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A transdiagnostic perspective on early mental health problems

*From adversity, digital markers, and putative mechanisms
to a hybrid ecological momentary intervention approach*

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ABBREVIATIONS

ACT	Acceptance and Commitment Therapy
AIDS	Acquired Immune Deficiency Syndrome
Amsterdam UMC	Amsterdam University Medical Centers
APS	Attenuated Psychotic Symptoms
ARMS	At-Risk Mental State
BLIPS	Brief Limited Intermittent Psychotic Symptoms
BSI	Brief Symptom Inventory
CAARMS	Comprehensive Assessment of At Risk Mental State
CBT	Cognitive Behavioural Therapy
CERQ-short	Cognitive Emotion Regulation Questionnaire
CFI	Compassion-Focused Intervention
CFT	Compassion-focused Therapy
CGI	Clinical Global Impression Scale
CHARMS	Broad Clinical High-Risk Mental State
CHR	Clinical High Risk
CI	Confidence Interval
CIMH	Central Institute of Mental Health
CMO	Context-mechanisms-outcomes
COVID-19	Coronavirus Disease 2019
CTQ	Childhood Trauma Questionnaire
DSM	Diagnostic and Statistical Manual of Mental Disorders
EMA	Ecological Momentary Assessment
EMI	Ecological Momentary Intervention
eHealth	Electronic Health
ESM	Experience Sampling Methodology
EU-GEI	European Network of National Networks studying Gene-Environment Interactions in Schizophrenia
GAF	Global Assessment of Functioning Scale
GSI	Global Severity Index
H	Hypothesis
HiTOP	Hierarchical Taxonomy of Psychopathology

HR	Hazard Ratio
ICD	International Statistical Classification of Diseases and Related Health Problems
JVQ	Juvenile Victimisation Questionnaire
K10	Kessler Psychological Distress Scale
M	Mean
mHealth	Mobile Health
N	Sample size
NA	Negative Affect
OASIS	Outreach and Support in South London
PA	Positive Affect
PACE	Personal Assessment and Crisis Evaluation clinic
PANSS	Positive and Negative Syndrome Scale
PE	Psychotic experiences
P_M	Proportion mediated
PQ-16	Prodromal Questionnaire
RCT	Randomised-Controlled Trial
RDoC	Research Domain Criteria
REML	Restricted Maximum Likelihood
SD	Standard Deviation
SE	Standard Error
TAU	Treatment As Usual
UHR	Ultra-High Risk
WAI-P/-T	Working Alliance Inventory for Patients and Therapists
WHO	World Health Organization
WLMHT	West London Mental Health NHS Trust

PROLOGUE

This thesis is a compilation of research articles, of which four are published and one is under review in international peer-reviewed journals. One chapter is an unpublished manuscript. A general introduction and a general discussion are provided to guide the reader.

An adapted version of *Chapter II* has been published as:

Paetzold, I., Hermans, K. S., Schick, A., Nelson, B., Velthorst, E., Schirmbeck, F., ... & Reininghaus, U. (2021). Momentary manifestations of negative symptoms as predictors of clinical outcomes in people at high risk for psychosis: Experience sampling study. *JMIR Mental Health*, 8(11), e30309. doi: https://doi.org/10.2196/30309

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An adapted version of *Chapter V* has been published as:

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An adapted version of *Chapter VI* is under review as:

Paetzold I., Schick A., Rauschenberg C., Hirjak D., Banaschewski T., Meyer-Lindenberg A., …& Reininghaus U. (under review). Exploring putative therapeutic mechanisms of change in a hybrid compassion-focused, ecological momentary intervention: Findings from the EMIcompass trial.

Throughout the papers, 'we' has consistently been used to reflect the collaborative work of all co-authors. The doctoral candidate's personal contributions comply with the criteria for first authorship in the guidelines for ensuring good scientific practice published by the Deutsche Forschungsgemeinschaft (2019) as well as international recommendations (e.g. recommendations by the International Committee of Medical Journal Editors (2022)). Details on the doctoral candidate's personal contributions to each of the publications are provided in Table 1.

Table 1. *Overview of the doctoral candidate's personal contributions.*

	Chapter				
	II	**III**	**IV**	**V**	**VI**
Conception (%)	30	30	70	80	80
Literature research (%)	90	100	90	100	100
Ethics approval (%)	0	0	0	50	50
Animal research proposal (%)	-	-	-	-	-
Data collection (%)	0	0	0	50	50
Data analysis (%)	100	100	80	100	100
Interpretation of results (%)	70	80	90	95	95
Manuscript writing (%)	90	100	100	100	100
Revision (%)	80	85	90	100	*
Figures		Supplementary Figures S1-S5	Supplementary Figure S6	Figures 2-3 Supplementary Figure S7	

Note. *=the paper is currently under review and has not been revised yet.

CHAPTER I:
GENERAL INTRODUCTION

1.1.   Mental health – a major global health challenge

Before COVID-19 has brought the word 'pandemic' into our everyday life vocabulary, Lake and Turner (2017) used this drastic term to describe the global mental health crisis: They called mental health problems a "pandemic of the 21st century" and identified mental health as "the next major global health challenge" (p.1). Indeed, mental health problems strongly contribute to the global disease burden (Vigo, Thornicroft, & Atun, 2016; Whiteford et al., 2013): the impact of neuropsychiatric conditions on the overall burden of disease has been reported to exceed the impact of either cardiovascular disease or cancer (Mathers & Loncar, 2006; Prince et al., 2007). By 2030, unipolar depression alone is anticipated to be among the three leading causes of illness worldwide – alongside with AIDS and ischaemic heart disease (Mathers & Loncar, 2006). A fifth of all disability adjusted years (i.e., the sum of life years lost attributable to premature mortality and disability) can be attributed to mental disorders, most prominently to affective, psychotic and substance abuse disorders (Anand & Hanson, 1997; C. J. Murray, 1994; C. J. Murray & Acharya, 1997; C. J. Murray & Lopez, 1997; Prince et al., 2007).

Youth are particularly affected by mental health problems. Most mental disorders first emerge in adolescence and young adulthood, 50% of all lifetime cases have their onset before the age of 14 and three-quarters emerge before the age of 24 (Kessler et al., 2005). Approximately one third of youth experience a mental disorder in their lifetime, and a quarter in the past 12 months (Merikangas, Nakamura, & Kessler, 2009). Worldwide, mental and substance abuse disorders are the primary cause of disability in children and adolescents (Erskine et al., 2015; Gore et al., 2011). These "chronic diseases of the young" (Insel & Fenton, 2005) place a heavy burden on youth (Insel & Fenton, 2005; WHO World Mental Health Survey Consortium, 2004).

Associations of mental and physical health problems (e.g. communicable and non-communicable diseases, intentional and unintentional injury) with disability are well-established (Bruce & Hoff, 1994; Bruce, Seeman, Merrill, & Blazer, 1994; Carroll, Cassidy, & Côté, 2003; Cole & Dendukuri, 2003; Firth et al., 2019; Härter, Conway, & Merikangas, 2003; Penninx et al., 1998; Prince et al., 2007), and the prevalence of poor physical health in service users with severe mental disorders is high (Scott & Happell, 2011). Prince et al. (2007) therefore proposed that there can be "no health without mental health". More recently, this has been extended further

in the debate about 'one health', which focuses on interdisciplinary collaboration of human and veterinary medicine, environmental and social science (World Health Organization, 2010; Zinsstag, Waltner-Toews, & Tanner, 2015). In addition, long-lasting social and economic impacts of mental health problems on individuals, their families, and society have been reported, for example on educational attainment, earnings, loss of societal output (Bloom et al., 2012; Breslau, Lane, Sampson, & Kessler, 2008; Kessler et al., 2008). Associations of poor mental health and poverty are well-established (Funk, Drew, & Knapp, 2012; Lund et al., 2010). Especially in youth, mental health problems are not isolated, but may – when not treated adequately – result in a downward spiral of disadvantage and missed opportunities for education, employment and development (Malla et al., 2018). From a public health perspective, it is therefore necessary to integrate mental health in all fields of health and social policy, health care system planning and primary and secondary health care delivery (Prince et al., 2007).

Despite high prevalence and immense disease burden worldwide across all age groups, a substantial treatment gap (i.e., the difference between true prevalence and treated prevalence) has been reported, showing that, alarmingly, the majority of individuals with mental disorders around the world does not receive adequate treatment by health care professionals (Dua et al., 2011; Thornicroft, 2007). For example, findings from the German Health Interview and Examination Survey for Adults (Gößwald, Lange, Kamtsiuris, & Kurth, 2012) indicate that the prevalence of service use (utilization of inpatient and outpatient services in the last 12 months: 4% of the total population for psychotherapists and 8% of the total population for neurologists/psychiatrists) deviates highly from prevalence estimates of mental health problems (Rattay et al., 2013). Moreover, the perceived stigma connected with mental health problems persists and may discourage individuals in need from seeking help (Franz et al., 2010; Henderson, Evans-Lacko, & Thornicroft, 2013). Self-stigma has been demonstrated to impact on self-esteem and there is evidence for associations with participation in mental health services and self-stigma as a barrier to recovery (Clement et al., 2015; Corrigan, Druss, & Perlick, 2014; Corrigan, Rafacz, & Rüsch, 2011; Göpfert, Conrad von Heydendorff, Dreßing, & Bailer, 2019; Oexle et al., 2018; Picco et al., 2016).

However, even for individuals receiving treatment, there is considerable room for improvement: For most mental diseases, the chance that a person in need of care would feel better after therapy has stagnated in recent years (Kilbourne et al., 2018; Lake & Turner, 2017) and service users may be confronted with persisting residual symptoms or relapse (Buckman et al., 2018; Fava, Ruini, & Belaise, 2007)

Thus, improving the understanding of transdiagnostic risk factors and underlying mechanisms to improve the prediction of onset, course and outcomes of mental disorders is a crucial first step. The development, implementation and improvement of innovative prevention and intervention approaches targeting the mechanisms identified and addressing needs and preferences of service users remain among society's major challenges.

1.2.   The complex and multifactorial aetiology of mental health conditions

Some of the difficulties the research field of mental health is currently confronted with may partly be rooted in the traditional conceptualisation of mental disorders in the prevailing medical model (Craddock & Owen, 2010; Kendler, 2012; van Os, Guloksuz, Vijn, Hafkenscheid, & Delespaul, 2019). The medical model conceptualises mental disorders as classifiable and distinguishable entities of disease with unique clinical and biological phenotypes that are associated with specific risk factors and mechanisms, and that need a specific treatment to be 'cured' (van Os et al., 2019). Mental health is seen as a dichotomy with mental disorders being qualitatively distinct from subclinical symptoms (Kendler, 2012). In addition, the medical model assumes that findings from experimental studies can be generalised to mental health problems in real-world contexts.

However, evidence has accumulated that subclinical and clinical expressions of affective symptoms, anxiety and psychotic experiences co-occur and overlap (Reininghaus, Böhnke, et al., 2016; Reininghaus, Priebe, & Bentall, 2013; Shevlin, McElroy, Bentall, Reininghaus, & Murphy, 2016) and transdiagnostic intervention approaches show beneficial effects (Craig, Hiskey, & Spector, 2020; Cuppage, Baird, Gibson, Booth, & Hevey, 2018; Gloster, Walder, Levin, Twohig, & Karekla, 2020; Kirby, Tellegen, & Steindl, 2017; Wilson, Mackintosh, Power, & Chan, 2019). Across a variety of mental health problems, a high degree of overlap on the levels of (poly-)genetics and biological systems (e.g. neuroimaging markers, patterns of brain activity, grey matter volume) is reported (Cross-Disorder Group of the Psychiatric Genomics Consortium et al., 2013; Jones et al., 2018; Sprooten et al., 2017; Stein et al., 2021; Vanes & Dolan, 2021). Various mental disorders seem to share common, transdiagnostic risk factors (e.g. early adversity) and putative mechanisms (C. Clark, Caldwell, Power, & Stansfeld, 2010; Greif Green et al., 2010; Hoppen & Chalder, 2018; Lynch, Sunderland, Newton, & Chapman, 2021; Merrick et al., 2017; Myin-Germeys et al., 2018; Myin-Germeys et al., 2003; Myin-Germeys & van Os, 2007; R. E. Norman et al., 2012; Rauschenberg et al., 2017;

Reininghaus, Kempton, et al., 2016; M. van Winkel et al., 2015; Wichers et al., 2009). In addition, there is a growing body of evidence pointing towards a continuum of mental health rather than dichotomous categories of 'ill' and 'healthy' (Constantino & Todd, 2003; Haslam, McGrath, Viechtbauer, & Kuppens, 2020; Judd, Schettler, & Akiskal, 2002; Linscott & Van Os, 2013; Tijssen et al., 2010; van Os, 2013; van Os & Reininghaus, 2016). In clinical trajectories, transitional staging process from mild distress and non-specific symptoms to attenuated symptoms or the emergence of severe mental disorders have been observed (McGorry, Hickie, Yung, Pantelis, & Jackson, 2006). Last, findings from experimental studies cannot always be generalised to real-world contexts outside the research laboratory (Myin-Germeys et al., 2018; Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001).

In reaction to these challenges, new conceptualisations of mental health problems have emerged: Cutting across traditional diagnostic boundaries defined by the International Classification of Diseases (ICD) and the Diagnostic and Statistical Manual of Mental Disorders (DSM), dimensional approaches acknowledging the overlapping and unspecific nature of mental health problems have been proposed (Reininghaus, Böhnke, et al., 2016; Reininghaus et al., 2013; van Os & Reininghaus, 2016): The Hierarchical Taxonomy of Psychopathology (HiTOP) consortium aims at quantifying disorders according to hierarchical levels of psychopathology and characterizing phenomena dimensionally (Kotov et al., 2017). As a descriptive system, HiTOP combines co-occurring phenomena to shared higher order factors. The HiTOP model comprises five levels (Kotov, Krueger, & Watson, 2018; Krueger et al., 2018): symptom components/traits (e.g. insomnia or emotional liability), syndromes (e.g. major depressive disorder), subfactors (e.g. distress dimension), spectra (internalizing dimension), and super-spectra (e.g. the general factor of psychopathology). The Research Domain Criteria (RDoC) framework is a dimensional classification approach of basic neurobiological processes that may be relevant for mental health problems (Cuthbert, 2014; Cuthbert & Insel, 2010; Cuthbert & Insel, 2013; Insel et al., 2010). RDoC aims at developing a nosology based on aetiology by integrating information from various levels to advance the knowledge of transdiagnostic dimensions of functioning. The complementary approaches of HiTOP and RDoC can be integrated in one interface (Michelini, Palumbo, DeYoung, Latzman, & Kotov, 2021; Reininghaus, Böhnke, et al., 2019). Moreover, concepts of mental health continua and clinical staging models have gained increasing attention (Cross et al., 2014; Hartmann et al., 2019; Hickie et al., 2013; Iorfino et al., 2019; McGorry et al., 2006; McGorry, Purcell, Hickie, Yung, et al., 2007; Shah et al., 2020; van Os, 2013). This is also reflected in the large body of research examining the At-Risk Mental State (ARMS), Ultra-High Risk for psychosis (UHR), or Clinical High Risk (CHR) state and their

predictive value for later transition to psychosis (Fusar-Poli, Borgwardt, et al., 2013; Riecher-Rössler & Studerus, 2017; Yung et al., 2021). In addition, the concept of psychosis as an 'extended and transdiagnostic phenotype' has emerged (van Os & Reininghaus, 2016). It builds on evidence suggesting both, disorder-specific factors and general, transdiagnostic phenotypic expressions across the general population, subclinical and clinical symptom levels (Reininghaus, Böhnke, et al., 2019; van Os & Reininghaus, 2016). Broadening these approaches to a pluripotent risk paradigm, transdiagnostic clinical staging models offer a broad set of criteria to identify individuals at risk taking into account the heterogeneous nature of pathways in early psychopathology (Hartmann et al., 2019; McGorry, Hartmann, Spooner, & Nelson, 2018). For example, the Broad Clinical High-Risk Mental State (CHARMS) with various clinical stages ranging from asymptomatic (stage 0), to help-seeking with distress (stage 1a), attenuated syndrome (stage 1b) and severe mental disorder with variation in recurrence and severity (stages 2-4) cutting across traditional boundaries of psychotic, bipolar, depressive, and personality disorders, has been proposed (Hartmann et al., 2021; Hartmann et al., 2019). Efforts have been made to explore transdiagnostic factors of risk and resilience as well as putative transdiagnostic mechanisms in the development of psychopathology (Lynch et al., 2021; Myin-Germeys et al., 2018). In addition, the role of contextual factors has gained increasing attention (Myin-Germeys et al., 2018).

In conclusion, new conceptualisations of mental health acknowledge the relevance of contextual factors, the transdiagnostic nature of socio-environmental and genetic risk factors, underlying mechanisms, symptoms and phenotypes, as well as the continuity of mental health (see figure 1). Building on this, the role of contextual factors, early adversity as prominent socio-environmental risk factor, and stress reactivity and threat anticipation as transdiagnostic mechanisms in the development of psychopathology will be delineated in the following chapters.
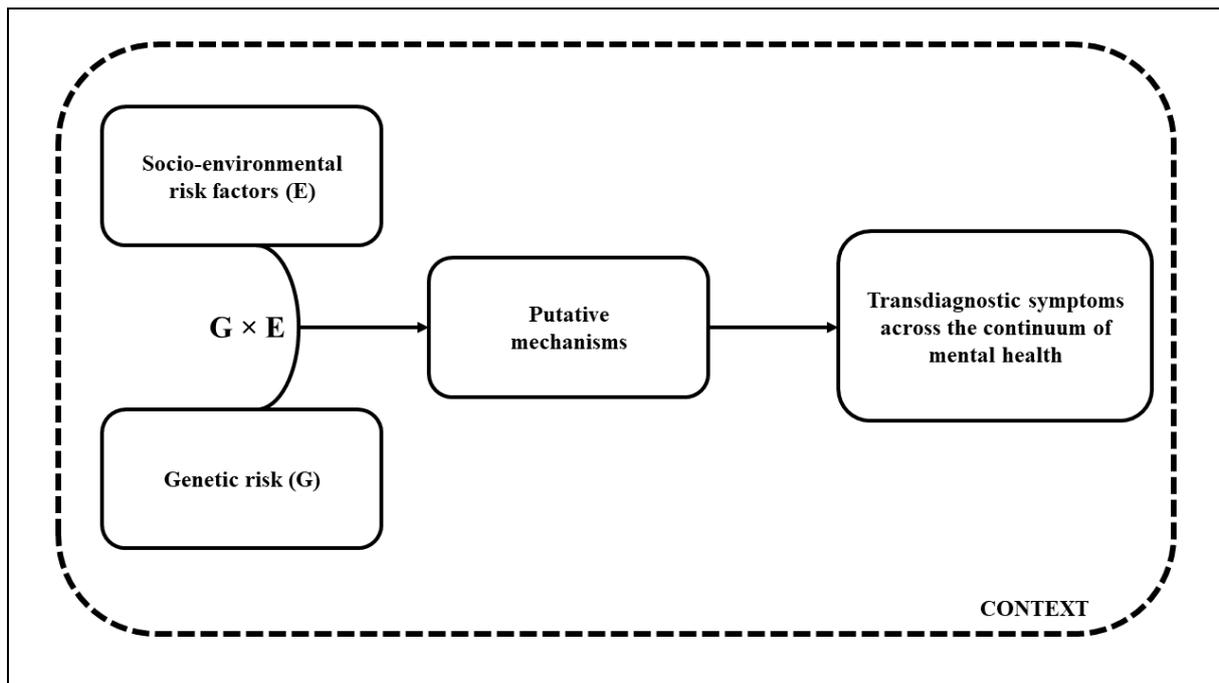
Figure 1. *New conceptualisation of mental health.*

1.3.   Contextual factors in mental health

As mentioned above, the role of contextual factors has gained increasing attention in the last years (Myin-Germeys et al., 2018). These developments have been pioneered by eco-epidemiology (M. Susser & Susser, 1996) and ecological psychology (Barker, 1968). Eco-epidemiology focuses on macro-level context factors (e.g. urbanicity, neighbourhood- or area-level factors, (Faris & Dunham, 1939; Heinz, Deserno, & Reininghaus, 2013; March et al., 2008; Schofield et al., 2017) and claims that environment is an interactive system with multiple levels (M. Susser & Susser, 1996). Ecological psychology (Barker, 1968) focuses on micro-level contextual factors and posits that experience can only be understood in its context.

Building on this, a growing body of research explores how mental health problems manifest in, and interact with, daily life contexts aiming at increasing ecological validity and generalisability of findings (Myin-Germeys et al., 2018). This approach may be especially interesting for mental health problems commonly assessed via observer ratings in interview situations (e.g. negative symptoms), as it may provide insight into the way service users experience symptoms in the real-world. Rapid advances in digital technology provide major opportunities for digitalised assessment of mental health problems in daily life. To capture emotion, cognition and behaviour in daily life contexts, the Experience Sampling Method (ESM) or synonymously Ecological Momentary Assessment (EMA), a structured self-report diary technique with high ecological

validity, is frequently used (Csikszentmihalyi & Larson, 1987; Ebner-Priemer & Trull, 2009; Myin-Germeys et al., 2018; Myin-Germeys et al., 2009; Shiffman, Stone, & Hufford, 2008; Stone & Shiffman, 1994). In ESM designs, participants are prompted several times a day (e.g. 10 times) over a number of consecutive days (e.g. 6 days) to answer short questionnaires enquiring about their momentary experiences and context on a smartphone or dedicated device to create fine-grained time-series data with multiple momentary observations for each participant. ESM has been used in various domains of mental health research aiming at improving the understanding of symptoms, and examining the complex interplay of context, experience and behaviour (Myin-Germeys et al., 2018; Schick et al., 2022). It offers an alternative to standard assessment of symptoms largely relying on retrospective self-reports and observer ratings as it allows for an assessment of symptoms as they occur (Myin-Germeys et al., 2018). Indeed, relevant discrepancies between momentary and retrospective assessment have been reported (Ben-Zeev, McHugo, Xie, Dobbins, & Young, 2012; Ben-Zeev & Young, 2010; Blum et al., 2015) and momentary symptoms have been discussed as digital markers predicting clinical outcomes (Paetzold, Hermans, et al., 2021). ESM may also be a powerful tool to empower service users by acknowledging their expertise for their own experience and may contribute to strengthening the contextual approach to personalised mental health care (Myin-Germeys et al., 2018).

1.4.   Early adversity as a transdiagnostic risk factor in mental health

As delineated above, converging evidence identified early adversity as a socio-environmental risk factor for various mental health problems, including affective and psychotic disorders (LeMoult et al., 2020; Morgan & Gayer-Anderson, 2016; Palmier-Claus, Berry, Bucci, Mansell, & Varese, 2016; Selous et al., 2020; Varese et al., 2012). Early adversity is defined as "experiences that are likely to require significant adaptation by an average child and that represent a deviation from the expectable environment" (McLaughlin, 2016, p.3), for example childhood trauma or bullying. There is evidence for dose-response relationships, indicating that individuals with higher levels of exposure to early adversity have progressively rising likelihoods of developing mental disorders (Croft et al., 2019).

Childhood trauma refers to potentially detrimental childhood experiences such as sexual, physical, and emotional abuse, as well as physical and emotional neglect (Morgan & Fisher, 2007). There is evidence for a high prevalence of childhood trauma in individuals at-risk for psychosis (Kraan, Velthorst, Smit, de Haan, & van der Gaag, 2015; Peh, Rapisarda, & Lee, 2019) and service users with severe mental disorders (Bonoldi et al., 2013; Larsson et al., 2013; Matheson,

Shepherd, Pinchbeck, Laurens, & Carr, 2013; Varese et al., 2012). For example, a recent meta-analysis demonstrated that service users with borderline personality disorder were over 13 times more likely to report childhood trauma than healthy controls (Porter et al., 2020). Childhood trauma is associated with a wide range of mental health problems and has been demonstrated to impact on both, internalizing and externalizing symptoms (Chen et al., 2010; R. Gilbert et al., 2009; Greif Green et al., 2010; McLaughlin et al., 2010). Meta-analytic evidence indicates an association of childhood trauma with diagnosis of depression and higher depression symptom scores (Humphreys et al., 2020). Exposure to childhood trauma increases the risk for bipolar disorder and has been identified as a prognostic marker associated with earlier onset, more severe clinical presentation (i.e., increased risk of suicide attempts and substance abuse) and unfavourable course of bipolar disorder over time (Aas et al., 2016; Agnew-Blais & Danese, 2016; Palmier-Claus et al., 2016). Childhood trauma has been found to increase the risk of developing anxiety disorders by the factor 1.9 to 3.6 (Fernandes & Osório, 2015). Furthermore, it has been demonstrated to be associated with psychotic experiences across the continuum of mental health: Previous research indicated an association with psychotic experiences in the general population and the persistence of psychotic symptoms in subclinical and clinical samples (T. Bailey et al., 2018; Croft et al., 2019; Janssen et al., 2004; Trotta, Murray, & Fisher, 2015; van Dam et al., 2015). In addition, there is evidence for an elevated risk for psychotic disorders (Morgan et al., 2020; Varese et al., 2012). In the research field of borderline personality disorder, a review posited that evidence points towards a causal relationship with childhood trauma when the relationship is considered in a multifactorial model of aetiology (Ball & Links, 2009). Taken together, there is compelling evidence for childhood trauma as an important transdiagnostic risk factor for mental health problems.

Bullying victimisation refers to intentional and repeated hostile behaviour of peers against others who experience problems to defend themselves (Olweus, 1993; Stanaway et al., 2018). Hostile behaviour may include for example "teasing, name calling, mockery, threats, harassment, taunting, hazing, social exclusion or rumours" (Srabstein & Leventhal, 2010, p. 403). The World Health Organization estimates that approximately 20% of youth are exposed to bullying at school (WHO Regional Office for Europe, 2012). For a long time, bullying has been considered an unpleasant, yet normal and transitory pattern of interaction in childhood and adolescence (Arseneault, Bowes, & Shakoor, 2010), that has not been seen to reflect a detrimental experience (Tolan, 2004). To date, however, there is convincing evidence that exposure to bullying is associated with various mental health problems including depression, anxiety, and psychosis as well as self-harming and suicidal behaviour (Brunstein Klomek et al., 2019; Copeland,

Wolke, Angold, & Costello, 2013; Koyanagi et al., 2019; Lee & Vaillancourt, 2018; Lereya, Copeland, Costello, & Wolke, 2015; Singham et al., 2017; Takizawa, Maughan, & Arseneault, 2014; Varese et al., 2012). In the general population, bullying is associated with more intense psychotic experiences in cross-sectional (Horrevorts, Monshouwer, Wigman, & Vollebergh, 2014) and longitudinal studies (Wolke, Lereya, Fisher, Lewis, & Zammit, 2014). The detrimental effects of exposure to bullying are not limited to childhood and adolescence, but extend to adult age (Koyanagi et al., 2019), as findings on associations of bullying victimisation in youth and adult psychopathology indicate (Brunstein Klomek, Sourander, & Elonheimo, 2015; Copeland et al., 2013; Sourander et al., 2016; Takizawa et al., 2014). Bullying is associated with the development of psychotic symptoms later in life (Cunningham, Hoy, & Shannon, 2016) and predicted the use of mental health services in adult life (Sourander et al., 2016). In parallel with the growing body of research on detrimental effects of bullying, it became a major concern among caregivers, pedagogues and local authorities (Department for Education, 2014; Department of Education, 2017). In summary, findings indicate that exposure to bullying may be an important transdiagnostic risk factor for mental health problems, which has also been acknowledged in the Global Burden of Disease Study 2017 (Stanaway et al., 2018).

Taken together, the relevance of early adversity as a transdiagnostic risk factor across a wide range of psychopathological outcomes is well demonstrated, tentatively indicating shared transdiagnostic mechanisms in the development of psychopathology.

1.5. Putative candidate mechanisms and processes linking early adversity to psychopathology

While converging evidence identified early adversity as a risk factor for psychopathology and findings point towards common, transdiagnostic processes in the development of mental health problems, putative candidate mechanisms involved remain largely unclear. Moreover, there are various potential ways of how adversity and putative mechanisms may combine in the development of psychopathology: On the one hand, adversity may modify the association of putative mechanisms and mental health problems (i.e., a moderation or interaction model). On the other hand, adversity may also connect with outcomes via pathways through putative mechanisms (i.e., a mediation model). To increase complexity further, both may be true at the same time – adversity may modify the association *and* connect with psychopathology via pathways through putative mechanisms (i.e., a mediated synergy model; Hafeman (2008); Hafeman and Schwartz

(2009)). In the following, two putative candidate mechanisms, stress reactivity and threat anticipation, and their potential interplay with early adversity and psychopathology will be delineated.

Stress reactivity comprises increased negative affect, decreased positive affect and increased psychotic experiences in response to minor daily stressors (Hammen, Henry, & Daley, 2000; Morgan, Charalambides, Hutchinson, & Murray, 2010; Myin-Germeys et al., 2018). It is proposed to be a behavioural marker of stress sensitization (Collip, Myin-Germeys, & Van Os, 2008; Myin-Germeys et al., 2018). Stress sensitization is the hypothesis that repeated or chronic exposure to adversity may gradually increase the stress response to further adversities and minor daily stressors (Collip et al., 2008; Myin-Germeys, Delespaul, & Van Os, 2005; Myin-Germeys et al., 2001; Wichers et al., 2009). As affect and psychotic experiences as well as minor daily stressors fluctuate highly, context-sensitive ESM data is especially well-suited to approximate stress reactivity in daily life by measuring exposure to daily stressors and responses in affect and psychotic experiences (Myin-Germeys et al., 2018; Myin-Germeys et al., 2001; Schick et al., 2022).

Elevated stress reactivity has been demonstrated in adult service users with depression and psychosis, individuals with UHR, subclinical psychosis phenotypes, relatives of service users with psychosis, and help-seeking adolescents (Lataster et al., 2009; Myin-Germeys et al., 2001; Myin-Germeys et al., 2003; Rauschenberg et al., 2017; van der Steen et al., 2017). Self-reported questionnaire ratings of stress reactivity have been found to be linked with poor clinical outcomes in individuals with a first episode of psychosis (Conus, Cotton, Schimmelmann, McGorry, & Lambert, 2009). Previous findings provided evidence for synergistic effects of early adversity and stress reactivity (i.e., an effect modification): Elevated stress reactivity was observed in individuals reporting high levels of early adversity across samples of adult and adolescent service users with clinical and subclinical mental health problems (Glaser, Van Os, Portegijs, & Myin-Germeys, 2006; Lardinois, Lataster, Mengelers, Van Os, & Myin-Germeys, 2011; Rauschenberg et al., 2017; Rauschenberg, van Os, Goedhart, Schieveld, & Reininghaus, 2021; Reininghaus, Gayer-Anderson, et al., 2016; Wichers et al., 2009). Furthermore, stress reactivity has also been examined as a potential mediator of the association of early adversity and psychopathological symptoms: There is evidence from cross-sectional studies using self-report questionnaires in community samples indicating that exposure to early adversity may impact on subclinical psychotic experiences via pathways through stress reactivity (Gibson et al., 2014; Rössler, Ajdacic-Gross, Rodgers, Haker, & Müller, 2016). Investigating the complex interplay of childhood and adult disadvantage, Morgan et al. (2014) used a mediated synergy

model (Hafeman, 2008; Hafeman & Schwartz, 2009) to examine both, effect modification and mediation, in the same analysis. Applying this approach to the interplay of early adversity, stress reactivity, and psychopathology, early adversity could modify the association of stress reactivity and psychopathology *and* be associated with psychopathology via pathways through stress reactivity. However, this has not been tested explicitly yet.

A second putative transdiagnostic candidate mechanism linking early adversity and psychopathology may be threat anticipation. Frequent or chronic exposure to adversity may lead to biased cognitive processes characterised by an increased anticipation of unpleasant events creating a persistent sense of threat (Bentall et al., 2014; Bentall et al., 2009; R. Corcoran et al., 2006; Morgan et al., 2010; Moutoussis, Williams, Dayan, & Bentall, 2007). As an integral part of theoretical models (Freeman, Garety, Kuipers, Fowler, & Bebbington, 2002; Garety, Bebbington, Fowler, Freeman, & Kuipers, 2007; Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001; Grupe & Nitschke, 2013), threat anticipation has frequently been examined in psychosis and anxiety research.

Current models of psychosis (Freeman et al., 2002; Garety et al., 2007; Garety et al., 2001) link early adversity with cognitive and affective changes and acknowledge the role of enhanced threat anticipation as a putative mechanism in the development of psychosis in general and especially in delusions. The models posit that early adversity may elicit negative schemas about oneself and the world. Exposure to adverse environments may evoke changes in cognition and emotion in vulnerable individuals, which, in turn, may trigger anomalous experiences. Negative schemas derived from past adverse experiences may result in biased cognitive processes such as enhanced threat anticipation. Biases in cognitive processing are posited to enhance the appraisal of anomalous experiences as threatening, which may be crucial for them to become symptomatic and create distress. Emotional distress may then drive the search for meaning and contribute to finding an interpretation of information that is congruent with the emotion, ultimately reinforcing dysfunctional cognitive and emotional processes that maintain psychotic symptoms.

A tendency to overestimate the likelihood of threatening events in the future has been observed in service users with delusions in cross-sectional and experimental studies (Bentall et al., 2008; R. Corcoran et al., 2006; Kaney, Bowen-Jones, Dewey, & Bentall, 1997). In addition, there is evidence from experience sampling studies elucidating momentary processes in the interplay of threat anticipation and psychotic experiences in daily life: Reininghaus, Kempton, et al. (2016) examined momentary threat anticipation and psychotic experiences in healthy controls,

individuals with UHR for psychosis and service users with a first episode of psychosis. Enhanced threat anticipation was associated with more intense psychotic experiences in daily life in all three groups. Magnitudes of effects were larger for service users with a first episode of psychosis compared to healthy controls and individuals with UHR for psychosis. Reininghaus, Gayer-Anderson, et al. (2016) showed that childhood trauma moderated the effects of momentary threat anticipation on psychotic experiences in the daily life of service users with a first episode of psychosis. In comparison to service users with low levels of childhood trauma, threat anticipation was associated with more intense psychotic experiences in participants with high levels of childhood trauma. Klippel et al. (2017) explored potential mediation effects and found evidence that threat anticipation mediated the association of stress and psychotic experiences in the daily life of individuals with a first episode of psychosis. Recently, Bloomfield et al. (2021) reviewed the existing literature on putative psychological processes linking early adversity and psychotic symptoms in adults and conducted a meta-analysis. They found evidence for the mediating role of avoidance and hyper-arousal and discussed that these symptoms, in turn, have been proposed to enhance threat anticipation and thereby increase vulnerability to psychosis (Mueser et al., 1998). In addition, there was some evidence for a mediation via negative schemata about the self and others.

Moreover, enhanced threat beliefs form the core of psychological conceptualisations of anxiety disorders (D. M. Clark, 1999). Enhanced threat anticipation is suggested to be associated with avoidance behaviour, hypervigilance and deficient safety learning, which, in turn, are posited to contribute highly to the development, maintenance and aggravation of anxiety disorders (Grupe & Nitschke, 2013). In line with the theoretical models, attentional biases towards threat stimuli have been demonstrated in a meta-analysis across various anxiety disorders (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007). In cognitive behavioural therapy (CBT) of anxiety disorders, the modification of negative beliefs and the reduction of threat anticipation are prominent targets for intervention. In line with the cognitive change model, behavioural experiments/confrontation approaches and verbal cognitive restructuring techniques are used to identify, test and modify service users' dysfunctional beliefs about of how dangerous the given situation is (D. M. Clark, 1999).

In conclusion, threat anticipation is a well-researched process and a target for intervention in several mental disorders, but has not been examined as a putative transdiagnostic mechanism linking early adversity and psychopathological symptoms across the continuum of mental health. Moreover, all studies discussed above are based on adult samples, so that to date, the

role of threat anticipation and early adversity in the development of psychopathology in adolescents – as a priority target population for prevention and early intervention – has not been examined yet.

Taken together, stress reactivity and threat anticipation represent promising putative candidate mechanisms in the development of psychopathology that need to be explored further. In addition, they may also be potentially relevant target mechanisms for novel approaches in early intervention and prevention.

1.6. From putative mechanisms and process to prevention and early intervention

There is compelling evidence on beneficial effects of early intervention and prevention approaches across a wide range of mental health problems. For example, a meta-analysis demonstrated the effectiveness of indicated prevention for higher education students with subclinical mental health problems such as mild depression, anxiety or interpersonal difficulties (Conley, Shapiro, Kirsch, & Durlak, 2017). In service users at risk for psychosis, meta-analytic evidence suggests that early intervention approaches reduce transition rates at follow-up compared to control conditions (Schmidt et al., 2015). Compared to treatment as usual, specialised early intervention services for psychosis have been demonstrated to be linked to more favourable outcomes regarding symptom severity, hospitalization, treatment discontinuation and involvement in school or work (Correll et al., 2018). Meta-analytic evidence shows beneficial effects with good effect sizes of standard cognitive behavioural therapy and third-wave approaches across various mental health problems (Cuijpers et al., 2013; Hofmann & Smits, 2008; Hunot et al., 2013; Johns et al., 2016; Kirby et al., 2017; Shawyer et al., 2017).

However, despite significant global research efforts, mental health care is confronted with various difficulties, such as stagnating quality of treatment (Kilbourne et al., 2018), residual symptoms and high relapse rates, especially for severe mental disorders (Buckman et al., 2018; Fava et al., 2007; Vittengl, Clark, Dunn, & Jarrett, 2007). This might partly be related to challenges in the translation of skills acquired in therapy into the context of service users' daily life. Besides these general difficulties, youth mental health care faces further challenges: Mental health care for adolescents and young adults is often delivered within adult services or institutions have developed only recently from exclusively focusing on young children (Patel, Flisher, Hetrick, & McGorry, 2007). On the one hand, adult services are predominantly specialised on

older service users with repeated or chronic mental health problems and mixing them with youth with early mental health problems may yield the potential of iatrogenic effects (Patel et al., 2007). Services deriving from an exclusive focus on younger children, on the other hand, often have difficulties providing appropriate care for adult patterns of disorders emerging in adolescence and young adulthood (Patel et al., 2007). The low availability, access and use of youth mental health services reported have been identified as problematic (Malla et al., 2016; Wang et al., 2005), as they may potentially result in a longer duration of untreated illness (Patel et al., 2007). A longer duration of untreated illness, in turn, is associated with poor prognosis, complicated course and unfavourable outcomes (Dell'Osso, Glick, Baldwin, & Altamura, 2013; Drancourt et al., 2013; Ghio, Gotelli, Marcenaro, Amore, & Natta, 2014; Marshall et al., 2005). Thus, low-threshold approaches of intervention and prevention tailored to the needs, preferences, and life realities of adolescents and young adults are urgently needed. Digitalization provides major opportunities for personalised mental health care and contributes to the emergence of various types of technology-enabled health services that may be promising approaches to address these aspects (Hollis et al., 2015; David C Mohr, Schueller, Montague, Burns, & Rashidi, 2014). Telemedical and internet-based (eHealth) interventions, as well as smartphone-based mobile health (mHealth) interventions, play an important role in this context (Lecomte et al., 2020; O'Connor, Munnelly, Whelan, & McHugh, 2018; Rauschenberg, Schick, Hirjak, et al., 2021). Both may lower the threshold to access mental health care and mHealth may enable the delivery of tailored interventions in real-time and real-world contexts (Myin-Germeys et al., 2018; Myin-Germeys, Klippel, Steinhart, & Reininghaus, 2016; Reininghaus, 2018; Schick et al., 2022). On the basis of transdiagnostic target mechanisms, the development, evaluation and implementation of novel digital intervention approaches across the continuum of public mental health (i.e., comprising mental health promotion and prevention as well as treatment of severe mental disorders) has become a thriving field of research (Hariman, Ventriglio, & Bhugra, 2019; Myin-Germeys et al., 2016; Reininghaus, 2018). This approach fits well with the concept of generalisation in cognitive behavioural therapy (McDevitt-Murphy, Luciano, & Zakarian, 2018). Moreover, subjectively stressful situations necessitating the application of skills acquired in treatment frequently result in the habitual activation of dysfunctional patterns of behaviour instead (Schwabe & Wolf, 2009). Regular use of recently acquired strategies in everyday life may enhance access and application in stressful situations and increase service users' self-efficacy, empowerment, and feeling of competence (Reininghaus, 2018; Steinhart,

Myin-Germeys, & Reininghaus, 2019; Vaessen et al., 2019). Mobile interventions may therefore facilitate the ecological translation of strategies learned into everyday life contexts (Reininghaus, 2018).

Ecological Momentary Interventions (EMIs) are a specific type of digital interventions (Heron & Smyth, 2010; Myin-Germeys, Birchwood, & Kwapil, 2011; Myin-Germeys et al., 2018; Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus, Depp, & Myin-Germeys, 2015). They extend ESM principles by suggesting that psychological mechanisms and processes in the development and maintenance of psychopathological symptoms may also best be modified in the context of service users' daily life (Reininghaus, 2018; Reininghaus et al., 2015). This embraces approaches of social psychiatry emphasizing the relevance of social interactions and context (Priebe, Burns, & Craig, 2013). The majority of EMIs have been developed and implemented as dedicated smartphone apps (Balaskas, Schueller, Cox, & Doherty, 2021; Bastiaansen, Ornée, Meurs, & Oldehinkel, 2020; Daemen et al., 2021; Schick et al., 2021; Vaessen et al., 2019; van Aubel et al., 2020). Smartphone ownership is prevalent and is predicted to rise to 7,5 billion users around the world by 2026 (Statista, 2021). EMIs therefore offer the unique opportunity to provide individuals in need – also from so called 'difficult-to-reach populations' (Barak, Hen, Boniel-Nissim, & Shapira, 2008; Giroux, Goulet, Mercier, Jacques, & Bouchard, 2017; Rauschenberg, Schick, Hirjak, et al., 2021) – with intervention components in the context of their everyday life and examine ecological interventionist causal models (Reininghaus, 2018; Reininghaus et al., 2015). By delivering intervention components in daily life, outside of standard care institutions, EMIs are inherently low-threshold (Balaskas et al., 2021; Heron & Smyth, 2010; Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus et al., 2015). In addition, the combination of ecological momentary assessment and intervention offers the opportunity to provide users with adaptive and personalised material, addressing current needs, symptoms and emotions in a given situation (Reininghaus, 2018). This may comprise personalised feedback as well as the delivery of tailored intervention strategies (Balaskas et al., 2021; Daemen et al., 2021; Kramer et al., 2014; Schick et al., 2021).

To date, EMIs have been applied for psychoeducation, self-monitoring of symptoms, enhancement of coping strategies, motivational interviewing and the delivery of CBT, Acceptance and Commitment (ACT) as well as Compassion Focused Therapy (CFT) based interventions across a wide range of subclinical and clinical mental health problems including anxiety, affective, psychotic and substance abuse disorders (Businelle et al., 2020; Daemen et al., 2021; Depp et al., 2015; Kazemi et al., 2019; Kroska et al., 2020; LaFreniere & Newman, 2016; Schick et al., 2021; Stevenson et al., 2020; van Aubel et al., 2020), for an overview see (Balaskas et al.,

2021). EMIs have been implemented as standalone interventions or as part of blended care approaches (Baumeister, Reichler, Munzinger, & Lin, 2014; Weisel et al., 2019). Previous research suggests preliminary, yet promising evidence on safety, feasibility, acceptability and beneficial effects of EMIs (Bell, Lim, Rossell, & Thomas, 2017; Colombo et al., 2019; Myin-Germeys et al., 2016) with higher acceptability and larger effect sizes for blended in comparison to standalone interventions (Baumeister et al., 2014; Lecomte et al., 2020; Topooco et al., 2017). Findings from a recent nationally representative survey suggested that youth use mHealth apps regularly and are more likely to do so when experiencing distress (Rauschenberg, Schick, Goetzl, et al., 2021), highlighting how well they may be suited to lower the threshold for, and address the needs of, a generation of digital natives. An important restriction is, however, that the majority apps currently available are not based on evidence and some even provide potentially harmful material (Larsen et al., 2019; Mercurio et al., 2020; Rauschenberg, Schick, Hirjak, et al., 2021; Weisel et al., 2019).

To contribute to addressing this pressing gap in youth mental health, evidence based novel intervention approaches targeting previously identified putative mechanisms in the development of psychopathology are urgently needed. A promising approach for targeting stress reactivity and threat anticipation as putative mechanisms in the development of psychopathology may be CFT (P. Gilbert, 2009, 2013, 2014). Following a quotation by the Dalai Llama, P. Gilbert (2013) defines compassion as "the sensitivity to suffering in self and others with a commitment to try to alleviate and prevent it" (p.16). CFT is rooted in evolutionary psychology and theories of attachment and social mentality (P. Gilbert, 2009, 2014). It broadly understands mental health problems as being caused by dysfunctional loops between 'old' and 'new' parts of the human brain (P. Gilbert, 2013, 2014): The 'old' parts encompass basic functions humans share with other animals (e.g. harm-avoidance, defensive behaviours and basic emotions). The 'new' parts of the brain comprise higher cognitive functions (e.g. imagination, planning and self-awareness but also rumination and worry). Both parts can interact in a coordinated and beneficial manner. In other cases, their interplay can result in maladaptive loops between negative emotions and defensive behaviours in 'old', and rumination and self-criticism in 'new' regions of the brain (P. Gilbert, 2013, 2014).

CFT suggests a model of emotional systems comprising three inter-related major emotional systems (P. Gilbert, 2009, 2013, 2014): The *threat* system is thought to aim to protect the individual from potential threats and includes emotions such as anger and anxiety. The *drive* system is posited to be characterised by activation and reward seeking, and it includes emotions like excitement and joy. The *soothing* system is suggested to signal safety and comprises emotions

like calmness, peacefulness, and contentment. CFT posits that mental problems are often associated with a hyperactive threat system, an overactive or blocked drive system and a hypoactive soothing system (P. Gilbert, 2014). As a consequence, CFT focuses on strengthening the soothing system, which is proposed to operate as an antagonist to an overactive threat system and provide a solid basis for a well-functioning drive system (P. Gilbert, 2009).

In line with its broad conceptualisation of psychopathology, CFT is not symptom-specific. Previous research has demonstrated that CFT is an effective treatment for a variety of mental health problems and psychological distress, that is appraised positively by service users (Ascone, Sundag, Schlier, & Lincoln, 2017; Craig et al., 2020; Cuppage et al., 2018; Gale, Gilbert, Read, & Goss, 2014; Heriot-Maitland, McCarthy-Jones, Longden, & Gilbert, 2019; Kirby et al., 2017; Leaviss & Uttley, 2015). Positive imagery is a key component of many CFT techniques. It is associated with increases in positive affect, behavioural activation and generalised positive expectations about the future and is reported to effectively reduce mental health problems (Blackwell & Holmes, 2017; Braehler et al., 2013; Holmes, Blackwell, Burnett Heyes, Renner, & Raes, 2016; Holmes & Mathews, 2010; Leaviss & Uttley, 2015; Pearson, Naselaris, Holmes, & Kosslyn, 2015; Renner, Ji, Pictet, Holmes, & Blackwell, 2017). The use of imagery-based compassion-focused interventions (CFIs) may be especially fruitful, as they have been reported to enhance the activation of the soothing system associated with positive affect as well as self-acceptance and calm emotional systems linked to threat and stress (P. Gilbert, 2009; Holmes, Blackwell, Heyes, Renner, & Raes, 2016; Lincoln, Hohenhaus, & Hartmann, 2013). Therefore, this approach may be particularly well-suited to be implemented in a transdiagnostic EMI for targeting stress reactivity and threat anticipation in daily life. First results are promising: Laboratory experiments showed that the use of compassion-focused techniques lowered state negative affect and paranoia in moments of high stress (Lincoln et al., 2013; Pearson et al., 2015). The development of a hybrid, CFI may therefore be a helpful contribution to lower the threshold and adequately address the needs of youth with early mental health problems. Indeed, a pilot study was suggestive of feasibility, safety and beneficial effects on stress reactivity and psychopathological symptoms for a hybrid compassion-focused intervention in help-seeking adolescents and young adults (Rauschenberg, Boecking, et al., 2021).

1.7. Elucidating putative therapeutic mechanisms of change in a hybrid CFI

While there is compelling evidence for beneficial effects of CFIs (Ascone et al., 2017; Cuppage et al., 2018; Gale et al., 2014; Heriot-Maitland et al., 2019; Kirby et al., 2017; Leaviss & Uttley,

2015), the therapeutic mechanisms of change involved remain largely unclear for standard delivery of CFT (Ferrari et al., 2019; Kirby et al., 2017) and much more so for hybrid interventions. In the following section, possible therapeutic mechanisms of change for a hybrid CFI will be delineated.

First, increased *self-compassion* has been suggested as a candidate mechanism of change in several publications (MacBeth & Gumley, 2012; Marsh, Chan, & MacBeth, 2018; Xavier, Pinto-Gouveia, & Cunha, 2016). Meta-analytic evidence indicates that CFIs moderately increase self-compassion (Ferrari et al., 2019). Self-compassion, in turn, has been reported to be associated with psychological distress and psychopathology with large effect sizes (MacBeth & Gumley, 2012; Marsh et al., 2018). Recently, Craig et al. (2020) reviewed the existing literature and suggested that compassion may have a direct impact on psychopathology. However, increased self-compassion has not been explored as a putative mechanism linking CFIs to clinical outcomes yet in a hybrid delivery format.

Second, a meta-analysis on RCTs (randomised controlled trials) using CFIs discussed improved *emotion regulation* as a putative candidate mechanism linking treatment to clinical improvement (Ferrari et al., 2019). Several strategies of emotion regulation have been postulated to be adaptive (e.g. reappraisal and acceptance) or maladaptive (e.g. rumination) and have been shown to be associated with psychopathology in a meta-analytic review (Aldao, Nolen-Hoeksema, & Schweizer, 2010). A recent longitudinal study found evidence suggesting that maladaptive emotion regulation may be a transdiagnostic mechanism linking child maltreatment with psychopathology (Weissman et al., 2019). Finlay-Jones (2017) posited that CFIs may improve adaptive emotion regulation, which, in turn, may have a positive effect on clinical outcomes. However, this is yet to be investigated in a hybrid CFI.

Third, findings from standard delivery of psychotherapy suggest *training frequency* may be a putative candidate mechanism of change: Meta-analyses demonstrated associations of homework compliance and therapy outcomes with small to moderate effect sizes (Kazantzis, Whittington, & Dattilio, 2010; Kazantzis et al., 2016; Mausbach, Moore, Roesch, Cardenas, & Patterson, 2010). Homework compliance is reported to be associated with response to treatment and remission (Callan et al., 2019). While training frequency seems to be relevant in standard care, this may be even more the case for a hybrid intervention explicitly aiming at training strategies in daily life. The reduced number and frequency of sessions in comparison to standard delivery of psychotherapeutic interventions could further increase the relevance of self-directed training of strategies learned. Again, the role of training frequency as a putative mechanism of change has not been explored in a hybrid CFI yet.

Fourth, *therapeutic working alliance* may also be taken into account as a putative candidate mechanism of change. There is evidence on the association of therapeutic working alliance and treatment outcomes across a variety of intervention approaches, mental health problems and age groups (Horvath, Del Re, Flückiger, & Symonds, 2011; Martin, Garske, & Davis, 2000; Murphy & Hutton, 2018; Shirk & Karver, 2003). A recent review concluded that alliance mediated the association between treatment and clinical outcomes in 70% of all studies included (Baier, Kline, & Feeny, 2020). Whereas the role of therapeutic working alliance in standard care seems quite well researched, this is not the case for hybrid interventions, as reviewed recently: Henson, Wisniewski, Hollis, Keshavan, and Torous (2019) could identify only five studies (three of them pilot studies) discussing therapeutic working alliance when a mobile application intervention was involved in treatment. Two studies used questionnaires to assess alliance (Reid et al., 2013; Richards & Simpson, 2015), three conducted qualitative thematic analyses (Bauer et al., 2018; Forchuk et al., 2016; Mackie et al., 2017). Henson et al. (2019) concluded that the assessment and optimization of therapeutic working alliance in interventions with mHealth applications is urgently needed to improve effectiveness and adherence.

Taken together, there are various putative therapeutic mechanisms of change not fully explored yet. Thus, deepening our understanding of mechanisms and processes involved in change is of great importance to develop new and improve existing mobile interventions.

1.8. Exploring the reach of an early intervention and prevention approach

When discussing improvements in health care, part of the truth is that gains in health outcomes achieved in the past did not benefit all members of society equally and that health inequalities have not improved or are even increasing (Frohlich & Potvin, 2008). In the United States, for example, discrepancies in life expectancy as large as 20 years between most and least advantaged groups can be observed (Marmot, 2005; C. J. Murray, Michaud, McKenna, & Marks, 1998) and additional burden of non-fatal diseases should be taken into account (Marmot, 2005). This has been central to the 'vulnerable population approach' (Frohlich & Potvin, 2008) as well as theories on 'social determinants of health inequalities' (Marmot, 2005, 2020) and 'fundamental causes of health inequalities' (Link & Phelan, 1995; Phelan, Link, & Tehranifar, 2010). The approaches converge to the suggestion of vulnerable populations sharing a fundamental cause of risk – their socio-economic status, their position in the social structure. Socio-economic status represents a 'fundamental cause' of risk as it 1) influences multiple health out-

comes, 2) is associated with various risk factors, 3) is associated with access to resources reducing risk or burden of existing disease, and 4) reproduces over time by replacing the intervening mechanisms (Link & Phelan, 1995). Therefore, Marmot (2005) concludes that "the major determinants of health are social" (p.8) and that reducing health inequalities therefore is a matter of social justice.

Digital prevention and intervention approaches, including mobile interventions, may not be exempt from inequalities. They may not work equally well and in the same way for all service users taking part in them. Reviewing studies of effectiveness of mHealth, Lui, Marcus, and Barry (2017) described the average participant as female, White and aged 30-45. Yet, this only describes a small proportion of the individuals in need of mental health care and the degree of generalisability of findings to service users with other characteristics remains largely unexplored. Reach of digital interventions has been discussed controversially and concerns have been expressed that new barriers to treatment may be created by this delivery format (Bucci, Berry, et al., 2019; Greer et al., 2019). It is therefore of crucial importance to understand which characteristics of service users are associated with treatment outcomes to improve reach and adapt interventions to the needs and preferences of service users. In order to obtain a comprehensive picture, it seems indispensable to conduct process evaluations considering both quantitative and qualitative data (G. F. Moore et al., 2015). In previous quantitative analyses, the predictive value of participants' characteristics for outcomes such as therapeutic change, dropout, and symptom severity at termination but also acceptability and adherence has been examined (Lewis, Simons, & Kim, 2012; Lincoln et al., 2014). For qualitative analyses in the context of process evaluations, a realist framework, aiming at understanding what works for whom, under which circumstances and how, has been reported to be particularly well-suited (Wong et al., 2016).

Based on evidence generated from process evaluations targeting reach, adaptions of existing interventions may be possible to address potential inequalities. For cultural adaptions for example, feasibility and beneficial effects on treatment outcomes have already been demonstrated (Rathod et al., 2013). In addition to adapting treatment for groups (e.g. in cultural adaptions), individual participants' needs could also be considered and addressed in a personalised intervention. Interventions can be adapted to individuals' current location, context, mood or level of symptoms (Myin-Germeys et al., 2018; Patrick et al., 2016; Patrick, Intille, & Zabinski, 2005; Reininghaus, 2018). While tailoring comprises the display of specific content such as self-set goals (Pijnenborg et al., 2010) or personal successes in a positive data log (Daemen et al., 2021) or the delivery of intervention components based on static decision rules (Daemen et al., 2021;

Schick et al., 2021) in EMIs, more complex approaches such as just-in-time adaptive interventions (Nahum-Shani et al., 2018; Spruijt-Metz et al., 2015) rely on algorithms to optimise and personalise systems over time (Balaskas et al., 2021; Goldstein et al., 2017; Schueller, Aguilera, & Mohr, 2017). Implementing intervention and prevention approaches, whose benefits are more equally distributed across the socio-economic continuum may be facilitated by applying co-creation and –evaluation methods explicitly including individuals from underserved and minoritized populations (Bucci, Schwannauer, & Berry, 2019; Hardy et al., 2018).

1.9. Aims and outline of this thesis

This thesis has three overarching goals. First, the thesis aims to investigate digital markers in the prediction of clinical outcomes *(Part 1)*. Second, the thesis aims to examine how early adversity may combine and interact with putative candidate mechanisms in the development of psychopathology *(Part 2)*. Third, the thesis aims at the development of a hybrid transdiagnostic intervention for enhancing resilience in youth with early mental health problems, exploring its reach, putative therapeutic mechanisms of change involved, and personalised intervention trajectories including context factors *(Part 3)*. The studies presented in this thesis investigated the following aims:

Part 1

Chapter II investigates the predictive value of momentary manifestations of negative symptoms for clinical outcomes in individuals at UHR for psychosis.

Part 2

Chapters III and IV examine the complex interplay of early adversity as a socio-environmental risk factor and putative candidate mechanisms in the development of psychopathology. More specifically, *Chapter III* investigates the interplay of exposure to childhood trauma and stress reactivity as a candidate mechanism in predicting clinical outcomes in individuals at UHR for psychosis in a longitudinal design. *Chapter IV* examines the interplay of childhood trauma, bullying and threat anticipation as a candidate mechanism in the development of psychopathology in a large community sample of adolescents.

Part 3

Chapters V, VI and VII examine the hybrid transdiagnostic EMIcompass intervention for enhancing resilience in youth with early mental health problems. More specifically, *Chapter V* delineates the intervention manual of the EMIcompass intervention and explores initial signals of the interventions' reach. *Chapter VI* examines change in self-compassion, change in emotion regulation, training frequency and therapeutic working alliance as putative therapeutic mechanisms of change in the EMIcompass intervention. *Chapter VII* presents findings from a process evaluation of the intervention incorporating realist methodology to explore what works for whom, in what respects, to what extent, in what contexts, and how.

CHAPTER II:

MOMENTARY MANIFESTATIONS OF NEGATIVE SYMPTOMS AS PREDICTORS OF CLINICAL OUTCOMES IN PEOPLE AT HIGH RISH FOR PSYCHOSIS: FINDINGS FROM THE EU-GEI HIGH RISK STUDY

2.1.   Abstract

Negative symptoms occur in individuals at UHR for psychosis. While there is evidence that observer-ratings of negative symptoms are associated with level of functioning, the predictive value of UHR individuals' subjective experience in daily life has not been studied yet. This study therefore aimed to investigate the predictive value of momentary manifestations of negative symptoms for clinical outcomes in UHR individuals. Experience sampling methodology was used to measure momentary manifestations of negative symptoms (blunted affective experience, lack of social drive, anhedonia, and social anhedonia) in the daily lives of N=79 UHR individuals. Clinical outcomes (level of functioning, illness severity, UHR status, transition status) were assessed at baseline, and at 1- and 2-year follow-up. Lack of social drive, operationalised as greater experienced pleasantness of being alone, was associated with poorer functioning at 2-year follow-up (b=-4.62, p=.013). Higher levels of anhedonia were associated with poorer functioning at 1-year follow-up (b=5.61, p=.017). Higher levels of social anhedonia were associated with poorer functioning (e.g. disability subscale: b=6.36, p=.006) and greater illness severity (b=-0.38, p=.045) at 1-year follow-up. In exploratory analyses, there was evidence that individuals with greater variability of positive affect (used as a measure of blunted affective experience) experienced a shorter time to remission from UHR status at follow-up (HR=4.93, p=.005). Momentary manifestations of negative symptoms in UHR individuals may

help to predict clinical outcomes and may be a promising target for interventions in the early stages of psychosis.

2.2.   Introduction

Background

Negative symptoms occur in individuals at UHR (also known as CHR) for psychosis and have been reported to be associated with reduced quality of life and impaired functioning in cross-sectional and longitudinal studies (Azar et al., 2018; Fulford et al., 2013; Schlosser et al., 2015; Svirskis et al., 2007). Recently, several studies have demonstrated the predictive value of negative symptoms for social aspects of functioning (Burton et al., 2019; Glenthøj, Kristensen, Wenneberg, Hjorthøj, & Nordentoft, 2020a). Furthermore, negative symptoms have been found to be predictive of transition to psychotic disorder in UHR samples (Alderman et al., 2015; Demjaha, Valmaggia, Stahl, Byrne, & McGuire, 2012; Oliver et al., 2020; Piskulic et al., 2012; Valmaggia et al., 2013; Zimmermann et al., 2010).

To date, clinical outcomes in UHR studies have primarily focused on transition to psychosis. Given that the majority of UHR individuals do not develop psychosis (71-76% in meta-analyses and systematic reviews; Addington et al., 2015; Ferrarelli & Mathalon, 2020; Fusar-Poli, Borgwardt, et al., 2013; Simon et al., 2011), investigating other outcomes has received increasing attention in recent years (Addington et al., 2011; Polari et al., 2018). Meta-analyses have found that most UHR individuals who do not transition to psychosis do not remit from UHR status within 2 years either (Simon et al., 2013). In addition, UHR individuals – regardless of whether or not they transition to psychosis – show other clinical symptoms and marked impairments in functioning that are comparable to those reported in patients with social phobia and major depressive disorder (Addington et al., 2011; K. Beck et al., 2019; Fusar-Poli, Rocchetti, et al., 2015; A. Lin et al., 2015; Michel, Ruhrmann, Schimmelmann, Klosterkötter, & Schultze-Lutter, 2018; Simon et al., 2013). The level of functioning in UHR individuals is more similar to that which is observed in patients with psychotic disorders than in controls (Fusar-Poli, Rocchetti, et al., 2015). Hence, level of functioning and persistence of clinical symptoms are important outcomes other than transition to psychosis.

Standard measures used to assess negative symptoms (e.g. the Positive and Negative Syndrome Scale, PANSS; Kay, Fiszbein, & Opler, 1987; Kay, Opler, & Lindenmayer, 1989), though valid in their own right, have been criticised for being overly reliant on behavioural observation and

third-party anamnesis (Blanchard et al., 2020; Galderisi, Mucci, Buchanan, & Arango, 2018; Oorschot et al., 2013). In addition, standardised self-report questionnaires and lab measures of negative symptoms in psychosis patients do not seem to converge with real-time and real-world reports generated using ESM and hence may capture different constructs (A. S. Cohen, Najolia, Brown, & Minor, 2011; Kring & Caponigro, 2010). ESM is a semi-structured diary method that captures daily behaviour and experience of company with high ecological validity (Myin-Germeys et al., 2018). A recent systematic review of experience sampling studies investigating everyday social experiences of individuals with schizophrenia (Mote & Fulford, 2020) concluded that, compared to other methods, experience sampling allows for a more granular assessment of social experience. This underscores the importance of examining the perspective of individuals' experience of negative symptoms in daily life (i.e., momentary manifestations of negative symptoms), as this is when psychiatric symptoms naturally emerge. Experience sampling studies have made important contributions to our understanding of psychosis, but until now, studies of momentary experience of social context and manifestations of negative symptoms have mainly focused on individuals with a psychotic disorder (Myin-Germeys, Delespaul, & deVries, 2000; Oorschot et al., 2013).

Previous experience sampling studies have investigated blunted affective experience, lack of social drive, anhedonia and social anhedonia as momentary manifestations of negative symptoms in daily life. Blunted affective experience has been operationalised as intensity (i.e., mean level), instability (i.e., differences in affect from one moment to the following), and variability (i.e., differences between affect in the moment and the average individual affect) of positive and negative affect (Dejonckheere et al., 2019; Hermans et al., 2020; Myin-Germeys et al., 2000; Oorschot et al., 2013). Lack of social drive has been assessed using the amount of time spent alone, the preference to be alone when in company and the experienced pleasantness of being alone (Hermans et al., 2020; Kwapil et al., 2009). Anhedonia has been operationalised as a smaller increase of positive affect in moments of pleasant events (Hermans et al., 2020; Oorschot et al., 2013). Similarly, social anhedonia has been operationalised as a smaller increase in positive affect associated with being in pleasant company (Hermans et al., 2020; Kwapil et al., 2009; Oorschot et al., 2013).

To our knowledge, only two experience sampling studies have, to date, investigated momentary manifestations of negative symptoms in UHR individuals (Gerritsen et al., 2019; Hermans et al., 2020). Although differing in focus and operationalization of constructs, both studies compared momentary manifestations of negative symptoms across UHR individuals, first episode psychosis patients and controls. In line with findings in enduring psychosis (Aghevli,

Blanchard, & Horan, 2003; Oorschot et al., 2013), both studies concluded that there may be a mismatch between what UHR individuals experience and how they express this in their behaviour, that may be interpreted as two distinct dimension of negative symptoms (i.e., experience vs. expression). Hence, assessing individuals' subjective experience of negative symptoms is important to gain a more comprehensive understanding of internal, experiential aspects (Blanchard et al., 2020). However, both studies used a cross-sectional design. No experience sampling study to date has used momentary manifestations of negative symptoms for predicting clinical outcomes in UHR individuals in a longitudinal design. This is an important gap that needs to be addressed, as a shift in research towards subjective experience of momentary symptoms may offer new insights into the social nature and development of negative symptoms in UHR and its outcomes.

Objectives

The current study aimed to investigate whether momentary manifestations of negative symptoms predict clinical outcomes (i.e., illness severity, level of functioning, and remission from ultra-high risk status and transition to psychosis) in individuals at ultra-high risk for psychosis at 1- and 2-year follow-up. We tested the following hypotheses:

Momentary manifestations of negative symptoms in daily life predict clinical outcomes in UHR individuals at 1- and 2-year follow-up, such that higher levels of

1) blunted affective experience (i.e., lower intensity, variability and instability of positive and negative affect, (hypothesis 1, H1),

2) lack of social drive (i.e., amount of time spent alone, pleasantness of being alone, and preference to be alone when in company, H2),

3) anhedonia (i.e., no/low increase of positive affect in moments of pleasant events, H3); and

4) social anhedonia (i.e., no/low increase of positive affect in moments of pleasant company, H4)

are associated with greater illness severity and poorer functioning at follow-up.

In exploratory analyses, we further aimed to examine whether momentary manifestations of negative symptoms are associated with time to transition to psychosis or remission from ultra-high risk status.

2.3.   Method

Sample

A sample of UHR individuals aged 15-35 years, who were assessed at baseline, 1- and 2-year follow-up, was recruited. Participants were recruited in London (United Kingdom), Melbourne (Australia), and Amsterdam/The Hague (the Netherlands) as a part of the High Risk Study of the European Network of National Networks studying Gene-Environment Interactions in Schizophrenia (EU-GEI; European Network of National Networks studying Gene-Environment Interactions in Schizophrenia, 2014). EU-GEI is a naturalistic prospective multicentre study that aims to identify the interactive genetic, clinical, and environmental determinants of schizophrenia.

To be eligible to participate, individuals had to meet at least one of the UHR criteria as defined by the Comprehensive Assessment of At-Risk Mental State (CAARMS; Yung et al., 2005): (1) Attenuated Psychotic Symptoms (APS): the presence of subthreshold positive psychotic symptoms for at least 1 month during the past year; (2) Brief Limited Intermittent Psychotic Symptoms (BLIPS): an episode of frank psychotic symptoms that lasted no longer than 1 week, which abated spontaneously; or, (3) Vulnerability: a first-degree relative with a psychotic disorder or schizotypal personality disorder in combination with a significant drop in functioning during at least 1 month in the previous year or enduring low functioning. Exclusion criteria were: (1) presence of a current or past psychotic disorder; (2) symptoms for inclusion explained by a medical disorder, drugs or alcohol dependency; or, (3) intelligence quotient < 60.

Data collection

Experience sampling measures

Data on momentary manifestations of negative symptoms were collected using experience sampling methodology (Myin-Germeys et al., 2018; Myin-Germeys et al., 2009). Subjects were asked to report their thoughts, feelings, and symptoms as well as the context (e.g. location, company, activity) and the appraisal of the context in their normal daily lives (Myin-Germeys et al., 2009; Palmier-Claus, Dunn, & Lewis, 2012; Palmier-Claus et al., 2011; Shiffman et al., 2008). For data collection, participants used a dedicated digital device (the Psymate®), which prompted participants with a 'beep' to complete a brief questionnaire ten times a day on six consecutive days at random moments within set blocks of time.

A detailed description of ESM items and compliance procedure is provided in Table 2. Momentary manifestations of negative symptoms were operationalised as follows: For blunted affective experiences, we computed mean levels of intensity, variability, and instability of positive and negative affect across beeps within subjects. We used three operationalizations for lack of social drive: the amount of time spent alone as the percentage of total time, the preference for being alone when in company and the pleasantness of being alone. To represent anhedonia, We obtained fitted values of positive affect predicted by event pleasantness. As anhedonia is by definition related to pleasant events, only ratings of 1 to 3 were used to test associations with positive affect (Hermans et al., 2020; Oorschot et al., 2013). Observations that indicated unpleasant events (-3 to -1) were excluded from analysis and neutral events (0) were set as the reference category (Oorschot et al., 2013). We fitted a two-level, linear mixed model with pleasantness of being in company as the independent and positive affect as the outcome variable and obtained fitted values for representing social anhedonia.

Consistent with previous research, psychometric properties for measures of momentary manifestations of negative symptoms were assessed by evaluating their convergent validity. Therefore, we examined the association between momentary manifestations and observer-rated measures of negative symptoms at baseline (assessed with the expanded Brief Psychiatric Rating Scale, BPRS; Overall & Gorham, 1962; Ventura et al., 1993; see Supplementary Material 1). We found small to moderate correlations between the BPRS total score and intensity of negative ($r=0.28$, $p=.017$) and positive affect ($r=-0.34$, $p=.004$), variability of negative affect ($r=0.26$, $p=.025$), anhedonia ($r=-0.34$, $p=.003$), and social anhedonia ($r=-0.31$, $p=.008$). We found no evidence that the BPRS negative symptom subscale was associated with momentary manifestations of negative symptoms. In addition, we used observer-rated measures of negative symptoms to predict momentary manifestations of negative symptoms in a multilevel model (see supplementary material 1). BPRS total score predicted intensity of positive ($b=0.04$, $p=.013$) and negative affect ($b=-0.04$, $p<.001$), instability ($b=0.04$, $p=.029$) and variability ($b=0.03$, $p=.003$) of negative affect, anhedonia ($b=-0.04$, $p=.001$) and social anhedonia ($b=-0.04$, $p=.001$). The BPRS negative symptoms scale did not predict momentary manifestations of negative symptoms in the multilevel model.

Clinical outcomes

Clinical outcomes were assessed at baseline, and around 1 and 2 years after the baseline assessment. As participants were not seen at exactly 1 and 2 years from their baseline appointment, the exact time points for follow-up assessments varied. Hence, the data closest to 1 and 2 years

after baseline was selected as follow-up data. Transition to psychosis and UHR status were assessed using the CAARMS (Yung et al., 2005). If participants could not be re-interviewed for the follow-up assessments, clinical notes were used to determine transition status. Participants' level of functioning was assessed using the symptoms and the functioning subscales of the Global Assessment of Functioning Scale (GAF; American Psychiatric Association, 2002). Illness severity was assessed using the severity of illness subscale of the Clinical Global Impression Scale (CGI; Guy, 1976). A detailed description of the outcome measures is provided in Table 2.

Statistical analysis

Momentary manifestations of negative symptoms – operationalised and computed as detailed above – were used as independent variables to predict clinical outcomes at 1- and 2-year follow-up using Stata 15. We fitted linear regression models using the command 'regress' with level of functioning and illness severity as outcome variables and momentary manifestations of negative symptoms as independent variables. In exploratory analyses, we examined the predictive value of momentary manifestations of negative symptoms for transition to psychosis and remission from UHR status as outcomes. Survival analyses using the Stata commands 'stset' and 'streg' were preformed to account for the time to event structure of the data. We used time to follow-up as a proxy for time to remission. In both survival analyses, a Weibull distribution was assumed.

Analyses were adjusted for a priori confounders (i.e., age, gender, ethnicity, centre, time to follow-up; for unadjusted results see online supplementary material 3). In a sensitivity analysis, we included current depressive episode (supplementary material 4) and comorbid disorders (supplementary material 5) as additional independent variables to control for potential confounding.

Table 2. *Overview of experience sampling and clinical outcome measures.*

Domain	Measure
Experience sampling	
Positive affect	Positive affect was measured by asking participants to rate how cheerful, relaxed, satisfied and enthusiastic they felt on a Likert scale ranging from 1 (not at all) to 7 (very much). We found satisfying internal consistency, Cronbach's α=.73. In line with previous studies (Dejonckheere et al., 2019; McManus, Siegel, & Nakamura, 2019), we used high and low physiological arousal items.
Negative affect	Negative affect was measured by asking participants to rate the extent to which they felt insecure, down, lonely, anxious and irritated on a Likert scale ranging from 1 (not at all) to 7 (very much). We found satisfying internal consistency, Cronbach's α=.73.
Blunted affect	*Intensity* was operationalised as the mean level of positive/negative affect. *Instability* was computed as the squared difference between beep-level positive and negative affect intensity at beep t and beep-level positive affect intensity at beep t-1 (previous beep), within days, within persons (MSSD) and only calculated if there was a maximum of two observations missing between two consecutive observations. Difference scores between two observations overnight were excluded (Myin-Germeys et al., 2000). *Variability* was computed as the squared difference between beep-level intensity of positive/negative affect at each observation and individual mean positive/negative affect over observations, over days within persons (Myin-Germeys et al., 2000).
Social drive	Lack of social drive was conceptualised as the amount of time spent alone in percentage of total time, the experienced pleasantness of being alone and the preference of being alone when in company. Pleasantness of being alone and preference to be alone when in company were rated on a Likert scale ranging from 1 (not at all) to 7 (very much). If participants were alone: 'I find it pleasant to be alone' and 'I would prefer to have company'. If participants were in company: 'I find being with these people pleasant.' and 'I would prefer to be alone.'
Anhedonia	Anhedonia was conceptualised as the relationship between positive affect and the occurrence of pleasant events. Participants were asked to 'think about the most important event that happened since the last beep'. The pleasantness of this event was rated on a bipolar scale ranging from -3 (very unpleasant) to 3 (very pleasant). We only used ratings of 1 to 3 to test associations with positive affect, as anhedonia is per definition related to pleasant events. Observations indicating unpleasant events (-3 to -1) were excluded, neutral events (0) were used as a reference category (Oorschot et al., 2013).
Social anhedonia	Social anhedonia was defined as the association between positive affect and pleasantness of being in company (Oorschot et al., 2013). Participants were asked whether they were alone or in company. If participants indicated to be in company, they were asked to rate 'I find being with these people pleasant.' on a Likert scale ranging from 1 (not at all) to 7 (very much).
Clinical outcome measures	
CAARMS	Transition to psychosis and UHR status were assessed using the CAARMRS (Yung et al., 2005), a semi-structured interview to assess attenuated psychotic symptoms in people at high risk for psychosis. The CAARMS comprises 27 items clustered in 7 subscales: Positive Symptoms, Cognitive Change, Attention and Concentration; Emotional Disturbance; Negative Symptoms; Behavioural Change; Motor/Physical Changes; and General Psychopathology. Scores on each item range from 0 (absent) to 6 (extreme).
GAF	The GAF (American Psychiatric Association, 2002) obtains ratings of burdening *symptoms* and *disabilities* in the last month on a scale from 100 (no symptoms/superior functioning in a wide range of activities) to 1 (persistent danger of severely hurting self or others or serious suicidal act with clear expectation of death/persistent inability to maintain minimal personal hygiene).
CGI	The CGI (Guy, 1976) symptoms severity subscale is an expert rating of average *illness severity* during the last week ranging from 1 (normal, not at all ill) to 7 (among the most extremely ill patients).

Note. Experience sampling procedure: During an initial briefing, the study team ensured that the week of data collection was a typical week for the participant. Each time the device emitted the beep signal, participants were asked to stop their activity and answer the questions. The experience sampling questionnaire was available to participants for the duration of 10 min after emission of the beep signal. Participants were contacted at least once during the assessment period to assess their adherence to instructions, identify any potential distress associated with the method, and maximize the number of observations per participant. At the end of the assessment period, participants' reactivity to, and compliance with, the method was examined in a debriefing session. Participants were required to provide valid responses to at least one-third (i.e., 20 valid answers) of the emitted beeps to be included in the analysis (Delespaul, deVries, & van Os, 2002). Procedures to ensure data quality are reported in supplementary material 2. CAARMS=Comprehensive Assessment of At Risk Mental State (Yung et al., 2005). GAF=Global Assessment of Functioning (American Psychiatric Association, 2002). CGI=Clinical Global Impression Scale (Guy, 1976).

We corrected for multiple testing to reduce the probability of type I errors as a consequence of the number of tests performed. We corrected within domains of momentary manifestations of negative symptoms and clinical outcomes. As in previous experience sampling studies (Janssens et al., 2012; R. van Winkel et al., 2008), Simes' correction method was used to account for multiple tests of significance (Simes, 1986). Simes'correction is a modified version of the more conservative Bonferroni correction in case of dependent hypotheses given significance tests in the current analyses were not independent (Simes, 1986). With the Simes' correction, the most significant p-value is tested against $\alpha=.05/n$ (total number of tests), the second most significant p-value is tested against $\alpha=.05/(n-1)$, the third p-value against $\alpha=.05/(n-2)$, etc. Simes-corrected significant results are highlighted with an asterisk (*) in text and tables.

2.4.   Results

Basic sample and clinical characteristics

The ESM sample comprised $N=79$ UHR individuals, of whom $N=9$ transitioned to psychosis during the study period. Data on clinical outcomes were obtained for $N=48$ at 1-year follow-up and $N=36$ at 2-year follow-up. Participants were on average 23 years old ($SD=4.93$) and 56% were women. The majority (67%) of the sample was white, followed by 15% with black ethnicity. In addition to their UHR status, 76% of the participants were diagnosed with a comorbid axis-I disorder (for further details see supplementary material 6). Compared to the sample of individuals included in the EU-GEI High Risk Study for whom experience sampling data was not collected (no ESM sample, $N=266$), the current study's sample showed no differences in demographic characteristics (age: $t(343)=-1.33$, $p=.185$, gender: $\chi^2(1)=3.58$, $p=.059$, ethnicity: $\chi^2(5)=6.53$, $p=.258$) or prevalence of comorbid disorders ($\chi^2(1)=1.82$, $p=.177$). However, the current sample showed poorer functioning (symptoms: $t(315)=2.29$, $p=.023$) and lower levels of observer-rated negative symptoms ($t(320)=2.27$, $p=.024$) at baseline. Comparing participants who completed follow-up assessments, the sample with no ESM data collected (1-year follow-up $N=134$, 2-year follow-up $N=89$) showed a lower BPRS total score at 1-year follow-up ($t(159)=-2.07$, $p=.040$). There were no significant differences in demographic or clinical characteristics at 2-year follow-up. Table 3 gives an overview of relevant sample characteristics.

Table 3. *Basic sample and clinical characteristics.*

	ESM sample			No ESM sample			ESM vs. no ESM		
	Baseline	1-year follow-up	2-year follow-up	Baseline	1-year follow-up	2-year follow-up	Baseline	1-year follow-up	2-year follow-up
N	79	48	36	266	134	89			
Age at baseline (years), mean (*SD*)	23.0 (4.93)	23.6 (5.24)	23.8 (5.18)	22.2 (4.89)	22.5 (4.82)	23.3 (5.14)	*t*(343)=-1.33, *p*=.185	*t*(180)=-1.30, *p*=.194	*t*(123)=-0.45, *p*=.654
Gender, *N* (%)							$\chi^2(1)$=3.58, *p*= .059	$\chi^2(1)$=3.76, *p*= .053	$\chi^2(1)$=2.74, *p*= .098
Male	35 (44%)	22 (46%)	16 (44%)	150 (56%)	83 (62%)	54 (61%)			
Female	44 (56%)	26 (54%)	20 (56%)	116 (44%)	51 (38%)	35 (39%)			
Ethnicity, *N* (%)							$\chi^2(5)$=6.53, *p*=.258	$\chi^2(5)$=6.74, *p*=.240	$\chi^2(5)$=6.25, *p*=.282
White	53 (67%)	33 (69%)	27 (75%)	193 (73%)	99 (74%)	63 (71%)			
Black	12 (15%)	9 (19%)	5 (14%)	22 (8%)	9 (7%)	6 (7%)			
Other	14 (18%)	6 (13%)	4 (11%)	50 (19%)	26 (19%)	20 (22%)			
Comorbidity at baseline *N* (%)	60 (76%)	37 (77%)	28 (78%)	220 (83%)	111 (83%)	79 (89%)	$\chi^2(1)$=1.82, *p*=.177	$\chi^2(1)$=0.77, *p*=.380	$\chi^2(1)$=2.51, *p*=.113
BPRS									
Total score, mean (*SD*)	44.00 (9.46)	39.69 (11.63)	37.31 (12.53)	43.37 (10.57)	36.01 (9.70)	33.45 (10.85)	*t*(314)=-0.46, *p*=.649	*t*(159)=-2.07, *p*=.040	*t*(111)=-1.97, *p*=.051
Negative symptom score, mean (*SD*)	4.49 (1.86)	4.04 (1.74)	3.75 (1.78)	5.21 (2.51)	4.42 (2.05)	4.12 (1.87)	*t*(320)=2.27, *p*=.024	*t*(160)=1.22, *p*=.264	*t*(112)=-0.98, *p*=.327
GAF									
Symptoms, mean (*SD*)	52.88 (9.85)	56.96 (10.76)	61.00 (11.73)	55.92 (10.23)	59.49 (13.08)	61.25 (15.02)	*t*(315)=2.29, *p*=.023	*t*(180)=1.20, *p*=.232	*t(123)*=0.09, *p*=.930
Disability, mean (*SD*)	56.27 (13.00)	58.92 (13.41)	63.78 (13.62)	55.36 (12.20)	60.40 (13.77)	61.81 (16.09)	*t*(330)=-0.57, *p*=.572	*t*(196)=0.65, *p*=.514	*t(132)*=-0.65, *p*=.514
CGI Illness severity, mean (*SD*)	3.57 (1.21)	3.15 (1.32)	2.89 (1.25)	3.60 (1.09)	3.33 (1.37)	3.22 (1.51)	*t*(319)=0.21, *p*=.831	*t*(203)=0.83, *p*=.409	*t*(148)=1.21, *p*=.228
UHR criteria met, *N* (%)		36 (73%)	23 (62%)		107 (73%)	71 (66%)		$\chi^2(1)$=0.00, *p*=.965	$\chi^2(1)$=0.15, *p*=.694

Note. Follow-up values for age, gender, ethnicity, and comorbidity based on individuals with valid Global Assessment of Functioning Scale at follow-up. SD=standard deviation. BPRS=Brief Psychiatric Rating Scale (Overall & Gorham, 1962; Ventura et al., 1993). GAF=Global Assessment of Functioning Scale (American Psychiatric Association, 2002). CGI=Clinical Global Impression Scale (Guy, 1976).

Blunted affective experience and clinical outcomes

Tables 4 and 5 show the results on clinical outcomes at follow-up predicted by blunted affective experience at baseline. We found no evidence that blunted affective experience predicted illness severity or level of functioning. In exploratory analyses, time to remission from UHR status was predicted by variability of positive affect (HR=4.93, 95% CI 1.61 – 15.11, p=.005*). Participants with greater variability were more likely to experience a shorter time to remission from UHR status. We found no evidence that blunted affective experience predicted transition to psychosis.

Lack of social drive and clinical outcomes

Tables 6 and 7 show findings on clinical outcomes predicted by lack of social drive. We found no evidence that the amount of time spent alone and the preference to be alone when in company predicted level of functioning or illness severity. Experienced pleasantness of being alone predicted the GAF disability subscale at 2-year follow-up (b=-4.62, 95% CI -8.19 – -1.04, p=.013*), such that individuals who experienced greater pleasantness of being alone showed poorer functioning. However, there was no evidence that pleasantness of being alone predicted illness severity and the GAF symptoms score. In exploratory analyses, there was no evidence that lack of social drive predicted time to transition or remission from UHR status.

Anhedonia and clinical outcomes

Tables 8 and 9 show findings on clinical outcomes at 1- and 2-year follow-up predicted by anhedonia. Anhedonia predicted the GAF disability subscale at 1-year follow-up (b=5.61, 95% CI 1.08 – 10.15, p=.017*). Lower positive affect in moments of pleasant events or, in other words, higher levels of anhedonia, were associated with poorer functioning. However, we found no evidence that anhedonia predicted functioning at 2-year follow-up. In addition, anhedonia did not predict illness severity at 1- and 2-year follow-up. In exploratory analyses, we found no evidence that anhedonia predicted time to remission or transition to psychosis.

Table 4. *Level of functioning at 1- and 2-year follow-up predicted by blunted affective experience at baseline (i.e., intensity, instability and variability of negative and positive affect) and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Intensity NA								
Outcome at baseline	0.18 (-0.16 – 0.52)	.292	0.00 (-0.61 – 0.61)	.996	0.34 (-0.01 – 0.70)	.057	0.55 (0.06 – 1.04)	.029
Intensity NA	-2.51 (-6.54 – 1.52)	.216	-1.36 (-6.89 – 4.18)	.618	-3.17 (-7.83 – 1.48)	.175	1.26 (-4.90 – 7.42)	.677
Predictor: Intensity PA								
Outcome at baseline	0.15 (-0.18 – 0.48)	.359	-0.01 (-0.62 – 0.60)	.973	0.34 (0.00 – 0.68)	.050	0.55 (0.06 – 1.05)	.029
Intensity PA	3.84 (-0.09 – 7.77)	.055	1.15 (-4.58 – 6.88)	.684	5.04 (0.59 – 9.49)	.028	0.07 (-6.34 – 6.48)	.982
Predictor: Instability NA								
Outcome at baseline	0.24 (-0.10 – 0.58)	.168	-0.02 (-0.62 – 0.58)	.936	0.36 (0.00 – 0.73)	.051	0.55 (0.08 – 1.01)	.024
Instability NA	0.80 (-1.43 – 3.04)	.471	-1.72 (-5.94 – 2.50)	.410	-0.36 (-2.98 – 2.27)	.785	-3.66 (-8.21 – 0.88)	.109
Predictor: Instability PA								
Outcome at baseline	0.22 (-0.12 – 0.56)	.205	-0.06 (-0.64 – 0.52)	.832	0.37 (0.01 – 0.73)	.046	0.55 (0.11 – 0.99)	.016
Instability PA	-0.24 (-3.75 – 3.28)	.893	-4.68 (-10.43 – 1.07)	.106	-0.46 (-4.57 – 3.64)	.821	-7.52 (-13.54 – -1.51)	.016
Predictor: Variability NA								
Outcome at baseline	0.23 (-0.11 – 0.56)	.184	0.00 (-0.59 – 0.60)	.995	0.37 (0.01 – 0.73)	.046	0.52 (0.07 – 0.98)	.027
Variability NA	1.60 (-3.30 – 6.50)	.514	-3.80 (-11.52 – 3.92)	.321	0.03 (-5.76 – 5.82)	.992	-7.96 (-16.15 – 0.22)	.056
Predictor: Variability PA								
Outcome at baseline	0.21 (-0.13 – 0.55)	.219	0.02 (-0.56 – 0.60)	.932	0.37 (0.01 – 0.73)	.043	0.47 (-0.01 – 0.95)	.053
Variability PA	1.12 (-4.54 – 6.77)	.692	-5.55 (-12.51 – 1.42)	.114	2.22 (-4.34 – 8.78)	.498	-6.30 (-14.23 – 1.63)	.114

Note. Results adjusted for age, gender, ethnicity, centre, and time to follow-up. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). CI=confidence interval. NA=negative affect. PA=positive affect.

Table 5. *Illness severity, remission from UHR status and transition status at 1- and 2-year follow-up predicted by blunted affective experience at baseline (i.e., intensity, instability and variability of negative and positive affect) and clinical outcome at baseline.*

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Intensity NA								
Outcome	0.43	.006	0.28	.238				
at baseline	(0.13 – 0.73)		(-0.19 – 0.75)					
Intensity	0.32	.108	-0.03	.912	0.34	.045	1.44	.356
NA	(-0.07 – 0.71)		(-0.59 – 0.53)		(0.12 – 0.98)		(0.66 – 3.13)	
Predictor: Intensity PA								
Outcome	0.44	.004	0.17	.463				
at baseline	(0.15 – 0.74)		(-0.30 – 0.64)					
Intensity	-0.31	.110	-0.35	.264	2.08	.097	0.62	.336
PA	(-0.69 – 0.07)		(-0.98 – 0.28)		(0.88 – 4.93)		(0.23 – 1.65)	
Predictor: Instability NA								
Outcome	0.52	.001	0.27	.232				
At baseline	(0.22 – 0.81)		(-0.18 – 0.72)					
Instability	-0.02	.805	-0.02	.941	1.19	.635	1.02	.924
NA	(-0.23 – 0.18)		(-0.46 – 0.42)		(0.57 – 2.48)		(0.67 – 1.54)	
Predictor: Instability PA								
Outcome	0.51	.001	0.28	.204				
at baseline	(0.22 – 0.81)		(-0.16 – 0.73)					
Instability	-0.06	.714	0.24	.427	1.75	.243	0.99	.971
PA	(-0.38 – 0.26)		(-0.38 – 0.86)		(1.69 – 4.44)		(0.50 – 1.94)	
Predictor: Variability NA								
Outcome	0.51	.001	0.26	.253				
at baseline	(0.22 – 0.81)		(-0.20 – 0.72)					
Variability	-0.10	.642	-0.08	.849	1.24	.769	1.21	.635
NA	(-0.53 – 0.33)		(-0.89 – 0.74)		(0.30 – 5.14)		(0.55 – 2.63)	
Predictor: Variability PA								
Outcome	0.51	.001	0.37	.114				
at baseline	(0.21 – 0.81)		(-0.09 – 0.83)					
Variability	0.04	.880	0.49	.205	4.93	.005*	1.49	.458
PA	(-0.47 – 0.54)		(-0.29 – 1.28)		(1.61 – 15.11)		(0.52 – 4.23)	

Note. Results adjusted for age, gender, ethnicity, centre, and time to follow-up. Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. NA=negative affect. PA=positive affect. HR=hazard ratio. *statistically significant after Simes' correction.

Social anhedonia and clinical outcomes

As displayed in Tables 8 and 9, reduced positive affect in moments of pleasant company or, in other words, higher levels of social anhedonia at baseline were associated with higher levels of illness severity (b=-0.38, 95% CI -0.74 – -0.01, p=.045*) and lower scores on both GAF sub-scales (symptoms: b=4.61, 95% CI 0.74 – 8.48, p=.021*, disability: b=6.36, 95% CI 1.97 – 10.74, p=.006*) at 1-year follow-up. However, we found no evidence that social anhedonia predicted clinical outcomes at 2-year follow-up. In exploratory analyses, we found no evidence that social anhedonia predicted time to remission or transition to psychosis.

Table 6. *Level of functioning at 1- and 2-year follow-up predicted by lack of social drive (i.e., amount of time spent alone, preference to be alone when in company and experienced pleasantness of being alone) and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Amount of time spent alone								
Outcome at baseline	0.22 (-0.12 – 0.56)	.197	-0.10 (-0.69 – 0.48)	.718	0.37 (0.01 – 0.73)	.045	0.49 (0.03 – 0.96)	.038
Amount of time spent alone	1.71 (-12.18 – 15.60)	.804	13.63 (-3.99 – 31.24)	.124	4.50 (-11.75 – 20.76)	.578	17.77 (-1.38 – 36.93)	.068
Predictor: Preference to be alone when in company								
Outcome at baseline	0.20 (-0.13 – 0.54)	.225	0.04 (-0.58 – 0.67)	.886	0.37 (0.01 – 0.72)	.042	0.54 (0.05 – 1.03)	.032
Preference to be alone	-1.61 (-4.20 – 0.97)	.213	-1.38 (-5.41 – 2.65)	.487	-1.88 (-4.90 – 1.15)	.217	-1.12 (-5.46 – 3.23)	.602
Predictor: Pleasantness of being alone								
Outcome at baseline	0.22 (-0.12 – 0.57)	.203	0.08 (-0.51 – 0.67)	.773	0.41 (0.04 – 0.79)	.032	0.51 (0.07 – 0.95)	.024
Pleasantness of being alone	0.04 (-2.88 – 2.96)	.977	-2.87 (-6.36 – 0.62)	.103	-1.38 (-4.86 – 2.10)	.428	-4.62 (-8.19 – -1.04)	.013*

Note. Results adjusted for age, gender, ethnicity, centre, and time to follow-up. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). CI=confidence interval. HR=hazard ratio. *statistically significant after Simes' correction.

Table 7. *Illness severity, remission from UHR status and transition status at 1- and 2-year follow-up predicted by lack of social drive (i.e., amount of time spent alone, preference to be alone when in company and experienced pleasantness of being alone) and clinical outcome at baseline.*

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Amount of time spent alone								
Outcome at baseline	0.49 (0.19 – 0.80)	.002	0.23 (-0.22 – 0.67)	.302				
Amount of time spent alone	-0.29 (-1.59 – 1.02)	.661	-1.17 (-3.00 – 0.66)	.202	3.91 (0.25 – 60.64)	.330	0.07 (0.00 – 2.07)	.125
Predictor: Preference to be alone when in company								
Outcome at baseline	0.48 (0.18 – 0.78)	.002	0.24 (-0.20 – 0.68)	.271				
Preference to be alone	0.11 (-0.14 – 0.36)	.373	0.23 (-0.17 – 0.63)	.243	0.97 (0.51 – 1.84)	.920	1.20 (0.65 – 2.22)	.564
Predictor: Pleasantness of being alone								
Outcome at baseline	0.51 (0.21 – 0.81)	.002	0.32 (-0.13 – 0.77)	.154				
Pleasantness of being alone	0.05 (-0.19 – 0.30)	.676	0.19 (-0.16 – 0.54)	.280	0.82 (0.44 – 1.54)	.542	1.39 (0.75 – 2.56)	.295

Note. Results adjusted for age, gender, ethnicity, centre, and time to follow-up. Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. HR=hazard ratio.

Table 8. *Level of functioning at 1- and 2-year follow-up predicted by anhedonia, social anhedonia and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Anhedonia								
Outcome at baseline	0.16 (-0.17 – 0.49)	.323	-0.02 (-0.62 – 0.59)	.955	0.34 (0.00 – 0.68)	.048	0.56 (0.06 – 1.05)	.028
Anhedonia events	3.73 (-0.32 – 7.78)	.070	0.25 (-5.37 – 5.88)	.927	5.61 (1.08 – 10.15)	.017*	-0.43 (-6.70 – 5.85)	.890
Predictor: Social anhedonia								
Outcome at baseline	0.17 (-0.15 – 0.49)	.282	0.01 (-0.59 – 0.61)	.974	0.33 (0.01 – 0.66)	.046	0.53 (0.04 – 1.01)	.035
Social anhedonia	4.61 (0.74 – 8.48)	.021*	2.29 (-3.65 – 8.23)	.435	6.36 (1.97 – 10.74)	.006*	3.09 (-3.51 – 9.70)	.345

Note. Results adjusted for age, gender, ethnicity, centre, and time to follow-up. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). CI=confidence interval. HR=hazard ratio. *statistically significant after Simes' correction.

Table 9. *Illness severity, remission from UHR status and transition status at 1- and 2-year follow-up predicted by anhedonia, social anhedonia and clinical outcome at baseline.*

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	p	b (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Predictor: Anhedonia								
Outcome at baseline	0.45 (0.15 – 0.75)	.004	0.19 (-0.29 – 0.66)	.422				
Anhedonia	-0.30 (-0.69 – 0.09)	.133	-0.30 (-0.91 – 0.32)	.336	2.02 (0.82 – 4.96)	.126	0.66 (0.23 – 1.88)	.439
Predictor: Social anhedonia								
Outcome at baseline	0.44 (0.15 – 0.73)	.004	0.14 (-0.30 – 0.59)	.519				
Social anhedonia	-0.38 (-0.74 – -0.01)	.045*	-0.57 (-1.18 – 0.05)	.068	2.22 (0.85 – 5.81)	.105	0.69 (0.26 – 1.80)	.446

Note. Results adjusted for age, gender, ethnicity, centre, and time to follow-up. Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. HR=hazard ratio. *statistically significant after Simes' correction.

2.5. Discussion

Principal findings

Using an experience sampling design, this study found no evidence that blunted affective experience predicted functioning or illness severity at follow-up (H1). However, there was some evidence that higher experienced pleasantness of being alone was associated with poorer functioning at 2-year follow-up (H2). In addition, our results tentatively suggest that higher levels of anhedonia were associated with poorer functioning at 1-year follow-up (H3). Finally, we found robust evidence that higher levels of social anhedonia were associated with higher levels of illness severity and poorer functioning at 1-year follow-up (H4). In our exploratory analysis, we found no evidence that momentary manifestations of negative symptoms in daily life predicted transition status. However, our results tentatively suggest that blunted affective experience predicted time to remission from UHR status.

Methodological considerations

Our findings should be interpreted in light of several methodological considerations. First, the sample selection should be critically evaluated: ESM is a burdensome research method, which may lead to selection bias, such that individuals with more intense symptoms might be underrepresented in the sample. However, compared to the no ESM sample of the EU-GEI High Risk Study the current study's participants showed comparable levels of illness severity and lower scores on the GAF symptoms subscale at baseline. In addition, the sample showed high comorbidity rates of non-psychotic disorders, which replicates findings from previous studies and systematic reviews (Albert, Tomassi, Maina, & Tosato, 2018; Lim et al., 2015). High rates of comorbidity, especially comorbid depressive disorders, may have attenuated the observed effects. However, when controlling for current depressive episodes or comorbid disorders in our sensitivity analysis, we found a similar pattern in terms of magnitude of associations but slightly wider 95% confidence intervals and some differences in statistical significance. In addition, it is important to consider the small to moderate sample size and the small absolute number of nine individuals (11% of the sample) who transitioned to psychosis within the follow-up period, although this transition rate is rather common in the field (Malda et al., 2019; Simon et al., 2011). Second, measuring social isolation and affect repeatedly over longer periods might provide a better prediction of outcomes. However, given burden on participants, this would require a less intense longitudinal data collection method, as is the case for ESM. Third,

it is important to consider some limitations regarding data collection at follow-up: while this was planned for 1- and 2-year follow-up, follow-up intervals varied in some individuals. Yet, analyses were controlled for time to follow-up and sensitivity analyses conducted with the sub-sample of individuals assessed +/- 6 months to the ideal follow-up time point showed a similar pattern of findings though varying statistical significance due to reduced sample size (see supplementary material 7). Moreover, experience sampling data was not collected at follow-up. Nonetheless, using CGI and GAF, we obtained ratings of several widely used outcome measures at follow-up. In addition, the follow-up period of 2 years was, arguably, rather short in the current study. However, previous research has demonstrated that the highest risk for transition in UHR samples is over the first 2 years after ascertainment (Nelson et al., 2013). Fourth, one should consider some statistical issues: For anhedonia and social anhedonia, we used fitted values of positive affect predicted by event pleasantness or pleasantness of social contact, to predict, in turn, clinical outcomes at follow-up. For blunted affective experience and lack of social drive, we aggregated data on the person-level. Aggregation of momentary manifestations of negative symptoms on the person-level led to a loss of information in comparison to the beep level, as the variance of beeps is not reflected in the aggregated scores. Nonetheless, compared to a single questionnaire assessment, the aggregated experience sampling measures used in the current study still provide higher levels of precision in measurement. The number of statistical analyses performed may have resulted in multiple testing problems. However, in order to control for type I error, results were corrected using the Simes' method (Simes, 1986) by momentary manifestation of negative symptom and outcome domain. In addition, time to follow-up was used as a crude proxy for time to remission from UHR status (e.g. for participants who remitted at any time between baseline and 1-year follow-up the date of the 1-year follow-up assessment was used as proxy), which might lead to imprecision in these exploratory survival analyses. Future research should attempt to establish a more precise data collection for time to remission.

Comparison with previous research

To our knowledge, this is the first study using an experience sampling design to investigate the predictive value of momentary manifestations of negative symptoms measured in UHR individuals. In accordance with our hypotheses, we found evidence for more intense momentary manifestations of negative symptoms to be associated with poorer functioning and higher ill-

ness severity at follow-up. In addition, we found evidence that individuals with greater variability of positive affect (as a measure of blunted affective experience), experienced a shorter time to remission from UHR status. This is in line with findings from previous studies using other operationalizations of negative symptoms (Burton et al., 2019; Fulford et al., 2013; Schlosser et al., 2015; Svirskis et al., 2007). Given that ESM measures of momentary manifestations of negative symptoms are intended to capture subjective experience of social context, our findings primarily pertain to the experiential level rather than to the level of expression (Blanchard et al., 2020).

Our findings tentatively suggest that blunted affect, lack of social drive and anhedonia are associated with some clinical outcomes, but findings on social anhedonia were most robust. We may speculate that changes in affective response to social contact (i.e., social anhedonia) in daily life may be most relevant in individuals at ultra-high risk, whereas other types of momentary manifestations of negative symptoms (e.g. lack of social drive) may be more relevant in later stages of psychosis. Social anhedonia may contribute to a loss of reinforcement of social contact, which might encourage a progressive decrease of social interaction and social functioning more downstream, closer to, or directly at, onset of psychotic disorder (C. M. Corcoran et al., 2011; Edwards, Cella, Emsley, Tarrier, & Wykes, 2018; Hermans et al., 2020; Reininghaus, Kempton, et al., 2016).

The findings have important implications for clinicians and researchers aiming to improve functional outcomes of UHR individuals. Recent meta-analyses found no evidence for psychosocial treatment to improve functioning in UHR individuals (Devoe, Farris, Townes, & Addington, 2019), with poor functioning at baseline being, in turn, a predictor for later psychopathology (Velthorst, Nelson, Wiltink, et al., 2013). Taken together, this may contribute to a vicious cycle of symptom burden and poor functioning amplifying each other in this group at risk. Therefore, new intervention approaches are urgently needed and the experience of momentary manifestations of negative symptoms, especially social anhedonia, in daily life may be a promising target. Possibly, improving social anhedonia may diminish social isolation and thereby improve outcomes.

In addition, we found only weak correlations between momentary manifestations of negative symptoms and the BPRS scores, highlighting the relevance of participants' subjective experience. These discrepancies may be interpreted in different ways. First, discrepancies may evolve due to varying modes of assessment and, hence, precision of measurement. Gerritsen et al. (2019) claim that some negative symptoms may be associated with no or very limited subjective

distress and, hence, difficult to measure via self-report. However, one may argue that aggregating multiple momentary measurements across several days may provide a more precise measure of affective and motivational processes than cross-sectional clinical interviews (Blanchard et al., 2020). Second, the discrepancies may, in fact, reflect two distinct dimensions of negative symptoms (i.e., experience vs. expression), and therefore, relying on purely behavioural indicators in assessing negative symptoms may result in a more limited understanding of internal, experiential aspects (Blanchard et al., 2020). Both interpretations highlight the potential of ESM as a diagnostic tool over and above traditional clinical measures of symptoms (van Os, Lataster, Delespaul, Wichers, & Myin-Germeys, 2014).

Conclusions

We found evidence for momentary manifestations of negative symptoms, especially social anhedonia, to predict clinical outcomes at follow-up. These findings emphasise that the assessment of momentary manifestations of negative symptoms in UHR individuals is of considerable potential value for both diagnostic assessment and early intervention. The assessment of momentary manifestations of negative symptoms may provide a more comprehensive picture of patients' symptoms in the context of their daily life for clinicians and researchers and contribute to a better understanding of individuals' subjective experience. In addition, the experience of momentary manifestations of negative symptoms, especially social anhedonia, in daily life may be a promising target for interventions aiming to improve clinical outcomes in the early stages of psychosis.

CHAPTER III:

STRESS REACTIVITY AS A PUTATIVE MECHANISM LINKING CHILDHOOD TRAUMA WITH CLINICAL OUTCOMES IN INDIVIDUALS AT ULTRA-HIGH RISK FOR PSYCHOSIS: FINDINGS FROM THE EU-GEI HIGH RISK STUDY

3.1. Abstract

Childhood trauma is associated with an elevated risk for psychosis, but the psychological mechanisms involved remain largely unclear. This study aimed to investigate emotional and psychotic stress reactivity in daily life as a putative mechanism linking childhood trauma and clinical outcomes in individuals at UHR for psychosis. Experience sampling methodology was used to measure momentary stress, affect and psychotic experiences in the daily life of N=79 UHR individuals in the EU-GEI High Risk Study. The Childhood Trauma Questionnaire was used to assess self-reported childhood trauma. Clinical outcomes were assessed at baseline, 1- and 2-year follow-up. The association of stress with positive (β=−0.14, p=.010) and negative affect (β=0.11, p=.020) was modified by transition status such that stress reactivity was greater in individuals who transitioned to psychosis. Moreover, the association of stress with negative affect (β=0.06, p=.019) and psychotic experiences (β=0.05, p=.037) was greater in individuals exposed to high v. low levels of childhood trauma. We also found evidence that decreased positive affect in response to stress was associated with reduced functioning at 1-year follow-up (b=6.29, p=.034). In addition, there was evidence that the association of childhood trauma with poor functional outcomes was mediated by stress reactivity (e.g. indirect effect: b=−2.13, p=.026), but no evidence that stress reactivity mediated the association between childhood trauma and transition (e.g. indirect effect: b=0.14, p=.506). Emotional and psychotic stress reactivity may be potential mechanisms linking childhood trauma with clinical outcomes in UHR individuals.

3.2. Introduction

Meta-analytic evidence suggests that childhood trauma (i.e. potentially harmful experiences as sexual, physical, and emotional abuse as well as physical and emotional neglect; Morgan & Fisher, 2007) increases transition risk in individuals at UHR for psychosis (Varese et al., 2012). Childhood trauma is associated with persistence of psychotic symptoms in subclinical and clinical samples (T. Bailey et al., 2018; Trotta et al., 2015; van Dam et al., 2015). A UHR state is commonly based on three criteria (Fusar-Poli et al., 2016; Fusar-Poli, Cappucciati, et al., 2015): Attenuated Psychotic Symptoms, Brief Limited Intermittent Psychotic Symptoms and Genetic Risk and Deterioration syndrome. Within 2 years, 20% of UHR individuals have been reported to transition to psychosis (Fusar-Poli et al., 2016) and a considerable proportion experience comorbid anxiety or depression (Fusar-Poli, Nelson, Valmaggia, Yung, & McGuire, 2014). However, in recent years, declining transition rates have been reported and various reasons for this have been discussed (e.g. different clinical profiles, earlier referrals, more effective treatment; Formica et al., 2020; Hartmann et al., 2016; Nelson et al., 2016; Yung et al., 2007). Meta-analyses show that the majority of UHR individuals who do not transition to psychosis do not remit from UHR status within 2 years either, and show marked impairments in functioning (Fusar-Poli, Rocchetti, et al., 2015; Simon et al., 2013). UHR individuals' functional level is comparable to that reported in patients with social phobia or major depressive disorder, and closer to that observed in psychosis patients than in healthy controls (Fusar-Poli, Rocchetti, et al., 2015). Hence, persistence of symptoms and functioning are important outcomes.

Although it is well accepted that childhood trauma is associated with clinical outcomes, psychological mechanisms involved remain largely unclear. Current models of psychosis suggest that childhood trauma amplifies stress reactivity, comprising increased negative affect, decreased positive affect and increased psychotic experiences in response to minor daily stressors (Collip et al., 2008; Hammen et al., 2000; Howes & Murray, 2014; Kendler, Kuhn, & Prescott, 2004; Morgan et al., 2010; Myin-Germeys & van Os, 2007). Stress reactivity is thought to be a behavioural marker of stress sensitization as a candidate mechanism underlying the association between childhood trauma and psychosis (Bentall et al., 2014; Hammen et al., 2000; Howes & Murray, 2014; Kendler et al., 2004; Morgan et al., 2010; Morgan et al., 2014; Myin-Germeys et al., 2001; Wichers et al., 2009). There is evidence that stress reactivity in daily life is elevated in patients with psychosis, individuals with familial risk for psychosis, subclinical psychosis phenotypes, and UHR individuals (Lataster et al., 2009; Myin-Germeys et al., 2003; Myin-Germeys et al., 2001; Reininghaus, Kempton, et al., 2016; van der Steen et al., 2017). Stress

reactivity, measured with self-report questionnaires, has also been found to be associated with worse clinical outcomes in patients with first-episode psychosis (Conus et al., 2009). Further, in adolescent service users, childhood trauma was associated with increased emotional and psychotic stress reactivity for individuals, who reported high vs. low levels of trauma (Rauschenberg et al., 2017). This is consistent with other experience sampling studies showing elevated stress reactivity in patients of general practitioners, UHR individuals and in patients with psychosis, who have experienced childhood trauma (Glaser et al., 2006; Lardinois et al., 2011; Reininghaus, Gayer-Anderson, et al., 2016). Taken together, these findings suggest effect modification of stress reactivity by childhood trauma or, in other words, synergistic effects of trauma and stress reactivity, in those at-risk or with psychotic disorder (i.e., an interaction or synergistic model).

Furthermore, other possibilities of how childhood trauma and stress reactivity may combine with each other may be relevant (Morgan et al., 2014; Schwartz & Susser, 2006). Stress reactivity may take on the role of a mediator, such that childhood trauma may impact on outcomes indirectly, via pathways through stress reactivity (i.e., a mediation model). In line with this, there is evidence from cross-sectional studies using self-report questionnaires in community samples that exposure to trauma in childhood may be linked to subclinical psychotic symptoms via stress reactivity (Gibson et al., 2014; Rössler et al., 2016). To increase complexity further, childhood trauma may both modify stress reactivity *and* connect with this putative mechanism along a causal pathway via mediation (Hafeman, 2008; Hafeman & Schwartz, 2009). In other words, exposure to trauma may interact with, and be predictive of, stress reactivity in pathways to psychosis (i.e., a mediated synergy model). To our knowledge, only one study to date has investigated both effect modification and mediation in the same analyses in relation to psychosis, suggesting that childhood and adult disadvantage may combine in complex ways (Morgan et al., 2014). While stress reactivity may be an important putative risk mechanism, no study to date has investigated whether stress reactivity in UHR individuals' daily life is greater in those exposed to high levels of childhood trauma, as well as its predictive value for clinical outcomes (Reininghaus, Gayer-Anderson, et al., 2016; Reininghaus, Kempton, et al., 2016). Therefore, the aim of the current study was to investigate the interplay of exposure to childhood trauma and stress reactivity as a candidate mechanism in predicting clinical outcomes in UHR individuals at 1- and 2-year follow-up using experience sampling data. We tested, in light of the theoretical models outlined above, the following hypotheses (see supplementary material 8 for a graphic illustration):

1) an increase in momentary stress is associated with increased negative affect, decreased positive affect, and increased psychotic experiences (H1);

2) the magnitude of associations between momentary stress and negative affect, positive affect, and psychotic experiences is modified by childhood trauma, such that these associations are greater in individuals exposed to high vs. low levels of childhood trauma (i.e., an effect modification or interaction model, H2).

3) stress reactivity (measured at baseline) predicts illness severity, functioning and symptom burden at 1- and 2-year follow-up (H3).

4) childhood trauma (measured at baseline) predicts illness severity, functioning and symptom burden at 1- and 2-year follow-up. The effects of childhood trauma will be mediated via pathways through stress reactivity (i.e., a mediation model, H4).

In exploratory analyses, we further aimed to investigate whether i) the magnitude of associations between momentary stress and negative affect, positive affect, and psychotic experiences is modified by transition status, ii) the effect of childhood trauma on transition status will be mediated via pathways through stress reactivity (i.e., a mediation model).

3.3.   Method

Sample

The sample comprises UHR individuals from London (United Kingdom, UK), Melbourne (Australia) and Amsterdam/The Hague (the Netherlands) recruited as a part of the EU-GEI High Risk study (European Network of National Networks studying Gene-Environment Interactions in Schizophrenia, 2014), a naturalistic prospective multicentre study that aimed to identify the interactive genetic, clinical and environmental determinants of schizophrenia. For the UK, participants were recruited from Outreach and Support in South London (OASIS), a clinical service for UHR individuals provided by the South London and Maudsley NHS Foundation Trust (Fusar-Poli, Byrne, Badger, Valmaggia, & McGuire, 2013), the West London Mental Health NHS Trust (WLMHT), and a community survey of General Practitioner practices (Reininghaus, Gayer-Anderson, et al., 2016). In Melbourne, participants were recruited from the Personal Assessment and Crisis Evaluation (PACE) clinic, a clinical arm of Orygen Youth Health, whose catchment area includes the north-western metropolitan region of Melbourne. Dutch participants were recruited from the Early Detection for Psychosis clinics of

Parnassia, The Hague, and Amsterdam University Medical Centers (Amsterdam UMC). All centres provide assessments and specialised clinical services for people with UHR.

UHR individuals, aged 15–35 years, were eligible to participate if they met at least one of the UHR criteria as defined by the CAARMS (Yung et al., 2005): (1) Attenuated Psychotic Symptoms: the presence of subthreshold positive psychotic symptoms for at least 1 month during the past year, (2) Brief Limited Intermittent Psychotic Symptoms: an episode of frank psychotic symptoms that have resolved in less than 1 week without receiving treatment, (3) Vulnerability: a first-degree relative with a psychotic disorder or diagnosed with schizotypal personality disorder in combination with a significant drop in functioning or chronic low functioning during at least 1 month in the previous year. Exclusion criteria were: (1) presence of a current or past psychotic disorder, (2) symptoms relevant for inclusion are explained by a medical disorder or drugs/alcohol dependency, (3) IQ<60.

Data collection

ESM measures

Momentary stress, affect and psychotic experiences were assessed using ESM (Myin-Germeys et al., 2001; Palmier-Claus et al., 2012), a structured diary method with high ecological validity, in which subjects are asked to report their thoughts, feelings and symptoms in daily life (Myin-Germeys et al., 2009; Palmier-Claus et al., 2011; Shiffman et al., 2008). At baseline, participants used a dedicated digital device for data collection (the Psymate®, www.psymate.eu/). The target constructs (i.e., stress, affect and psychotic experiences) show high and continuous variation over time. To obtain a representative sample of participants' experiences in daily life and to capture relevant variation in these target constructs with high resolution, a time-contingent sampling design with a blocked random schedule and a high sampling frequency was used for ESM data collection, i.e., 10 times a day on 6 consecutive days at random moments within set blocks of time (Myin-Germeys et al., 2018; Shiffman et al., 2008). In line with previous literature, data was included if ≥20 valid responses were provided over the assessment period (Bentall et al., 2008; Bentall et al., 2009; R. Corcoran et al., 2006; Delespaul et al., 2002; Freeman et al., 2013; Myin-Germeys et al., 2005; Myin-Germeys et al., 2001; Reininghaus, Kempton, et al., 2016). A detailed description of the ESM procedure and measures is provided in supplementary material 9.

Childhood trauma

Childhood trauma was assessed using the short form of the Childhood Trauma Questionnaire (CTQ), an established 25-item self-report measure enquiring about traumatic experiences during childhood (for detailed information see supplementary material 9; Bernstein, Ahluvalia, Pogge, & Handelsman, 1997; Bernstein & Fink, 1998; Bernstein et al., 2003; Scher, Stein, Asmundson, McCreary, & Forde, 2001; Wingenfeld et al., 2010).

Clinical outcomes

Clinical outcomes were assessed at baseline, 1- and 2-year follow-up. As the time points for follow-up assessments varied, the data closest to 1 and 2 years after baseline was selected as follow-up data. Illness severity was assessed using the CGI (Guy, 1976). Level of functioning was assessed using the GAF (American Psychiatric Association, 2002). Symptoms were assessed using the unusual thought content, perceptual abnormalities, anxiety and tolerance to normal stress subscales of the CAARMS (Yung et al., 2005). To ensure data quality, extensive training was provided (see supplementary material 10).

Statistical analysis

As ESM data have a multilevel structure with multiple observations (level-1) nested within participants (level-2), the 'mixed' command in Stata 15 was used to fit two-level, linear mixed models (StataCorp, 2017). Continuous variables of momentary stress, affect, psychotic experiences and childhood trauma were z-standardised for interpreting significant interaction terms. First, we included the composite stress measure as an independent variable and negative affect, positive affect, and psychotic experiences as outcome variables (H1). Second, we added two-way interaction terms for stress × childhood trauma to examine whether the associations between momentary stress, negative affect, positive affect and psychotic experiences were modified by childhood trauma (H2). The hypothesis that the associations of momentary stress with affect and psychotic experiences were greater in individuals exposed to high vs. low levels of childhood trauma (+/- 1 *SD* of standardised CTQ scores, mean=0, *SD*=1) was tested by using the 'testparm' command for computing Wald tests to assess statistical significance of two-way interaction terms and the 'lincom' command to compute linear combinations of coefficients (Aiken & West, 1991; J. Cohen, Cohen, West, & Aiken, 2003). Third, we used the 'predict' option to obtain fitted values of psychotic experiences and affect predicted by the composite stress measure. We used linear regression analysis to investigate whether these fitted values

representing stress reactivity predicted illness severity, level of functioning and symptom burden at follow-up, while controlling for baseline values (H3). Finally, we performed mediation analysis using the 'gsem' command to investigate whether the effects of childhood trauma on illness severity, level of functioning and symptom burden were mediated by stress reactivity (H4). The total effect of childhood trauma on clinical outcomes was apportioned into a direct effect and an indirect effect through stress reactivity. The indirect effect was computed using the product of coefficients strategy. The indirect and the total effect were computed and tested on significance using the 'nlcom' command.

Restricted maximum likelihood (H1 and H2) or maximum likelihood estimation (H3 and H4) were applied, allowing for the use of all available data under the relatively unrestrictive assumption that data is missing at random and if all variables associated with missing values are included in the model (Little & Rubin, 1987; Mallinckrodt, Clark, & David, 2001). Following previous studies (Hermans et al., 2020; Rauschenberg et al., 2017; Reininghaus, Gayer-Anderson, et al., 2016; Reininghaus, Kempton, et al., 2016), all analyses were adjusted for age, gender, ethnicity, and centre as these are known a priori confounders (based on evidence on the basic epidemiology of psychosis). To control for confounding of findings by comorbid disorders, all analyses were controlled for comorbid major depressive and anxiety disorders. In addition, analyses for testing H3 and H4 were controlled for time to follow-up to account for variation in time to follow-up. Unadjusted analyses and sensitivity analyses in a restricted sample assessed in a +/- 6 month time interval around the expected follow-up time points are displayed in supplementary materials 11-13.

3.4. Results

Basic sample and clinical characteristics

A total of $N=108$ participants were assessed with the ESM during the study period. Of these, $N=79$ participants completed ESM assessment with ≥20 valid responses (i.e., 73% of 108; valid responses: $M=38$, range 20 – 57). Assessment of clinical outcomes was completed for $N=48$ participants at 1-year follow-up (61% of the full sample; months away from optimal 1-year follow-up time point: median=0.5, range -8.7 – 4.6) and $N=36$ participants at 2-year follow-up (46% of the full sample; months away from optimal 2-year follow-up time point: median=0.5, range -5.6 – 22.6). Nine individuals (11%) transitioned to psychosis by the final follow-up time point. Participants were on average 23 years old ($SD=4.93$) and 56% were women. The majority

(67%) of the sample was white, followed by 15% with black ethnicity. Seventy-six percent of the participants were diagnosed with a comorbid axis-I disorder. Comparing the current study's participants to individuals included in the EU GEI High-Risk study, for whom ESM data was not collected *(N=266)*, there were no differences in demographics (age: t=-1.33, p=.185, gender: χ^2=3.58, p=.059, ethnicity: χ^2=6.53, p=.258) or overall prevalence of comorbid disorders (χ^2=1.82, p=.177). However, the current sample showed higher levels of childhood trauma (t=-2.59, p=.010), a higher prevalence of specific phobias (χ^2=4.86, p=.027) and a lower prevalence of major depressive disorder (χ^2=4.67, p=.031) compared to participants, for whom ESM data was not collected (see Table 10).

Association between momentary stress, affect and psychotic experiences (H1)

Momentary stress was associated with small to moderate increases in negative affect (β=0.31, 95% CI 0.27 – 0.36, p<.001) and psychotic experiences (β=0.16, 95% CI 0.13 – 0.20, p<.001) as well as with a moderate decrease in positive affect (β=-0.38, 95% CI -0.43 – -0.34, p<.001).

Association between momentary stress, affect and psychotic experiences by childhood trauma (H2)

Childhood trauma modified the associations of momentary stress with negative affect (stress × childhood trauma: β=0.03, 95% CI 0.00 – 0.06, p=.019) and psychotic experiences (stress × childhood trauma: β=0.02, 95% CI 0.00 – 0.05, p=.044, see Table 11). These associations were greater in individuals with higher levels of childhood trauma (outcome negative affect: high vs. low childhood trauma: β=0.06, 95% CI 0.01 – 0.11, p=.019; outcome psychotic experiences: high vs. low childhood trauma: β=0.05, 95% CI 0.00 – 0.09, p=.044). Further, we found a non-significant indication that childhood trauma modified the association between momentary stress and positive affect (stress × childhood trauma: β=0.03, 95% CI 0.00 – 0.06, p=.081).

Table 10. *Basic sample and clinical characteristics.*

	ESM sample			No ESM sample	ESM vs. no ESM
	Baseline	1-year follow-up	2-year follow-up	Baseline	Baseline
N	79	48	36	266	
Age at baseline (years), mean (*SD*)	23.0 (4.93)	23.6 (5.24)	23.81 (5.18)	22.2 (4.82)	t=-1.33, p=.185
Gender, *N* (%)					χ^2=3.58, p=.059
Male	35 (44%)	22 (46%)	16 (44%)	150 (56%)	
Female	44 (56%)	26 (54%)	20 (56%)	116 (44%)	
Ethnicity, *N* (%)					χ^2=6.53, p=.258
White	53 (67%)	33 (69%)	27 (75%)	193 (73%)	
Black	12 (15%)	9 (19%)	5 (14%)	22 (8%)	
Other	14 (18%)	6 (13%)	4 (11%)	50 (19%)	
Comorbidity at baseline, *N* (%)	60 (76%)	37 (77%)	28 (78%)	220 (83%)	χ^2=1.82, p=.177
Major depressive disorder, *N* (%)	29 (37%)	14 (31%)	11 (31%)	123 (51%)	χ^2=4.67, p=.031
Current depressive episode, *N* (%)	22 (28%)	11 (24%)	8 (22%)	88 (35%)	χ^2=1.26, p=.262
Bipolar disorder, *N* (%)	7 (9%)	4 (9%)	5 (14%)	17 (6%)	χ^2=0.57, p=.449
Any anxiety disorder, *N* (%)	42 (53%)	26 (57%)	17 (47%)	117 (44%)	χ^2=2.06, p=.151
Panic disorder, *N* (%)	19 (24%)	12 (27%)	6 (17%)	52 (21%)	χ^2=0.30, p=.584
Panic disorder + agoraphobia, *N* (%)	6 (8%)	4 (9%)	1 (3%)	25 (11%)	χ^2=0.46, p=.496
Agoraphobia only, *N* (%)	2 (3%)	0	0	4 (2%)	χ^2=0.26, p=.607
Social phobia N, *N* (%)	19 (24%)	14 (30%)	9 (25%)	42 (17%)	χ^2=1.87, p=.172
Specific phobia, *N* (%)	14 (18%)	9 (20%)	5 (14%)	22 (9%)	χ^2=4.86, p=.027
Generalized anxiety disorder, *N* (%)	11 (14%)	7 (15%)	5 (14%)	26 (11%)	χ^2=0.67, p=.413
Not otherwise specified anxiety disorder, *N* (%)	3 (4%)	1 (2%)	0	14 (6%)	χ^2=0.49, p=.485
Obsessive-compulsive disorder, *N* (%)	3 (4%)	2 (4%)	3 (9%)	26 (12%)	χ^2=3.41, p=.065
Posttraumatic stress disorder, *N* (%)	11 (14%)	4 (9%)	0	23 (6%)	χ^2=1.40, p=.237
Any eating disorder, *N* (%)	10 (13%)	7 (15%)	6 (17%)	22 (8%)	χ^2=1.39, p=.238
Anorexia nervosa, *N* (%)	5 (6%)	3 (7%)	3 (8%)	10 (4%)	χ^2=0.69, p=.408
Bulimia nervosa, *N* (%)	5 (6%)	3 (7%)	2 (6%)	10 (4%)	χ^2=0.66, p=.417
Binge eating disorder, *N* (%)	1 (1%)	1 (2%)	1 (3%)	6 (3%)	χ^2=0.44, p=.508
Any somatoform disorder, *N* (%)	2 (3%)	1 (2%)	1 (3%)	9 (3%)	χ^2=0.14, p=.705
Somatization disorder, *N* (%)	1 (1%)	0	0	4 (2%)	χ^2=0.06, p=.812

Chronic pain, *N* (%)	1 (1%)	0	0	1 (<1%)	χ^2=0.70, *p*=.403
Hypochondriasis, *N* (%)	1 (1%)	1 (2%)	1 (3%)	4 (2%)	χ^2=0.07, *p*=.789
Body dismorph disorder, *N* (%)	0	0	0	2 (1%)	χ^2=0.67, *p*=.412
Childhood trauma questionnaire total score at baseline, mean (*SD*)	51.54 (17.00)	50.13 (15.60)	47.33 (13.31)	46.23 (14.97)	*t*=-2.59, *p*=.010
Clinical global impression scale					
Illness severity, mean (*SD*)	3.57 (1.21)	3.15 (1.32)	2.89 (1.26)	3.60 (1.09)	*t*=0.21, *p*=.831
Global assessment of functioning					
Disability, mean (*SD*)	56.27 (13.00)	58.92 (13.41)	63.78 (13.62)	55.36 (12.20)	*t*=-0.57, *p*=.572
Comprehensive assessment of at-risk mental states					
Unusual thought content, mean (*SD*)	2.89 (1.77)	2.13 (1.94)	1.62 (1.95)	2.68 (1.85)	*t*=-0.88, *p*=.378
Perceptual abnormalities, mean (*SD*)	3.08 (1.65)	2.42 (1.69)	1.85 (1.84)	2.84 (1.67)	*t*=-1.13, *p*=.261
Anxiety, mean (SD)	3.29 (1.29)	2.89 (1.45)	2.59 (1.83)	2.99 (1.68)	*t*=-1.47, *p*=.144
Tolerance to normal stress, mean (SD)	2.09 (1.85)	1.04 (1.57)	1.00 (1.61)	2.13 (1.77)	*t*=0.19, *p*=.850

Note. SD=standard deviation.

Stress reactivity and clinical outcomes at follow-up (H3)

Decreased positive affect in response to stress was associated with higher illness severity (*b*=-0.51, 95% CI -0.97 – -0.06, *p*=.028) and lower level of functioning (*b*=7.92, 95% CI 1.39 – 14.45, *p*=.019) at 1-year follow-up (see Table 12).

In addition, level of functioning at 2-year follow-up was predicted by psychotic stress reactivity (*b*=11.62, 95% CI 1.70 – 21.54, *p*=.024)[1]. Increased negative affect in response to stress predicted unusual thought content at 2-year follow-up (*b*=1.74, 95% CI 0.36 – 3.11, *p*=.016). Moreover, perceptual abnormalities at 1-year follow-up were predicted by emotional (negative affect: *b*=1.24, 95% CI 0.54 – 1.93, *p*=.001; positive affect: *b*=-1.03, 95% CI -1.81 – -0.25, *p*=.011) and psychotic stress reactivity (*b*=1.06, 95% CI 0.29 – 1.83, *p*=.009). There was no evidence that emotional or psychotic stress reactivity predicted anxiety or tolerance to normal stress.

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[1] This counterintuitive finding can be explained by centre and time to follow-up acting as suppressor variables (i.e., these variables suppressed, in part the variance of the independent variable of psychotic stress reactivity). When we examined the associations among independent and outcome variables, we found the typical pattern as it would be expected for suppressor effects: centre and time to follow-up were not correlated with the outcome variable but showed substantial associations with other independent variables.

Table 11. *Modification of the association between momentary stress and affect/psychotic experiences by childhood trauma.*

	β	95% CI	SE	p
Outcome: Negative affect				
Stress	0.31	0.28 – 0.34	0.01	<.001
Childhood trauma	0.23	0.08 – 0.38	0.08	.003
Stress × childhood trauma	0.03	0.00 – 0.06	0.01	.019
High childhood trauma	0.34	0.31 – 0.37	0.02	<.001
Low childhood trauma	0.28	0.24 – 0.32	0.02	<.001
High vs. low childhood trauma	0.06	0.01 – 0.11	0.03	.019
Outcome: Positive affect				
Stress	-0.39	-0.42 – -0.36	0.02	<.001
Childhood trauma	-0.07	-0.21 – 0.07	0.07	.311
Stress × childhood trauma	0.03	0.00 – 0.06	0.02	.081
Outcome: Psychotic experiences				
Stress	0.15	0.13 – 0.17	0.01	<.001
Childhood trauma	0.28	0.12 – 0.44	0.08	.001
Stress × childhood trauma	0.02	0.00 – 0.05	0.01	.044
High childhood trauma	0.17	0.14 – 0.20	0.02	<.001
Low childhood trauma	0.13	0.09 – 0.16	0.02	<.001
High vs. low childhood trauma	0.05	0.00 – 0.09	0.02	.044

Note. Results adjusted for age, gender, ethnicity, centre, comorbid major depressive disorder, and anxiety disorders. Childhood trauma assessed with the CTQ (Bernstein & Fink, 1998; Wingenfeld et al., 2010). CI=confidence interval, SE=standard error.

Table 12. *Clinical outcomes at 1- and 2-year follow-up predicted by emotional and psychotic stress reactivity at baseline and clinical outcome at baseline.*

	Clinical Outcomes			
	Illness severity		Level of functioning Disability	
	1-year follow-up	2-year follow-up	1-year follow-up	2-year follow-up
N	46	35	47	35
	b (95% CI) *p*	*b* (95% CI) *p*	*b* (95% CI) *p*	*b* (95% CI) *p*
Predictor: Emotional reactivity (increased negative affect in response to stress)				
Outcome at baseline	0.62 <.001 (0.35 – 0.89)	0.27 .290 (-0.24 – 0.77)	0.35 .047 (0.01 – 0.70)	0.51 .041 (0.02 – 1.00)
Emotional reactivity	0.38 .156 (-0.15 – 0.91)	0.02 .963 (-0.92 – 0.96)	-5.17 .163 (-12.54 – 2.20)	1.31 .782 (-8.38 – 11.01)
Predictor: Emotional reactivity (decreased positive affect in response to stress)				
Outcome at baseline	0.60 <.001 (0.35 – 0.86)	0.16 .520 (-0.34 – 0.66)	0.34 .044 (0.01 – 0.66)	0.50 .046 (0.01 – 0.99)
Emotional reactivity	-0.51 .028 (-0.97 – -0.06)	-0.50 .282 (-1.44 – 0.44)	7.92 .019 (1.39 – 14.45)	-0.17 .971 (-9.48 – 9.15)
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)				
Outcome at baseline	0.70 <.001 (0.42 – 0.98)	0.38 .129 (-0.12 – 0.88)	0.41 .021 (0.07 – 0.76)	0.54 .016 (0.11 – 0.98)
Psychotic reactivity	-0.04 .863 (-0.64 – 0.55)	-0.58 .283 (1.68 – 0.51)	-1.59 .669 (-9.08 – 5.90)	11.62 .024 (1.70 – 21.54)

	Unusual thought content		Perceptual abnormalities	
	1-year follow-up	2-year follow-up	1-year follow-up	2-year follow-up
N	43	33	43	32
	b (95% CI) *p*	*b* (95% CI) *p*	*b* (95% CI) *p*	*b* (95% CI) *p*
Predictor: Emotional reactivity (increased negative affect in response to stress)				
Outcome at baseline	0.43 .016 (0.09 – 0.78)	-0.12 .595 (-0.58 – 0.34)	0.40 .002 (0.16 – 0.64)	0.37 .142 (-0.13 – 0.87)
Emotional reactivity	0.47 .331 (-0.50 – 1.45)	1.74 .016 (0.36 – 3.11)	1.24 .001 (0.54 – 1.93)	-0.11 .878 (-1.55 – 1.34)
Predictor: Emotional reactivity (decreased positive affect in response to stress)				
Outcome at baseline	0.43 .016 (0.08 – 0.77)	-0.08 .727 (-0.58 – 0.41)	0.45 .001 (0.19 – 0.71)	0.42 .093 (-0.08 – 0.92)
Emotional reactivity	-0.71 .162 (-1.71 – 0.30)	-1.09 .105 (-2.44 – 0.25)	-1.03 .011 (-1.81 - -0.25)	-0.51 .416 (-1.79 – 0.77)
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)				
Outcome at baseline	0.42 .029 (0.05 – 0.79)	-0.14 .592 (-0.65 – 0.38)	0.33 .018 (0.06 – 0.59)	0.38 .121 (-0.11 – 0.86)
Psychotic reactivity	0.27 .599 (-0.77 – 1.32)	1.26 .103 (-0.28 – 2.81)	1.06 .009 (0.29 – 1.83)	0.51 .460 (-0.90 – 1.91)

	Anxiety		Tolerance to normal stress	
	1-year follow-up	2-year follow-up	1-year follow-up	2-year follow-up
N	43	33	43	33
	b (95% CI) *p*	*b* (95% CI) *p*	*b* (95% CI) *p*	*b* (95% CI) *p*
Predictor: Emotional reactivity (increased negative affect in response to stress)				
Outcome at baseline	0.29 .207 (-0.17 – 0.75)	0.54 .312 (-0.54 – 1.62)	0.35 .016 (0.07 – 0.63)	0.25 .191 (-0.13 – 0.63)
Emotional reactivity	0.14 .699 (-0.61 – 0.89)	-0.64 .402 (-2.19 – 0.91)	-0.10 .816 (-0.94 – 0.74)	-0.48 .447 (-1.77 – 0.81)
Predictor: Emotional reactivity (decreased positive affect in response to stress)				
Outcome at baseline	0.23 .268 (-0.19 – 0.64)	0.37 .455 (-0.65 – 1.40)	0.34 .017 (0.07– 0.62)	0.20 .265 (-0.16 – 0.57)
Emotional reactivity	-0.68 .057 (-1.39 – 0.02)	0.00 .997 (-1.32 – 1.32)	0.22 .609 (-0.65 – 1.09)	0.10 .850 (-1.01 – 1.21)

Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)							
Outcome at baseline	0.31 (-0.13 – 0.75)	.156	0.54 (-0.45 – 1.53)	.272	0.35 (0.07 – 0.63)	.016	0.25 (-0.14 – 0.64)	.197
Psychotic reactivity	0.08 (-0.64 – 0.80)	.824	-1.07 (-2.49 – 0.35)	.131	-0.10 (-0.95 – 0.75)	.815	-0.44 (-1.75 – 0.87)	.489

Note. Results adjusted for age, gender, ethnicity, centre, comorbid major depressive disorder, and anxiety disorders and time to follow-up. Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Unusual thought content, perceptual abnormalities, anxiety, and tolerance to normal stress assessed with Comprehensive Assessment of At-Risk Mental States(Yung et al., 2005). CI=confidence interval.

Emotional and psychotic stress reactivity as mediators of the association between childhood trauma and clinical outcomes (H4)

Table 13 shows findings on total, direct, and indirect effects of childhood trauma and stress reactivity on clinical outcomes at follow-up. Increased negative affect in response to stress mediated the association of childhood trauma and illness severity at 1-year follow-up (indirect effect: b=0.20, 95% CI 0.02 – 0.38, p=.033). We found no evidence that emotional and psychotic stress reactivity mediated the association of childhood trauma and level of functioning. The association of childhood trauma and unusual thought content at 2-year follow-up was mediated by increased negative affect in response to stress (b= 0.42, 95% CI 0.04 – 0.80, p=.030). In addition, the association of childhood trauma and perceptual abnormalities at 1-year follow-up was mediated by increased negative affect (indirect effect: b=0.39, 95% CI 0.09 – 0.69, p=.011) and psychotic experiences in response to stress (indirect effect: b=0.44, 95% CI 0.13 – 0.75, p=.005). High levels of childhood trauma were associated with more intense reactivity in form of a stronger increase of negative affect and psychotic experiences in response to stress, which, in turn, was associated with higher illness severity, unusual thought content and perceptual abnormalities at follow-up. We found no evidence for direct effects of childhood trauma on anxiety and tolerance to normal stress and no mediation via stress reactivity.

In exploratory analyses, there was no evidence for a direct effect of childhood trauma on transition status and no mediation via stress reactivity (see supplementary material 14)

Table 13. *Emotional and psychotic stress reactivity as mediators of the association of childhood trauma and clinical outcomes.*

	Clinical Outcomes							
	Illness severity				**Level of functioning Disability**			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	47		36		47		35	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	0.39 (0.06 – 0.72)	.022	-0.43 (-0.90 – 0.04)	.074	-3.48 (-7.47 – 0.51)	.087	3.55 (-1.84 – 8.95)	.197
Direct effect	0.19 (-0.12 – 0.51)	.224	-0.57 (-1.07 – -0.06)	.027	-1.82 (-5.79 – 2.16)	.371	4.27 (-1.59 – 10.14)	.153
Indirect effect	0.20 (0.02 – 0.38)	.033	0.14 (-0.06 – 0.33)	.170	-1.67 (-3.65 – 0.32)	.100	-0.72 (-2.98 – 1.54)	.531
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	0.33 (0.02 – 0.65)	.038	-0.40 (-0.86 – -0.06)	.089	-3.38 (-7.20 – 0.45)	.083	3.44 (-1.96 – 8.83)	.212
Direct effect	0.24 (-0.05 – 0.54)	.110	-0.48 (-0.93 – -0.03)	.037	-2.30 (-5.93 – 1.32)	.213	3.69 (-1.73 – 9.11)	.182
Indirect effect	0.09 (-0.03 – 0.22)	.142	0.08 (-0.04 – 0.20)	.188	-1.07 (-2.47 – 0.33)	.133	-0.25 (-1.19 – 0.68)	.592
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	0.36 (0.02 – 0.69)	.039	-0.42 (-0.90 – 0.07)	.091	-2.96 (-6.97 – 1.05)	.148	4.26 (-1.10 – 9.62)	.119
Direct effect	0.22 (-0.12 – 0.55)	.202	-0.42 (-0.93 – 0.09)	.103	-2.72 (-6.92 – 1.48)	.205	1.58 (-3.86 – 7.03)	.569
Indirect effect	0.14 (-0.04 – 0.32)	.132	0.01 (-0.23 – 0.24)	.949	0.24 (-2.32 – 1.84)	.821	2.67 (-0.28 – 5.63)	.076

	Unusual thought content				**Perceptual abnormalities**			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	43		33		43		32	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	-0.21 (-0.77 – 0.35)	.469	0.41 (-0.36 – 1.18)	.297	0.03 (-0.44 – 0.51)	.886	-0.08 (-0.87 – 0.72)	.852
Direct effect	-0.42 (-1.02 – 0.18)	.166	-0.01 (-0.78 – 0.76)	.983	-0.36 (0.81 – 0.09)	.120	0.01 (-0.83 – 0.85)	.986
Indirect effect	0.22 (-0.06 – 0.50)	.125	0.42 (0.04 – 0.80)	.030	0.39 (0.09 – 0.69)	.011	-0.08 (-0.39 – 0.23)	.598
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	-0.15 (-0.71 – 0.41)	.598	0.37 (-0.41 – 1.16)	.350	0.10 (-0.37 – 0.58)	.667	-0.06 (-0.86 – 0.73)	.874
Direct effect	-0.25 (-0.79 – 0.30)	.374	0.26 (-0.52 – 1.04)	.511	0.00 (-0.46 – 0.45)	.990	-0.10 (-0.90 – 0.71)	.812
Indirect effect	0.10 (-0.06 – 0.25)	.226	0.11 (-0.07 – 0.29)	.215	0.11 (-0.05 – 0.26)	.179	0.03 (-0.09 – 0.16)	.604
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	-0.20 (-0.76 – 0.36)	.490	0.48 (-0.32 – 1.28)	.241	0.05 (-0.42 – 0.52)	.825	0.00 (-0.81 – 0.80)	.993
Direct effect	-0.47 (-1.07 – 0.13)	.126	0.19 (-0.61 – 0.99)	.642	-0.39 (-0.84 – 0.07)	.095	-0.16 (-0.97 – 0.65)	.701
Indirect effect	0.27 (-0.03 – 0.58)	.080	0.29 (-0.06 – 0.64)	.105	0.44 (0.13 – 0.75)	.005	0.16 (-0.18 – 0.49)	.363

	Anxiety				Tolerance to normal stress			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	43		33		43		33	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	-0.19 (-0.56 – 0.18)	.315	-0.46 (-1.25 – 0.33)	.255	-0.15 (-0.62 – 0.32)	.531	-0.01 (-0.68 – 0.67)	.982
Direct effect	-0.34 (-0.75 – 0.08)	.111	-0.42 (-1.25 – 0.41)	.326	-0.19 (-0.72 – 0.33)	.464	0.04 (-0.67 – 0.75)	.913
Indirect effect	0.14 (-0.04 – 0.32)	.137	-0.04 (-0.34 – 0.26)	.791	0.04 (-0.17 – 0.26)	.688	-0.05 (-0.31 – 0.21)	.719
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	-0.14 (-0.50 – 0.22)	.453	-0.45 (-1.24 – 0.34)	.260	-0.16 (-0.64 – 0.31)	.502	0.00 (-0.68 – 0.67)	.994
Direct effect	-0.23 (-0.57 – 0.11)	.187	-0.46 (-1.26 – 0.33)	.253	-0.14 (-0.61 – 0.34)	.576	0.00 (-0.69 – 0.68)	.989
Indirect effect	0.09 (-0.04 – 0.22)	.162	0.01 (-0.11 – 0.13)	.855	-0.03 (-0.12 – 0.07)	.577	0.00 (-0.10 – 0.10)	.964
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	-0.18 (-0.55 – 0.19)	.332	-0.54 (-1.33 – 0.24)	.176	-0.15 (-0.62 – 0.32)	.536	-0.01 (-0.70 – 0.67)	.968
Direct effect	-0.30 (-0.71 – 0.11)	.152	-0.32 (-1.11 – 0.47)	.425	-0.22 (-0.75 – 0.31)	.413	0.01 (-0.68 – 0.71)	.968
Indirect effect	0.11 (-0.08 – 0.31)	.241	-0.22 (-0.55 – 0.11)	.193	0.07 (-0.17 – 0.31)	.562	-0.03 (-0.30 – 0.25)	.841

Note. Results adjusted for age, gender, ethnicity, centre, comorbid major depressive disorder, anxiety disorders, and time to follow-up. Childhood trauma assessed with the Childhood Trauma Questionnaire (Bernstein & Fink, 1998; Wingenfeld et al., 2010). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Unusual thought content, perceptual abnormalities, anxiety and tolerance to normal stress assessed with the Comprehensive Assessment of At Risk Mental State (Yung et al., 2005). CI=confidence interval.

3.5.   Discussion

Main findings

Using an experience sampling design, we found strong evidence that minor daily stressors were associated with emotional and psychotic stress reactivity in UHR individuals (H1). Childhood trauma modified the effect of daily stressors on negative affect and psychotic experiences, with more intense psychotic experiences and stronger increases in negative affect for individuals exposed to high levels of childhood trauma (H2). In addition, we found some evidence to suggest stress reactivity predicts clinical outcomes at follow-up (H3). Finally, there was partial evidence that stress reactivity mediates the association of childhood trauma and clinical outcomes (H4).

Methodological considerations/Limitations

The reported findings should be interpreted in the light of several methodological considerations. First, childhood trauma was measured with a retrospective self-report questionnaire. A common concern about retrospective self-report is that recall bias and cognitive distortions might lead to invalid ratings (Colman et al., 2016; Dill, Chu, Grob, & Eisen, 1991; Morgan & Fisher, 2007; Saykin et al., 1991; E. Susser & Widom, 2012). However, good reliability and validity for these measures have been reported in individuals with psychosis (Fisher et al., 2011). Similar levels of agreement between self-report and interviewer-rated retrospective reports of childhood trauma have been observed in individuals with first-episode psychosis and population-based controls (Gayer-Anderson et al., 2020). Other types of early adversity not assessed (e.g. bullying victimisation) might also be relevant (Cunningham et al., 2016). Second, ESM is a burdensome research method, which may lead to sampling and selection bias. For example, one way this may have operated on findings may be that individuals with more intense symptoms may have been underrepresented in the sample, as assessment burden may have discouraged eligible individuals with severe symptoms from participation. In addition, it may be more challenging for individuals with more severe symptoms to reach sufficient compliance, which may lead to underrepresentation due to the exclusion of these participants. However, we found no differences in clinical characteristics at baseline when comparing participants included in the analysis to individuals for whom ESM data were not available. Third, follow-up intervals varied, which was accounted for by controlling for time to follow-up and conducting sensitivity analyses with a restricted sample (leading to similar results in terms of magnitude of associations but some variation in statistical significance due to varying sample sizes). Fourth, unmeasured confounders (e.g. polygenic risk) may have influenced the reported findings. Fifth, although an increasingly common finding in the field (Formica et al., 2020; Hartmann et al., 2016; Nelson et al., 2016; Simon et al., 2011), we need to consider the small number of nine individuals (11%) who transitioned to psychosis within the follow-up period. The findings should therefore be re-evaluated in a larger sample with higher transition rates. In addition, comorbidity, especially comorbid major depressive and anxiety disorders, should be taken into account. Therefore, all analyses were controlled for comorbid major depressive and anxiety disorders. Sixth, the use of a composite stress measure should be critically discussed. In line with previous studies, we aggregated event-related, activity-related and social stress for each beep to reduce multiple testing (Klippel et al., 2021; Pries et al., 2020). Still, type I error should be taken into account when interpreting the results.

Comparison with previous research

In accordance with previous ESM studies, we found that momentary stress was associated with small to moderate increases in negative affect and psychotic experiences and moderate decreases in positive affect in UHR individuals (Reininghaus, Kempton, et al., 2016; van der Steen et al., 2017). When considering the role of childhood trauma and stress reactivity in clinical trajectories, several possibilities of how these may combine with each other may be relevant (Morgan et al., 2014; Schwartz & Susser, 2006). Following Morgan et al. (2014), we investigated both effect modification and mediation in the same analyses. In accordance with suggested models and recent ESM studies, we found that childhood trauma amplifies reactivity to minor stress in daily life (Hammen et al., 2000; Kendler et al., 2004; Morgan et al., 2010; Myin-Germeys et al., 2001; Rauschenberg et al., 2017; Reininghaus, Gayer-Anderson, et al., 2016). Furthermore, we found some evidence that stress reactivity predicted clinical outcomes at follow-up. This extends findings from a previous ESM study in the general population and an observational study in patients with first-episode psychosis (Collip et al., 2013; Conus et al., 2009). Going one step further, there was some evidence that stress reactivity mediated the association of childhood trauma and clinical outcomes at follow-up. High levels of childhood trauma were associated with an increased stress reactivity, which, in turn, was associated with worse clinical outcomes at follow-up. Hence, this tentatively suggests that childhood trauma may both modify stress reactivity <u>and</u> exert detrimental effects via stress reactivity and push individuals along more severe clinical trajectories. Overall, this adds evidence in support of a mediated synergy model (Hafeman & Schwartz, 2009).

Conclusion

Taken together, our findings underscore the relevance of reactivity to daily stressors as a putative mechanism linking childhood trauma with clinical outcomes in UHR individuals. Adding evidence to the mediated synergy model, the study suggests early adversity in childhood links to more severe clinical trajectories via, and in interaction with, subsequently elevated stress reactivity in adulthood. Therefore, the findings underline the relevance of ecological momentary interventions targeting stress reactivity in daily life (e.g. EMIcompass, a transdiagnostic ecological momentary intervention for improving resilience in youth; Schick et al., 2021) as an important next step towards improving clinical outcomes in UHR individuals at an early stage (Addington, Marshall, & French, 2012; Myin-Germeys et al., 2018; Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus, Klippel, et al., 2019).

CHAPTER IV:

THE ROLE OF THREAT ANTICIPATION IN THE DEVELOPMENT OF PSYCHOPATHOLOGY IN ADOLESCENCE: FINDINGS FROM THE SIGMA STUDY

4.1. Abstract

Early adversity is associated with psychopathology. First evidence in adults suggests that threat anticipation, i.e., an enhanced anticipation of unpleasant events creating an enduring sense of threat, may be a putative mechanism linking early adversity to psychopathology. This study aimed to test the indirect effect of early adversity on psychopathology via threat anticipation in a large community sample of adolescents. We measured childhood trauma and bullying victimisation (as indicators of early adversity), threat anticipation, general psychopathology and prodromal psychotic symptoms in adolescents aged 12-16 years (full sample size N=1,682; minimum sample size in the complete case sample N=449) in wave I of the SIGMA study. We found strong evidence that early adversity (e.g. childhood trauma, β=0.54, p<.001) and threat anticipation (e.g. β=0.36, p<.001) were associated with general psychopathology and prodromal psychotic symptoms. Moreover, there was evidence that the association between early adversity, general psychopathology and prodromal psychotic symptoms is mediated via pathways through threat anticipation (e.g. childhood trauma, $\beta_{indirect\ effect}$=0.13, p<.001). Threat anticipation may be a potential mechanism linking early adversity and psychopathology in adolescents.

4.2. Introduction

Most mental disorders first emerge during adolescence and young adulthood. Three quarters of all lifetime cases have their onset before the age of 24 (Kessler et al., 2005). With approximately one fourth of youth having experienced a mental disorder during the past year (Merikangas et al., 2009), mental disorders contribute substantially to the disease burden in young age groups (Erskine et al., 2015). Trajectories are often characterised by transitional staging processes from relatively mild distress and subclinical symptoms to clinical severity highlighting the potential and relevance of early intervention (Kessler et al., 2005; McGorry, Purcell, Hickie, Yung, et al., 2007). In addition, dimensional classification frameworks cutting across traditional boundaries of diagnoses have emerged (Insel et al., 2010; Kotov et al., 2017). However, underlying mechanisms in the development of psychopathology remain unclear, so deepening our understanding of these mechanisms is a crucial step towards improving existing and developing new preventive and early intervention strategies (Reininghaus et al., 2015).

Converging evidence identified early adversity as a risk factor for psychopathology. McLaughlin (2016) defines early adversity as "experiences that are likely to require significant adaptation by an average child and that represent a deviation from the expectable environment" (p.3), for example, childhood trauma and bullying. Early adversity is associated with a heightened risk for mental disorders in youth, but also in later life (Greif Green et al., 2010; R. E. Norman et al., 2012). Previous research tentatively indicates specificity in the links of different types of early adversity with anxiety, affective or personality disorders (Porter et al., 2020; Spinhoven et al., 2010), but not with psychosis (Varese et al., 2012).

Childhood trauma refers to potentially harmful experiences including sexual, physical and emotional abuse as well as physical and emotional neglect (Morgan & Fisher, 2007). Previous research indicates a high prevalence in the general population (Witt, Brown, Plener, Brähler, & Fegert, 2017), individuals at ultra-high risk for psychosis (Kraan et al., 2015) and with severe mental disorder (Larsson et al., 2013; Varese et al., 2012). Childhood trauma has been shown to be associated with internalizing and externalizing problems (Greif Green et al., 2010), psychotic experiences in the general population, the persistence of psychotic symptoms in subclinical and clinical samples, and an increased risk for psychosis (Trotta et al., 2015; Varese et al., 2012).

Bullying refers to an individual or a group engaging in hostile behaviour against others who have problems defending themselves (Olweus, 1993), for example "teasing, name calling, mockery, threats, harassment, taunting, hazing, social exclusion or rumours" (Srabstein &

Leventhal, 2010, p. 403). With the increasing availability of technologies, cyber bullying (i.e. bullying using technology; Campbell, 2005) has emerged. Experiences of bullying are highly prevalent in youth (WHO Regional Office for Europe, 2012). Evidence has accumulated linking bullying to general psychopathology (Forbes, Magson, & Rapee, 2020) and various mental disorders (Brunstein Klomek et al., 2019; Varese et al., 2012). Moreover, bullying is associated with the later development of psychotic symptoms (Cunningham et al., 2016) as well as with higher levels of psychotic experiences in the general population (Wolke et al., 2014).

In summary, early adversity has been found to be relevant across a range of psychopathological outcomes (Greif Green et al., 2010; R. E. Norman et al., 2012), tentatively suggesting common, transdiagnostic mechanisms in their development (Rauschenberg et al., 2017). A putative transdiagnostic mechanism linking early adversity and psychopathology may be threat anticipation: Repeated or chronic exposure to adversity may lead to a cognitive bias comprising enhanced anticipation of unpleasant events creating an enduring sense of threat (Bentall et al., 2008; Bentall et al., 2009; R. Corcoran et al., 2006). Maladaptive high levels of threat anticipation are postulated as a core factor in the development and maintenance of anxiety disorders (Grupe & Nitschke, 2013). There is evidence for an association between threat anticipation and psychotic experiences in general (Reininghaus, Kempton, et al., 2016), and especially paranoia (Bentall et al., 2008; Freeman et al., 2013). Klippel et al. (2017) showed that the effect of stress on psychotic experiences was mediated via threat anticipation. Further, threat anticipation was associated with more intense psychotic experiences in participants with a first-episode of psychosis and high levels of childhood trauma (Reininghaus, Gayer-Anderson, et al., 2016).

The role of threat anticipation has been investigated in several mental disorders, especially psychosis, but to date has not been studied as a putative transdiagnostic mechanism linking early adversity and psychopathology. Above-mentioned studies are based on adult samples, so that to date, the role of threat anticipation has not been explored in adolescents yet as a priority target population for prevention and early intervention. Drawing on a large sample of adolescents, the current study aimed to investigate whether of the association between early adversity and psychopathology is mediated via pathways through threat anticipation. We tested the following hypotheses (for graphic illustration see supplementary material 16):

1) Higher levels of threat anticipation are associated with higher levels of a.) general psychopathology, and b.) prodromal psychotic symptoms (i.e., anomalous experiences and perceived distress, H1).

2) Higher levels of early adversity, characterised by childhood trauma and experiences of bullying, are associated with higher levels of a.) general psychopathology, and b.) prodromal psychotic symptoms (i.e., anomalous experiences and perceived distress, H2).

3) The association between early adversity, characterised by childhood trauma and experiences of bullying, and a.) general psychopathology, and b.) prodromal psychotic symptoms (i.e., anomalous experiences and perceived distress) is mediated via pathways through threat anticipation (H3).

In exploratory analyses, we further aimed to examine the specificity of different types of adversity with respect to their association with psychopathology. Furthermore, we sought to investigate the associations between early adversity and specific dimensions of psychopathology.

4.3. Methods

Sample

This study used data from the SIGMA study, a large cohort study with adolescents aged 12 to 16 years conducted in Flanders, Belgium, focusing on the socio-developmental origins of alterations in psychological mechanisms associated with psychopathology (Kirtley et al., 2021). Inclusion criteria were: (1) age of 12 to 16 years, (2) ability to understand the study procedures, (3) adequate command of Dutch language. Written informed consent from at least one caregiver and the adolescent was required. Further details on recruitment, procedures, ethics and consent are described elsewhere (Kirtley et al., 2021). For the current study, cross-sectional data collected as part of wave I was used. Data was collected between January 2018 and May 2019.

Data collection

Threat anticipation

Threat anticipation was assessed with a shortened version of the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). Participants were asked to predict the likelihood of five threatening events (e.g. 'you are being followed by someone') happening to them in the coming week using a scale of 1 ('not at all') to 7 ('very likely'). In line with previous work, threat anticipation was operationalised as a sum score for the anticipated likelihood of threatening events (Freeman et al., 2013). Cronbach's alpha was $\alpha=.67$.

Early adversity

Childhood trauma was assessed using the Juvenile Victimisation Questionnaire (JVQ; Finkelhor, Ormrod, Turner, & Hamby, 2005), a self-report questionnaire comprising 5 sub-scales ('any conventional crime', 'any child maltreatment', 'any peer or sibling victimisation', 'any sexual victimisation', and 'any witnessing or indirect victimisation'). The full version includes 34 potential victimisations scored dichotomously with 0 ('no') and 1 ('yes'). 12-year old participants completed a shortened version with 25 items (omitting the scale 'any conventional crime'). Childhood trauma was operationalised as a mean score. The scoring of all composite items was aggregated and divided by the total number of items administered (i.e., 34 items for participants aged 14 and older, 25 items for 12-year old participants). We observed good internal consistency for childhood trauma (α=.85).

Bullying victimisation was assessed with two self-constructed items on severity and frequency devised and included based on an amended questionnaire version of the Retrospective Bullying Interview (European Network of National Networks studying Gene-Environment Interactions in Schizophrenia, 2014; Kirtley et al., 2021). Participants were asked to rate their prevalence of bullying on a scale from 0 ('never') to 4 ('often, every week or several times per week'). Bullying severity was reported on a scale from 0 ('You've never been bullied or just a little teased that didn't bother you.') to 3 ('Severe, very bad bullying that you have had a lot of trouble with; you have become very upset about this; this has prevented you from daring or wanting to go to some places or people; you have had nightmares about this before.'). Moderate correlations with peer and sibling victimisation indicate concurrent validity (r=.43 for severity and frequency).

Psychopathology

To assess general psychopathology, we used the Brief Symptom Inventory (BSI-53; Derogatis, 1993), a self-report questionnaire consisting of nine subscales measuring different relevant dimensions of mental disorders (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) and four additional items (appetite, sleeping problems, thoughts about death and dying, and feelings of guilt). Participants were asked to indicate to what extend they experienced the listed symptoms in the last 7 days on a scale ranging from 0 ('not at all') to 4 ('very strong'). The Global Severity

Index (GSI), operationalised as the mean score, was used as a measure of general psychopathology. We observed excellent internal consistency for the GSI (α=.96).

Prodromal psychotic symptoms were assessed using a brief version of the Prodromal Questionnaire (PQ-16), a self-report screening questionnaire for psychosis risk (Ising et al., 2012). It comprises 16 items on anomalous experiences rated with 'yes'/'no'. If participants confirmed a symptom, perceived distress ('How much distress did you experience?') was assessed on a scale ranging from 0 ('none') to 3 ('severe'). If participants negated a symptom, the perceived distress variable was not presented. The PQ-16 was omitted for 12-year old participants. We used a total score (i.e., number of items answered with 'yes') as a measure of anomalous experiences and a sum score of the perceived distress by any given prodromal psychotic symptoms. For anomalous experiences, we observed satisfying internal consistency (α=.76).

Sociodemographic and intellectual characteristics

Age, gender and self-reported ethnicity were assessed as sociodemographic characteristics. In the assessment of self-reported ethnicity, participants were asked to indicate to which groups other than Belgian they felt related to, multiple answers were allowed. In addition, the THINC-it application (McIntyre et al., 2017) was used to screen for impairments in cognitive functioning.

Statistical analysis

The study was registered on the open science framework prior to accessing the data (Paetzold, Gugel, Schick, & Reininghaus, 2021), deviations from the preregistration are made transparent in supplementary material 17. As the data have a multilevel structure with multiple students (level-1) nested within schools (level-2), the 'mixed' command in Stata 16 (StataCorp, 2019) was used to fit two-level, linear mixed models. First, we included threat anticipation as an independent variable and general psychopathology (H1a) and prodromal psychotic symptoms (H1b) as outcome variables. Second, we included childhood trauma, bullying prevalence and severity as independent variables and general psychopathology (H2a) and prodromal psychotic symptoms (H2b) as outcome variables. Third, we performed mediation analysis using the 'gsem' command to investigate the indirect effects of childhood trauma, bullying prevalence and severity on general psychopathology (H3a) and prodromal psychotic symptoms (H3b) via pathways through threat anticipation. The total effect of early adversity on outcomes was apportioned into a direct effect and an indirect effect through threat anticipation. The indirect

effect was computed using the product of coefficients strategy. We computed the proportion mediated (i.e., the ratio of the indirect effect to the total effect) as a measure of effect size.

In exploratory analyses (see supplementary material 18), we used specific types of trauma and bullying as independent variables and general psychopathology and prodromal psychotic symptoms as outcome variables. In addition, we examined whether childhood trauma and bullying were associated with different dimensions of psychopathology (operationalised by the BSI subscales) and investigated differential indirect effects for dimensions of prodromal psychotic symptoms.

We used random intercept and slope models and applied restricted maximum likelihood (H1 and H2) or maximum likelihood estimation (H3), allowing for the use of all available data under the relatively unrestrictive assumption that data is missing at random and all variables associated with missing values are included in the model (see supplementary material 19 for an overview of missing values; Little & Rubin, 1987; Mallinckrodt et al., 2001). Results were bootstrapped with 1.000 repetitions. For sensitivity analyses with restrictions on missing values, exclusion of outliers and robust standard errors see supplementary material 20. All analyses were adjusted for potential confounders (i.e., age, gender, self-reported ethnicity, and deviations in cognitive functioning; for unadjusted analyses see supplementary material 21). We corrected for multiple testing within each hypothesis to reduce the probability of type I errors as a consequence of the number of tests performed. We used Simes' correction, a modified version of the more conservative Bonferroni correction in case of dependent hypotheses given significance tests in the current analyses were not independent (Simes, 1986). With the Simes' correction, the most significant p-value is tested against $\alpha=.05/n$ (total number of tests), the second most significant p-value is tested against $\alpha=.05/(n-1)$, etc. Simes-corrected significant results are highlighted with an asterisk (*) in text and tables. The study is reported based on STROBE criteria for reporting for cross-sectional studies (von Elm et al., 2007).

4.4.   Results

Basic sample characteristics

Table 14 displays relevant sample characteristics. The sample comprised $N=1,682$ adolescents with a mean age of 13.4 years ($SD=1.47$), 63% were girls. The majority (70%) reported to be Belgian only, 9% reported Moroccan and 5% Turkish ethnicity in addition to Belgian. The lifetime prevalence of trauma ranged from 21% (sexual victimisation) to 65% (peer or sibling

victimisation). In addition, 58% of all participants reported to have experienced bullying victimisation at least once. A majority of 71% reported at least one prodromal psychotic symptom, 28% of all participants reached the cut-off for relevant prodromal psychotic symptomatology (i.e., six symptoms). The mean level of general psychopathology was M=0.82 (SD=0.59).

The association between threat anticipation and psychopathology (H1)

As displayed in table 15, threat anticipation predicted psychopathology, such that higher levels of threat anticipation were associated with more severe general psychopathology (β=0.36, 95% CI 0.28 – 0.41, p<.001*, n=3 for Simes correction), more anomalous experiences (β=0.28, 95% CI 0.17 – 0.38, p<.001*, n=3 for Simes correction) and higher levels of perceived distress (β=0.36, 95% CI 0.24 – 0.47, p<.001*, n=3 for Simes correction).

The association between early adversity and psychopathology (H2)

Table 16 shows the association between early adversity and psychopathology. Individuals reporting higher levels of childhood trauma (β=0.54, 95% CI 0.48 – 0.61, p<.001*, n=9 for Simes correction) as well as higher prevalence (β=0.36, 95% CI 0.28 – 0.42, p<.001*, n=9 for Simes correction) and severity of bullying (β=0.42, 95% CI 0.35 – 0.48, p<.001*, n=9 for Simes correction) experienced more severe general psychopathology. Moreover, participants with higher levels of childhood trauma reported more anomalous experiences (β=0.32, 95% CI 0.24 – 0.41, p<.001*, n=9 for Simes correction) and higher levels of perceived distress (β=0.34, 95% CI 0.25 – 0.42, p<.001*, n=9 for Simes correction). Higher bullying prevalence and severity were associated with more anomalous experiences (e.g. prevalence: β=0.23, 95% CI 0.13 – 0.33, p<.001*, n=9 for Simes correction) and higher levels of perceived distress (e.g. severity: β=0.28, 95% CI 0.14 – 0.37, p<.001*, n=9 for Simes correction).

Table 14. *Basic sample characteristics of the full sample.*

	Full sample
N	1,682
Age (years), mean (*SD*)	13.4 (1.47)
Gender, *N* (%)	
Male	619 (37%)
Female	1,053 (63%)
Other	6 (0.4%)
Self-reported ethnicity, *N* (%)	
Only Belgian	1,183 (70%)
Moroccan	146 (9%)
Turkish	84 (5%)
Berbers	65 (4%)
Italian	42 (3%)
Polish	21 (1%)
Kurdish	16 (1%)
Other	238 (14%)
Lifetime prevalence of at least one experience of early adversity, *N* (%)	
Conventional crime	512 (30%)
Indirect victimisation	783 (47%)
Child maltreatment	596 (35%)
Peer or sibling victimisation	1,100 (65%)
Sexual victimisation	348 (21%)
Bullying prevalence	707 (58%)
Cyber bullying prevalence	367 (30%)
Physical bullying prevalence	613 (50%)
Threat anticipation, mean (*SD*)	10.24 (6.10)
Lifetime prevalence of prodromal symptoms, *N* (%)	
At least one symptom	
At least six symptoms (cut-off)	464 (71%)
	181 (28%)
General psychopathology, mean (*SD*)	0.82 (0.59)

Note. The full sample size was 1,682, sample sizes varied over the different scales due to missing values. Identification as Belgian was assumed, participants were asked to state all other nationalities they identify with, multiple answers were allowed on this scale, so that the number does not add up to the full sample of 1,682 participants. The conventional crime scale was not answered by participants in the first year (~12 years old). For prodromal symptoms, a cut-off score of ≥6 on the PQ-16 identifies people at ultra-high-risk for developing psychosis with a sensitivity and specificity of 87% each (Ising et al., 2012). SD=standard deviation.

The association between early adversity and psychopathology is mediated via pathways through threat anticipation (H3)

Table 17 shows findings on total, direct, and indirect effects of early adversity and threat anticipation on psychopathology. For the associations between early adversity and general psychopathology we observed evidence for mediation effects via threat anticipation (e.g. childhood trauma, indirect effect: β=0.13, 95% CI 0.09 – 0.16, $p<.001$*, $n=9$ for Simes correction). In addition, there was evidence for mediation effects via threat anticipation for the associations between early adversity and prodromal psychotic symptoms (e.g. childhood trauma, indirect effect on perceived distress: β=0.08, 95% CI 0.03 – 0.13, $p<.001$*, $n=9$ for Simes correction). The pathway via threat anticipation (i.e., the proportion mediated) accounted for 12-25% of the total effect.

Exploratory analyses

Results of exploratory analyses are displayed in supplementary material 18. Examining specific types of childhood trauma, we observed variation in the magnitude of associations with general psychopathology (indicated by confidence intervals not including point estimates). We found a larger association with peer or sibling victimisation (β=0.49, 95% CI 0.39 – 0.59, $p<.001$) in comparison to sexual or indirect victimisation (e.g. β=0.26, 95% CI 0.19 – 0.34, $p<.001$). Examining specific dimensions of psychopathology, we found an especially strong association between childhood trauma and paranoid ideation (β=0.55, 95% CI 0.49 – 0.61, $p<.001$). Examining differential mediation effects, we found evidence for a mediation effect threat anticipation for the association between childhood trauma and delusions (indirect effect: β=0.06, 95% CI 0.02 – 0.09, $p=.004$), but not for the association between childhood trauma and hallucinations (indirect effect: β=0.04, 95% CI 0.00 – 0.07, $p=.063$). However, there was evidence for mediation effects of threat anticipation for the association between bullying prevalence and severity and hallucinations and delusions.

Table 15. *General psychopathology and prodromal symptoms predicted by threat anticipation.*

	General psychopathology			Prodromal symptoms					
				Anomalous experiences			Perceived distress		
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Threat anticipation	0.36 (0.28 – 0.41)	< .001*	1,384	0.28 (0.17 – 0.38)	< .001*	607	0.36 (0.24 – 0.47)	< .001*	607

Note. Results were bootstrapped with 1.000 repetitions. Results were adjusted for age, gender, self-reported ethnicity, and cognitive deviance. CI=confidence interval. *=statistically significant after Simes' correction with *n*=3.

Table 16. *General psychopathology and prodromal symptoms predicted by early adversity.*

	General psychopathology			Prodromal symptoms					
				Anomalous experiences			Perceived distress		
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Childhood trauma	0.54 (0.48 – 0.61)	< .001*	1,239	0.32 (0.24 – 0.41)	< .001*	563	0.34 (0.25 – 0.42)	< .001*	563
Bullying prevalence	0.36 (0.28 – 0.42)	< .001*	1,045	0.23 (0.13 – 0.33)	< .001*	449	0.24 (0.14 – 0.34)	< .001*	449
Bullying severity	0.42 (0.35 – 0.48)	< .001*	1,059	0.26 (0.15 – 0.35)	< .001*	452	0.28 (0.14 – 0.37)	< .001*	452

Note. Results were bootstrapped with 1.000 repetitions. Results were adjusted for age, gender, cultural identification, and cognitive deviance. CI=confidence interval. *=statistically significant after Simes' correction with *n*=9.

Table 17. *The association between early adversity and psychopathology is mediated via pathways through threat anticipation.*

	General psychopathology				Prodromal symptoms							
					Anomalous experiences				Perceived distress			
	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M
Childhood trauma			1,239				563				563	
Total effect	0.55 (0.49 – 0.61)	< .001			0.31 (0.23 – 0.42)	< .001			0.33 (0.25 – 0.43)	< .001		
Direct effect	0.42 (0.35 – 0.49)	< .001			0.26 (0.17 – 0.36)	< .001			0.25 (0.16 – 0.36)	< .001		
Indirect effect	0.13 (0.09 – 0.16)	< .001*		0.24	0.05 (0.01 – 0.09)	.008*		0.16	0.08 (0.03 – 0.13)	< .001*		0.24
Bullying prevalence			1,045				449				449	
Total effect	0.35 (0.29 – 0.41)	< .001			0.24 (0.15 – 0.32)	< .001			0.20 (0.09 – 0.30)	< .001		
Direct effect	0.30 (0.24 – 0.37)	< .001			0.20 (0.12 – 0.29)	< .001			0.20 (0.09 – 0.30)	< .001		
Indirect effect	0.05 (0.03 – 0.07)	< .001*		0.14	0.04 (0.02 – 0.07)	.001*		0.17	0.05 (0.03 – 0.09)	< .001*		0.25
Bullying severity			1,059				452				452	
Total effect	0.41 (0.35 – 0.47)	< .001			0.27 (0.18 – 0.38)	< .001			0.29 (0.20 – 0.40)	< .001		
Direct effect	0.36 (0.31 – 0.43)	< .001			0.24 (0.14 – 0.34)	< .001			0.25 (0.15 – 0.36)	< .001		
Indirect effect	0.05 (0.03 – 0.07)	< .001*		0.12	0.04 (0.02 – 0.07)	.001*		0.15	0.05 (0.02 – 0.08)	< .001*		0.17

Note. Results were bootstrapped with 1.000 repetitions. Results were adjusted for age, gender, self-reported ethnicity, and cognitive deviance. N_{min}=due to varying numbers of missing values, different paths of the mediation analyses comprised varying sample sizes. Therefore, the minimum sample size is displayed here. CI=confidence interval. P_M=Proportion mediated. *=statistically significant after Simes' correction with n=9.

4.5. Discussion

Main findings

We found evidence that threat anticipation was associated with psychopathology (H1). In addition, experiences of early adversity were associated with psychopathology (H2). We observed medium to large associations with childhood trauma and small to medium associations with bullying. Moreover, there was evidence for mediation effects via pathways through threat anticipation for the associations between early adversity and psychopathology (H3). In exploratory analyses, we found some evidence for differential associations of specific types of early adversity and specific dimensions of psychopathology.

Methodological considerations

The reported findings should be interpreted in the light of several methodological considerations: First, the cross-sectional design should be taken into account. As temporal precedence is an important criterion of causality (M. Susser, 1991), the current study focuses on reporting associations and longitudinal designs are needed to further strengthen evidence on the role of threat anticipation. However, as SIGMA is a cohort study, it may be possible to further explore temporal associations with data from future waves of data collection. Second, limitations regarding the data structure should be considered. Measures of psychopathology and early adversity were affected by missing values. However, missing values on the perceived distress score are inherent to the instrument used. In addition, sensitivity analyses in restricted samples (see supplementary material 20) indicated a similar pattern of findings. Caregivers' reports were affected by a low response rate and it was not possible to control for social disadvantage. Therefore, we adjusted the analyses for adolescents' self-reports of known a priori confounders (i.e., age, gender, ethnicity, and deviances in cognitive functioning). In addition, unmeasured confounders (e.g. polygenic risk) may have influenced the reported findings. Third, statistical limitations should be evaluated critically. The number of analyses performed may have resulted in multiple testing problems. In order to control for type I error, results were corrected using the Simes' method (Simes, 1986) within each hypothesis. Data were left-skewed on several scales, as one would expect in a community sample. In addition, scatter plots revealed slightly pro-

nounced heteroscedasticity for some tests. Sensitivity analyses based on univariate outlier analyses for skewed data (Hubert & Van der Veeken, 2008) and robust standard errors replicated the pattern of findings (see supplementary material 20).

Comparison to previous research

Consistent with previous research we found evidence for an association between early adversity and psychopathology in a large community sample of adolescents (Greif Green et al., 2010; S. E. Moore et al., 2017). The current study extends findings on threat anticipation (Bentall et al., 2009; Reininghaus, Kempton, et al., 2016) by showing an association with general psychopathology and prodromal psychotic symptoms. Examining momentary processes, Klippel et al. (2017) found that the effect of stress on psychotic experiences was mediated by threat anticipation. The current study broadens the perspective by elucidating the role of threat anticipation as a potential mediator in a larger context linking early adversity and psychopathology. In line with previous suggestions of transdiagnostic risk and resilience mechanisms (Rauschenberg et al., 2017; Reininghaus, Gayer-Anderson, et al., 2016) and a recent review on cognitive mediators (Aafjes-van Doorn, Kamsteeg, & Silberschatz, 2020), the partial mediation indicates that threat anticipation may be one of multiple mechanisms underlying this association. Future research should therefore examine threat anticipation in combination with other putative mechanisms.

Exploratory analyses demonstrated an especially strong association of childhood trauma and paranoid ideation. In line with the model of psychosis (Garety et al., 2007), the current findings underscore the relevance of childhood trauma as a potential risk factor in the development of psychotic experiences. In addition, exploratory analyses indicated a potential mediating effect of threat anticipation for the association between childhood trauma and delusions, but not for the association between childhood trauma and hallucinations. These findings are consistent with the hypothesis of different pathways from childhood trauma to hallucinations and from childhood trauma to delusions (Bentall et al., 2008): For hallucinations, childhood trauma is expected to cause unwanted, intrusive cognitions which, in interaction with dysfunctional, metacognitive beliefs and poor source monitoring, then cause hallucinations. The hypothesised pathway from childhood trauma to delusions or paranoid beliefs is postulated to operate via externalizing explanatory bias and threat anticipation.

Conclusion

Taken together, our findings underscore the relevance of threat anticipation as putative transdiagnostic mechanism linking early adversity with psychopathology in adolescents. Threat anticipation may therefore be a potential transdiagnostic target mechanism in the development of prevention and early intervention (Reininghaus et al., 2015). Future research could elaborate on this by applying a longitudinal approach. A first example of an intervention targeting threat anticipation as a candidate mechanism is EMIcompass, a hybrid compassion-focused intervention to enhance resilience in help-seeking youth, which is currently tested in an exploratory randomised controlled trial (Schick et al., 2021).

CHAPTER V:

A HYBRID ECOLOGICAL MOMENTARY COMPASSION-FOCUSED INTERVENTION FOR ENHANCING RESILIENCE IN HELP-SEEKING YOUNG PEOPLE: A PROSPECTIVE STUDY OF BASELINE CHARACTERISTICS IN THE EMICOMPASS TRIAL

5.1.   Abstract

Young people are a target population for mental health related early intervention and prevention. Whereas evidence for early intervention is promising, availability and access of youth mental health services remain limited. Therefore, the development of an evidence-based hybrid intervention is urgently needed. The current paper aims to 1) present a manual for a hybrid intervention, combining an EMI and face-to-face sessions aimed for enhancing resilience in help-seeking young people based on CFIs and 2) explore whether participants' baseline characteristics are associated with putative mechanisms and outcomes of the EMIcompass intervention. Specifically, we aimed to explore initial signals as to whether a) participants' sociodemographic, clinical and functional characteristics at baseline are associated with putative mechanisms (i.e., change in self-compassion, change in emotion regulation, working alliance, training frequency); b) participants' sociodemographic, clinical and functional characteristics, self-compassion, and emotion regulation at baseline are associated with clinical outcomes (i.e., psychological distress and general psychopathology at post-intervention and four-week follow-up) in the experimental condition and obtain first parameter estimates. We recruited young people aged 14 to 25 with psychological distress, clinical high-at-risk mental states or first episodes of severe mental disorder for an exploratory randomised controlled trial with assessments at baseline, post-intervention and at four-week follow-up. A structured manual was developed and optimised based on a pilot study's manual, a scoping review of existing literature and manuals,

exchange with experts, the team's clinical experience of working with CFIs and the principles of EMIs. The current analysis focuses on the experimental condition receiving the EMIcompass intervention. Forty-six young individuals were randomised to the experimental condition. There was evidence for initial signals of effects of age (b=0.11, 95% CI 0.00 – 0.22), general psychopathology (b=0.08, 95% CI -0.01 – 0.16) and clinical stage (b=1.50, 95% CI 0.06 – 2.93) on change in momentary self-compassion and change in emotion regulation from baseline to post-intervention assessments. There was no evidence for associations of other baseline characteristics (e.g. gender, minority status, level of functioning) and putative mechanisms (e.g. overall self-compassion, working alliance, training frequency). In addition, except for an initial signal for an association of momentary self-compassion at baseline and psychological distress (b=-2.83, 95% CI -5.66 – 0.00), we found no evidence that baseline characteristics related to clinical outcomes. Findings indicated reach of participants by the intervention largely independently from sociodemographic, clinical, and functional baseline characteristics. The findings need to be confirmed in a definitive trial.

5.2. Introduction

Background

Young people constitute a priority target population for mental health related prevention and early intervention as they are particularly affected by mental health problems. Mental disorders primarily emerge in adolescence and young adulthood, more than 60% of all lifetime cases have their onset before the age of 25 (Solmi et al., 2022). With a worldwide pooled prevalence of 21% of mental disorders in adolescents aged 12-18 (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015), mental health problems contribute substantially to the disease burden (Erskine et al., 2015; Kassebaum et al., 2017). Addressing the co-occurrence and overlap of subclinical and clinical experiences and symptoms (Reininghaus, Böhnke, et al., 2016; Reininghaus et al., 2013; Shevlin et al., 2016; van Os & Reininghaus, 2016), especially in early stages of psychopathology, dimensional classification frameworks (Forbes, Tackett, Markon, & Krueger, 2016; Insel et al., 2010) cutting across traditional diagnostic boundaries, including HiTOP (Kotov et al., 2017), have been proposed. Clinical staging models take early, overlapping and nonspecific psychopathological symptoms and transitional staging processes into account (Hartmann et al., 2019; McGorry, Purcell, Hickie, Yung, et al., 2007).

There is convincing evidence on risk factors that are modifiable, on mental health problems that can be changed and on protective factors that can be strengthened to enhance resilience (Bayer et al., 2009; Forbes, Rapee, & Krueger, 2019; Patel et al., 2007). Traditional psychotherapeutic interventions, including standard cognitive behavioural therapy, as well as third-wave approaches, show moderate to high effect sizes in RCTs and meta-analyses (Cuijpers et al., 2013; Hofmann & Smits, 2008; Kirby et al., 2017; Tai & Turkington, 2009). However, there is considerable room for improvement, as - even after successful treatment - many service users suffer from significant residual symptoms or relapse (Fava et al., 2007). In addition, availability and access of youth mental health services remain limited (Malla et al., 2018; McGorry & Mei, 2018). More downstream, this may result in a longer duration of untreated illness, an important marker of poor prognosis and complex course and outcome (Ghio et al., 2014; Marshall et al., 2005).

Some of these problems of standard care might be due to difficulties transferring preventive and therapeutic strategies developed in face-to face sessions to service users' daily life. mHealth may be a promising approach to address these challenges by improving access to mental health care for young people by using mobile devices for the delivery of prevention and intervention (Myin-Germeys et al., 2018; Myin-Germeys et al., 2016; Rauschenberg, Schick, Goetzl, et al., 2021; Rauschenberg, Schick, Hirjak, et al., 2021; Reininghaus, 2018). With ESM, often also referred to as EMA, a structured diary method, momentary fluctuations in experience and behaviour can be assessed in real-time and real-life (Csikszentmihalyi & Larson, 1987; Ebner-Priemer & Trull, 2009; Myin-Germeys et al., 2018; Myin-Germeys et al., 2009; Shiffman et al., 2008; Stone & Shiffman, 1994). EMIs (Heron & Smyth, 2010; Myin-Germeys et al., 2011; Myin-Germeys et al., 2018; Reininghaus, 2018; Reininghaus et al., 2015) offer the opportunity to deliver adaptive and personalised intervention components in daily life. The digital approach may help to lower the threshold for young people to access interventions meeting their needs and preferences and facilitates the ecological translation of techniques learned into service users' everyday lives (Reininghaus, 2018). A recent nationally representative survey indicated that young people do frequently use mHealth apps and are even more likely to do so when feeling distressed (Rauschenberg, Schick, Goetzl, et al., 2021).

However, digital approaches are also confronted with challenges: Most applications currently available in major app stores are not evidence-based and some even include potentially harmful content (Larsen et al., 2019; Rauschenberg, Schick, Hirjak, et al., 2021). In addition, reach of digital interventions has been subject to controversial debate as concerns have been expressed

that barriers to treatment may be created rather than removed (Bucci, Berry, et al., 2019; Greer et al., 2019). A review indicated that studies of effectiveness of mHealth apps mostly include samples of predominantly female, white participants with an average age of 30-45 years (Lui et al., 2017) and the degree of generalisability of findings to service users with other characteristics remains largely unexplored. Therefore, the development of evidence-based, low-threshold interventions that specifically target established candidate mechanisms that have been linked to the development and persistence of mental health conditions across various groups and settings are urgently needed. In addition, it is crucial to explore the association of participants' baseline characteristics with putative mechanisms and outcomes to examine reach of the intervention.

Extensive research identified stress reactivity as a putative transdiagnostic mechanism in the development of psychopathology and a promising target for prevention and early intervention (Myin-Germeys et al., 2018). Stress reactivity (i.e., increases in negative affect in response to minor daily stressors) is thought to be a behavioural marker of stress sensitization, positing that frequent or chronic experiences of adversity may gradually increase individuals' stress response to subsequent adversities and minor stressors in everyday life (Collip et al., 2008; Myin-Germeys et al., 2018; Wichers et al., 2009).

CFIs may be a promising approach to target stress reactivity in daily life. Building on a combination of evolutionary psychology, attachment theory and social mentality theory, the compassion-focused approach claims that various psychological problems are caused by unhelpful loops between distressing emotions, defensive behaviours and cognitive processes such as rumination, worry and self-criticism (P. Gilbert, 2014). A model with three inter-related major emotional systems is suggested (P. Gilbert, 2009, 2013, 2014): threat, drive and soothing. Many people experience an overactive threat system, an overactive or somehow blocked drive system and an underactive soothing system (P. Gilbert, 2014). Therefore, CFIs focus on strengthening the soothing system, as it is thought to be an antagonist to an overactive threat system and a good basis for a well-functioning drive system. CFIs are not symptom-specific and previous studies demonstrated that they are an effective treatment for various mental health problems (Cuppage et al., 2018; Heriot-Maitland et al., 2019; Kirby et al., 2017; Leaviss & Uttley, 2015). Positive imagery, a key component of CFIs, has been shown to effectively reduce a wide range of mental health problems and increases positive affect, optimism and behavioural activation (Holmes, Blackwell, Burnett Heyes, et al., 2016; Holmes & Mathews, 2010; Leaviss & Uttley,

2015; Pearson et al., 2015; Renner et al., 2017). In laboratory studies the application of compassion-focused techniques has been shown to reduce state negative affect and paranoia in moments of high stress. (Lincoln et al., 2013; Pearson et al., 2015).

Combining digital approaches and CFIs in a hybrid intervention using imagery-based techniques may be particularly well-suited to target stress reactivity in the daily life of young people. Previous research indicated higher acceptability and larger effect sizes for hybrid interventions in comparison to standalone internet- and mobile-based interventions (Baumeister et al., 2014; Topooco et al., 2017). Therefore, EMIcompass was developed as a hybrid intervention combining an EMI with guided face-to-face sessions. A pilot study provided initial evidence for feasibility, safety and beneficial effects of a compassion-focused EMI for enhancing resilience in help-seeking young people (Rauschenberg, Boecking, et al., 2021). Feasibility and initial signals of efficacy of the intervention have been investigated in a registered exploratory RCT in Germany (Reininghaus, 2019), comparing treatment as usual (TAU) with TAU + EMIcompass in young people with early mental health problems.

Objectives

The current paper aims to:

1) present the intervention manual for EMIcompass, a hybrid intervention combining an EMI and face-to-face sessions aiming at enhancing resilience in help-seeking young people based on compassion-focused principles (P. Gilbert, 2009, 2013, 2014)

2) explore whether participants' baseline characteristics are associated with putative mechanisms and outcomes of the EMIcompass intervention. To this end, we aimed to obtain first parameter estimates and explore initial signals as to whether: a) sociodemographic, clinical, and functional characteristics at baseline (i.e., clinical stage, psychological distress, general psychopathology, level of functioning, age, gender, and minority status) are associated with putative mechanisms (i.e., change in self-compassion, change in emotion regulation, working alliance, and training frequency); b) sociodemographic, clinical and functional characteristics (i.e., clinical stage, psychological distress, general psychopathology, level of functioning, age, gender, and minority status) as well as self-compassion and emotion regulation at baseline are associated with clinical outcomes (i.e., psychological distress and general psychopathology, at post-intervention and four-week follow-up) in the experimental condition and obtain 95% confidence intervals.

5.3.   Method

Study design

In our exploratory RCT, participants were randomly allocated to a control condition TAU or an experimental condition of TAU + EMIcompass in a 50:50 ratio. For the current analyses, data from the experimental condition was used to examine the impact of participants' baseline characteristics on the putative mechanisms and outcomes of the intervention. In the RCT, candidate mechanisms (primary: stress reactivity; secondary: resilience, interpersonal sensitivity, threat anticipation and negative affective appraisals) and outcomes (primary: psychological distress; secondary: primary psychiatric symptoms, general psychopathology and quality of life) were assessed at baseline (i.e., before randomization), at the end of the intervention period and at four-week follow-up. Observer ratings were performed by blinded assessors. The sample size was based on a power simulation for the primary outcome of the trial (Schick et al., 2021). The RCT was conducted between August 2019 and September 2021. Appointments were held in person or (due to the COVID-19 pandemic) via video calls. Further details on study procedures are described in the study protocol (Schick et al., 2021).

Ethical considerations

The trial has received ethical approval by the local Ethics Committee of the Medical Faculty Mannheim, Heidelberg University (2017-602N-MA). All participants and, in case of minors, parents/legal guardians, provided written informed consent before inclusion in the study.

Manual for the EMIcompass intervention

To ensure consistent delivery of the intervention, a structured manual was developed and refined building on the manual from the pilot study (for changes to the pilot version see supplementary material 22; Rauschenberg, Boecking, et al., 2021). The development and optimization process comprised a scoping review of available literature and existing manuals. In addition, local CFI experts were consulted and the team's clinical experience of working with these approaches was considered. The intervention was designed based on principles of EMIs (Myin-Germeys et al., 2018; Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus et al., 2015).

The development and optimization process resulted in a structured manual for a six-week intervention combining four individual sessions with daily training via a dedicated smartphone app. The manual is reported in supplementary material 23 in line with state-of-the art guidelines such as WHO guidelines for reporting health interventions using mobile phones (Agarwal et al., 2016) as well as the Template for Intervention Description and Replication Checklist (Hoffmann et al., 2014). An overview of the intervention structure and the types of tasks is provided in figure 2, figure 3 displays a summary of the intervention content. The intervention can be aligned to participants' personal needs, for example sessions or training weeks can be repeated if necessary. Moreover, the intervention provides two different study tracks with varying foci and demand levels. Based on the trained psychologists' impression and the participants' experiences in the first two weeks of the intervention, participants were allocated to the basic or the elaborate track of the intervention. The basic study track focused on creating feelings of safeness and calmness by introducing breathing techniques and soothing imagery. The elaborate track extended breathing exercises and soothing imagery by introducing self-compassionate imagery and writing.

The intervention comprised three guided sessions to introduce compassion-focused principles and practical tasks to activate participants' soothing system and to provide feedback on their current progress and a short review session. The content was presented on the smartphone and was discussed with the trained psychologist. All sessions could be delivered in person or via video calls. The in-person sessions were delivered in dedicated treatment/assessment rooms. For sessions delivered via video call, participants attended the sessions at home. Psychologists were trained in delivering the EMIcompass intervention and supervised by an expert in CFIs (BB) to ensure intervention quality.

To facilitate interactive, real-time and -world translation of techniques into participants' daily lives, an EMI was administered through a mHealth app (movisensXS) on a study smartphone which they received in the first guided session. To learn new techniques, participants were asked to complete one *enhancing* task per week, which were subsequently extended over the intervention period. In the weeks with sessions, the new task was introduced in the contact with the trained psychologists, in the weeks without session, participants familiarised with the new enhancing task autonomously. Short *consolidating* tasks were offered to practise the techniques previously introduced in enhancing tasks. Once a day, at a time set by the participants, a signal was prompted to offer participants a consolidating task. In addition, on demand consolidating

tasks were available at any time during the intervention period. Further, participants could decide whether they also wanted to allow for *interactive* tasks. To present interactive tasks, the smartphone prompted a signal six times per day on three consecutive days per week at random within set blocks of time. At each signal, participants were asked to complete a short ESM questionnaire on momentary stress and affect. If participants indicated high stress or negative affect in the ESM questionnaire, they were offered an interactive task. Thereby, the interactive tasks guided participants to use previously learned compassion-focused techniques in moments of distress, which is an essential element of CFIs (P. Gilbert, 2009). A gamification element was used to provide feedback on the progress made. If appropriate, participants could choose between reading the instructions on the smartphone's screen and a guided audio version of the tasks.

Between sessions, participants received weekly feedback on their progress and were offered e-mail and/or phone contact to discuss questions and technical problems. At the beginning of weeks without scheduled session (i.e., weeks 2, 4 and 6), participants were contacted to notify them about a new enhancing task becoming available for them to try out autonomously. To proceed with the subsequent study week, participants had to complete at least one consolidating task per week. If this was not the case, the intervention week was repeated.

Participants

In line with a modified version of the clinical staging model (Hartmann et al., 2019; Schick et al., 2021), the EMIcompass study recruited young individuals aged 14 to 25 with current psychological distress, broad clinical high at-risk mental state or a first treated episode of severe mental disorder (for a detailed description of the modified criteria see supplementary material 24, age range based on suggestions of the youth mental health reform and local regulations; Malla et al., 2016). Participants were recruited from mental health services at the Central Institute of Mental Health (CIMH), Mannheim, Germany, via local registries and online advertisements on the institute's webpage and social media. Self-reported and observer-rated measures were used to assess eligibility to participate. All participants (including caregivers for minors) provided informed consent and were reimbursed for their time and travel expenses. Further details on inclusion and exclusion criteria are provided in the study protocol (Schick et al., 2021).

Enhancing tasks	**Once per week to learn new content:** Session 1 · Session 2 · Session 3 · Short review session Week 1 · Week 2 · Week 3 · Week 4 · Week 5 · Week 6 **Intervention period: 6 weeks** E · E · E · E · E · E
Consolidating tasks	**Once per day at a self-set time:** DAY 1 · 2 · 3 · 4 · 5 · 6 · 7 One week in the intervention C · C · C · C · C · C · C **On demand:** Train now!
Interactive tasks	**Optional:** ESM questionnaires (3 days a week, 6 times a day) + interactive task in moments of high stress or high negative affect DAY 1 · · · · · 2 One day in the intervention with interactive tasks I · I · I · I · I · I

Figure 2. *Overview of the intervention structure and the types of tasks.*
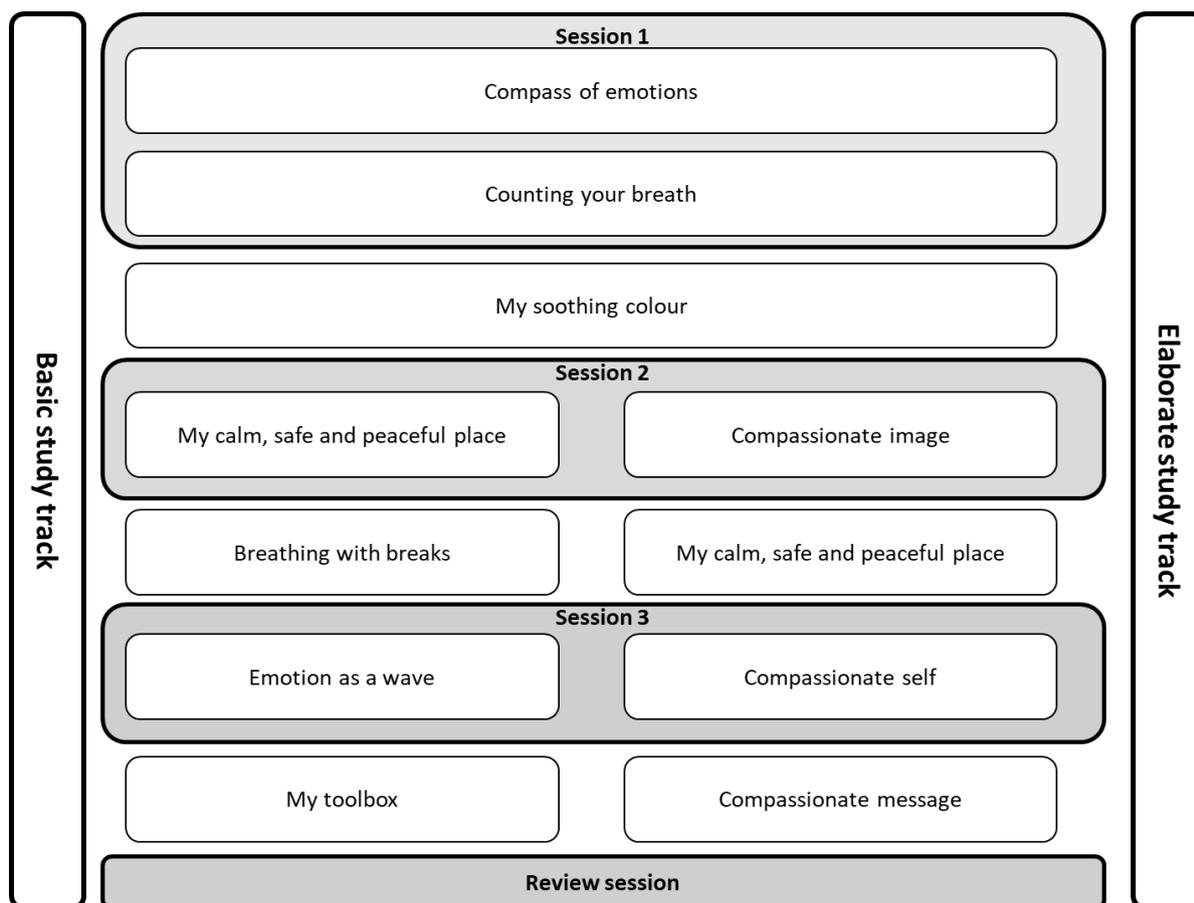
Figure 3. *Summary of the intervention content.*

Measures

Table 18 provides an overview of the measures used and the time points of administration. We used self-reports and, in the case of ethnicity, family assessments to collect data on sociodemographic characteristics. Clinical characteristics (i.e., clinical stage, psychological distress, general psychopathology, level of functioning) were assessed using self-report questionnaires, observer ratings and standardised interviews. Self-report questionnaires were used to assess overall self-compassion, emotion regulation and working alliance. Momentary self-compassion was assessed using ESM. The total number of training tasks completed in the EMI was used as an indicator of training frequency. Supplementary material 25 displays a correlation table of the measures used.

Table 18. *Description of measures and time points of their administration.*

Measures	Assessment method	Instrument und further information	Time point
Sociodemographic characteristics			
Age	Self-report		Screening
Gender	Self-report		Screening
Ethnicity	Self-report, family assessment	Citizenship, country of birth, first language and family assessment.	Screening, T0
Clinical characteristics			
Clinical stage	Standardised interviews, self-report, observer ratings	Allocation to stage 1a (i.e., current psychological distress), stage 1b (i.e., broad Clinical High At-Risk Mental State, CHAARMS) with attenuated symptoms of psychosis, mania, depression, or anxiety) or stage 2 (i.e., first episode of severe mental disorder) based on a modified version of the clinical staging model (Hartmann et al., 2019; Schick et al., 2021). Further details on the criteria are provided elsewhere (Schick et al., 2021) and in supplementary material 24.	Screening
Psychological distress	Self-report questionnaire	Assessment with the Kessler Psychological Distress Scale (K10; Kessler et al., 2002; Kessler et al., 2005), a 10-item questionnaire assessing psychological distress in the last month on a scale from 1 (=never) to 5 (=always). To obtain a measure of psychological distress, a sum score across all items was calculated. α=.73 at baseline.	Screening, T1, T2
General psychopathology	Self-report questionnaire	Assessment with the 18-item version of the Brief Symptom Inventory (BSI-18;Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Participants were asked to rate to what extend they experienced the listed 18 symptoms in the last seven days on a 5-point Likert-scale ranging from 0 (=not at all) to 4 (=very strong). We used the Global Severity Index, the sum score across all items, as a measure of general psychopathology. α=.79 at baseline.	T0, T1, T2
Level of functioning	Observer rating	Trained assessors rated participants' level of functioning using the Social and Occupational Functioning Assessment Scale (SOFAS; Goldman, Skodol, & Lave, 1992). Ratings range from 0 to 100, with lower scores indicating lower levels of functioning. A random set of audiotaped interviews rated by a fixed set of trained raters was used to determine interrater-reliability using JASP (i.e. ICC 3.1, JASP version 0.16.1; JASP Team, 2022; Shrout & Fleiss, 1979). In line with the literature (Hilsenroth et al., 2000), we observed excellent interrater-reliability (ICC 0.96; 95% CI 0.86 – 0.99).	Screening
Baseline levels of putative mechanisms			
Self-compassion		Overall self-rating and momentary ESM ratings in participants' daily life. To indicate change in self-compassion from baseline to post-intervention, we calculated difference scores ($\delta_{\text{post-intervention – baseline}}$).	
Overall self-compassion	Self-report questionnaire	Assessment with the Self-Compassion Scale (Hupfeld & Ruffieux, 2011) with 26 items. In line with Neff (2003), we re-coded items from the subscales self-judgement, isolation and over-identification. We then	T0, T1

		calculated a mean for each of the subscales, and finally summed the means to create a total self-compassion score. α=.90 at baseline.	
Momentary self-compassion	ESM	Three items: "I feel safe.", "I feel benevolent.", "I like myself.", 7-point Likert-scale ranging from 1 (=not at all) to 7 (=very much). Assessments eight times a day at six consecutive days at baseline and post-intervention.	T0, T1
		We aggregated participants' ratings of momentary self-compassion to a mean score for each assessment week (baseline, post-intervention). α=.84 at baseline.	
Emotion regulation	Self-report questionnaire	Assessment with the Cognitive Emotion Regulation Questionnaire (CERQ-short), an 18-item questionnaire capturing nine strategies (self-blame, other-blame, rumination, catastrophizing, positive refocusing, planning, positive reappraisal, putting into perspective and acceptance) on a 5-point Likert scale ranging from 1 (= almost never) to 5 (=almost always) (Garnefski & Kraaij, 2006). In line with the CERQ scoring manual (Garnefski, Kraaij, & Spinhoven, 2002), we calculated sum scores for each subscale. Following the approach of Martins, Freire, and Ferreira-Santos (2016), we classified the coping strategies as adaptive (acceptance, putting into perspective, positive refocusing, refocus on planning and positive reappraisal) or maladaptive (self-blame, rumination, catastrophizing and other-blame). We aggregated the values to a mean score for adaptive and a mean score for maladaptive coping strategies. Adaptive emotion regulation α=.82, maladaptive emotion regulation α=.77 at baseline.	T0, T1
		To indicate change in emotion regulation from baseline to post-intervention, we calculated a difference score ($\delta_{\text{post-intervention – baseline}}$).	
Working alliance	Self-report questionnaire	Assessment with the Working Alliance Inventory for Patients and Therapists (WAI-P/WAI-T; Horvath & Greenberg, 1989). We used sum scores of the 12 items for patient and therapist ratings to obtain measures of working alliance. Patient ratings: α=.92, therapist ratings α=.93.	T1
Training frequency		Total number of training tasks completed in the EMI.	Intervention period

Note. A correlation table of the measures used is displayed in supplementary material 25. T0 = baseline assessment. T1 = post-intervention assessment. T2 = follow-up assessment.

Statistical analysis

The study was registered on the open science framework prior to accessing the data (Paetzold, Schick, Rauschenberg, Hirjak, Banaschewski, Meyer-Lindenberg, Butz, et al., 2021). To obtain parameter estimates for the effect of sociodemographic, clinical and functional characteristics on putative mechanisms and processes, we fitted linear regression models with change in self-compassion ($\delta_{\text{post-intervention – baseline}}$), change in adaptive and maladaptive emotion regulation ($\delta_{\text{post-intervention – baseline}}$), working alliance (patient and therapist ratings, total scores) and training

frequency (total score) as dependent variables. Independent variables in the models were: clinical stage (stage 1a, stage 1b, stage 2), psychological distress, general psychopathology, level of functioning, age, gender (female, male) and ethnic minority status (minority, majority). Parameter estimates (95% confidence intervals) were obtained for the main effects of baseline characteristics on change in self-compassion, change in adaptive and maladaptive emotion regulation, working alliance and training frequency. We computed partial η^2 as estimators of effect size for the predictors.

To obtain parameter estimates for the effect of sociodemographic, clinical and functional characteristics and baseline level of self-compassion, adaptive and maladaptive emotion regulation on clinical outcomes, we fitted mixed effects regression models with psychological distress and general psychopathology at post-intervention/follow-up as the dependent variables. Independent variables in these models were: time (post-intervention, follow-up), clinical stage (stage 1a, stage 1b, stage 2), level of functioning at baseline, age, gender (female, male), ethnic minority status (minority, majority), momentary and overall self-rated self-compassion at baseline, adaptive and maladaptive emotion regulation at baseline, psychological distress at baseline (as independent variable in the model with general psychopathology at post-intervention/follow-up as outcome and as control variable with psychological distress at post-intervention/follow-up as outcome) and general psychopathology at baseline (as independent variable in the model with psychological distress at post-intervention/follow-up as outcome and as control variable with general psychopathology at post-intervention/follow-up as outcome). We took into account the within-subject clustering of repeated measures by adding a level-2 random intercept. The model was fitted using restricted maximum likelihood (REML) estimation. Parameter estimates (95% confidence intervals) were obtained for the main effects of baseline characteristics on outcomes across the two follow-up time points (i.e., post-intervention, four-week follow-up). In a next step, given the exploratory nature of this trial, 95% confidence intervals for the two time-specific contrasts were obtained. For this, the above model was extended by time × characteristic interactions (time × clinical stage, time × psychological distress, time × general psychopathology, time × level of functioning, time × age, time × gender, time × self-compassion, time × adaptive emotion regulation, and time × maladaptive emotion regulation). The 'margins' command was used for each interaction to obtain predicted means for both time points and all manifestations of categorical variables (e.g. 'margins time point #clinical stage'). For continuous variables, the 'margins' command was used with z-standardised continuous variables to obtain predicted means for both time points and low (mean - 1 *SD*), mean and high

(mean + 1 *SD*) levels of the given continuous variable (e.g. 'margins, at (z_age = (-1 0 1)) over (time)').

To transform the results into an effect size, the model was run including only a random intercept for participants, the estimated target relationship as well as the baseline control to obtain the conditional and pooled variance across both assessment time points (Bijleveld et al., 1998; Hoffman & Stawski, 2009; Xiao, Kasim, & Higgins, 2016). The resulting estimate of variance therefore approximates the variation in the dependent variable at any cross-section in the post-intervention and follow-up periods. The resulting estimate is on a similar scale as other typical d-type effect sizes (at "0" of any random slopes, if included) and if additional random effects were strong, these variances are underestimations and the effect sizes in the following likely at the upper possible limit.

The analysis was conducted according to intention-to-treat principles, with data from all participants entered into the analysis including those who have low adherence to, or who dropped out of the intervention. To screen for potential collinearity problems, we computed variance inflation factors and tolerance values (see supplementary material 26).

5.4.   Results

Basic sample and clinical characteristics

An overview of basic sample and clinical characteristics is displayed in table 19. The sample of those randomised to the experimental condition comprised *N*=46 individuals (50% of the total sample in the exploratory RCT of *N*=92) with a mean age of 21.30 years (*SD*=2.84, range 14 – 25 years). A majority of 76% identified as girls/women, 24% as boys/men, no participant identified as non-binary. We identified 70% of the participants as White majority (German), 9% as white other, and 22% as other or mixed ethnicity. Most participants were classified as stage 1a (psychological distress, 57%), 28% of the participants met criteria for stage 1b (CHARMS), and 15% were classified as stage 2 (first episode of severe mental disorder). The mean level of psychological distress at baseline was *M*=28.20 (*SD*=5.08), the mean level of general psychopathology at baseline was *M*=24.55 (*SD*=9.94). The average level of functioning was *M*=71.83 (*SD*=9.89). Participants showed comparable levels of overall self-rated self-compassion (*p*=.326), adaptive (*p*=.574) and maladaptive emotion regulation (*p*=.212) at baseline and post-intervention. We observed increases in momentary self-compassion at post-intervention (*p*=.023).

Table 19. *Basic sample and clinical characteristics.*

	Baseline	Post-intervention	Follow-up	Baseline vs. post-intervention
N_{max}	46	45	45	
Age at baseline (years), mean (*SD*)	21.30 (2.84)	-	-	
Gender, *N* (%)		-	-	
Female	35 (76%)			
Male	11 (24%)			
Non-binary	0			
Ethnicity, *N* (%)				
White majority	32 (70%)	-	-	
Minority				
Mixed white majority/white other	3 (7%)	-	-	
White other	4 (9%)	-	-	
Turkish	3 (7&)	-	-	
Mixed other	2 (4%)	-	-	
Middle east	1 (2%)	-	-	
Asian	1 (2%)			
Level of education, *N* (%)				
School: GCSEs	7 (15%)	-	-	
Further: A levels	14 (30%)	-	-	
Higher: university	25 (54%)	-	-	
Employment status, *N* (%)				
Student	39 (85%)	-	-	
School	4 (9%)	-	-	
Vocational training, University	35 (76%)	-	-	
Employed	4 (9%)	-	-	
Unemployed	3 (7%)	-	-	
Clinical stage at baseline, *N* (%)				
1a	26 (57%)	-	-	
1b	13 (28%)	-	-	
2	7 (15%)	-	-	
Level of functioning at baseline, mean *(SD)*	71.83 (9.89)	-	-	
Psychological distress, mean (*SD*)	28.20 (5.08)	24.11 (6.55)	22.73 (7.16)	
General psychopathology, mean *(SD)*	24.55 (9.94)	18.0 (12.03)	16.20 (10.68)	
Self-compassion				
Overall self-rating, mean *(SD)*	18.34 (2.77)	18.70 (2.06)	-	$t(42)=-0.99$, $p=.326$
Momentary rating, mean *(SD)*	3.89 (0.87)	4.30 (1.06)	-	$t(44)=-2.35$, $p=.023$
Emotion regulation				
Adaptive, mean *(SD)*	5.51 (1.45)	5.61 (1.57)	-	$t(42)=-0.57$, $p=.574$
Maladaptive, mean *(SD)*	5.97 (1.46)	5.64 (1.45)	-	$t(42)=1.27$, $p=.212$
Training frequency, mean *(SD)*	-	75.84 (85.09)	-	
Working alliance				
Patient rating, mean *(SD)*	-	48.07 (8.37)	-	
Therapist rating, mean *(SD)*	-	46.74 (6.47)	-	

Note. Sample sizes varied due to missing values at baseline ($N_{max}=46$, $N_{min}=45$). SD=standard deviation. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002; Kessler et al., 2005). General psychopathology assessed with the 18-item version of the Brief Symptom Inventory (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Global Assessment of Functioning (American Psychiatric Association, 2002).

Sociodemographic, clinical and functional characteristics at baseline associated with putative mechanisms and processes of change

Table 20 shows the associations of sociodemographic, clinical and functional characteristics at baseline with change in self-compassion and emotion regulation. There was no evidence for initial signals that participants' characteristics at baseline were associated with change in overall self-rated self-compassion ($\delta_{\text{post-intervention – baseline}}$). For change in momentary self-compassion, we observed a tendency for an association with age (b=0.11, 95% CI 0.00 – 0.22): Older participants tended to show more pronounced change in momentary self-compassion from baseline to post-intervention. Clinical stage was associated with change in adaptive emotion regulation such that participants in stage 2 showed more pronounced positive changes in adaptive emotion regulation compared to participants in stage 1a (b=1.50, 95% CI 0.06 – 2.93). For change in maladaptive emotion regulation, we found a tendency for an association with general psychopathology such that participants with lower levels of psychopathology at baseline tended to show more pronounced reductions in maladaptive emotion regulation (b=0.08, 95% CI -0.01 – 0.16).

Table 21 shows the associations of sociodemographic, clinical and functional characteristics at baseline with working alliance and training frequency. We found no evidence for initial signals of associations of working alliance and training frequency with baseline characteristics.

Sociodemographic, clinical and functional characteristics, self-compassion and emotion regulation at baseline associated with clinical outcomes

Table 22 shows findings on associations of psychological distress with participants' characteristics and level of putative mechanisms at baseline, and predicted marginal means. There was some evidence for a main effect of momentary self-compassion such that higher momentary self-compassion at baseline tended to be associated with, on average, lower levels of psychological distress across post-intervention and follow-up assessments (b=-2.83, 95% CI -5.66 – 0.00). There was no evidence for main effects of sociodemographic or clinical characteristics, overall self-rated self-compassion, and emotion regulation on psychological distress.

Table 23 shows findings on associations of general psychopathology with participants' characteristics and level of putative mechanisms at baseline, and predicted marginal means. There was no evidence for initial signals of main effects of sociodemographic, clinical and functional characteristics on general psychopathology. Cross differences between high and low levels of baseline characteristics at the time points are presented in supplementary material 27.

Table 20. *Associations of sociodemographic, clinical and functional characteristics at baseline with change in self-compassion and emotion regulation.*

	Putative mechanisms and processes of change							
	Change in overall self-rated self-compassion		Change in momentary self-compassion		Change in adaptive emotion regulation		Change in maladaptive emotion regulation	
N	43		45		43		43	
	b (95% CI)	Effect size	*b* (95% CI)	Effect size	*b* (95% CI)	Effect size	*b* (95% CI)	Effect size
Age	-0.05 (-0.40 – 0.29)	0.00	0.11 (0.00 – 0.22)	0.10	-0.10 (-0.23 – 0.04)	0.05	-0.09 (-0.26 – 0.09)	0.03
Gender	0.81 (-1.68 – 3.29)	0.01	-0.07 (-0.85 – 0.71)	0.00	-0.70 (-1.70 – 0.30)	0.06	0.45 (-0.81 – 1.72)	0.02
Ethnic minority status	0.91 (-1.28 – 3.10)	0.02	-0.20 (-0.89 – 0.49)	0.01	0.07 (-0.81 – 0.95)	0.00	0.51 (-0.60 – 1.62)	0.02
Clinical stage		0.01		0.04		0.15		0.00
Stage 1b	0.57 (-1.66 – 2.81)		-0.31 (-1.03 – 0.40)		0.70 (-0.20 – 1.60)		0.18 (-0.95 – 1.32)	
Stage 2	-0.34 (-3.91 – 3.23)		0.27 (-0.81 – 1.34)		1.50 (0.06 – 2.93)		0.13 (-1.68 – 1.94)	
Psychological distress	-0.01 (-0.38 – 0.35)	0.00	0.03 (-0.09 – 0.14)	0.01	-0.02 (-0.16 – 0.13)	0.00	-0.15 (-0.34 – 0.03)	0.08
General psychopathology	-0.01 (-0.18 – 0.16)	0.00	0.03 (-0.02 – 0.09)	0.04	-0.04 (-0.11 – 0.03)	0.03	0.08 (-0.01 – 0.16)	0.09
Level of functioning	-0.01 (-0.11 – 0.10)	0.00	-0.02 (-0.06 – 0.01)	0.04	0.00 (-0.04 – 0.05)	0.00	0.01 (-0.05 – 0.07)	0.00

Note. CI=confidence interval. Effect size=partial η2. Stage 1a (individuals with psychological distress) were used as a reference category. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002; Kessler et al., 2005). General psychopathology assessed with the 18-item version of the Brief Symptom Inventory (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Global Assessment of Functioning (American Psychiatric Association, 2002).

Table 21. *Associations of sociodemographic, clinical and functional characteristics at baseline with working alliance and training frequency.*

	Putative mechanisms and processes of change					
	Working alliance – participant rating		Working alliance – therapist rating		Training frequency	
N	44		43		45	
	b (95% CI)	Effect size	*b* (95% CI)	Effect size	*b* (95% CI)	Effect size
Age	0.57 (-0.33 – 1.46)	0.05	0.17 (-0.59 – 0.94)	0.01	2.69 (-7.38 – 12.77)	0.01
Gender	2.55 (-3.93 – 9.03)	0.02	2.72 (-2.93 – 8.37)	0.03	12.80 (-85.02 – 9.43)	0.00
Ethnic minority status	1.89 (-3.65 – 7.44)	0.01	1.54 (-3.18 – 6.26)	0.01	-26.31 (88.48 – 35.86)	0.02
Clinical stage		0.09		0.04		0.05
Stage 1b	5.03 (-0.68 – 10.74)		-1.22 (-5.93 – 3.49)		26.07 (-38.45 – 90.60)	
Stage 2	-0.41 (-9.47 – 8.65)		3.51 (-4.00 – 11.02)		-41.07 (-141.05 – 58.91)	
Psychological distress	0.70 (-0.24 – 1.65)	0.06	0.33 (-0.46 – 1.12)	0.02	4.83 (-5.80 – 15.47)	0.02
General psychopathology	0.00 (-0.44 – 0.44)	0.00	-0.13 (-0.49 – 0.23)	0.02	-1.82 (-6.74 – 3.11)	0.02
Level of functioning	0.01 (-0.28 – 0.29)	0.00	0.11 (-0.14 – 0.36)	0.02	-0.31 (-3.50 – 2.87)	0.00

Note. CI=confidence interval. Effect size=partial η2. Stage 1a (individuals with psychological distress) were used as a reference category. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002; Kessler et al., 2005). General psychopathology assessed with the 18-item version of the Brief Symptom Inventory (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Global Assessment of Functioning (American Psychiatric Association, 2002).

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Table 22. *Associations of psychological distress with participants' characteristics, and level of putative mechanisms and processes at baseline, and predicted marginal means.*

	Post-intervention		Follow-Up			
	Predicted marginal mean (95% CI)	*SE*	Predicted marginal mean (95% CI)	*SE*	*b* (95% CI)	Effect size
Time					-7.46 (-37.20 – 22.29)	-1.16
Age					-0.31 (-1.04 – 0.42)	-0.05
Low	24.92 (22.26 – 27.57)	1.36	24.99 (22.33 – 27.65)	1.36		
Mean	24.03 (22.33 – 25.73)	0.87	22.62 (20.93 – 24.32)	0.87		
High	23.15 (20.44 – 25.86)	1.38	20.26 (17.55 – 22.96)	1.38		
Gender					-0.51 (-5.26 – 4.23)	-0.08
Female	24.16 (22.15 – 26.17)	1.03	23.90 (21.89 – 25.91)	1.03		
Male	23.65 (19.61 – 27.69)	2.06	18.45 (14.41 – 22.49)	2.06		
Ethnic minority status					2.39 (-4.40 – 9.18)	0.37
White majority	23.83 (22.02 – 25.64)	0.92	22.71 (20.91 – 24.52)	0.92		
Minority	26.22 (19.81 – 32.62)	3.27	22.11 (15.70 – 28.52)	3.27		
Clinical stage					-0.19 (-3.62 – 3.24)	-0.03
Stage 1 a	25.42 (23.12 – 27.73)	1.18	23.75 (21.44 – 26.05)	1.18		
Stage 1b	21.84 (18.58 – 25.10)	1.66	20.21 (16.95 – 23.46)	1.66		
Stage 2	22.62 (16.44 – 28.79)	3.15	23.37 (17.19 – 29.55)	3.15		
General psychopathology at baseline					0.04 (-0.29 – 0.38)	0.01
Low	23.62 (19.88 – 27.37)	1.91	18.79 (15.05 – 22.54)	1.91		
Mean	24.03 (22.33 – 25.74)	0.87	22.56 (20.86 – 24.26)	0.87		
High	24.45 (20.85 – 28.04)	1.83	26.33 (22.73 – 29.92)	1.83		
Level of functioning at baseline					-0.10 (-0.30 – 0.11)	-0.02
Low	25.02 (22.34 – 27.70)	1.37	22.27 (19.59 – 24.95)	1.37		
Mean	24.07 (22.37 – 25.77)	0.87	22.65 (20.95 – 24.35)	0.87		
High	23.12 (20.52 – 25.72)	1.33	23.03 (20.43 – 25.63)	1.33		
Overall self-rated self-compassion at baseline					0.06 (-0.83 – 0.94)	0.01
Low	23.81 (19.66 – 27.95)	2.11	21.28 (17.14 – 25.43)	2.11		
Mean	24.02 (22.29 – 25.76)	0.89	22.53 (20.79 – 24.26)	0.89		
High	24.24 (20.74 – 27.74)	1.79	23.77 (20.27 – 27.28)	1.79		
Momentary self-compassion at baseline					-2.83 (-5.66 – 0.00)	-0.37
Low	26.60 (23.53 – 29.68)	1.57	23.05 (19.97 – 26.12)	1.57		
Mean	24.17 (22.47 – 25.88)	0.87	22.68 (20.98 – 24.38)	0.87		
High	21.74 (18.88 – 24.60)	1.46	22.31 (19.45 – 25.17)	1.46		
Adaptive emotion regulation at baseline					-0.36 (-1.96 – 1.24)	-0.06
Low	24.57 (21.68 – 27.45)	1.47	24.01 (21.13 – 26.90)	1.47		
Mean	24.01 (22.35 – 25.74)	0.87	22.66 (20.96 – 24.63)	0.87		
High	23.52 (20.64 – 26.41)	1.47	21.30 (18.42 – 24.19)	1.47		
Maladaptive emotion regulation at baseline					0.03 (-1.74 – 1.80)	0.00
Low	24.00 (20.92 – 27.08)	1.57	20.53 (17.45 – 23.62)	1.57		
Mean	24.05 (22.35 – 25.74)	0.87	22.66 (20.96 – 24.36)	0.87		
High	24.09 (21.01 – 27.17)	1.57	24.78 (21.70 – 27.86)	1.57		

Note. Results were adjusted for baseline levels of psychological distress. CI=confidence interval. SE=standard error. Effect size=d-type effect size. Low=mean – 1 SD. High=mean + 1 SD. Stage 1a (individuals with psychological distress) was used as a reference category. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002; Kessler et al., 2005). General psychopathology assessed with the 18-item version of the Brief Symptom Inventory (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Global Assessment of Functioning (American Psychiatric Association, 2002)

Table 23. *Associations of general psychopathology with participants' characteristics, and level of putative mechanisms and processes at baseline, and predicted marginal means.*

	Post-intervention		Follow-Up			
	Predicted marginal mean (95% CI)	SE	Predicted marginal mean (95% CI)	SE	b (95% CI)	Effect size
Time					-25.10 (-56.83 – 6.63)	-2.38
Age					-0.79 (-2.05 – 0.46)	-0.08
Low	19.75 (15.20 – 24.29)	2.32	18.27 (13.72 – 22.81)	2.32		
Mean	17.49 (14.58 – 20.39)	1.48	16.06 (13.15 – 18.96)	1.48		
High	15.23 (10.61 – 19.86)	2.36	13.85 (9.22 – 18.48)	2.36		
Gender					-2.14 (-10.25 – 5.97)	-0.20
Female	18.01 (14.57 – 21.45)	1.76	17.44 (14.00 – 20.88)	1.76		
Male	15.87 (8.96 – 22.78)	3.53	11.49 (4.58 – 8.40)	3.53		
Ethnic minority status					1.40 (-10.21 – 13.02)	0.13
White majority	17.40 (14.30 – 20.49)	1.58	15.69 (12.60 – 18.78)	1.58		
Minority	18.80 (7.84 – 29.75)	5.59	20.10 (9.15 – 31.06)	5.59		
Clinical stage					-0.97 (-6.84 – 4.89)	-0.09
Stage 1a	19.07 (15.13 – 23.01)	2.01	18.29 (14.35 – 22.23)	2.01		
Stage 1b	14.32 (8.75 – 19.88)	2.84	11.60 (6.03 – 17.17)	2.84		
Stage 2	17.82 (7.26 – 28.39)	5.39	16.34 (5.77 – 26.91)	5.39		
Psychological distress at baseline					-0.27 (1.55 – 1.01)	-0.03
Low	18.83 (12.03 – 25.63)	3.47	19.44 (12.64 – 26.25)	3.47		
Mean	17.52 (14.61 – 20.42)	1.48	16.07 (13.17 – 18.98)	1.48		
High	16.20 (9.35 – 23.06)	3.50	12.71 (5.85 – 19.56)	3.50		
Level of functioning at baseline					-0.13 (-0.48 – 0.22)	-0.01
Low	18.84 (14.26 – 23.43)	2.34	15.01 (10.43 – 19.60)	2.34		
Mean	17.56 (14.65 – 20.46)	1.48	16.06 (13.16 – 18.97)	1.48		
High	16.27 (11.82 – 20.72)	2.27	17.11 (12.66 – 21.57)	2.27		
Overall self-rated self-compassion at baseline					0.31 (-1.20 – 1.83)	0.03
Low	16.18 (9.09 – 23.27)	3.62	10.90 (3.81 – 17.99)	3.62		
Mean	17.39 (14.43 – 20.36)	1.51	15.60 (12.63 – 18.57)	1.51		
High	18.61 (12.62 – 24.60)	3.05	20.29 (14.31 – 26.28)	3.05		
Momentary self-compassion at baseline					-3.24 (-8.08 – 1.61)	-0.31
Low	20.45 (15.19 – 25.70)	2.68	15.26 (10.01 – 20.52)	2.68		
Mean	17.67 (14.76 – 20.58)	1.49	16.05 (13.14 – 18.96)	1.49		
High	14.89 (9.99 – 19.79)	2.50	16.84 (11.94 – 21.73)	2.50		
Adaptive emotion regulation at baseline					0.32 (-2.42 – 3.06)	0.03
Low	17.06 (12.13 – 22.00)	2.52	19.47 (14.53 – 24.41)	2.52		
Mean	17.52 (14.62 – 20.43)	1.48	16.09 (13.19 – 19.00)	1.48		
High	17.98 (13.05 – 22.92)	2.52	12.71 (7.78 – 17.65)	2.52		
Maladaptive emotion regulation at baseline					0.97 (-2.42 – 3.06)	0.09
Low	16.11 (10.84 – 21.38)	2.69	14.42 (9.15 – 19.69)	2.69		
Mean	17.52 (14.62 – 20.43)	1.48	16.09 (13.19 – 19.00)	1.48		
High	18.93 (13.67 – 24.20)	2.69	17.76 (12.49 – 23.03)	2.69		

Note. Results were adjusted for baseline levels of psychological distress. CI=confidence interval. SE=standard error. Effect size=d-type effect size. Low=mean – 1 SD. High=mean + 1 SD. Stage 1a (individuals with psychological distress) was used as a reference category. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002; Kessler et al., 2005). General psychopathology assessed with the 18-item version of the Brief Symptom Inventory (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Global Assessment of Functioning (American Psychiatric Association, 2002)

5.5.   Discussion

Main findings

First, we developed a hybrid six-week CFI comprising two intervention tracks with varying foci and demand levels. Second, we observed initial signals of effects of age, general psychopathology and clinical stage on change in momentary self-compassion and change in emotion regulation. Older participants tended to show greater differences in momentary self-compassion comparing baseline and post-intervention assessments. Participants classified as stage 2 were found to show greater differences in adaptive emotion regulation comparing baseline and post-intervention assessments. In addition, participants with lower levels of psychopathology at baseline showed more pronounced reductions in maladaptive emotion regulation from baseline to post-intervention assessments. There was no evidence for associations of other baseline characteristics (e.g. gender, minority status, level of functioning) and putative mechanisms (i.e., overall self-rated self-compassion, working alliance, training frequency). Third, there was some evidence that higher momentary self-compassion at baseline tended to be associated with, on average, lower levels of psychological distress across post-intervention and follow-up assessments. We observed no other initial signals that clinical or functional characteristics at baseline impacted on clinical outcomes.

Methodological considerations

The reported results should be interpreted in the light of several methodological considerations and limitations: First, sample size and selection as well as the exploratory nature of the analyses need to be critically appraised. Although the analyses were prospectively registered, they reflect secondary analyses with an increased risk of type I error. As noted, our findings reflect initial signals of associations of participants' baseline characteristics with putative mechanisms, processes and outcomes. Moreover, it should be taken into account that boys/men, individuals identifying as non-binary, and participants from stage 2 (first episode of severe mental disorder) were considerably underrepresented in the sample. However, the gender difference in recruitment may partly be explained by higher prevalence of depressive and anxiety disorders in women and adolescent girls (Afifi, 2007; Parker & Roy, 2001) and the exclusion of mental health problems that are especially prevalent in men and adolescent boys (e.g. primary

substance abuse disorder; Kessler et al., 2005). Randomization in a future definitive trial may therefore need to stratify by gender to rule out potential confounding by this factor. In addition, we assessed ethnicity taking into account participants' self-report of citizenship, country of birth, first language and information provided in participants' family assessment. Grouping participants to broad categories of ethnicity inevitably implies that some participants may have assigned to a category they do not consider to belong to and, hence, misclassification. In general, the concept of using categories, for example with regard to ethnicity or gender, may be criticised as – of course – there is considerable heterogeneity within groups which needs to be further explored in qualitative analyses (Bhopal, 1997; Morgan et al., 2007). These limitations can be tolerated at the exploratory stage of developing a complex intervention, but should be addressed in future, definitive trials.

Second, operationalizations of putative mechanisms were not measured at multiple time points during the intervention period and difference scores were used as proxies for change in self-compassion and emotion regulation. While proxies are acceptable in this exploratory study, a future definitive trial may use multiple assessments during the intervention period to yield more fine-grained data on potential changes in mechanisms.

Third, the assessment of self-compassion needs to be critically appraised: In our analyses, overall self-rated self-compassion and momentary self-compassion were not correlated, indexing low convergent validity (see supplementary material 25). Similar phenomena have been observed before, for example, for negative symptoms measured with ESM and interviewer-rated measures, which may tap distinct but related constructs (Paetzold, Hermans, et al., 2021). This may be viewed as underscoring the relevance of assessment under real-time and real-world conditions, which is supported by moderate to large correlations of momentary self-compassion with clinical characteristics (i.e., clinical stage, psychological distress, general psychopathology, and level of functioning), indicating high concurrent validity. However, as the items for assessing momentary self-compassion were used for the first time in the current study, they may also not fully capture the construct of self-compassion as operationalised by the subscales in the SCS (i.e., they are more similar in content to items from the self-kindness than mindfulness subscale). In addition, we aggregated ESM data on momentary self-compassion at the person-level, which led to a loss of information in comparison to the level of ESM observations, given the repeated measurement and temporal variability ESM captures as an intensive longitudinal data collection method (Schick et al., 2022). Nonetheless, aggregated experience sampling measures may still capture the target constructs with less noise and greater sensitivity than

recall measures (Shiffman et al., 2008), so this may not reduce the current study's informative value substantially.

Forth, potential influences of the COVID-19 pandemic have not been statistically accounted for in current analyses and should be considered when interpreting the findings. Due to local regulations (e.g. lockdowns, contact restrictions), the intervention sessions were shifted from face-to-face contact to video calls. Recent systematic reviews and meta-analyses indicated no differences in telehealth and in-person psychotherapy (Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2018), but generalisability to settings in which both in-person sessions and an online format are used flexibly remains unclear and the impact cannot be determined with certainty without further research.

Comparison with previous research

To our knowledge, the EMIcompass intervention is the first hybrid CFI blending an EMI and face-to-face sessions designed to enhance self-compassion and resilience in young people with non-specific psychological distress, CHARMS, and first episode of severe mental disorder. Building on principles of EMIs (Myin-Germeys et al., 2018; Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus et al., 2015), EMIcompass combined different intervention elements: enhancing tasks provided participants with new CFI strategies. Consolidating tasks facilitated training in different contexts and translation into daily life increasing the chances of generalisation. Elements of experience sampling were used to increase reflective processing improving insight and awareness of own cognitive and emotional processes (Telford, McCarthy-Jones, Corcoran, & Rowse, 2012). This may be further improved by incorporating elements of feedback into future versions of the intervention (Kramer et al., 2014). In addition, assessing stress and affect in daily life allows the EMI to offer useful techniques in moments of high distress (i.e., interactive tasks) providing participants with support in challenging life situations.

For the EMIcompass intervention, results from an uncontrolled pilot study (Rauschenberg, Boecking, et al., 2021) indicated a reduction of stress reactivity at post-intervention and follow-up and reduced clinical symptoms at follow-up when compared to baseline. A recent exploratory RCT (Reininghaus et al., under review; Schick et al., 2021) indicated that all feasibility criteria were met and a reduction of stress reactivity in the experimental condition as the primary candidate mechanism in comparison to a control condition of TAU. In addition, it suggests initial signals that the EMIcompass intervention may have beneficial effects on resilience

in daily life and quality of life. Detailed findings on feasibility and initial signals of efficacy are described elsewhere (Reininghaus et al., under review).

Apart from an association of age and change in momentary self-compassion, participants' sociodemographic characteristics were not associated with putative processes, mechanisms and outcomes of the EMIcompass intervention. This is at variance with findings in traditional psychotherapy for depression and psychosis, where reviews indicate differential treatment effects for various sociodemographic characteristics (e.g. age, gender, marital status; K. E. Hamilton & Dobson, 2002; O'Keeffe, Conway, & McGuire, 2017). In an Acceptance and Commitment Therapy-based EMI in individuals at ultra-high-risk for psychosis and with a first episode of psychosis, ethnic minority status was associated with lower compliance and higher app usefulness, whereas being female predicted lower usefulness of the app's metaphor images (van Aubel et al., 2021).

When examining the impact of clinical and functional characteristics, we observed associations of clinical stage and general psychopathology with putative mechanisms and processes (i.e., change in momentary self-compassion and change in emotion regulation). Interestingly, *later* clinical stage was associated with a more pronounced increase in adaptive emotion regulation, whereas *lower* levels of general psychopathology tended to be associated with a more pronounced reduction of maladaptive emotion regulation. However, findings on clinical stage must be interpreted with caution given the small number of participants from stage 2 included in the study. The possibility of ceiling effects for a particular clinical stage could be ruled out, as the mean levels of adaptive emotion regulation were in the middle range of the scale for all clinical stages. An RCT of cognitive behavioural therapy in patients with psychotic disorders investigating predictors of improvement and drop-out indicated that higher symptom severity and poor level of functioning do not pose a barrier to improvement (Lincoln et al., 2014). Findings from an Acceptance and Commitment Therapy-based EMI in individuals at ultra-high-risk for psychosis and with a first episode of psychosis show a differentiated perspective on symptom severity: the severity of affective symptoms was associated with higher, the severity of negative symptoms was associated with lower perceived usefulness of the intervention (van Aubel et al., 2021). Besides sociodemographic, clinical and functional characteristics at baseline, we moved beyond these previous studies and examined potential associations of baseline levels of self-compassion and emotion regulation with outcomes of the intervention. We found some evidence that higher levels of momentary self-compassion at baseline were associated with, on average, lower levels of psychological distress across assessment time points. By showing this in a longitudinal intervention study, the current findings extend evidence from a meta-analysis

indicating associations of self-compassion and psychological distress in general (Marsh et al., 2018). However, in the current study, this did not hold true for overall self-compassion. Apart from the effects delineated above, there were no initial signals of associations, tentatively suggesting that participants' sociodemographic, clinical, and functional characteristics had little influence on their response to the EMIcompass intervention. This may indicate – within the limits of the variables assessed – that the EMIcompass intervention is relatively inclusive and reach of participants is largely independent from their sociodemographic, clinical, and functional baseline characteristics.

The role of digital approaches in improving reach of those in need within broader conceptualisations has been subject to controversial debate: Qualitative studies with health professionals and service users indicate that digital approaches were viewed as having the potential to improve inclusion, but also as having the risk of digital exclusion (Berry, Bucci, & Lobban, 2017; Bucci, Berry, et al., 2019; Greer et al., 2019). Concerns have been raised that digital approaches and the digital divide may further reinforce health inequalities (i.e. systematic, avoidable and unfair differences in health outcomes; McCartney, Popham, McMaster, & Cumbers, 2019) in marginalised and underserved populations, for example in racial and ethnic minorities (Friis-Healy, Nagy, & Kollins, 2021). Digital inequalities are suggested to comprise multiple continuous dimensions, for example, socioeconomic and educational background, migrant and ethnic minority status, and health literacy (S. C. Bailey et al., 2015; Cruz-Jesus, Vicente, Bacao, & Oliveira, 2016; Haight, Quan-Haase, & Corbett, 2014). To further improve our understanding of the consequences of digital inequalities for individuals' response to the EMIcompass intervention, future studies may broaden their perspective by including further aspects of marginalised and underserved populations (e.g. sexual minority status, socioeconomic background) and examining other criteria (e.g. level of functioning, satisfaction with the intervention, goal attainment, and quality of life) in addition to those considered so far.

To address digital exclusion of marginalised and underserved populations, demands for evidence-based digital inclusion strategies have been articulated (Robotham, Satkunanathan, Doughty, & Wykes, 2016) and potential pathways for improving inclusion in digtial approaches have been discussed. On the one hand, adaptations of interventions have been suggested: For example, feasibility and beneficial effects of cultural adaptation of interventions have already been demonstrated (Rathod et al., 2013). In addition to adapting interventions for specific groups, the needs and perspectives of individual participants should be taken into account in process evaluations combining quantitative and qualitative data (G. F. Moore et al., 2015). In line with this, we conducted a qualitative study incorporating realist methodology (Wong et al.,

2016) examining what works for whom under which circumstances in the EMIcompass study, the findings of which are reported elsewhere (Paetzold et al., in preparation). An emerging research field targets the adaptation of digital interventions on an individual level aiming at personalizing assessment and intervention (Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus et al., 2015). On the other hand, the creation of interventions for diverse populations has been suggested, for example, in the REACT recommendations (Friis-Healy et al., 2021). In line with this approach, a recent review of digital mental health interventions specifically designed for marginalised populations indicated promising results on feasibility and acceptability in pilot studies but also a lack of larger-scale examinations (Schueller, Hunter, Figueroa, & Aguilera, 2019).

Conclusions

We developed the first hybrid CFI combining an EMI and face-to-face sessions with two intervention tracks and varying foci and demand levels to enhance resilience in young people with early mental health problems. We aimed at exploring whether participants' characteristics at baseline were associated with putative mechanisms and outcomes of the EMIcompass intervention. Findings indicated reach of participants by the intervention largely independently from sociodemographic, clinical, and functional baseline characteristics. The findings need to be confirmed in a definitive trial.

CHAPTER VI:

EXPLORING PUTATIVE THERAPEUTIC MECHANISMS OF CHANGE IN A HYBRID COMPASSION-FOCUSED, ECOLOGICAL MOMENTARY INTERVENTION: FINDINGS FROM THE EMICOMPASS TRIAL

This chapter is currently under review as 'Paetzold I., Schick A., Rauschenberg C., Hirjak D., Banaschewski T., Meyer-Lindenberg A., … & Reininghaus U. (under review). Exploring putative therapeutic mechanisms of change in a hybrid compassion-focused, ecological momentary intervention: Findings from the EMIcompass trial.'

6.1.   Abstract

Compassion-focused interventions represent a promising transdiagnostic approach, but the mechanisms involved in hybrid delivery combining face-to-face sessions and an ecological momentary intervention remain unexplored. The current study aimed at exploring associations of putative mechanisms with clinical outcomes at post-intervention/follow-up and mediation of outcome at follow-up by preceding pre- to post-intervention changes in putative mechanisms. The compassion-focused EMIcompass intervention was applied in an exploratory randomised controlled trial (TAU vs. TAU + EMIcompass) with youth with early mental health problems. Data was collected before randomization, at post-intervention and at four-week follow-up. We recruited N=92 participants, N=46 were allocated to the experimental condition. After control for baseline levels of the target outcomes, baseline- to post-intervention improvement in adaptive emotion regulation was associated with lower levels of clinical outcomes (e.g. psychological distress b=-1.15; 95% CI -1.92 – -0.39) across time points. We did not detect indirect effects, but we observed associations of change in self-compassion and adaptive emotion regulation with outcomes at follow-up in the mediation analysis (e.g. β=-0.35, 95% CI -0.52 – -0.16). If successfully targeted by interventions, self-compassion and emotion regulation may be promising putative therapeutic mechanisms of change.

6.2. Introduction

Adolescents and young adults are particularly affected by mental health problems and therefore reflect a priority target population for prevention and early intervention (McGorry, Purcell, Hickie, & Jorm, 2007). Three-quarters of all lifetime cases emerge before the age of 24 (Kessler et al., 2005) and there is evidence for a 12-month prevalence of mental disorders in youth of approximately 25% (Merikangas et al., 2009). As the "chronic diseases of the young" (Insel & Fenton, 2005; WHO World Mental Health Survey Consortium, 2004), mental health problems contribute substantially to the disease burden in young age groups (Erskine et al., 2015; Gore et al., 2011).

Evidence has accumulated that various (sub)clinical symptoms often co-occur and overlap and clinical trajectories have been described to develop from relatively mild or non-specific symptoms and psychological distress to attenuated symptoms and the emergence of severe mental disorders (McGorry et al., 2006; Reininghaus, Böhnke, et al., 2016; Reininghaus et al., 2013; Shevlin et al., 2016; van Os & Reininghaus, 2016). Consequently, dimensional approaches of classification and clinical staging models taking into account the overlapping and nonspecific nature of early psychopathology have been proposed (Cross et al., 2014; Forbes et al., 2016; Hartmann et al., 2019; Hickie et al., 2013; Insel et al., 2010; Iorfino et al., 2019; Kotov et al., 2017; McGorry et al., 2006; McGorry, Purcell, Hickie, Yung, et al., 2007; Shah et al., 2020). Acknowledging the heterogeneous pathways for youth with subclinical symptoms, transdiagnostic clinical staging models provide a broad set of at-risk criteria and highlight the relevance of tailored prevention and early intervention approaches that may help to delay or prevent severe mental disorder (Hartmann et al., 2019).

Stress reactivity (i.e., increased negative affect in response to minor daily stressors) may be an especially promising transdiagnostic target mechanism in the context of prevention and early intervention (Myin-Germeys et al., 2018). Elevated stress reactivity has been reported in adults with depression, clinical and subclinical phenotypes of psychosis, and help-seeking adolescent service users (Lataster et al., 2009; Myin-Germeys et al., 2001; Myin-Germeys et al., 2003; Rauschenberg et al., 2017; van der Steen et al., 2017). CFIs may be especially suitable to target stress reactivity, as they aim to strengthen individuals' 'soothing system' comprising emotions such as calmness and peacefulness to balance a mostly overactive 'threat system' comprising emotions such as anxiety, anger or shame (P. Gilbert, 2009, 2013, 2014). The compassion-focused approach is not symptom-specific and can be used to support individuals struggling with a wide range of mental health problems (Ascone et al., 2017; Cuppage et al., 2018; Gale

et al., 2014; Heriot-Maitland et al., 2019; Kirby et al., 2017; Leaviss & Uttley, 2015). Imagery-based compassion-focused techniques activate positive affect, self-acceptance and -compassion (P. Gilbert, 2009; Holmes, Blackwell, Heyes, et al., 2016; Lincoln et al., 2013) and may therefore be especially appropriate to target stress reactivity in daily life. Laboratory studies provided initial evidence that CFIs reduced state negative affect and paranoia in moments of high stress (Lincoln et al., 2013; Pearson et al., 2015).

Despite convincing evidence on beneficial effects for standard approaches of (early) intervention (Correll et al., 2018; Cuijpers et al., 2013; Hofmann & Smits, 2008; Hunot et al., 2013; Kirby et al., 2017; Shawyer et al., 2017), important challenges, especially for youth mental health, remain: e.g. a large treatment/ care gap (Alonso et al., 2018; Dua et al., 2011; Evans-Lacko et al., 2018; Pathare, Brazinova, & Levav, 2018; Rice, Eyre, Riglin, & Potter, 2017; Thornicroft, 2007), persistence of residual symptoms and relapse after successful intervention (Buckman et al., 2018; Fava et al., 2007), low availability, access and use of youth mental health services (Malla et al., 2016; Wang et al., 2005). These challenges may be targeted by smartphone-based mHealth interventions offering the opportunity to extend therapy and prevention beyond standard settings and facilitate low-threshold access to mental health services for the generation of digital natives (Myin-Germeys et al., 2016; Rauschenberg, Schick, Goetzl, et al., 2021; Rauschenberg, Schick, Hirjak, et al., 2021; Reininghaus, 2018; Reininghaus et al., 2015; Schick et al., 2021). EMA or ESM, structured self-report diary methods, can be used to obtain highly ecologically valid assessments of appraisals of symptoms, experiences, context and behaviour in real-time and under real-world conditions (Csikszentmihalyi & Larson, 1987; Myin-Germeys et al., 2018; Myin-Germeys et al., 2009; Schick et al., 2022; Shiffman et al., 2008). EMIs embrace the principle of experience sampling that experience and behaviour are situated in the given context and therefore also are best modified in the context of service users' daily life (Heron & Smyth, 2010; Myin-Germeys et al., 2011; Myin-Germeys et al., 2018; Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus et al., 2015). Recent findings from a nationally representative survey in Germany demonstrated that adolescents and young adults do already use mHealth apps frequently and that distressed young individuals are even more likely to do so (Rauschenberg, Schick, Goetzl, et al., 2021). However, the majority of apps currently available in major app stores is not based on scientific evidence (Larsen et al., 2019; Mercurio et al., 2020; Rauschenberg, Schick, Hirjak, et al., 2021; Weisel et al., 2019).

To contribute to addressing this pressing gap in youth mental health, EMIcompass was developed as a transdiagnostic intervention for enhancing resilience in youth with early mental health problems. It is a six-week hybrid intervention combining three face-to-face training sessions

and a review session with a trained psychologist with an EMI aiming at enhancing self-compassion, improving self-care and reducing stress reactivity in daily life (Paetzold, Schick, et al., 2022; Schick et al., 2021). EMIcompass builds on compassion-focused principles (P. Gilbert, 2009, 2013, 2014). An uncontrolled pilot study provided initial evidence on feasibility, safety and beneficial effects in the form of reductions in stress reactivity and clinical symptoms for a prototype version of the EMIcompass intervention (Rauschenberg, Boecking, et al., 2021). Based on these findings, the intervention was optimised and applied in an exploratory RCT registered in Germany (Reininghaus, 2019; Schick et al., 2021). The RCT compares a control condition of TAU with an experimental condition of TAU + EMIcompass in youth with early mental health problems. There is evidence on beneficial effects of CFIs, but the mechanisms involved remain largely unclear for standard delivery and even more so for mHealth interventions building on compassion-focused principles (Ferrari et al., 2019; Kirby et al., 2017). In the following, we will present and discuss several putative therapeutic mechanisms of change for the hybrid EMIcompass intervention.

Increased *self-compassion* may be a putative key mechanism of change to consider (MacBeth & Gumley, 2012; Marsh et al., 2018; Xavier et al., 2016). Meta-analyses reported moderate effect sizes of CFIs on self-compassion (Ferrari et al., 2019) and large effect sizes for the associations between self-compassion, psychological distress and psychopathology (MacBeth & Gumley, 2012; Marsh et al., 2018). Recently, a systematic review concluded that CFIs increase self-compassion and suggested that compassion may directly reduce psychopathology (Craig et al., 2020). However, to our knowledge, this pathway has not been explored in a hybrid CFI yet.

In addition, improvement in *emotion regulation* has been discussed as a putative mechanism linking CFIs and clinical improvements (Ferrari et al., 2019). Over the last decades, theoretical models of emotion regulation have postulated several strategies to be adaptive or maladaptive (for an overview, see Aldao et al., 2010), and a meta-analytic review demonstrated associations of emotion regulation strategies with general psychopathology across different mental health problems (Aldao et al., 2010). Furthermore, there is initial evidence from a longitudinal study suggesting that maladaptive emotion regulation strategies may be putative transdiagnostic mechanisms underlying the association of child maltreatment and psychopathology in later life (Weissman et al., 2019). Finlay-Jones (2017) proposed that CFIs may enhance adaptive emotion regulation strategies which, in turn, may positively impact on clinical outcomes. Again, this has not been explored in a hybrid CFI yet.

Moreover, *training frequency* may be an important putative mechanism. Practicing between sessions is an integral part of many psychotherapeutic interventions (e.g. Cognitive Behavioural Therapy, Mindfulness-Based Cognitive Therapy; Kazantzis, Deane, Ronan, & L'Abate, 2005; Kazantzis et al., 2016; Segal, Williams, & Teasdale, 2012) and programmes for mental health promotion (e.g. Mindfulness-Based Stress Reduction, Progressive Muscle Relaxation; Kabat-Zinn & Hanh, 1990; McGuigan & Lehrer, 2007). Meta-analytic evidence indicates associations of homework compliance/ home practice and outcomes of small to moderate effect size in clinical and non-clinical populations (Kazantzis et al., 2010; Kazantzis et al., 2016; Mausbach et al., 2010; Parsons, Crane, Parsons, Fjorback, & Kuyken, 2017). For a hybrid intervention with a reduced number and frequency of face-to-face sessions, training frequency may be even more important.

In addition*, working alliance*, conceptualised as the agreement between service user and clinician on the goals of the treatment and about the tasks to achieve these goals as well as the quality of the bond between the service user and the clinician (Bordin, 1979), may also be considered. Meta-analyses and reviews provide convincing evidence on the association of working alliance and outcomes across non-clinical coaching (e.g. career counselling, executive coaching (e.g. career counselling, executive coaching; Pandolfi, 2020; Whiston, Rossier, & Barón, 2016) and clinical settings, including therapy for different mental health problems in adults and adolescents (Horvath et al., 2011; Martin et al., 2000; Murphy & Hutton, 2018; Shirk & Karver, 2003). A review of the existing literature demonstrated that alliance mediated effects of treatment on outcomes in 70% of all studies included (Baier et al., 2020). Whereas the role of working alliance is well researched in classic coaching and psychotherapeutic settings, a recent review identified only five studies that discuss working alliance when a mobile application intervention is involved in treatment (Henson et al., 2019).

To further improve mobile interventions, elucidating putative mechanisms of change is of crucial importance. The current study therefore aimed at examining change in self-compassion, change in emotion regulation, training frequency and working alliance as putative therapeutic mechanisms in the EMIcompass trial. In light of the above, we aimed to obtain first parameter estimates and explore initial signals as to whether:

1) putative mechanisms (i.e., change in self-compassion ($\delta_{\text{post-intervention – baseline}}$), change in adaptive and maladaptive emotion regulation ($\delta_{\text{post-intervention – baseline}}$), training frequency (total score), and working alliance (total score)) are associated with psychological distress and general psychopathology as outcome variables across post-intervention and

four-week follow-up, whilst controlling for baseline levels of outcome variables and sociodemographic characteristics, and obtain 95% confidence intervals.

2) the effects of experimental condition on psychological distress and general psychopathology as outcome variables at four-week follow-up are mediated via

    a. change in overall self-rated and momentary self-compassion ($\delta_{\text{post-intervention – baseline}}$),

    b. change in adaptive and maladaptive emotion regulation ($\delta_{\text{post-intervention – baseline}}$),

whilst controlling for baseline levels of outcome variables and sociodemographic characteristics.

6.3.   Method

Study design

We examined young individuals in an exploratory RCT comparing a control condition of TAU and an experimental condition of TAU + EMIcompass. The RCT was conducted between August 2019 and September 2021. An independent researcher conducted randomization using a computer-generated sequence. Data on candidate mechanisms and outcomes was collected before randomization (i.e., at baseline), at the end of the intervention period, and at four-week follow-up. The study protocol (Schick et al., 2021) provides further information on the trial's methods.

Participants

Based on a modification of the clinical staging model (Hartmann et al., 2019; Schick et al., 2021), we recruited youth aged 14 to 25 with current psychological distress (stage 1a), clinical high at-risk mental state (stage 1b) or a first treated episode of severe mental disorder (depression, bipolar disorder, anxiety disorder and psychosis, stage 2). Eligibility to participate was assessed using self-report questionnaires and observer ratings. Participants (and caregivers for minors) provided informed consent and received compensation for their time and travel expenses.

Measures

Sociodemographic characteristics

Self-reported age and gender were used as sociodemographic characteristics. We constructed a proxy for ethnicity based on participants' self-reports of citizenship, country of birth, first language and family anamnesis assessed by the research team.

Putative mechanisms and processes of change

Self-compassion

We used an overall self-rating questionnaire and ESM measures to assess participants' self-compassion. To obtain overall ratings of self-compassion, we used the Self-Compassion Scale (Hupfeld & Ruffieux, 2011). In line with Neff (2003), we re-coded items from the subscales self-judgement, isolation and over-identification. We then calculated a mean for each subscale, and finally summed the means to create a total self-compassion score. We observed excellent internal consistency (α=.90, full sample) at baseline. We used three experience sampling items ("I feel safe.", "I feel benevolent.", "I like myself.") with a 7-point Likert-scale ranging from 1 (=not at all) to 7 (=very much) to assess momentary self-compassion. Experience sampling questionnaires were offered eight times a day at six consecutive days at baseline and post-intervention. We aggregated participants' ratings of momentary self-compassion to a mean score for each assessment week (baseline, post-intervention) and observed good internal consistency for this score (α=.88, full sample). To indicate change in self-compassion from baseline to post-intervention, we calculated difference scores ($\delta_{\text{post-intervention – baseline}}$) for overall self-rated and momentary self-compassion.

Emotion regulation

A short version of the Cognitive Emotion Regulation Questionnaire (CERQ-short), an 18-item questionnaire capturing nine cognitive emotion regulation strategies (self-blame, other-blame, rumination, catastrophizing, positive refocusing, planning, positive reappraisal, putting into perspective and acceptance) on a 5-point Likert scale ranging from 1 (=almost never) to 5 (=almost always), was used to assess emotion regulation (Garnefski & Kraaij, 2006). Following the scoring manual (Garnefski et al., 2002), we calculated sum scores for each subscale. In line with the approaches of Martins et al. (2016) and R. J. Murray et al. (2021), we classified the

coping strategies as adaptive (acceptance, putting into perspective, positive refocusing, refocus on planning and positive reappraisal) or maladaptive (self-blame, rumination, catastrophizing and other-blame) and aggregated the values to mean scores for adaptive and maladaptive coping strategies. We observed satisfying or good internal consistency (adaptive emotion regulation α=.82, maladaptive emotion regulation α=.71, full sample) at baseline. To indicate change from baseline to post-intervention, we calculated difference scores ($\delta_{\text{post-intervention} - \text{baseline}}$) for adaptive and maladaptive emotion regulation.

Training frequency

The total number of training exercises completed in the EMI was used as a proxy for training frequency.

Working alliance

The Working Alliance Inventory for Patients and Therapists (WAI-P/WAI-T; Horvath & Greenberg, 1989) was used to obtain sum scores for patient and therapist ratings as measures of working alliance. We obseverved excellent internal consistencies for both versions (participant ratings: α=.92, therapist ratings α=.93, experimental condition).

Outcome variables

Psychological distress

The Kessler Psychological Distress Scale (K10; Kessler et al., 2002; Kessler et al., 2005) was used to assess psychological distress. The K10 is a 10-item questionnaire capturing psychological distress in the last month on a scale from 1 (=never) to 5 (=always). To obtain a measure of psychological distress, a sum score was calculated. We observed good internal consistency (α=.76 – .87, full sample across time points).

General psychopathology

General psychopathology was assessed using a short version of the Brief Symptom Inventory with 18 items (BSI-18; Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Participants rated to what extend they experienced the listed 18 symptoms in the last seven days on a 5-point Likert-scale ranging from 0 (=not at all) to 4 (=very strong). We used the Global Severity Index (GSI,

the sum score across all items) as a measure of general psychopathology. Internal consistency at baseline was good (α=.85 – .90, full sample across time points).

Statistical analysis

The study was registered on the open science framework prior to accessing the data (Paetzold, Schick, Rauschenberg, Hirjak, Banaschewski, Meyer-Lindenberg, Boehnke, et al., 2021). Given the exploratory nature of the analysis, parameter estimates (95% confidence intervals) were obtained for all aims. To explore aim 1, we fitted separate models for each putative mechanism. First, we examined main effects of putative mechanisms (i.e., change in self-compassion and change in adaptive and maladaptive emotion regulation ($\delta_{post-intervention – baseline}$), working alliance (total scores for participants and psychologists at post-intervention), and training frequency (total score)) on outcomes across the two time points (i.e., post-intervention, four-week follow-up). Therefore, we fitted mixed effects regression models with psychological distress and general psychopathology as dependent variables. Independent variables in these models were: time (2-level factor), putative mechanisms of change, baseline levels of outcome variables, age, gender (2-level factor), and ethnic minority status (2-level factor). For change in self-compassion and change in emotion regulation, difference scores ($\delta_{post-intervention – baseline}$) were used and the analysis was performed in the full sample. For working alliance and training frequency, total scores were used. As working alliance and training frequency could only be measured in the experimental condition, the analysis was limited to the experimental condition. We took into account the within-subject clustering of repeated measures by adding a level-2 random intercept. We obtained parameter estimates for the main effects of mechanisms on outcomes across the two time points (i.e., post-intervention, four-week follow-up). Second, the above models were extended by a mechanism × time interaction. Predicted margins were calculated (Stata: 'margins' command) for each interaction for both time points and low (- 1 *SD*), mean, and high (+ 1 *SD*) levels of putative mechanisms of change. To facilitate the interpretation of predicted margins, we used unstandardised variables. Third, results were transformed into an effect size. Therefore, the model was run including only a random intercept for participants, the estimated target relationship as well as the baseline control to obtain the conditional and pooled variance across both assessment time points. The resulting estimate is on a similar scale as other typical d-type effect sizes and if additional random effects were strong, these variances are underestimations and the effect sizes in the following likely at the upper possible limit.

To explore whether the effects of experimental condition on psychological distress and general psychopathology as outcome variables at four-week follow-up were mediated via change in self-compassion and change in emotion regulation (aim 2), we fitted mediation models with psychological distress and general psychopathology at four-week follow-up as the dependent variables, change in self-compassion ($\delta_{\text{post-intervention – baseline}}$, aim 2a) and change in emotion regulation ($\delta_{\text{post-intervention – baseline}}$, aim 2b) as mediators and condition as independent variable in the full sample. We controlled for baseline levels of outcome variables, age, gender (2-level factor), and ethnic minority status (2-level factor). In additional sensitivity analyses, we also controlled for clinical stage (3-level factor; stage 1a vs stage 1b vs stage 2, see supplementary material 28). We obtained parameter estimates for the main effects of condition and change in self-compassion/ change in emotion regulation on outcomes at four-week follow-up and of condition on change in self-compassion/ change in emotion regulation. The total effects of experimental condition on psychological distress and general psychopathology were apportioned into direct and indirect effects through change in self-compassion/ change in emotion regulation. The indirect effects were computed using the product of coefficients strategy. We computed the proportion mediated (i.e., the ratio of the indirect effect to the total effect) as a measure of effect size (MacKinnon, Fairchild, & Fritz, 2007; Shrout & Bolger, 2002). Continuous variables were z-standardised. In line with recommendations of Preacher, Rucker, and Hayes (2007), we used bootstrapping for the mediation analyses.

The analysis was conducted according to intention to treat principles, with data from all participants entered into the analysis including those who have low adherence to, or who dropped-out from, the intervention. We applied restricted maximum likelihood (aim 1) or maximum likelihood estimation (aim 2), allowing for the use of all available data under the relatively unrestrictive assumption that data is missing at random and all variables associated with missing values are included in the model.

6.4.   Results

Basic sample characteristics

An overview of basic sample characteristics is displayed in table 24. The full sample comprised N=92 individuals, of which N=46 were randomised to the experimental condition of TAU + EMIcompass. The mean age was 21.7 years (SD=2.48, range 14 – 25 years), 73% were women.

Table 24. *Basic sample characteristics.*

	Full sample	Experimental condition	Control condition
N	92	46	46
Age (years), mean (*SD*)	21.7 (2.48)	21.3 (2.84)	22.0 (2.04)
Gender, *N* (%)			
Male	25 (27%)	11 (24%)	14 (30%)
Female	67 (73%)	35 (76%)	32 (70%)
Ethnicity, *N* (%)			
White majority German	72 (78%)	35 (76%)	32 (70%)
Minority			
Mixed white majority	5 (5%)	3 (7%)	2 (4%)
White other	5 (5%)	4 (9%)	1 (2%)
Turkish	4 (4%)	3 (7%)	1 (2%)
Mixed other	3 (3%)	2 (4%)	1 (2%)
Middle east	2 (2%)	1 (2%)	1 (2%)
Asian	1 (1%)	1 (2%)	0 (0%)
Group status, *N* (%)			
1a	52 (58%)	26 (57%)	26 (59%)
1b	27 (29%)	13 (30%)	14 (28%)
2	13 (13%)	7 (13%)	6 (13%)
Psychological distress, mean (*SD*)			
At baseline	28.08 (5.12)	28.20 (5.08)	27.96 (5.21)
At post-intervention	23.76 (6.53)	24.11 (6.55)	23.41 (6.56)
At follow-up	22.50 (6.71)	22.73 (7.16)	22.26 (6.27)
General psychopathology, mean *(SD)*			
At baseline	23.28 (10.49)	24.55 (9.34)	22.00 (10.97)
At post-intervention	17.45 (11.27)	18.00 (12.03)	16.89 (10.54)
At follow-up	15.69 (10.36)	16.20 (10.68)	15.16 (10.11)
Overall self-compassion, mean (*SD*)			
At baseline	17.84 (3.37)	18.34 (2.77)	17.34 (3.84)
At post-intervention	18.32 (2.24)	18.70 (2.06)	17.93 (2.40)
Momentary self-compassion, mean (*SD*)			
At baseline	3.98 (0.92)	3.89 (0.87)	4.06 (0.96)
At post-intervention	4.35 (1.02)	4.30 (1.06)	4.39 (0.99)
Adaptive emotion regulation, mean (*SD*)			
At baseline	5.64 (1.42)	5.51 (1.45)	5.77 (1.40)
At post-intervention	5.76 (1.51)	5.61 (1.57)	5.91 (1.45)
Maladaptive emotion regulation, mean (*SD*)			
At baseline	5.72 (1.29)	5.97 (1.46)	5.48 (1.06)
At post-intervention	5.50 (1.38)	5.64 (1.45)	5.35 (1.31)
Training frequency, mean (*SD*)	-	77.16 (87.66)	-
Working alliance, mean (*SD*)	-		-
Participant rating		48.07 (8.37)	
Psychologist rating		46.74 (6.47)	

Note. SD=standard deviation. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002; Kessler et al., 2005). General psychopathology assessed with the 18-item version of the Brief Symptom Inventory (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Self-compassion assessed with the Self-Compassion Scale (Hupfeld & Ruffieux, 2011) and ESM measures. Emotion regulation assessed with Cognitive Emotion Regulation Questionnaire. (Garnefski & Kraaij, 2006). Training frequency operationalized as total number of training exercises completed in the EMI. Working alliance assessed with the Working Alliance Inventory (Horvath & Greenberg, 1989).

Approximately a fifth (22%) of all participants were identified as having an ethnic minority background. The majority was classified as stage 1a (psychological distress, 58%), 29% ful-filled CHARMS criteria (stage 1b) and 13% were classified as stage 2 (first episode of a severe mental disorder).

Aim 1: Putative mechanisms of change are associated with outcome variables

Tables 25 and 26 show main effects of putative mechanisms of change and time on psycholog-ical distress and general psychopathology across post-intervention/follow-up and predicted marginal means for post-intervention and follow-up.

There was evidence for an association of greater differences in adaptive emotion regulation after the intervention with lower psychological distress (b=-1.15; 95% CI -1.92 – -0.39). In addition, there were initial signals of an association of change in maladaptive emotion regula-tion with psychological distress (b=0.74; 95% CI -0.01 – 1.66). Greater reductions in maladap-tive emotion regulation after the intervention tended to be associated with lower levels of psy-chological distress. Moreover, there were initial signals of a potential main effect of psycholo-gist-rated working alliance (b=0.19; 95% CI -0.02 – 0.41). There was no evidence of initial signals of associations of psychological distress with self-compassion or training frequency.

There was evidence for an association of general psychopathology with change in adaptive emotion regulation such that greater differences in emotion regulation after the intervention were associated with lower general psychopathology (b=-2.53; 95% CI -3.70 – -1.40). There was no evidence of initial signals of associations of general psychopathology with overall self-rated and momentary self-compassion, maladaptive emotion regulation, training frequency or working alliance.

Table 25. *Psychological distress predicted by putative mechanisms of change.*

	Post-intervention		Follow-Up			
	Marginal mean (95% CI)	*SE*	Marginal mean (95% CI)	*SE*	*b* (95% CI)	Effect size
Change in overall self-compassion					-0.19 (-0.51 – 0.29)	-0.03
Time					-1.37 (-3.08 – -0.04)	-0.23
Low change in overall self-rated self-compassion	24.48 (22.03 – 26.94)	1.25	23.43 (20.96 – 25.91)	1.26		
Mean change in overall self-rated self-compassion	23.73 (22.47 – 25.00)	0.65	22.63 (21.35 – 23.91)	0.65		
High change in overall self-rated self-compassion	22.98 (20.82 – 25.14)	1.10	21.82 (19.66 – 23.99)	1.10		
Change in momentary self-compassion					-1.02 (-2.43 – 0.51)	-0.17
Time					-0.88 (-2.52 – 0.63)	-0.15
Low change in momentary self-compassion	24.61 (22.89 – 26.33)	0.88	24.36 (22.62 – 26.10)	0.89		
Mean change in momentary self-compassion	23.72 (22.52 – 24.92)	0.61	22.46 (21.25 – 23.67)	0.62		
High change in momentary self-compassion	22.84 (21.11 – 24.57)	0.88	20.56 (18.83 – 22.30)	0.88		
Change in adaptive emotion regulation					-1.15 (-1.92 – -0.39)	-0.19
Time					-1.08 (-2.62 – 0.35)	-0.18
Low change in adaptive emotion regulation	25.09 (23.36 – 26.82)	0.88	24.59 (22.85 – 26.33)	0.89		
Mean change in adaptive emotion regulation	23.66 (22.46 – 24.86)	0.61	22.55 (21.33 – 23.76)	0.62		
High change in adaptive emotion regulation	22.23 (20.50 – 23.97)	0.88	20.50 (18.76 – 22.24)	0.89		
Change in maladaptive emotion regulation					0.74 (-0.01 – 1.66)	0.12
Time					-1.17 (-2.91 – 0.25)	-0.19
Low change in maladaptive emotion regulation	22.66 (20.89 - 24.44)	0.90	21.79 (20.00 – 23.58)	0.91		
Mean change in maladaptive emotion regulation	23.66 (22.42 – 24.90)	0.63	22.55 (21.30 – 23.81)	0.64		
High change in maladaptive emotion regulation	24.66 (22.89 – 26.42)	0.90	23.31 (21.52 – 25.11)	0.91		
Training frequency					0.00 (-0.05 – 0.05)	0.00
Time					-0.66 (-5.95 – 4.93)	-0.11
Low training frequency	23.56 (20.87 – 26.26)	1.37	23.14 (20.44 – 25.83)	1.37		
Mean training frequency	24.04 (22.18 – 25.91)	0.95	22.68 (20.82 – 24.55)	0.95		
High training frequency	24.53 (21.84 – 27.21)	1.37	22.23 (19.55 – 24.91)	1.37		

Working alliance – participant ratings					0.03 (-0.23 – 0.23)	0.00
Time					1.94 (-15.44 – 14.49)	0.32
Low working alliance	23.78 (21.02 – 26.54)	1.41	22.99 (20.22 – (25.75)	1.41		
Mean working alliance	24.05 (22.18 – 25.91)	0.95	22.68 (20.81 – 24.55)	0.95		
High working alliance	24.31 (21.55 – 27.07)	1.41	22.38 (19.61 – 25.14)	1.41		
Working alliance – psychologist ratings					0.19 (-0.02 – 0.41)	0.03
Time					10.85 (-3.71 – 25.51)	1.81
Low working alliance	22.48 (19.86 – 25.10)	1.34	23.25 (20.64 – 25.87)	1.34		
Mean working alliance	23.70 (21.89 – 25.50)	0.92	22.86 (21.06 – 24.67)	0.92		
High working alliance	24.91 (22.30 – 27.53)	1.34	22.47 (19.85 – 25.09)	1.34		

Note. Continuous variables z-standardised (*M*=0, *SD*=1). Adjusted for age, gender, ethnic minority status, and baseline levels of psychological distress. CI=confidence interval. SE=standard error. Effect size=d-type effect size. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002; Kessler et al., 2005). Self-compassion assessed with the Self-Compassion Scale (Hupfeld & Ruffieux, 2011) and ESM measures. Emotion regulation assessed with Cognitive Emotion Regulation Questionnaire. (Garnefski & Kraaij, 2006). Training frequency operationalized as total number of training exercises completed in the EMI. Working alliance assessed with the Working Alliance Inventory (Horvath & Greenberg, 1989).

Table 26. *General psychopathology predicted by putative mechanisms of change.*

	Post-intervention	Follow-Up			
	Marginal mean (95% CI)	Marginal mean (95% CI)	*SE*	*b* (95% CI)	Effect size
Change in overall self-compassion				-0.23 (-0.64 – 0.45)	-0.02
Time				-1.48 (-3.82 – 0.45)	-0.16
Low change in overall self-rated self-compassion	17.61 (13.70 – 21.53)	16.31 (12.37 – 20.25)	2.01		
Mean change in overall self-rated self-compassion	17.19 (15.18 – 19.20)	15.88 (13.85 – 17.90)	1.03		
High change in overall self-rated self-compassion	16.77 (13.32 – 20.21)	15.44 (12.00 – 18.88)	1.76		
Change in momentary self-compassion				-1.16 (-3.38 – 0.84)	-0.12
Time				-0.86 (-2.90 – 1.40)	-0.09
Low change in momentary self-compassion	18.49 (15.69 – 21.29)	18.77 (15.95 – 21.59)	1.44		
Mean change in momentary self-compassion	17.48 (15.53 – 19.44)	15.70 (13.73 – 17.67)	1.00		
High change in momentary self-compassion	16.48 (13.67 – 19.29)	12.63 (9.81 – 15.45)	1.44		
Change in adaptive emotion regulation				-2.53 (-3.70 – -1.40)	-0.27
Time				-1.22 (-3.74 – 0.83)	-0.13
Low change in adaptive emotion regulation	20.29 (17.59 – 22.99)	19.26 (16.55 – 21.97)	1.39		
Mean change in adaptive emotion regulation	17.15 (15.28 – 19.02)	15.83 (13.95 – 17.71)	0.96		
High change in adaptive emotion regulation	14.01 (11.31 – 16.71)	12.40 (9.69 – 15.11)	1.38		
Change in maladaptive emotion regulation				0.71 (-0.51 – 2.26)	0.07
Time				-1.34 (-3.32 – 1.05)	-0.14
Low change in maladaptive emotion regulation	16.19 (13.36 – 19.02)	15.50 (12.65 – 18.35)	1.45		
Mean change in maladaptive emotion regulation	17.15 (15.16 – 19.13)	15.83 (13.84 – 17.83)	1.02		
High change in maladaptive emotion regulation	18.11 (15.28 – 20.93)	16.17 (13.32 – 19.03)	1.46		
Training frequency				0.00 (-0.09 – 0.08)	0.00
Time				-1.57 (-8.66 – 6.26)	-0.17
Low training frequency	17.63 (13.11 – 22.15)	16.29 (11.77 – 20.80)	2.30		
Mean training frequency	18.07 (14.94 – 21.20)	16.27 (13.14 – 19.40)	1.60		
High training frequency	18.50 (14.01 – 23.00)	16.26 (11.76 – 20.75)	2.29		
Working alliance – participant ratings				-0.03 (-0.30 – 0.26)	0.00
Time				6.17 (-12.58 – 27.41)	0.65
Low working alliance	18.28 (13.72 – 22.83)	17.86 (13.31 – 22.42)	2.32		
Mean working alliance	18.07 (14.96 – 21.18)	16.27 (13.16 – 19.38)	1.59		
High working alliance	17.86 (13.30 – 22.41)	14.68 (10.13 – 19.24)	2.32		

Working alliance – psychologist ratings				0.06 (-0.30 – 0.41)	0.01
Time				0.49 (-22.27 – 26.34)	0.05
Low working alliance	17.18 (12.73 – 21.64)	16.29 (11.84 – 20.74)	2.27		
Mean working alliance	17.56 (14.49 – 20.62)	16.44 (13.38 – 19.51)	1.56		
High working alliance	17.93 (13.48 – 22.38)	16.60 (12.14 – 21.05)	2.27		

Note. Continuous variables z-standardised (*M*=0, *SD*=1). Adjusted for age, gender, ethnic minority status, and baseline levels of psychological distress. CI=confidence interval. SE=standard error. Effect size=d-type effect size. General psychopathology assessed with the 18-item version of the Brief Symptom Inventory (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Self-compassion assessed with the Self-Compassion Scale (Hupfeld & Ruffieux, 2011) and ESM measures. Emotion regulation assessed with Cognitive Emotion Regulation Questionnaire. (Garnefski & Kraaij, 2006). Training frequency operationalized as total number of training exercises completed in the EMI. Working alliance assessed with the Working Alliance Inventory (Horvath & Greenberg, 1989).

Aim 2: The indirect effects of experimental condition on psychological distress and general psychopathology at four-week follow-up via pathways through change in self-compassion and change in emotion regulation

Table 27 shows findings on total, direct, and indirect effects of experimental condition and change in self-compassion (aim 2a) and change in emotion regulation (aim 2b) on psychological distress and general psychopathology at four-week follow-up. There was no evidence for signals of indirect effects via pathways through change in self-compassion (aim 2a). We observed an association of change in momentary self-compassion with psychological distress (β=-0.27, 95% CI -0.50 – -0.07) and general psychopathology (β=-0.28, 95% CI -0.50 – -0.10). There were no signals of potential indirect effects via pathways through change in adaptive or maladaptive emotion regulation (aim 2b). We observed an association of change adaptive emotion regulation with psychological distress (β=-0.35, 95% CI -0.52 – -0.16) and general psychopathology (β=-0.34, 95% CI -0.52 – -0.14).

6.5. Discussion

Main findings

In the current study, we aimed at examining change in self-compassion, change in emotion regulation, training frequency and working alliance as putative therapeutic mechanisms of change in the EMIcompass trial. We observed initial signals of associations of putative mechanisms with outcomes across post-intervention and four-week follow-up (aim 1). More specifically, there was evidence for an association of greater differences in adaptive emotion regulation after the intervention with lower psychological distress and general psychopathology across time points. In addition, there were initial signals that greater reductions in maladaptive emotion regulation were associated with lower levels of psychological distress across time points. Moreover, we observed initial signals of an association of higher levels of psychologist rated working alliance with higher levels of psychological distress across time points. We did not detect initial signals of indirect effects of condition on outcomes via putative mechanisms (aim 2), but we observed associations of change in self-compassion and change in adaptive emotion regulation with outcomes at follow-up.

Table 27. *The indirect effects of experimental condition on psychological distress and general psychopathology at four-week follow-up via pathways through change in self-compassion and emotion regulation.*

	Psychological distress			General psychopathology		
	β	95% CI	P_M	β	95% CI	P_M
Pathways through change in overall self-compassion						
Total effect	-0.05	-0.48 – 0.32		-0.06	-0.46 – 0.36	
Direct effect of condition on outcome	-0.06	-0.51 – 0.33		-0.06	-0.49 – 0.35	
Effect of condition on mediator	-0.08	-0.38 – 0.19		-0.08	-0.38 – 0.20	
Effect of mediator on outcome	-0.15	-0.39 – 0.26		-0.07	-0.31 – 0.30	
Indirect effect	0.01	-0.03 – 0.13	0.20	0.01	-0.03 – 0.09	0.17
Pathways through change in momentary self-compassion						
Total effect	-0.02	-0.39 – 0.39		-0.05	-0.43 – 0.35	
Direct effect of condition on outcome	0.01	-0.39 – 0.39		-0.02	-0.39 – 0.37	
Effect of condition on mediator	0.12	-0.30 – 0.53		0.12	-0.29 – 0.57	
Effect of mediator on outcome	-0.27	-0.50 – -0.07		-0.28	-0.50 – -0.10	
Indirect effect	-0.03	-0.19 – 0.06	1.50*	-0.03	-0.21 – 0.08	0.60
Pathways through change in adaptive emotion regulation						
Total effect	-0.05	-0.46 – 0.34		-0.05	-0.41 – 0.41	
Direct effect of condition on outcome	-0.08	-0.46 – 0.30		-0.08	-0.40 – 0.33	
Effect of condition on mediator	-0.08	-0.52 – 0.37		-0.08	-0.56 – 0.34	
Effect of mediator on outcome	-0.35	-0.52 – -0.16		-0.34	-0.52 – -0.14	
Indirect effect	0.03	-0.11 – 0.22	0.60	0.03	-0.11 – 0.24	0.60
Pathways through change in maladaptive emotion regulation						
Total effect	-0.05	-0.44 – 0.35		-0.06	-0.45 – 0.37	
Direct effect of condition on outcome	-0.03	-0.41 – 0.36		-0.05	-0.42 – 0.38	
Effect of condition on mediator	-0.18	-0.66 – 0.27		-0.18	-0.63 – 0.27	
Effect of mediator on outcome	0.12	-0.07 – 0.35		0.04	-0.18 – 0.22	
Indirect effect	-0.02	-0.18 – 0.02	0.40	-0.01	-0.14 – 0.03	0.17

Note. Continuous variables z-standardised (*M*=0, *SD*=1). Adjusted for age, gender, ethnic minority status, and baseline levels of outcomes. CI=confidence interval. P_M=Proportion mediated. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002; Kessler et al., 2005). General psychopathology assessed with the 18-item version of the Brief Symptom Inventory (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Self-compassion assessed with the Self-Compassion Scale (Hupfeld & Ruffieux, 2011) and ESM measures. Emotion Regulation assessed with Cognitive Emotion Regulation Questionnaire. (Garnefski & Kraaij, 2006). *=exceeds 1.0 in case of suppression effects (i.e., if direct effect is opposite in sign to the indirect effect (Shrout & Bolger, 2002).

Methodological considerations

Several methodological considerations and limitations should be taken into account when interpreting the current study's findings: First, the trial was not powered for the mediation analyses, so effects should be considered in terms of magnitude – not significance. However, the current study provided initial evidence on effect sizes that can be used to inform future studies. Second, the sample selection needs to be appraised critically. Boys/men and individuals identifying as non-binary were underrepresented in the current study. The rather low number of male participants may partly be explained by the exclusion of primary substance abuse disorder, which is especially prevalent in men and male adolescents (Kessler et al., 2005; Linzer et al., 1996), and a higher prevalence of depression and anxiety in females (Afifi, 2007; Linzer et al., 1996; Parker & Roy, 2001). A future definitive trial may therefore need to stratify randomization by gender to rule out potential confounding by this factor. In addition, the number of participants included varied markedly across the three clinical stages. However, a sensitivity analysis controlling for group status replicated the pattern of findings (see supplementary material 28).

Third, the operationalizations of putative mechanisms of change should be considered. To operationalize change from baseline to post-intervention, difference scores were calculated for self-compassion and emotion regulation. Future research could improve this by measuring putative mechanisms at multiple time points throughout the intervention to better model changes and provide more fine-grained data. Moreover, momentary self-compassion was aggregated on the person-level to compute a difference score. This resulted in loss of information, as the within-person variation is not taken into account. Nonetheless, aggregated ESM measures may be still superior in sensitivity and minimization of noise compared to retrospective judgments in single questionnaire assessments (Shiffman et al., 2008). Training frequency was operationalised by the total number of exercises completed in the app, a proxy that disregards that participants could have performed the exercise without using the smartphone, which a substantial proportion of participants did in a hybrid intervention with a different focus (Vaessen et al., 2019). In addition, other mechanisms not considered in this analysis could affect outcome variables. For example, aspects of the therapeutic relationship other than working alliance or quality rather than quantity of training could be relevant (Kazantzis et al., 2016). Results from accompanying qualitative research could provide target mechanisms of change for future research (Paetzold et al., in preparation).

Forth, due to the COVID-19 pandemic, intervention sessions were mostly shifted from in-person contacts to video-conferencing. Whereas systematic reviews and meta-analyses indicate equivalent effects for in-person and tele-psychotherapy (Berryhill et al., 2019; Carlbring et al., 2018; Greenwood et al., 2022), generalisability to settings in which both formats were used flexibly remains unexplored. In addition, the pandemic may also have influenced participants' mental health. A nationally representative study in Germany indicated that social isolation, worries and anxiety were associated with psychological distress and concluded that infection control measures in the pandemic may be associated with poor youth mental health (Rauschenberg, Schick, Goetzl, et al., 2021).

Comparison to previous research

To our knowledge, this is the first study to examine putative therapeutic mechanisms of change in a hybrid compassion-focused intervention aiming at enhancing resilience in youth with early mental health problems.

Previous research in adults and adolescents indicated strong associations of self-compassion with psychological distress and psychopathology and highlighted the relevance of self-compassion for well-being (MacBeth & Gumley, 2012; Marsh et al., 2018; Zessin, Dickhäuser, & Garbade, 2015). CFIs are reported to increase self-compassion and a review suggested that compassion may directly reduce psychopathology (Craig et al., 2020). The current findings provide a mixed picture of the role of self-compassion: while we could not detect initial signals of change in self-compassion to be associated with outcomes across time points (as examined in aim 1), we observed that change in momentary self-compassion was associated with improved clinical outcomes at follow-up in the mediation analyses (as examined in aim 2). However, this did not extend to overall self-rated self-compassion. The findings may partly be explained by suggestions of higher sensitivity to change of momentary assessments in comparison to self-report questionnaires (R. C. Moore, Depp, Wetherell, & Lenze, 2016; Moskowitz & Young, 2006; Myin-Germeys et al., 2011; Myin-Germeys et al., 2018). Moving beyond previous research, we examined mediation effects and did not detect initial signals of an indirect effect of condition on clinical outcomes via change in self-compassion. Alongside with self-compassion being increasingly seen as an important target of interventions, the concept of fear of self-compassion has gained attention (P. Gilbert, McEwan, Matos, & Rivis, 2011). Fear of self-compassion has been observed in various mental health problems, including depression

and anxiety disorders (Merritt & Purdon, 2020). In a study with survivors of childhood maltreatment, fear of self-compassion has been identified as a barrier to treatment (Boykin et al., 2018). Future adaptions of the intervention should therefore address fear of self-compassion and the concept should be taken into account in future studies.

Meta-analyses in children, adolescents and adults concluded that adaptive emotion regulation is linked to lower levels of psychopathological symptoms (Aldao et al., 2010; Compas et al., 2017). In line with pervious findings, we found that changes towards more adaptive and less maladaptive emotion regulation were associated with lower levels of clinical outcomes. Based on suggestions of emotion regulation as a potential link between self-compassion interventions and clinical improvements (Ferrari et al., 2019; Finlay-Jones, 2017), we examined mediation effects and did not detect signals for a mediation via pathways through change in emotion regulation.

In line with the focus on quantitative aspects in the literature (Kazantzis et al., 2010; Kazantzis et al., 2016; Mausbach et al., 2010), the current study focused on training frequency. We did not detect signals for associations with clinical outcomes. However, there is also evidence for the relevance of qualitative aspects of homework (Kazantzis et al., 2016), which have not been assessed in the current study. Future studies could take ratings of the quality of exercises performed into account to assess both, quantitative and qualitative aspects of training.

A recent review highlighted that working alliance has often been overlooked when mobile application interventions are involved in therapy (Henson et al., 2019). The current study therefore adds evidence to this under-researched topic. We observed initial signals of an effect of psychologist rated working alliance on psychological distress across post-intervention/follow-up such that higher working alliance was associated with higher psychological distress. When examining predicted margins, it can be determined that the effect was driven by post-intervention assessments. At follow-up, however, these differences were lower and psychological distress was lowest in the group of individuals with high working alliance at follow-up. The association of high distress and high working alliance may be explained by trained psychologists increasing the intensity of interventions for those who showed signs of worsening mental health problems during the intervention period, which may in turn improve working alliance. As mentioned above, due to the exploratory nature of the trial, only a small number of clinicians delivered the intervention and, thus, these effects must be interpreted with caution. Contrary to the majority of findings in standard delivery of psychotherapy (Baier et al., 2020), we did not detect initial signals of effects of participant rated working alliance on outcomes. However, it should be taken into account that – in absence of a specific measure for the intervention's setting – we

used standard assessments constructed for classic psychotherapy settings with significantly longer treatment periods, higher session frequency and without digital intervention components to examine working alliance in the current study. Future research should focus more directly on specific aspects of digital working alliance. In this respect, a specific measure to evaluate the digital working alliance, as proposed by Henson et al. (2019), may yield important insights. For the previously described effects of putative mechanisms on clinical outcomes, we observed small effect sizes for our hybrid six-week intervention. In the mediation analyses, we did not detect initial signals of effects of condition on putative mechanisms or indirect effects of condition on clinical outcomes via putative mechanisms. However, the intervention has been examined in an exploratory RCT indicating a reduction of stress reactivity in the experimental condition as a primary candidate mechanism (Reininghaus et al., under review). Recently, a systematic review on CFIs in clinical populations concluded that CFIs may be especially promising when delivered in a group format over at least 12 hours (Craig et al., 2020). In combination with calls for more personalised intervention approaches (Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus et al., 2015), these findings may lead to future versions of the intervention with varying scope and format for subclinical and clinical severity of symptoms.

Conclusion

In the current study, we aimed at examining change in self-compassion, change in emotion regulation, training frequency and working alliance as putative therapeutic mechanisms in the EMIcompass trial. We observed initial signals of associations of some putative mechanisms with outcomes across post-intervention and four-week follow-up, but could not detect initial signals of indirect effects of condition on outcomes at follow-up via putative mechanisms. Findings suggest that, if successfully targeted by interventions, self-compassion and adaptive emotion regulation may be putative therapeutic mechanisms of change associated with clinical outcomes in youth with early mental health problems. Future studies powered for these analyses should further explore whether a hybrid CFI may be able to target these mechanisms.

CHAPTER VII:

EXPLORING THE IMPLEMENTATION OF A NOVEL, TRANSDIAGNOSTIC, HYBRID ECOLOGICAL MOMENTARY INTERVENTION FOR IMPROVING RESILIENCE IN YOUTH (EMICOMPASS): A REALIST EVALUATION

7.1. Abstract

Previous research indicated that the hybrid compassion-focused intervention EMIcompass may reduce stress reactivity and improve quality of life. Our aim was to investigate which components of the intervention work for whom, how and under which circumstances to contribute to the enhancement of resilience.

We conducted a process evaluation using a realist framework. First, we developed initial programme theories using CFI and EMI documents, in addition to conducting a focus group and an interview with an individual expert. Second, we tested the initial programme theories based on qualitative data from 20 participants. Third, we refined the programme theories by analysing and interpreting the data.

We identified four programme components experienced as enhancing the activation of the soothing system and the application of compassion-focused principles. EMIcompass was perceived as lowering barriers to, and burden of, treatment and facilitated the translation into daily life. Intra- and inter-personal context factors interacted with the mechanisms, leading to improvement in well-being, which was identified as a main outcome.

The intervention worked by strengthening participants' soothing system and facilitated ecological translation leading to improved well-being. Adaptions to improve the intervention may allow for more flexibility in individual intervention trajectories acknowledging different needs and preferences.

7.2. Introduction

Background

Mental and substance abuse disorders are the leading cause of disability in youth and place a heavy burden on young individuals (Erskine et al., 2015; Gore et al., 2011). Mental health problems may – particularly in youth and when not treated adequately – result in a vicious circle of disadvantage characterised by missed opportunities for development, education, and employment (Malla et al., 2018). Youth mental health services are a powerful tool for prevention and early intervention (Conley et al., 2017; Correll et al., 2018; Schmidt et al., 2015). Risk factors and mental health problems can be changed and resilience can be increased by strengthening protective factors (Bayer et al., 2009; Forbes et al., 2019; Patel et al., 2007). However, youth mental health services are confronted with various problems in their organisational structure (e.g. delivering youth mental health care in adult services; Patel et al., 2007), as well as low availability, access and use (Malla et al., 2016; Wang et al., 2005). This is especially problematic as it may lead to a longer duration of untreated illness, which, in turn, represents a marker of poor prognosis and a potential entry point to the vicious circle of disadvantage (Dell'Osso et al., 2013; Drancourt et al., 2013; Ghio et al., 2014; Marshall et al., 2005). Consequently, it is urgently necessary to lower the threshold for youth to access prevention and early intervention services tailored to their needs and preferences.

Digital approaches provide major opportunities to lower the threshold to accessing mental health care. EMIs enable the delivery of personalised interventions in the everyday life of service users and facilitate ecological translation of strategies acquired, making them inherently low-threshold (Balaskas et al., 2021; Heron & Smyth, 2010; Myin-Germeys et al., 2011; Myin-Germeys et al., 2018; Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus et al., 2015). Behavioural sensitization, a widely studied putative transdiagnostic mechanism positing that experiencing frequent or chronic adversity may gradually increase individuals' stress response to subsequent adverse experiences and minor daily stressors resulting in increased stress reactivity, may be a promising target for digital prevention and early intervention (Collip et al., 2008; Myin-Germeys et al., 2018). CFIs (P. Gilbert, 2009, 2013, 2014) may be especially well suited to target stress reactivity as their techniques are associated with increases in positive affect, behavioural activation, as well as self-acceptance and are reported to reduce mental health problems and calm threat and stress (P. Gilbert, 2009; Holmes, Blackwell, Burnett Heyes, et al., 2016; Holmes & Mathews, 2010; Leaviss & Uttley, 2015; Lincoln et al., 2013;

Pearson et al., 2015; Renner et al., 2017). In the light of the above, EMIcompass has been developed as a transdiagnostic, hybrid CFI aiming to enhance resilience in youth.

The EMIcompass intervention

EMIcompass is a manualised, hybrid six-week CFI delivered by trained psychologists in addition to treatment as usual. The intervention included biweekly training sessions and a compassion-focused EMI administered through a smartphone app installed on dedicated study smartphones. The intervention was based on compassion-focused techniques aiming at strengthening participants' soothing system associated with emotions such as calmness and peacefulness. In the sessions, various CFIs (e.g. breathing exercises, compassionate imagery or compassionate writing) were introduced and trained. Sessions were offered as in person contacts or via video-conferencing. The EMI provided participants with new techniques once a week and offered on demand training of strategies acquired so far. In addition, the EMI sent daily reminders to complete an exercise at a self-set time point. An optional function offered participants CFIs in moments of high stress or negative affect based on brief ESM assessments. The intervention and the exploratory RCT are presented in detail elsewhere (Paetzold, Schick, et al., 2022; Reininghaus et al., under review).

Objectives

For the EMIcompass intervention, there is evidence from an uncontrolled pilot study (Rauschenberg, Boecking, et al., 2021) and an exploratory RCT (Reininghaus et al., under review) suggesting feasibility, safety, and initial signals for reducing stress reactivity and improving quality of life. However, it is acknowledged that contexts impact on outcomes and that programmes do not work equally for all individuals taking part in them (Pawson & Tilley, 1997; Westhorp et al., 2011). It is therefore of crucial importance to explore the interactions between contexts and mechanisms (i.e., service users' responses to the resources provided by the programme) and how these lead to outcomes. The aim of this process evaluation was to investigate which components of the EMIcompass intervention work for whom, how and under which circumstances to contribute to enhancing resilience in youth with early mental health problems.

7.3.   Method

Evaluation design

For the process evaluation, a realist evaluation design was used. This design reflects an evidence informed and theory-driven approach of evaluation aiming to explore what works, for whom, in what respects, to what extent, in what contexts, and how (Westhorp et al., 2011). Therefore, complex interactions of contexts, mechanisms (i.e., participants' response to resources provided by the programme) and outcomes involved in the programme are examined (Jagosh, 2019). The evaluation comprised three overarching phases: developing, testing and refining the programme theory (Punton, Vogel, & Lloyd, 2016).

Setting and participants

The EMIcompass intervention was offered to participants between August 2019 and August 2021 at the Central Institute of Mental Health in Mannheim, Germany. Participants were recruited from mental health services in Mannheim, Germany, as well as via online advertisements on the institute's webpage, social media and local registries. Sessions were delivered in person or via video-conferencing. The exploratory RCT included individuals aged 14 to 25 with current psychological distress, clinical high at-risk mental state or a first treated episode of severe mental disorder based on a modified version of the clinical staging model (Hartmann et al., 2019; Schick et al., 2021). For further information on recruitment and inclusion/exclusion criteria of the exploratory RCT, see Schick et al. (2021). From December 2020 on, all participants finishing the EMIcompass intervention were invited to participate in the realist evaluation.

Sampling, recruitment, and data collection

To understand how the EMIcompass programme was expected to work to achieve intended outcomes, we conducted a focus group with the experts involved in the development and implementation of the intervention and drew on an individual interview with an expert in EMIs. Data collection aimed at examining the programme's rationale as well as assumptions about mechanisms and outcomes. Supplementary material 29 displays the topic guide for the focus group. The collected data was combined with previous publications on CFIs and EMIs to develop the initial programme theory.

The initial programme theory was tested and refined using data from semi-structured interviews with twenty participants who received the EMIcompass intervention. Interviews were conducted by trained researchers (IP, MS, CF) via video-conferencing. Using findings from previous interviews, the interview guide (supplementary materials 30 and 31) was revised to focus on elucidating unclear aspects and use active reflection to explicitly test theories (Manzano, 2016).

Analysis

Using data from the focus group, the expert interview and previous research, we produced a matrix comprising context, mechanisms and outcomes and formulated overarching initial programme theories on the EMIcompass intervention. In a second step, we conducted qualitative data analysis on participants' interviews. Transcripts were coded independently by two members of the research team (IP, CF), discrepancies were discussed in consensus meetings. Similar codes were grouped and considered together. Data were summarised and synthesised to find evidence supporting or refuting initial programme theories. MAXQDA (GmbH, 2020) was used to facilitate the analysis. Last, the initial programme theories we revised focusing on explanations about how the programme unfolded in practice.

7.4. Results

Initial programme theories

Based on data from the focus group, the expert interview and previous research, we proposed a matrix of CMO-configurations as initial programme theories (table 28). We identified various context factors (affinity to psychology and mental health, prior experiences, symptom severity, participants' needs, affinity to technology) that we expected to interact with the mechanisms to impact on outcomes. From the data collected in phase 1, we derived putative resources (intervention content, interpersonal contact, self-compassionate attitude) that were posited to result in responses (establishment compassion-focused skills, feeling of being connected, motivation and encouragement, compliance, corrective interpersonal experiences, knowledge and understanding of emotional states, self-efficacy) potentially leading to improvements in participants' overall well-being and reductions of the symptom burden. In addition, the initial programme theory posits that situations of high stress (context) interact with the application of self-compassion techniques (resource) leading to an activated soothing system, increased self-compassion, inner safeness, a changed perspective on emotional experience and reduced stress reactivity (response) that may result in momentary reduced stress, negative affect and momentary increased well-being (outcomes).

Table 28. *Initial programme theory in form of a Context-Mechanism-Outcome configurations matrix.*

CONTEXT	MECHANISM		OUTCOME LEVEL 1	OUTCOME LEVEL 2
	Resource	**Response**		
Affinity to psychological topics and therefore higher interest and involvement in…	the strategies provided in the intervention…	guiding participants to establish a soothing breathing rhythm, compassionate imagery and writing…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Participants' needs and personality fit with…	the strategies provided in the intervention…	guiding participants to establish a soothing breathing rhythm, compassionate imagery and writing…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Positive prior experiences with counselling or therapy and therefore higher interest and involvement in…	the strategies provided in the intervention…	guiding participants to establish a soothing breathing rhythm, compassionate imagery and writing…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden..
Affinity to psychological topics and therefore higher interest and involvement with…	the self-compassionate attitude modelled in the intervention…	will enable participants to more easily take over and embody a self-compassionate attitude, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Participants' needs and personality fit with …	the self-compassionate attitude modelled in the intervention…	will enable participants to more easily take over and embody a self-compassionate attitude, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Positive prior experiences with counselling or therapy and therefore higher interest and involvement with…	the self-compassionate attitude modelled in the intervention…	will enable participants to more easily take over and embody a self-compassionate attitude, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden. which increase well-being, reduce symptom burden.
Lower symptom severity combined with…	the self-compassionate attitude modelled in the intervention…	will enable participants to more easily take over and embody a self-compassionate attitude, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Participants' needs and personality fit with…	the structure provided through regular sessions and feedback…	will give participants an increased feeling of being connected, increases motivation and encouragement and may increase participants' compliance, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.

		will give participants an increased feeling of being connected, increases motivation and encouragement and may increase participants' compliance, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Higher symptom severity will make participants benefit more from…	the structure provided through regular sessions and feedback…			
Affinity to psychological topics and therefore higher interest and involvement makes participants more open to perceive…	the clinician as a reference person…	offering the possibility to make corrective experience in therapeutic relationship, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Participants' needs and personality fit with…	the clinician as a reference person…	offering the possibility to make corrective experience in therapeutic relationship, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Positive prior experiences with counselling or therapy and therefore higher interest and involvement makes participants more open to perceive…	the clinician as a reference person…	offering the possibility to make corrective experience in therapeutic relationship, which will…	increase participants' self-compassion and inner safeness…	which increase well-being, reduce symptom burden.
Affinity to psychological topics and therefore higher interest and involvement with…	the information on mental health and emotional systems provided in the intervention…	increasing participants' knowledge and enhancing the understanding of emotional states participants experience will…	change participants' perspective on emotional states they experience…	which increase well-being, reduce symptom burden.
Participants' needs and personality fit with…	the information on mental health and emotional systems provided in the intervention…	increasing participants' knowledge and enhancing the understanding of emotional states participants experience will…	change participants' perspective on emotional states they experience…	which increase well-being, reduce symptom burden.
Affinity to psychological topics and therefore higher interest and involvement with…	the self-compassionate attitude modelled in the intervention…	will enable participants to more easily take over and embody a self-compassionate attitude, which will…	change participants' perspective on emotional states they experience…	which increase well-being, reduce symptom burden.
Participants' needs and personality fit with …	the self-compassionate attitude modelled in the intervention…	will enable participants to more easily take over and embody a self-compassionate attitude, which will…	change participants' perspective on emotional states they experience…	which increase well-being, reduce symptom burden.

Positive prior experiences with counselling or therapy and therefore higher interest and involvement with…	the self-compassionate attitude modelled in the intervention…	will enable participants to more easily take over and embody a self-compassionate attitude, which will…	change participants' perspective on emotional states they experience…	which increase well-being, reduce symptom burden.
Lower symptom severity combined with…	the self-compassionate attitude modelled in the intervention…	will enable participants to more easily take over and embody a self-compassionate attitude, which will…	change participants' perspective on emotional states they experience…	which increase well-being, reduce symptom burden.
Affinity to psychological topics and therefore higher interest and involvement makes participants more open to perceive…	the clinician as a reference person…	offering the possibility to make corrective experience in therapeutic relationship, which will…	change participants' perspective on interpersonal support…	which increase well-being, reduce symptom burden.
Participants' needs and personality fit with…	the clinician as a reference person…	offering the possibility to make corrective experience in therapeutic relationship, which will…	change participants' perspective on interpersonal support…	which increase well-being, reduce symptom burden.
Positive prior experiences with counselling or therapy and therefore higher interest and involvement makes participants more open to perceive…	the clinician as a reference person…	offering the possibility to make corrective experience in therapeutic relationship, which will…	change participants' perspective on interpersonal support…	which increase well-being, reduce symptom burden.
Exposure to situations of high stress combined with…	the application of compassion-focused techniques provided by the intervention…	activates the soothing system, increases self-compassion, inner safeness, changes the perspective on emotional experience, and reduces stress reactivity which will…	reduce participants' momentary negative affect and increase their well-being.	

Testing the initial programme theories

In the analyses, we identified four main components of the programme: 1) intervention content, 2) interpersonal contact, 3) delivery via smartphone and training in daily life, 4) intervention in acute moments of stress or negative affect. In addition, we identified context factors directly associated with given components and context factors impacting on participants more generally. We observed discrete associations of specific mechanisms and outcomes, but participants also reported outcomes that could not be attributed to a single component of the programme. In the following sections, we first present general context factors and then provide findings on the identified components of the programme, context factors interacting with them as well as outcomes attributed to the components. Last, we will provide an overview of outcomes that could not be attributed to a single component of the programme. Findings on further components will be displayed in the supplementary material 32.

General context factors

We identified context factors within the participants and factors in their personal environment impacting on their involvement with all intervention components:

Within the participant, we identified level of symptom severity, personality traits and attitudes as relevant factors in the interaction with the programme. Participants were ambiguous on whether higher levels of symptom severity would hinder or facilitate positive effects of the intervention. Some claimed that too severe symptoms may have made them less open and less motivated to get involved. A medium symptom severity may be optimal, as the majority indicated that distress made them take the intervention seriously and motivated them to work for change:

> *I was able to profit the most from it now, because before that or so I felt I was stuck and it pulled me out. […] (EMI0122, 50)*

Participants named several personality traits that they perceived as helpful or hindering context factors in interaction with the intervention. Some described themselves as determined and goal-oriented, which increased commitment to and involvement with the intervention leading to better outcomes. Others mentioned imagination and creativity as facilitating traits helping to increase the effects of imagery exercises. Openness for new experiences as well as openness to reflect and share thoughts and feelings was mentioned in many interviews. Participants described being curious and willing to reflect and learn new aspects about oneself as a helpful

trait. Many reported positive attitudes towards the intervention, meditation, and psychology as helpful context factors. Others also indicated that previous positive experiences (e.g. with mediation, psychology, mental health services) facilitated opening up and made it easier to involve themselves in the techniques. In addition, seeing the complaints as distressing but modifiable motivated participants to work for change.

> *Because, at that time, I didn't perceive it as a problem that I could change. Instead, it was for me like "that's the way it is and always will be". That's why I wouldn't have known that I could change it. And now I have this idea "I can change it - if I want to" and that has made me more open to say "I'll give it a go" (EMI0097, 27)*

Participants' personal circumstances emerged as a crucial variable. Many participants experienced distressing life circumstances and perceived the COVID-19 pandemic as an important stressor associated with insecurity, doubt, loss of structure and loneliness. Others reported that changes in everyday life due to the pandemic enabled their participation in the intervention as home schooling/ office introduced more flexibility in their daily schedules. Opportunities to participate from home made the intervention more accessible and lowered barriers to get involved.

> *It was definitely practical in my situation that I could also have video calls that way. That made the whole thing a bit more accessible, that I didn't always have to go to Mannheim. And also because I'm at home, I also had a bit more time to answer the prompts and without being distracted [...] (EMI0164, 87)*

Most participants reported that feedback from their social environment did not affect their intervention outcomes. Some received positive feedback, which further motivated them.

Intervention components

1) Intervention content

a) Techniques presented and trained in the intervention

We identified direct and indirect pathways via which the intervention techniques led to responses in participants' soothing system.

First, the techniques directly activated participants' soothing system by inducing pleasant emotions, feelings of calmness and safety while reducing negative affect.

> *This soothed me very much any case, and yes, it was just very pleasant. (EMI0117, 198)*

Participants also reported that the techniques helped to enhance self-compassion and reduced self-criticism. We found evidence that the intervention techniques transported the concept of common humanity ('you're not struggling alone'). The exercises were seen as small moments of self-care and increased participants' mindfulness (for cognitive, emotional, physical and behavioural processes).

> *[...] question and reduce especially self-criticism and things like that. (EMI0089, 185)*
>
> *Supported, I would say, not alone with one's thoughts (EMI0123, 157)*

Moreover, we found evidence for indirect effects on participants' self-compassion and soothing system. Psycho-educative elements helped participants to attain a better understanding of internal processes, which, in turn, was associated with feelings of relief ('de-shaming') and self-compassion.

> *It simply created relief and that you can just say "okay that's how it is and that's why it's negative in the moment" (EMI0115, 89)*

Participants also reported that the techniques triggered self-reflective processes. This self-reflection helped participants to get to know themselves better und to gain more insight in internal processes. Emotional states became clearer, easier to distinguish and to explain, which made them less threatening and enhanced an accepting attitude.

> *That you understood why you feel the way you do - and that this is okay. (EMI0112, 177)*

In addition, participants were enabled to distance themselves from distressing emotions and cognitions more easily. This broadened their scope of action in moments of stress and negative affect and highlighted potential opportunities to intervene with an activation of the soothing system.

> *It helps me to keep my distance: 'Okay, I experience the emotion, but it doesn't define me and won't overwhelm me, it will go away again'. So really this certainty that an emotion has ever remained forever [...] (EMI0162, 204)*
>
> *[...] you have always managed to bring yourself back into another area and you will also manage that in the future. (EMI0162, 168)*

Self-reflection was also reported to enhance the perception of positive aspects. For participants with high levels of experiential avoidance, however, enhanced self-reflection was associated with unpleasant emotions in the first instance.

> *It decreased the mood a bit because I had chosen such a negative emotion, but that's also a bit of the point of dealing with it. (EMI0134, 206)*

Participants also highlighted that the tasks helped them to gain new knowledge and experiences that changed their perspectives on others, themselves (e.g. experienced themselves as source of soothing and support), their situation and inner processes. This reduced stress and distressing thoughts and enhanced functional coping, self-compassion and the activation of the soothing system.

> *It enabled a new way of thinking, because I never had the idea before of how I treat myself in the first place (EMI0041, 83)*

No positive or even negative effects were reported when participants experienced uncertainties or difficulties with the tasks, which led to an activation of self-criticism. High levels of perfectionism were identified as a context variable for these processes. For example, single participants reported that they were disappointed when experiencing difficulties with the tasks, again triggering self-criticism and negative affect.

b) ESM in the intervention

Within an optional part of the intervention app, participants were asked to complete ESM questionnaires, which were then sent 6 times at random within set blocks of time on 3 consecutive days per week.

In the interviews, self-reflection was identified as the key feature of the ESM questionnaires. Participants reported that self-reflection enhanced their acceptance for own emotional states and helped them to uncover cognitive biases towards negativity and dysfunctional cognitive patterns.

> *I would also say that I have generally noticed that I'm not doing so badly! Because often, when I was asked how I felt, I have actually stated that I was relaxed and that I was actually doing well totally often. And then I thought about 10 situations a day that were good and maybe one bad, but that that was then but still actually a good day. (EMI0144, 47)*

The ESM questionnaires encouraged participants to prioritize mental health and stimulated participants to reflect on their needs and act to meet them. Being prompted regularly to reflect about mood and stress helped participants to establish a routine of self-reflection independent of external triggers.

> *Exactly, those [i.e., mood queries] made my head rethink and to say 'hey, why am I feeling that way now?' and 'what could you change that it goes from 0 to the 10 in the mood query?'. (EMI0154, 73)*

However, participants also clearly highlighted the burden associated with the ESM. This was especially evident in participants with high need for autonomy, who felt restricted by prompts. Participants suggested individualization and more flexibility (e.g. individualised sets of questions, 'I don't know' option, personalised choice of ringtone, individual sampling schemes that can be changed at any time) as potential improvements.

> *It's really helpful when you can access it on your own and when you're not bound to anything...there are too many things I'm bound to right now. (EMI0101, 227)*

2) Interpersonal contact

Findings on interpersonal contact focus on the sessions with the trained psychologists. Participants reported that guidance in acquiring the strategies and having someone to refer to for questions and problems was helpful. This ensured the correct application of strategies and provided participants with a feeling of connectedness.

> *I thought it was really nice to talk to someone human, also just because I could have my questions answered and partly she also did the exercises with me. That was kind of...yes you didn't feel so alone, that was cool (EMI0144, 141)*

The sessions were also reported to enhance the intervention content presented on the smartphone and were highlighted as crucial for their progress by some participants.

> *They [i.e., the sessions] were the things that have totally worked for me. They were such an aha-experience and I would not have had that, if I only read through it on the phone (EMI0162, 131)*
>
> *I would almost say that the sessions were the crux of the matter. [...] Without the sessions, this thought process wouldn't have started at all. (EMI0134, 86)*

Participants perceived the psychologists as competent and trustworthy, they felt understood and validated in the sessions. This increased their engagement with and their trust in the strategies and perspectives presented in the sessions and created a safe atmosphere, where participants could be sure that they were treated with care, benevolence, genuine interest, and the wish to work for change, which encouraged them to open up. Talking openly about problems and worries was experienced as relieving by many participants.

> *I had the feeling she knows what I need and I thought that was amazing (EMI0162, 159)*
>
> *[...] very abstract, but I found it quite good to know that within this therapy, the other person is not pursuing his or her own interests, but only wants to help. (EMI0122, 72)*

The atmosphere also allowed entering reflections about the process, which helped to develop new perspectives on participants' emotions, cognitions, behaviour and interpersonal dynamics.

> *I'd rather think that I found them [i.e., feelings] through this in the first place (EMI0122, 82)*

> *I think overcoming this barrier, that is, that she got me to participate in it, that was also something that actually helped. (EMI0134, 92)*

Some participants were even able to make profound corrective experiences of interpersonal contact as validating, supportive and benevolent in the sessions.

> *When I turn to my parents, for example, with such things, then they really just say "I'm not interested in that, don't annoy me with it". That's why I first had an insecure feeling when I start to talk about it all, because then I thought I'm not annoying my parents with it, but someone else. But just when I realised that it was okay in the situation and that they wanted to help me, it was the atmosphere...that always made the sessions very beautiful (EMI0156, 155)*

Participants successfully transferred experiences of validation, modelling of care and compassion-focused principles by the trained psychologists to the way they viewed and treated themselves. This was reported for various compassion-focused key principles such as self-kindness, common humanity, de-shaming and normalizing, "not your fault":

> *Sometimes, I also became aware of the fact that things are not my fault and that I am just too hasty in judging myself (EMI0101, 122)*

> *You felt like you were part of a community, because you had the feeling that you were not alone with your thoughts and things in your head. (EMI0143. 122)*

> *[...] I also felt appreciated and understood and not crazy or anything - just as if my problem was something normal that could be worked on. (EMI0144, 135)*

In addition, participants highlighted the importance of tailored interventions and the feeling of being seen as an individual with individual strength and difficulties as relevant for their engagement with the intervention.

> *If I had felt like I was just one of many participants, I would have been less motivated and would not have seen the point, if one had only been 'processed' (EMI0162, 147)*

3) Delivery via smartphone and training in daily life

We identified accessibility of information and availability of techniques, daily reminders, flexibility and a fit to participants' lifestyle as aspects that lowered the hurdles to apply techniques regularly.

The smartphone provided quick and easy access to information and made techniques highly available.

> *That [i.e., other forms of delivery] would have been simply larger barrier again […](EMI0123, 215)*

Daily reminders to train were described as a valuable support by many participants. The prompts helped to establish a training routine and were described as helpful nudging towards more self-care.

> *[…] I need little nudges in the right direction, that's why I thought it was so good with the reminders. […] (EMI0144, 43)*

Some participants would, however, have preferred to have more flexibility in the timing of prompts and the type of tasks offered. The desire for more flexibility was addressed in the on-demand options giving participants the possibility to decide on what, where, when and how to train.

> *But I also liked that you can be proactive yourself. You can do it when you want and when you have the feeling that you need it. (EMI0097, 85)*

The majority did not describe themselves as especially "technophile", but the delivery via smartphone was seen as timely, increasing flexibility and fitting their lifestyle by most participants. Some, however, also perceived the smartphone as a source of stress. We identified participants' attitude towards the use of digital devices, rather than mere affinity to technology or digital literacy, as a context variable determining whether the resource smartphone impacted positively or negatively on training frequency.

> *The phone helped me a lot to integrate it into my everyday life. I liked that I knew 'okay, you can do it from everywhere, you can just integrate it into your everyday life' (EMI0162, 216-218)*
>
> *I just don't want to be the slave of such a device (EMI0115, 41)*

4) Intervention in moments of acute stress or negative affect

Participants reported the techniques to be helpful in acute moments of stress or negative affect. Applying the strategies in distressing situations, participants were able to activate their soothing

system, which reduced negative affect, increased positive affect, reduced stress reactivity and improved well-being. In addition, participants reported increases in their experienced scope of action and coping skills in challenging situations.

> *So in any case, in bad situations I just felt much better [...] and could deal with it better. (EMI0112, 191)*

Moreover, using the strategies changed participants' perspective on acute emotions they were experiencing.

> *This helps me keep my distance like 'okay, I feel the emotion, but it doesn't define me and doesn't overwhelm me either. (EMI0162, 204)*

One the one hand, this holds true for interactive tasks triggered if participants reported high levels of momentary stress or negative affect in the optional experience sampling questionnaires. Participants, who made use of this option, perceived it as helpful. On the other hand, participants also developed a routine in initiating tasks themselves when anticipating or experiencing high stress or negative affect.

> *Then, it [i.e., an exercise suggested by the phone] is like a friend who knocks on your door somehow unexpectedly and then you do something nice together...that's how I'd imagine it (EMI0156, 223)*
>
> *In the end, every time such an exercise was suggested, it helped me (EMI0162; 230)*
>
> *In fact, in everyday life, just when I noticed that it was getting stressful, I really did an exercise. And I would never have thought of doing that before and I'd say, that it has made a difference (EMI0125, 27)*

Many participants described their current life situation as distressing and indicated that the programme, and especially this component, may be especially helpful under these circumstances. This was further amplified by the COVID-19 pandemic, which was perceived as a source of additional stressors.

> *I think the complete situation with the corona pandemic at the moment is definitely such an external factor. In the last few months, I often find myself and I have often found myself in situations, where I have simply questioned everything [...] So I think I had a lot of opportunity to apply it (EMI0089, 43)*

Outcomes

As delineated above, participants' soothing system and self-compassion was perceived as being strengthened by the programme, leading to improvements in well-being and reduced symptoms.

We identified outcomes associated with a well-functioning drive system, such as increases in self-confidence and level of functioning.

Moreover, some participants with more severe symptoms were encouraged to engage in longer-term psychotherapeutic treatment by the positive experiences with EMIcompass:

> *The session helped me to lower the barrier of opening up to others, as a consequence, I started a therapy afterwards (EMI0041, 19)*

Refined programme theory

Table 29 displays the refined programme theory matrix based on the analyses presented above. We identified various intra- and some inter-personal context factors (e.g. personality traits, attitude towards key features of the intervention, current life situation, COVID-19) and 4 core components of the programme (i.e., intervention content, interpersonal contact, delivery via smartphone and training in daily life, intervention in acute moments of stress or negative affect) leading to the activation of participants' soothing system and the incorporation of compassion-focused principles, improved accessibility of techniques and the translation of strategies into daily life. This caused improvements in well-being as a core outcome of the programme.

7.5.   Discussion

The study was designed to evaluate how and why the EMIcompass intervention could contribute to enhance resilience in youth with early mental health problems. We used a realist evaluation approach to gain insight in the relevant context factors, mechanisms and outcomes to understand how the programme worked. Findings suggest that EMIcompass largely worked via activating the soothing system and the application of compassion-focused principles. In addition, we were able to generate information with regard to how the programme could be improved. As the intervention has been examined in a multimethod-approach, interpreting current findings in the light of quantitative results will offer a more comprehensive perspective on the intervention. The results will be discussed in the sequence of Context - Mechanisms – Outcomes.

Table 29. *Refined programme theory in form of a Context-Mechanism-Outcome configurations matrix.*

CONTEXT	MECHANISM		OUTCOME LEVEL 1	OUTCOME LEVEL 2
	Resource	Response		
INTERVENTION CONTENT				
Involvement with the intervention combined with…	the strategies provided in the intervention…	guiding participants to establish a soothing breathing rhythm, compassionate imagery & writing…	activate participants' soothing system with feelings of calmness, safeness, enhance positive and reduce negative emotions, increase self-compassion, mindfulness, self-care and the feeling of common humanity, decrease self-criticism…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Low levels of emotional avoidance combined with…	the strategies provided in the intervention…	guiding participants to reflect regularly and thereby enhancing the understanding of emotional states participants experience…	make emotions easier to understand and less threatening, make it easier to distance from distressing internal processes, increase participants' scope of action, and their perception of positive aspects…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Involvement with the intervention combined with…	the information on mental health and emotional systems provided in the intervention…	increasing participants' knowledge and enhancing the understanding of emotional states participants experience will…	lead to de-shaming and increased self-compassion…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Involvement with the intervention combined with…	the information on mental health and emotional systems provided in the intervention…	supporting participants to get a new perspective on others, themselves (e.g. experienced themselves as source of soothing and support), their situation and inner processes	reduces stress and distressing thoughts and enhance functional coping, self-compassion and the activation of the soothing system…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Creativity and fantasy, combined with…	the imagery based techniques provided in the intervention…	increasing positive effects of the strategies applied…	lead to a stronger activation of participants' soothing system with feelings of calmness, safeness, enhance positive and reduce negative emotions, increase self-compassion, mindfulness, self-care and the feeling of common humanity, decrease self-criticism…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Low levels of emotional avoidance combined with…	the experience sampling questionnaires…	guiding participants to reflect regularly…	increase their acceptance for emotional states, uncover cognitive bias towards negativity, help to focus on needs and actions to meet them and to prioritize mental health…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).

Involvement with the intervention combined with…	the experience sampling questionnaires…	guiding participants to reflect regularly…	helps to establish a routine of self-reflection without external trigger and thereby increase mindfulness…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Involvement with the intervention combined with…	the experience sampling questionnaires…	guiding participants to reflect regularly…	helps to identify dysfunctional cognitive and behavioural patterns and show possibilities to change them…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Perfectionism combined with…	a lack of clarity or difficulties with an exercise…	creating uncertainty…	causes increases in unpleasant emotions and self-criticism…	leading to a feeling of burden and reactivity.
High need for autonomy combined with…	the sampling scheme and/or fixed settings…	making participants feel restricted by the prompts…	causes increases in unpleasant emotions and self-criticism…	leading to a feeling of burden and reactivity.

INTERPERSONAL CONTACT

Involvement with the intervention combined with…	the guidance provided by clinicians…	ensuring the correct application of strategies…	strengthens participants' soothing system and self-compassion…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Involvement with the intervention combined with…	the guidance provided by clinicians…	creating a feeling of connectedness..	strengthens participants' soothing system and self-compassion…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Involvement with the intervention combined with…	the interpersonal contact in the sessions…	perceived as helpful and supportive…	leads to an augmentation of the content presented on the smartphone, aha-experiences, and triggered processes…	leading to increases well-being, hope and self-esteem, and strengthening of the drive system (increased motivation, performance, concentration).
Involvement with the intervention combined with…	the clinician as reference person…	perceived as competent and trustworthy…	makes participants feel understood and validated…	increasing engagement with and trust in the strategies presented and increasing success expectations.
Involvement with the intervention combined with…	the clinician as reference person…	perceived as competent and trustworthy…	creates a safe atmosphere, where participants feel treated with care, benevolence, genuine interest, and the wish to work for change…	encouraging participants to open up, which was experienced as relief.
Involvement with the intervention combined with…	the clinician as reference person…	perceived as competent and trustworthy…	create a safe atmosphere, where participants feel treated with care, benevolence, genuine interest, and the wish to work for change…	allowing to go in to reflections about the process, which help to develop new perspectives on their emotions, cognitions, behaviour and interpersonal dynamics.

Involvement with the intervention combined with…	the clinician as a reference person…	offering the possibility to make corrective experience in therapeutic relationship, which …	change participants' perspective on interpersonal support positively…	leading to increased well-being.
Involvement with the intervention combined with…	the self-compassionate key principles modelled by the clinicians…	enable participants to more easily take over and embody a similar attitude, which …	helps participants to view and treat themselves with more care, self-compassion and –kindness, and less shaming…	leading to increased well-being.
Involvement with the intervention combined with…	the individualization of the content by the clinician	was perceived by the participants and created a feeling of being seen as an individual with individual strengths and difficulties	increased engagement with and trust in the strategies presented…	leading to increased well-being.
The pandemic situation leading to loneliness combined with…	regular contact opportunities with the study team…	meeting participants need for interpersonal contact…	creating feelings of connectedness and being cared for…	leading to increased well-being.
The pandemic situation leading to loneliness combined with…	regular contact opportunities with the study team…	meeting participants need for interpersonal contact…	activating participants' soothing system…	leading to increased well-being.

DELIVERY VIA SMARTPHONE

Positive attitude towards digital devices combined with…	the delivery via smartphone…	increases availability and accessibility of information…	lowering the hurdles for participants to train strategies to activate their soothing system, increasing engagement with the app and enhancing translation to everyday life…	leading to increased well-being.
Positive attitude towards digital devices combined with…	the delivery via smartphone…	is seen as timely, increasing flexibility and fitting their lifestyle…	lowering the hurdles for participants to train strategies to activate their soothing system, increasing engagement with the app and enhancing translation to everyday life…	leading to increased well-being.
Enhanced flexibility due to home office/ home schooling, combined with…	the delivery via smartphone allowed to send participants daily reminders…	which helped participants to establish a training routine and nudged them towards more self-care…	enhancing translation to everyday life…	leading to increased well-being.
Enhanced flexibility due to home office/ home schooling, combined with…	the delivery via smartphone allowed for on demand training…	providing participants with the flexibility to decide on what, where, when and how to train…	lowered the hurdles for participants to train strategies to activate their soothing system, increased engagement with the app, enhanced translation to everyday life and the application of the strategies perceived as helpful…	leading to increased well-being.

Affinity to gaming combined with…	the delivery via smartphone allowing for gamification elements…	motivating participants…	leading to increased engagement with the app training strategies to activate their soothing system..	leading to increased well-being.
Negative attitude towards digital devices combined with…	delivery via smartphone…	lowers participants' motivation and commitment…	impact on training frequency and therefore translation to everyday life negatively and creating reactivity…	leading to increased well-being.

INTERVENTION IN ACUTE MOMENTS OF STRESS

Exposure to situations of high stress combined with…	compassion-focused techniques provided by the intervention's interactive tasks…	applied by participants…	activate the soothing system and lead to increases self-compassion and inner safeness…	leading to increases in momentary well-being and reductions participants' momentary symptom burden.
Exposure to situations of high stress combined with…	compassion-focused techniques provided by the intervention's interactive tasks…	applied by participants…	increase participants' experienced scope of action and competence in handling challenging situations…	leading to increases in momentary well-being and reductions participants' momentary symptom burden.
Exposure to situations of high stress combined with…	compassion-focused techniques provided by the intervention's interactive tasks…	applied by participants…	changes the perspective on emotional experience…	leading to increases in momentary well-being and reductions participants' momentary symptom burden.
Exposure to situations of high stress combined with…	on demand exercises on the smartphone…	triggered by participants…	activate the soothing system and lead to increases self-compassion and inner safeness…	leading to increases in momentary well-being and reductions participants' momentary symptom burden.
Exposure to situations of high stress combined with…	on demand exercises on the smartphone…	triggered by participants…	increase participants' experienced scope of action and competence in handling challenging situations…	leading to increases in momentary well-being and reductions participants' momentary symptom burden.
Exposure to situations of high stress combined with…	on demand exercises on the smartphone…	triggered by participants...	changes the perspective on emotional experience…	leading to increases in momentary well-being and reductions participants' momentary symptom burden.
Anticipation of stressful situations combined with...	compassion-focused techniques provided by the intervention…	applied by participants…	activate the soothing system, increases self-compassion, inner safeness, and changes the perspective on emotional experience…	leading to increases in momentary well-being and reductions participants' momentary symptom burden.
Participants' current life circumstances perceived as distressing combined with...	compassion-focused techniques provided by the intervention…	applied by participants…	activate the soothing system, increases self-compassion, inner safeness, and changes the perspective on emotional experience…	leading to increases in momentary well-being and reductions participants' momentary symptom burden.

The COVID-19 pandemic, as a source of additional stressors such as insecurity and doubt, loss of structure and loneliness combined with…

compassion-focused techniques provided by applied by participants… the intervention…

activate the soothing system, increases self-compassion, inner safeness, and changes the perspective on emotional experience, which will…

leading to increases in momentary well-being and reductions participants' momentary symptom burden.

Context

First, contradicting the initial programme theory, affinity to digital tools could not be identified as a relevant context factor in the current study. Most participants did not describe themselves as especially "technophile", potentially indicating that the delivery format was not creating barriers for most young people with self-described average digital literacy. Findings may therefore contribute to the debate about digital interventions lowering or creating barriers (Berry et al., 2017; Bucci, Schwannauer, et al., 2019; Friis-Healy et al., 2021; Greer et al., 2019).

Second, we identified various context factors improving participants' involvement with the intervention, such as medium symptom severity and positive attitudes towards aspects of the intervention. Involvement, in turn, was an important context factor reported by participants to optimize their outcomes. In quantitative analyses, however, reach was largely independent from baseline characteristics such as symptom severity (Paetzold, Schick, et al., 2022). This may indicate that context factors may unfold their effect before participants sign up for the intervention rather than in the course of the intervention. In future process evaluations, this could be explored by interviewing individuals who have been informed about the intervention and decided not to participate. On the other hand, taken together with findings on personality traits interacting with specific components of the intervention (e.g. need for autonomy and the structure provided), one may conclude that the fit of participants' individual characteristics with the intervention may impact on outcomes more than belonging to a broad group, such as gender, clinical stage or ethnic minority background. This is at variance with findings from standard psychotherapy studies indicating differential treatment effects depending on sociodemographic characteristics (K. E. Hamilton & Dobson, 2002; O'Keeffe et al., 2017).

Third, the COVID-19 pandemic was an important external context factor that impacted on participants in various ways: As indicated in recent publications (Panchal et al., 2021; Rauschenberg, Schick, Goetzl, et al., 2021), some experienced loss of daily structure, loneliness and their mental health was negatively affected by the situation. For others, the changed occupational or educational situation enabled them to participate in the intervention in the first place. Findings on context factors strengthened the concept of EMIs tailoring interventions to service users' daily lives (Myin-Germeys et al., 2018; Myin-Germeys et al., 2016; Reininghaus, 2018) and implied that introducing more flexibility to acknowledge considerable differences in the needs and preference of young individuals may improve the programme. Echoing suggestions of 'stepped-care' models of services (Bower & Gilbody, 2005; Kaltenthaler et al., 2002; Marks

et al., 2003; Scogin, Hanson, & Welsh, 2003), gradable hybrid approaches with flexible delivery schemes and adaptive determination of the number and frequency of sessions may address different needs of treatment intensity, autonomy, structure, interpersonal contact and guidance. Interviewing trained psychologists in future evaluations may help to gain more insight in context factors.

Mechanisms

Adding evidence to findings on improved stress reactivity and momentary resilience in quantitative analyses (Reininghaus et al., under review), we found evidence that participants improved their ability to cope with minor daily stressors by applying self-compassion strategies. As suggested by Myin-Germeys et al. (2018), participants perceived the EMI helped them in "moments when intervention is most needed" (p.127). Qualitative results imply that this may even be extended to anticipatory application of CFIs when expecting stress.

The majority of participants highly appreciated the delivery via smartphone and optional video-conferencing as timely and lowering barriers to and the burden of both, accessing treatment and translating skills into everyday life (Reininghaus, 2018). Participants experienced the hybrid approach as beneficial, but differed in their evaluation of the relative importance of self-directed training via app and the sessions. The programme may therefore be improved further by introducing more flexibility in the intensity of personal contact, tailored to participants' individual needs and personality.

Extending evidence from quantitative analyses (Paetzold et al., under review; Reininghaus et al., under review) and replicating findings from a recent meta-analysis (Ferrari et al., 2019) with qualitative results, the incorporation of compassion-focused principles and the activation of participants' soothing systems were key elements of the intervention's content and the interpersonal contact in the current analyses. Qualitative findings showed improved understanding of affective process, emotional resilience and emotion regulation skills and provided evidence for emotion regulation as a putative link between CFIs and clinical outcomes (Ferrari et al., 2019; Finlay-Jones, 2017; Paetzold et al., under review). Taken together, the current study goes beyond quantitative findings by showing perceived effects on the subjective level of participants' experience that have not been detected in quantitative measures yet.

In line with literature from non-clinical coaching and clinical settings (Baier et al., 2020; Murphy & Hutton, 2018; Pandolfi, 2020), the current study highlights the relevance of the in-

terpersonal contact within the programme. This discrepancy to findings from quantitative analyses, which could not identify working alliance as a mechanism (Paetzold et al., under review), may partly be attributed to the assessment of working alliance in the quantitative investigation, which may not have fully grasped participants' subjective experience.

Outcomes

Replicating meta-analytical findings (Ferrari et al., 2019; Marsh et al., 2018; Wilson et al., 2019), we found evidence that the intervention strengthened participants' soothing system and self-compassion which improved well-being and reduced negative affect. Interestingly, participants also reported improvement in aspects associated with the drive system, such as higher motivation, better concentration and improved self-confidence. This is consistent with compassion-focused theories positing that a strong soothing system provides a good basis for an adaptive and well-functioning drive system (P. Gilbert, 2014). Moreover, positive experiences with the intervention seemed to encourage participants with more severe symptoms to engage in a longer-term therapeutic relationship. This may indicate that EMIcompass may help to lower barriers to more intense forms of treatment.

Limitations

The findings should be evaluated in the light of several limitations. First, the process evaluation was conducted by staff that was also involved in the development and delivery of the programme. This is associated with strengths and limitations of the project. On the one hand, the research team has an enormous depth of understanding and insight in the programme that can hardly be reached in an external process evaluation. On the other hand, the internal evaluation may also be associated with a biased view of the programme. We addressed this with external interviewers and supervision to reduce bias. Second, it was not possible to evaluate all aspects of the intervention in detail. We address this with providing further details in the supplementary material 32. Third, potential self-selection biases cannot be ruled out as participants were not chosen randomly from the full sample receiving the intervention. However, a large proportion of the participants invited agreed to take part.

Conclusion

In the current study, we aimed at examining context factors, mechanisms and outcomes to understand which components of the intervention work for whom, how and under which circumstances. Our findings are encouraging for future of digital mental health interventions in general and future versions of EMIcompass in particular. They provide evidence that EMIs enhance ecological translation of intervention strategies into daily life and highlight the relevance of tailoring intervention delivery and content to service users and their contexts.

CHAPTER VIII:
GENERAL DISCUSSION

For this thesis, I have presented 6 studies devoted to three overarching goals:

First, I aimed to examine digital markers in the prediction of clinical outcomes and investigate the predictive value of momentary manifestations of negative symptoms in individuals at UHR for psychosis (*Part 1, Chapter II*). Second, I aimed to examine the complex interplay of early adversity as a socio-environmental risk factor and putative candidate mechanisms in the development of psychopathology *(Part 2, Chapters III and IV)*. Therefore, *Chapter III* aimed to examine the interplay of exposure to childhood trauma and stress reactivity as a candidate mechanism in predicting clinical outcomes in individuals at UHR for psychosis in a longitudinal design. *Chapter IV* investigated the interplay of childhood trauma, bullying and threat anticipation as a candidate mechanism in the development of psychopathology in a large community sample of adolescents. Third, I presented a hybrid transdiagnostic CFI for enhancing resilience in youth with early mental health problems, explored its reach, putative mechanisms of change involved, and individual intervention trajectories including context factors *(Part 3, Chapters V-VII)*.

This concluding chapter focuses on a critical appraisal of the principal findings with regard to the thesis' aims stated in the introduction. I will discuss methodological considerations as well as potential implications in the light of existing and newly generated evidence.

8.1.   Part 1: Investigating digital markers in the prediction of clinical outcomes

Experience sampling acknowledges service users' expertise for their own experience and allows for a more granular assessment of social experience in real-time and -world contexts (Myin-Germeys et al., 2018). Considerable discrepancies between momentary and other assessment methods (e.g. retrospective self-report questionnaires, laboratory measures) have been reported, indicating that they may capture different constructs (Ben-Zeev et al., 2012; Ben-Zeev & Young, 2010; Blum et al., 2015; A. S. Cohen et al., 2011; Kring & Caponigro, 2010). Consequently, findings suggesting that negative symptoms are associated with level of functioning and transition to psychosis (Alderman et al., 2015; Burton et al., 2019; Demjaha et al., 2012; Glenthøj et al., 2020a; Piskulic et al., 2012; Valmaggia et al., 2013; Zimmermann et al., 2010) cannot simply be transferred to momentary manifestations of negative symptoms as digital markers. Examining the predictive value of subjective experience in daily life may therefore

offer new insights into the social nature and development of negative symptoms in UHR and its outcomes. *Chapter II* was the first study to address this gap in the literature using an experience sampling design to investigate whether momentary manifestations of negative symptoms predict clinical outcomes (i.e., illness severity, level of functioning, and remission from UHR status and transition to psychosis) in individuals at UHR for psychosis at 1- and 2-year follow-up. Robust evidence indicated that higher levels of social anhedonia were associated with higher levels of illness severity and poorer functioning. In addition, there was some evidence that higher experienced pleasantness of being alone and higher levels of anhedonia were associated with poorer functioning at different follow-up assessment points. In exploratory analyses, there was no evidence that momentary manifestations of negative symptoms were associated with transition, but the results tentatively suggested that blunted affective experience predicted time to remission from UHR status.

There are several methodological considerations that should be taken into account when interpreting findings from this chapter. First, the use of an experience sampling design is associated with both, strengths and limitations: On the one hand, it allows for an assessment of momentary manifestations of negative symptoms in real-time and real-world and provides unique insights into participants' subjective experiences. On the other hand, ESM is a burdensome research method, which may have led to selection biases. However, rates of comorbidity and transition were comparable to those observed in previous studies (Albert et al., 2018; Lim et al., 2015; Malda et al., 2019; Simon et al., 2011) and, compared to all participants of the EU-GEI High Risk Study, there was no evidence for an underrepresentation of individuals with more intense symptoms in the ESM sample. Moreover, a recent review concluded that there is compelling evidence that ESM is feasible in vulnerable populations such as participants with severe mental disorders (Myin-Germeys et al., 2018). Given the burden of ESM, the time interval for data collection was rather short (i.e., 6 days), which increased susceptibility to potential sampling biases. This was addressed in the debriefing sessions by ensuring that the ESM period was a 'normal week' for the participants. Despite the potential biases discussed above, ESM is a powerful research method that is particularly well suited to investigate the hypotheses formulated for *Chapter II*.

Second, potential measurement biases need to be considered. Follow-up intervals varied markedly for some individuals, introducing time as a potential confounder. This was addressed by controlling analyses for time to follow-up and conducting sensitivity analyses in a restricted sample of individuals assessed around the ideal follow-up time points, which did not show

substantial deviations from the pattern of results observed in the main analyses. In the exploratory analyses, the use of a proxy for time to remission from UHR may have led to imprecision. Given the focus on generating initial signals of evidence in the exploratory analyses, this may be seen as acceptable at this stage. In addition, the rather short follow-up interval of 2 years is a relevant limitation of *Chapter II*. Conclusions about the predictive value of momentary manifestations of negative symptoms for clinical outcomes can only be drawn for this time interval, as findings cannot be automatically extrapolated to longer periods. Although follow-up intervals of 2 years are rather common in the field (Glenthøj, Kristensen, Wenneberg, Hjorthøj, & Nordentoft, 2020b; Nelson et al., 2013; Salazar de Pablo et al., 2021; Simon et al., 2013) and the highest risk for transition has been demonstrated within the first 2 years after ascertainment (Nelson et al., 2013; Salazar de Pablo et al., 2021), further research adopting longer follow-up intervals is needed to extend evidence on the predictive value of momentary manifestations of negative symptoms.

Third, aggregating data on the person-level rather than acknowledging its multilevel structure did not make optimal use of the data's richness (Schick et al., 2022). Consequently, the variance within participants was not reflected in the aggregated scores, which may have led to imprecision in the analyses. Nonetheless, compared to a single questionnaire assessment, the aggregated experience sampling measures used in *Chapter II* still provide higher levels of sensitivity and minimization of noise (Shiffman et al., 2008). Future research may address this limitation by applying more elaborated methods of analysis to fully use the data's potential.

Although the results must be interpreted with some caution in light of these methodological considerations, we may conclude that *Chapter II* has contributed to deepening our understanding of momentary manifestations of negative symptoms and provided first evidence for their predictive value for clinical outcomes.

Several implications for future research can be derived from *Chapter II*. First, findings on the predictive value of momentary manifestations of negative symptoms as digital markers for clinical outcomes underscore the relevance of service users' momentary experiences of negative symptoms. In line with conceptualisations of social psychiatry (Priebe et al., 2013), ecological psychology (Barker, 1968) and eco-epidemiology (E. Susser, 2004; M. Susser & Susser, 1996), this approach acknowledges the importance of social interactions and contextual factors. Future research may build on this by increasingly incorporating service users' momentary perspective in their everyday life contexts in their studies. This may contribute to understanding how mental health problems manifest in, and interact with, daily life contexts. Moreover, using experience

sampling designs may lead to an empowerment of participants by acknowledging them as experts for their own experiences (Myin-Germeys et al., 2018) and may, for example, introduce opportunities to enhance shared decision making (Reininghaus & Schick, 2022). Second, I observed discrepancies in findings for changes in affective response to social contact (i.e., social anhedonia) and other types of momentary manifestations of negative symptoms (e.g. lack of social drive). One may speculate that various negative symptoms may be especially relevant at different stages in the development of psychopathology. Social anhedonia may be most relevant in individuals at UHR, whereas the impact of other types of momentary manifestations of negative symptoms may unfold in later stages. The findings suggest that social anhedonia may contribute to social interaction losing its reinforcement character, which may stimulate a continuously progressing decrease of social contact and functioning more downstream (C. M. Corcoran et al., 2011; Edwards et al., 2018; Hermans et al., 2020; Reininghaus, Kempton, et al., 2016). This may be elucidated further in future studies. Third, the weak correlations between momentary manifestations of negative symptoms and the BPRS scores should be investigated in more detail. Future research may determine whether the discrepancies – if replicated – may, in fact, reflect distinct dimensions of negative symptoms, such as experience vs expression (Blanchard et al., 2020). If that holds true, this may introduce a whole new facet to the research of negative symptoms in UHR. Fourth, the methodological shortcomings of *Chapter II* may be addressed in future studies. Although the current sample represents the largest set of prospective experience sampling data in individuals at UHR for psychosis to date, longitudinal data from larger samples with repeated ESM measurements and longer follow-up periods need to be collected in the future. This may help to deepen our understanding of momentary manifestations of negative symptoms and their predictive value for various clinical outcomes. Future research may apply more elaborated methods of analyses to make use of the data's full capacity.

Furthermore, implications for practice touching both, diagnostics and intervention, can be derived from *Chapter II*. Findings on the predictive value of momentary manifestations of negative symptoms and low correlations with BPRS scores highlight the relevance of experience sampling as a diagnostic tool over and above traditional clinical measures of symptoms that empowers service users by acknowledging their expertise for their own experience (Myin-Germeys et al., 2018). A recent meta-analysis did not show improvements in functioning by psychosocial treatment in individuals at UHR (Devoe et al., 2019). With poor functioning being a predictor for later psychopathology (Velthorst, Nelson, O'Connor, et al., 2013), it may contribute to a vicious cycle of symptom burden and poor functioning amplifying each other in this group at risk. If replicated, findings from *Chapter II* may therefore inform new intervention

approaches that are urgently needed and the experience of momentary manifestations of negative symptoms, especially anhedonia, may be a promising target for such approaches. Interventions improving social anhedonia may diminish social isolation, and thereby improve service users' outcomes.

8.2. Part 2: Exploring the complex interplay of early adversity as a socio-environmental risk factor and putative candidate mechanisms in the development of psychopathology

Converging evidence from prior research identified early adversity as a socio-environmental risk factor for psychopathology: Adverse experiences in young age, such as childhood trauma or bullying, are associated with a heightened risk of mental-ill health across the lifespan (Greif Green et al., 2010; Kessler et al., 2010; R. E. Norman et al., 2012). For bullying and childhood trauma, associations with general psychopathology (Forbes et al., 2020), various sub-dimensions of psychopathology (Brunstein Klomek et al., 2015; Greif Green et al., 2010) and numerous mental disorders (Brunstein Klomek et al., 2019; Chapman et al., 2004; Dube et al., 2003; Palmier-Claus et al., 2016; Porter et al., 2020; Varese et al., 2012; Weich, Patterson, Shaw, & Stewart-Brown, 2009) have been demonstrated. This compelling evidence on the relevance of early adversity across a wide range of psychopathological outcomes is suggestive of common, transdiagnostic mechanisms in their development (Rauschenberg et al., 2017). In Part 2, I aimed to explore the complex interplay of early adversity as a socio-environmental risk factor and two putative mechanisms in the development of psychopathological outcomes: Stress reactivity (*Chapter III*) and threat anticipation (*Chapter IV*).

As a behavioural marker of stress sensitization (Collip et al., 2008; Myin-Germeys et al., 2018), stress reactivity has been demonstrated to be elevated in various clinical and subclinical populations, especially in the spectrum of psychosis (Lataster et al., 2009; Myin-Germeys et al., 2001; Myin-Germeys et al., 2003; Reininghaus, Kempton, et al., 2016; van der Steen et al., 2017). While previous work accumulated evidence for synergistic effects of adversity and stress reactivity (Glaser et al., 2006; Lardinois et al., 2011; Rauschenberg et al., 2017; Reininghaus, Gayer-Anderson, et al., 2016), other possibilities of how early adversity and stress reactivity may combine with each other, such as a mediation or a mediated synergy model, may also be relevant (Hafeman, 2008; Hafeman & Schwartz, 2009; Morgan et al., 2014; Schwartz & Susser, 2006)). Although stress reactivity may be a crucial putative risk mechanism, *Chapter III* was the first study to investigate the complex interplay of early adversity and stress reactivity as

well as its predictive value for clinical outcomes. To address this pressing gap in the literature, *Chapter III* drew on the largest set of prospective experience sampling data in individuals at UHR for psychosis to date. There was evidence that childhood trauma modified the effect of daily stressors on negative affect and psychotic experiences. In addition, findings were suggestive of stress reactivity as a mediator of the association of childhood trauma and clinical outcomes.

Similar to stress reactivity, threat anticipation has been examined in various clinical and subclinical populations, most prominently in the psychosis spectrum (Bentall et al., 2008; Bentall et al., 2009; R. Corcoran et al., 2006; Grupe & Nitschke, 2013; Reininghaus, Gayer-Anderson, et al., 2016; Reininghaus, Kempton, et al., 2016). *Chapter IV* was the first study to explore the putative transdiagnostic nature of threat anticipation and the first to examine threat anticipation in a sample of adolescents to elucidate the putative mechanism in young age groups. More specifically, *Chapter IV* aimed at investigating the interplay of early adversity, threat anticipation and psychopathology. Threat anticipation, childhood trauma and bullying victimisation were associated with psychopathology. There was evidence for partial mediation of the association between early adversity and psychopathology via threat anticipation. In exploratory analyses, evidence was suggestive of differential associations of specific types of early adversity and specific dimensions of psychopathology.

The findings derived from Part 2 should be interpreted in the light of several methodological considerations. *Chapter III* was a prospective study with a modest sample size; *Chapter IV* was a cross-sectional study drawing on a large community sample. Consequently, both chapters have, in part, complementary strengths and limitations, which will be discussed in the following.

First, the sample sizes should be considered. In *Chapter III*, the sample was of modest size and included few individuals who transitioned to psychosis within the follow-up period. On the one hand, the sample represents the largest set of prospective experience sampling data in individuals at UHR for psychosis to date and transition rates in the observed range are increasingly common in the field (Formica et al., 2020; Hartmann et al., 2016; Nelson et al., 2016; Simon et al., 2011). On the other hand, existing effects may not have been detected due to lack of statistical power, especially in the analyses focusing on transition. In contrast, *Chapter IV* drew on a remarkably large community sample of adolescent leading to high statistical power, which allows to detect rather small effects in the data. As levels of significance are influenced by sample

size, it is important to consider the magnitudes of effects rather than mere statistical significance in both cases (Kirk, 2007; M. Lin, Lucas, & Shmueli, 2013).

Second, the varying designs need to be taken into account. The prospective study design is a major strength of *Chapter III*. It allows to examine stress reactivity as a mediator of the association of childhood trauma and outcomes at follow-up and investigate its predictive value. *Chapter IV* used a cross-sectional design. Consequently, the study did only report associations and further evidence on temporal precedence is mandatory to support criteria for potential causality (M. Susser, 1991). As SIGMA is a cohort study, data collected in future waves of SIGMA may contribute to this.

Third, biases in measurement should be considered. *Chapter IV* assessed various types of early adversity, whereas *Chapter III* focused on childhood trauma and did not consider other relevant forms, such as bullying victimisation (Cunningham et al., 2016). However, findings on associations of mental health problems and different types of early adversity seem to point in the same direction (Brunstein Klomek et al., 2019; Chen et al., 2010; Copeland et al., 2013; R. Gilbert et al., 2009; Greif Green et al., 2010; Koyanagi et al., 2019; Lee & Vaillancourt, 2018; Lereya et al., 2015; McLaughlin et al., 2010; Singham et al., 2017; Takizawa et al., 2014; Varese et al., 2012). In addition, *Chapter III* focused on exploring complex ways of how putative mechanisms may combine and interact with early adversity to exert detrimental effects on mental health. Therefore, both effect modification and mediation have been examined in the same analyses. To my knowledge, only one study in relation to psychosis had investigated both in the same analyses before. Given the focus of the study and the novelty of this approach, it may therefore be deemed appropriate to focus on childhood trauma in the first instance. Future studies may adopt this approach and explore whether findings can be extended to other types of early adversity. In addition, potential measurement biases discussed for Part 1 (i.e., potential biases resulting from the rather short follow-up period and varying follow-up intervals for some individuals) need to be taken into account for *Chapter III* as well. Further, unmeasured potential confounders need to be discussed. Caregiver reports were strongly affected by a low response rate in *Chapter IV*. Consequently, social disadvantage, which has been identified as an a priori cofounder in the preregistration (Paetzold, Gugel, et al., 2021), could not be included in the analyses. Instead, analyses were adjusted for adolescents' self-reports of known a priori confounders (i.e., age, gender, ethnicity, and deviances in cognitive functioning) as an approximation of social disadvantage. However, this can only partly address the limitation and further research is needed to rule out alternative explanations of the data.

In conclusion, the evidence presented in Part 2 is informed by two studies, which differ significantly in their designs and the strengths and limitations associated with them. This is a major strength of Part 2, as the joint interpretation of both chapters, with their respective strengths and limitations, allows for a fusion of complementing perspectives. Taken together, the findings yield exciting insights into the interplay of early adversity and putative mechanisms in the development of psychopathology, whose implications will be discussed below.

Implications for future research can be derived from the results and limitations presented in Part 2. Extending previous findings, evidence highlights the relevance of early adversity in the development of psychopathology and suggests stress reactivity and threat anticipation as relevant putative mechanisms. This is in line with existing models of psychopathology, for example models of psychosis or anxiety disorders (Bar-Haim et al., 2007; D. M. Clark, 1999; Freeman et al., 2002; Garety et al., 2007; Garety et al., 2001; Grupe & Nitschke, 2013; Myin-Germeys & van Os, 2007). However, findings from *Chapter IV* may also be taken to suggest that a shift from specific models of disorders to a more transdiagnostic perspective on the development of psychopathology may be promising. In line with this, evidence derived from Part 2 may also be interpreted in the light of the transdiagnostic conceptualisation of psychopathology posited by compassion-focused approaches (P. Gilbert, 2009, 2014): Stress reactivity and threat anticipation share the concept of an enduring over-activation of emotions related to stress and threat and may be seen as expressions of an hyperactive threat system, which, in turn, CFT posits to be at the core of many mental health problems (P. Gilbert, 2009, 2014). To further strengthen this transdiagnostic perspective on mental health, transdiagnostic investigations of risk factors and putative mechanisms are urgently needed in the future. To increase complexity further, *Chapter III* showed that putative mechanisms may combine with early adversity in various ways to exert detrimental effects on mental health. The findings add evidence to the mediated synergy model suggesting that childhood trauma may link to more severe clinical trajectories via, and in interaction with, subsequently elevated stress reactivity in adulthood. In line with a recent review on putative cognitive mediators (Aafjes-van Doorn et al., 2020), evidence suggestive of partial mediation implies the presence of additional mechanisms linking early adversity to psychopathology.

Future research should therefore aim to better understand the numerous factors contributing to this link and how they may combine. This may be achieved by broadening the perspective in various ways: First, future research may benefit from broadening the perspective with regard to samples and study design. Examining large, transdiagnostic samples with participants from

different stages and age groups in a prospective study with long follow-up intervals may be promising as it allows to generate evidence on transdiagnostic risk factors and mechanisms. A cohort study offers the opportunity to further elucidate potential causal relationships as temporal precedence, which is mandatory to support criteria for potential causality (M. Susser, 1991), can be established. In addition, large samples providing sufficient statistical power to test small effects may help to address some of the limitations of *Chapter III*. Second, future research may broaden the perspective by investigating various risk factors and putative mechanisms and thereby acknowledge the poly-etiological nature of mental health problems. Third, broadening the perspective on how relevant risk factors and putative mechanisms combine may be beneficial. *Chapter III* has provided initial evidence for a mediated synergy model and future research may extend this by investigating both effect modification and mediation in other risk factors and putative mechanisms. Fourth, alternative explanations for the patterns observed need to be ruled out by replication studies that adjust for all relevant a priori confounders, such as social disadvantage. Taken together, these approaches may further extend our understanding of the complex interplay of factors contributing to the development of mental health problems and provide promising targets for prevention and intervention.

Incorporating the perspectives of public health and clinical practice, the findings from Part 2 offer promising targets for prevention and intervention. First, early adversity is a massive public health challenge and must be acknowledged and treated as such (Committee on Psychosocial Aspects of Child and Family Health et al., 2012; Dube, 2018; Juwariah et al., 2022; Sara & Lappin, 2017). Adverse childhood experiences are contributors to the global disease burden that can potentially be modified (Sara & Lappin, 2017). Symonds (2020) posits that protecting children from exposure to early adversity will improve the health of a large proportion of the population (e.g. 60% of the US population). Screening, prevention, and intervention approaches for individuals at risk or already afflicted by early adversity have emerged and need to be extended further (Flynn et al., 2015; Machir, 2014; Murphey & Bartlett, 2019; Oral et al., 2016). In addition, programmes targeting potential offenders have been initiated. This includes, for example, services for undetected, help-seeking people with pedo- and hebephilia in projects like "Dunkelfeld" (Beier et al., 2015) and "kein Täter werden" (von Heyden & Stockmann, 2021) in Germany. Incorporating a public health perspective in these considerations may encourage the development of prevention approaches on different levels (i.e., individual family, community and societal level) and increase reach of measures taken (Magruder, Kassam-Adams, Thoresen, & Olff, 2016). Protecting children will save lives, avoid illness, improve

quality of life and life expectancy and reduce the financial burden on social systems at the same time (Ottley et al., 2022; Symonds, 2020).

Second, while 'curing the cause' completely may unfortunately not be realistic, *Chapters III and IV* provide targets for transdiagnostic prevention and intervention approaches more down-stream, where early adversity may combine with putative mechanisms in the development of psychopathology. As discussed above, the findings suggestive of partial mediation converge with evidence from a recent review that identified multiple putative cognitive mediators of the association of early adversity and psychopathology (Aafjes-van Doorn et al., 2020). The candidate mechanisms identified so far may be targeted successfully by various established strategies: Standard CBT approaches provide a rich repertoire of techniques that can be applied to restructure cognitive bias and improve emotion regulation (Barnow, Reinelt, & Sauer, 2016; A. T. Beck, Rush, Shaw, & Emery, 2010; Ellis, 2013). In addition, third-wave CBT approaches offering an alternative set of strategies, such as ACT (Hayes, Strosahl, & Wilson, 1999), Metacognitive Therapy (Wells, 2011) or CFT (P. Gilbert, 2009, 2014), have gained increasing attention in recent years. Compassion-focused interventions may be especially well suited to target the mechanisms examined in Part 2: Stress reactivity and threat anticipation may both be interpreted as indicators of a hyperactive threat system (P. Gilbert, 2009, 2014) and compassion-focused approaches aim to directly access emotional systems to strengthen the soothing system as an antagonist of a hyperactive threat system (P. Gilbert, 2009, 2014).

Beyond specific techniques, the findings' implications for the delivery mode of prevention and intervention content may not be overlooked. Stress reactivity is a key construct in experience sampling research and has extensively been examined as a momentary process (Myin-Germeys et al., 2005; Myin-Germeys et al., 2003; Myin-Germeys & van Os, 2007; Myin-Germeys et al., 2001; Palmier-Claus et al., 2012; Rauschenberg et al., 2022; Rauschenberg et al., 2017; Reininghaus, Gayer-Anderson, et al., 2016; Reininghaus, Kempton, et al., 2016; Rössler et al., 2016). Threat anticipation has been investigated as a momentary process in various publications as well (Klippel et al., 2017; Reininghaus, Gayer-Anderson, et al., 2016; Reininghaus, Kempton, et al., 2016). Therefore, it may be especially fruitful to use cutting-edge digital technology, such as EMIs, to target these mechanisms where they emerge - on a momentary level in individuals' daily life (Myin-Germeys et al., 2018; Reininghaus, 2018).

8.3. Part 3: A hybrid transdiagnostic intervention for enhancing resilience in youth with early mental health problems – exploring its reach, putative mechanisms of change involved, and individual intervention trajectories

EMIcompass was developed as a hybrid CFI combining an EMI and face-to-face sessions with trained psychologists to enhance resilience in youth with early mental health problems. Part 3 provided details on the intervention manual, as well as first quantitative evidence on its reach and the mechanisms of change involved. Moreover, qualitative results contribute to elucidating which components of the intervention work for whom, how and under which circumstances to enhance resilience.

Chapter V presented the EMIcompass intervention and explored potential associations between participants' baseline characteristics, putative mechanisms and outcomes of the intervention. A structured manual was developed and optimised based on existing literature and manuals including a pilot study's manual (Rauschenberg, Boecking, et al., 2021), the team's clinical experience of working with CFIs, exchange with experts and the principles of EMIs (Myin-Germeys et al., 2016; Reininghaus, 2018). Findings suggested that the reach of the intervention was largely independent of participants' sociodemographic, clinical and functional baseline characteristics.

As delineated above, a combination of compassion-focused and EMI techniques was deemed especially promising to target stress reactivity and threat anticipation in the daily life of young individuals with early mental health problems. While findings from an uncontrolled pilot study (Rauschenberg, Boecking, et al., 2021) and an exploratory RCT (Reininghaus et al., under review) were suggestive of beneficial effects of the EMIcompass intervention, therapeutic mechanisms of change involved remained largely unexplored. Therefore, *Chapter VI* explored change in self-compassion, change in emotion regulation, training frequency and working alliance as putative therapeutic mechanisms of change in the intervention, more specifically their associations with clinical outcomes and mediation of outcome at follow-up by preceding pre- to post-intervention changes in putative mechanisms. Controlling for baseline levels of target outcomes, change in emotion regulation was associated with clinical outcomes across time points. In the mediation analyses, associations of change in self-compassion and change in adaptive emotion regulation with outcomes at follow-up were observed, but no indirect effects were detected. There was no evidence for associations of training frequency with clinical out-

comes. Higher levels of psychologist rated working alliance were associated with higher psychological distress. The effect was driven by post-intervention assessments and did not hold true for follow-up assessments.

Chapter VII aimed to enrich the picture with a qualitative perspective and investigated which components of EMIcompass work for whom, how and under which circumstances by conducting a realist evaluation. I identified 4 programme components (i.e., intervention content, interpersonal contact, delivery via smartphone and training in daily life, intervention in acute moments of distress) that were perceived to enhance the activation of the soothing system and the incorporation of compassion-focused principles. The intervention delivery was perceived as lowering barriers to and burden of treatment and facilitating translation into daily life. EMIcompass was perceived to improve well-being as a main outcome but was also reported to enhance the functioning of participants' drive system. Various context factors, such as personality traits or the COVID-19 pandemic, interacting with the mechanisms were identified. The qualitative analyses provided rich information on potential improvements of the intervention, for example increasing the flexibility in individual intervention trajectories to further tailor EMIcompass to different needs and preferences.

Several methodological considerations should be taken into account when evaluating the quantitative and qualitative findings presented in Part 3. First, aspects of the sample need to be discussed, in particular the sample size, potential biases due to imbalance in the sample, and potential self-selection biases in the qualitative analyses. As the studies presented in Part 3 reported findings from secondary analyses of an exploratory RCT (Reininghaus et al., under review; Schick et al., 2021), they were based on a sample of modest size. Consequently, potential lack of statistical power is a shared limitation of *Chapters V* and *VI*. I addressed this by interpreting effects in terms of magnitude rather than significance. This approach was deemed tolerable given the exploratory nature of the analyses and the early stage of developing a complex intervention. A definitive trial with a larger sample is now warranted. Furthermore, the underrepresentation of participants identifying as male or non-binary may have led to biases in the sample. For a definitive trial, one may therefore consider to stratify randomisation by gender to rule out potential confounding by this factor. Despite intense efforts to recruit participants from a large-scale secondary mental health service, the sample included only few individuals with a first episode of severe mental disorder. Reininghaus et al. (under review) discuss potential explanations: On the one hand, this may be explained by a restriction of the age range to the upper limit of 25 years. In line with international specialist services for individuals with first

episode psychosis (Malla et al., 2016), the upper limit may be extended to 35 years for stage 2 in future studies. On the other hand, the low intensity of the intervention may also be considered as a potential explanation, as it may have prevented individuals from being referred to, or participating in, the intervention. Future research may therefore develop and evaluate versions of the intervention with increased intensity to fit the needs of service users with a first episode of a severe mental disorder. To avoid imbalances between conditions, stratifying recruitment and randomization by clinical stage may be considered in future trials. The qualitative analyses in *Chapter VII* were based on a subsample of the experimental condition receiving the EMIcompass intervention: All participants completing the intervention from December 2020 on were invited to participate in the realist evaluation. Although a comprehensive sample of 20 individuals consented, this raises the question of a potential self-selection bias. It may be possible that individuals finishing the intervention and agreeing to participate in the realist evaluation and individuals declining to do so have distinct characteristics. One may for example speculate whether individuals consenting may have had a strong (either positive or negative) opinion about the intervention, which they wanted to express in the interviews. Therefore, some caution is advised when interpreting the findings of *Chapter VII*.

Second, potential biases in measurement and data collection should be considered. The use of several proxies (e.g. for ethnicity or therapeutic mechanisms of change) may have led to imprecise measurement and is therefore a relevant limitation of *Chapters V and VI*. Ethnicity was assessed taking into account participants' self-reports of citizenship, country of birth, first language and information provided in participants' family assessment, which may have led to misclassification of some individuals. In general, the use of categorical classifications, for example with regard to ethnicity or gender, may be criticised in the light of considerable heterogeneity within groups (Bhopal, 1997; Morgan et al., 2007). By using proxies for putative therapeutic mechanisms of change I may only have been able to map processes roughly, whereas more fine-grained quantitative process data remained unexplored. Furthermore, it cannot be ruled out that unmeasured constructs, or unmeasured aspects of the constructs examined, affected outcome variables. Fear of compassion as a potential barrier to improvement (Boykin et al., 2018; P. Gilbert et al., 2011; Merritt & Purdon, 2020) has not been assessed in the current data set and operationalisations of putative mechanisms under investigation may not fully have grasped all facets of the constructs. Moreover, potential confounding context effects of the COVID-19 pandemic cannot be ruled out. There is evidence suggesting that infection control measures in the pandemic may be associated with poor youth mental health (Rauschenberg, Schick, Goetzl, et al., 2021). In addition, the pandemic directly impacted on the intervention delivery as formats

were changed flexibly between in-person contacts and video-conferencing to comply with local infection control measures. Equivalent effects for both delivery formats have been demonstrated in systematic reviews and meta-analyses (Berryhill et al., 2019; Carlbring et al., 2018; Greenwood et al., 2022), but generalisability to settings in which both formats were used flexibly remains to be tested. Although these limitations may be considered acceptable at this early stage in the development of the intervention, the results should be interpreted with the appropriate caution. Replication of findings with more elaborated assessment procedures and measures, of which some are yet to be developed, is needed to validate the conclusions drawn from *Chapter V* and *VI*.

Third, several aspects of the analyses need to be appraised critically. As delineated for Part 1, the aggregation of data on the person-level is associated with limitations and more elaborate methods of analyses are warranted in future studies. Furthermore, the realist evaluation was conducted by staff also delivering the intervention, which may be associated with a biased view of the programme in the analyses. However, an 'internal' process evaluation may also benefit from the staff's enormous depth of understanding and insight in the programme that can hardly be reached in an 'external' process evaluation. Future research may benefit from combining findings of 'internal' and 'external' process evaluations to create a more comprehensive picture of the programme.

Overall, the limitations discussed for *Chapters V-VII* can be considered acceptable for exploratory analyses at this stage of the development of a complex intervention. In accordance with the predefined aims for Part 3, the chapters generated initial evidence that now needs to be replicated and extended in a definitive trial addressing the limitations described.

The results and methodological considerations presented in Part 3 yield important implications for future versions of the EMIcompass intervention, future trials and research in general. Part 3 provides promising evidence for the intervention, its reach and the delivery format in the transdiagnostic sample of young individuals with early mental health problems. Findings show a mixed picture on putative therapeutic mechanisms of change and emphasise the added value of qualitative methods.

Findings from *Chapter V* suggest that the intervention's reach is largely independent from participants' characteristics. Qualitative results indicating personality traits, rather than sociodemographic aspects, impact on participants' outcomes further support this. The reach of the EMIcompass intervention needs to be further explored in a future definitive trial. This may

include examining reach in more balanced samples, in populations exposed to emerging vulnerabilities as those resulting from armed conflicts, climate crisis and forced displacement, as well as other aspects of marginalised and underserved populations and investigating potential associations with outcomes not considered yet. Future process evaluations may provide more information about relevant context factors by including trained psychologists' perspectives, investigating why participants drop out or decline to participate in the intervention, or by focusing on aspects of the programme not explored in detail yet.

More broadly, against the background of marked health inequalities (Barr, Kinderman, & Whitehead, 2015; Frohlich & Potvin, 2008; Kuntz et al., 2018; Marmot, 2005, 2020; C. J. Murray et al., 1998), reach is a topic that is not reserved for practice but should be considered at all stages in the 'life' of a prevention or intervention approach – from development and conceptualisation to piloting, evaluation and implementation. Although innovation in prevention and treatment is of course much to be welcomed and is driven by the desire to improve the situation of individuals in need, improvements in reach do not necessarily go hand in hand with this. On the contrary, Phelan et al. (2010) noted "developing new interventions, even when beneficial to health, is very likely to increase social inequalities in health outcome" (p. 36) – or in other words, gains in health outcomes achieved by innovations do not benefit all members of society equally (Frohlich & Potvin, 2008). While much effort is going into advances that improve overall health, accompanying increasing health inequalities are often overlooked. However, improving overall health without further widening health inequalities is possible if we can 1) achieve reductions in social inequalities or 2) implement interventions that are more equally distributed across the socio-economic continuum (Phelan et al., 2010). Research may contribute to the first by highlighting the need to intervene and suggesting approaches of change in policy briefs and expert panels. The latter may, for example, be facilitated by using iterative, participative stakeholder-centred design and evaluation processes (Dockweiler & Razum, 2016; David C. Mohr, Weingardt, Reddy, & Schueller, 2017) especially considering minoritized and underserved populations, as suggested as part of the REACT recommendations (Friis-Healy et al., 2021). Increased awareness in the research community and routine examinations of reach in the development of prevention and intervention approaches may further advance the establishment of treatments beneficial to all members of society.

This may be especially important for digital interventions, as concerns have been raised that this delivery format may create, rather than lower, barriers to treatment (Berry et al., 2017; Bucci, Berry, et al., 2019; Friis-Healy et al., 2021; Greer et al., 2019). The current findings are

at variance with evidence of differential treatment effects depending on sociodemographic characteristics in standard psychotherapy studies (K. E. Hamilton & Dobson, 2002; O'Keeffe et al., 2017). If future studies replicated these findings and even moved beyond them for EMIcompass and other digital interventions, this may contribute to a better understanding of the opportunities and limitations of digital interventions in comparison to standard formats of delivery and help to address associated concerns.

Although more research is required, the current findings already yield implications for digital intervention formats in general and EMIs in particular. *Chapter VII* indicates that digital tools (i.e., the EMI, video-conferencing formats for sessions) were highly appreciated by young individuals participating in the EMIcompass trial and were reported to lower barriers to and burden of treatment. This indicates feasibility and may be seen as an encouragement for further digital intervention projects to target a generation of digital natives. Digital intervention approaches may therefore have the potential to address low availability, access and use reported for youth mental health services (Malla et al., 2016; Wang et al., 2005) and contribute to narrow the existing treatment gap (Thornicroft, 2007). Despite positive signals, potential downsides of these delivery formats should not be overlooked and future research should take concerns of stakeholders seriously (Aafjes-van Doorn, Békés, & Prout, 2021; Topooco et al., 2017). Generalisability for other samples and ecological validity for clinical and public health practice, especially against the background of the digital divide (Lythreatis, Singh, & El-Kassar, 2022; Makri, 2019), remains to be demonstrated. Across different types of digital interventions (i.e., video therapy, hybrid approaches combining face to face sessions with internet- and mobile-based intervention), clinicians are reported to anticipate barriers such as impersonality and difficulties in building a stable therapeutic relationship (Connolly, Miller, Lindsay, & Bauer, 2020; Sucala, Schnur, Brackman, Constantino, & Montgomery, 2013; Titzler, Saruhanjan, Berking, Riper, & Ebert, 2018; Topooco et al., 2017). In the course of the COVID-19 pandemic however, many clinicians began to provide online treatment and future research may investigate whether the experiences gained during these times may have changed their view of digital intervention formats (Aafjes-van Doorn et al., 2021). Measures explicitly acknowledging digital contexts, such as an assessment of digital working alliance, as proposed by Henson et al. (2019), are urgently needed and may contribute to addressing clinicians' concerns.

To my knowledge, *Chapter VII* is the first qualitative study to show that an EMI is perceived to provide support in "moments when intervention is most needed" (Myin-Germeys et al., 2018, p. 127) as posited in influential publications of the field (Heron & Smyth, 2010; Myin-Germeys et al., 2018; Myin-Germeys et al., 2016). Interestingly, current findings extend this even further

by providing initial evidence for a preventive application of intervention techniques when anticipating distress. Taken together, with findings suggestive of a reduction of momentary threat anticipation (Reininghaus et al., under review), this adds a completely new perspective to EMIs and needs to be explored in more detail. Therefore, future research may investigate processes leading participants to trigger on-demand intervention content within the app (i.e., by asking why participants have decided to trigger the task before or after completing it) or in qualitative interviews. These findings are in line with calls of social psychiatry to acknowledge social interactions and contextual factors (Priebe et al., 2013) and provide encouraging evidence for approaches aiming to modify symptoms in the context in which they emerge (Myin-Germeys et al., 2018; Reininghaus, 2018).

Moreover, findings from Part 3 improve our understanding of compassion-focused interventions in general and especially in the context of the hybrid delivery format. While quantitative analyses could not detect evidence for a mediation effect via change in self-compassion or change in emotion regulation, *Chapter VII* largely supports current theoretical models of CFIs in the transdiagnostic sample of youth with early mental health problems. In line with theoretical papers, meta-analyses, and review articles (Craig et al., 2020; Ferrari et al., 2019; Finlay-Jones, 2017; P. Gilbert, 2009, 2014), EMIcompass was perceived to strengthen participants' soothing system. This included increases in self-compassion and improvements in emotion regulation leading to improved well-being. Further, as postulated in compassion-focused models (P. Gilbert, 2009, 2014), EMIcompass was reported to improve the functioning of the drive system. This may be taken to suggest that EMIcompass, as a hybrid intervention, may work similarly to standard delivery of CFIs in transdiagnostic samples.

The observed inconsistencies between quantitative and qualitative findings allow several interpretations: On the one hand, they may be explained by the limitations of the current studies, which may be addressed in future research. In the context of an EMI, it may be fruitful to examine putative therapeutic processes of change, such as improvements in self-compassion or emotion regulation, on a momentary level throughout the intervention to provide more fine-grained data (Schick et al., 2022). The assessment of momentary constructs is developing rapidly and future research may benefit from relying on open resources for ESM items, such as the Experience Sampling Item Repository (Kirtley et al., 2019). In line with this focus on momentary processes, the hypothesised modes of action of intervention components will be examined in a detailed investigation of micro-level processes of change that is currently being prepared for postregistration (Gugel, Paetzold, Schick, & Reininghaus, in preparation). On the other

hand, the inconsistencies in the findings may also be taken to emphasise the relevance of multimethod approaches. Part 3 illustrates the potential of quantitative and qualitative research to complement each other. Qualitative analyses seem to go beyond quantitative findings by showing perceived effects on the subjective level of participants' experience that have not been detected in quantitative measures yet. The promise of a more comprehensive picture of the programme under examination may attract more attention in the future and increase the rate of multimethod evaluations of (digital) intervention and prevention approaches.

Findings may also have research implications for the putative therapeutic mechanisms of change examined. *Chapter VI* provided a mixed picture of the role of self-compassion. Quantitative analyses did not detect initial signals of change in self-compassion to be associated with outcomes across time points, but change in momentary self-compassion was associated with improved clinical outcomes at follow-up in the mediation analyses. As mentioned above, the assessment of momentary self-compassion may be aligned more to the postulated facets (Hupfeld & Ruffieux, 2011; Neff, 2003) and fear of compassion may be assessed as a potential barrier to improvement (P. Gilbert et al., 2011) in future studies.

Emotion regulation strategies have been demonstrated to be associated with psychopathology (Aldao et al., 2010; Compas et al., 2017) and have been discussed as a putative link between CFIs and clinical improvement (Ferrari et al., 2019; Finlay-Jones, 2017). Replicating previous findings (Conklin et al., 2015), change in adaptive and maladaptive emotion regulation strategies was associated with psychopathology in *Chapter VI*. However, I did not detect initial signals for a mediation via emotion regulation. In addition, the magnitude of effects observed in *Chapter VI* were at variance with the literature reporting more robust associations with psychopathology for maladaptive than for adaptive emotion regulation (Aldao et al., 2010). Future research may further investigate emotion regulation in the context of EMIcompass, also taking into account more complex ways of how emotion regulation may interact with CFIs and psychopathology. For example, one may consider the compensatory hypothesis of psychopathology suggesting the elevated use of maladaptive emotion regulation strategies may be compensated by adaptive strategies (Aldao & Nolen-Hoeksema, 2012).

Although meta-analytic evidence indicated small to moderate associations with outcomes (Kazantzis et al., 2010; Kazantzis et al., 2016; Mausbach et al., 2010; Parsons et al., 2017), training frequency was not associated with clinical outcomes in *Chapter VI*. Training frequency was operationalised as the amount of exercises completed in the EMI. In line with findings from a hybrid intervention with a different focus (Vaessen et al., 2019), several participants reported in the qualitative analyses that they occasionally applied strategies without using the phones.

Future EMIs may therefore include a function, which allows participants to note the application of techniques without the phone, if training frequency is further investigated. Besides quantitative aspects, future studies may also focus on qualitative aspects of training. Therefore, the revised version of the intervention will assess training quality ratings and potential difficulties experienced by the participants. This can be used for scientific and clinical purposes as it may broaden the perspective on training effects in research and inform trained psychologists about potential difficulties when preparing the next session.

Contrary to findings from standard delivery of psychotherapy (Baier et al., 2020), participants' rating of working alliance were not associated with outcomes in Part 3. This may partly be attributed to the small number of contacts with the trained psychologists in comparison to standard psychotherapy as well as the guided self-help nature of the intervention. In qualitative analyses, however, the interpersonal contact was described as the "the crux of the matter" by some participants. Furthermore, higher psychologist rated working alliance tended to be associated with higher psychological distress at post-intervention but not at follow-up, potentially indicating trained psychologists may have increased the intensity of interventions for those who showed signs of worsening mental health problems during the intervention period. To elucidate these ambiguous findings further, future versions may rely on other forms of measurement of working alliance more appropriate for the given context that are probably yet to be developed (Henson et al., 2019).

All these interesting aspects derived from Part 3 can be used to inform future EMIs, CFIs and approaches combining both. The EMIcompass intervention is currently being revised informed by quantitative and qualitative results. Recommendations to further improve acceptability and feasibility of the intervention (e.g. updating and optimizing the app design, offering the use of own smartphones, feedback on app usage) have been formulated in this thesis and elsewhere (Reininghaus et al., under review) and will be implemented in the revised version. In line with calls for more personalization in intervention approaches (Myin-Germeys et al., 2016; Reininghaus, 2018; Reininghaus et al., 2015), this refers in particular to a flexibilization of individual intervention trajectories including, for example, tailored sampling schemes for interactive tasks, a personalised session frequency and the opportunity to augment treatment for individuals with more severe symptoms (Paetzold, Schueltke, Boecking, & Reininghaus, 2022). In addition, fear of compassion will be addressed with dedicated materials provided in a resource pool for potential difficulties in the intervention manual. Future research may also consider to investigate EMIcompass in a group format, as evidence from a systematic review suggests that CFIs may be especially promising when delivered in a group format over at least 12

hours (Craig et al., 2020). Moreover, a process evaluation by external researchers not involved in the development and delivery of the intervention may contribute to deepen our understanding of which components of EMIcompass work for whom, how and under which circumstances.

Furthermore, various implications for public health approaches and clinical practice can be derived from Part 3. First, findings on the intervention presented in Part 3 and elsewhere (Reininghaus et al., under review) encourage the application of hybrid transdiagnostic compassion-focused approaches in young individuals with early mental health problems. The intervention was demonstrated to be feasible and first signals of reduced stress reactivity have been detected (Reininghaus et al., under review). Change in self-compassion and change in emotion regulation were associated with clinical outcomes and may therefore represent promising targets for future intervention and prevention approaches.

Second, quantitative findings for reach were promising and the qualitative analyses indicated that the digital forms of delivery lowered barriers and burden for the given sample. Digital options in treatment, such as video therapy or the use of digital mental health interventions, may therefore be a useful extension of services to increase reach. In addition, some participants used EMIcompass as a possibility to familiarize with mental health care services and get a first impression of treatment, which then encouraged them to access more intensive forms of care. Positive experiences with low-threshold, low-intensity services may therefore be helpful to build trust and encourage young individuals with early mental health problems to seek more intensive care if needed. This is in line with key concepts of the youth mental health reform and early intervention aiming at reducing the duration of untreated illness (Malla et al., 2016; McGorry, Purcell, Hickie, & Jorm, 2007; R. M. G. Norman & Malla, 2001) and may help to prevent young individuals from getting entangled in a downward spiral of disadvantage and missed opportunities for education, employment and development (Malla et al., 2018). Taken together, a shift in our perspective may be needed to prioritize reach – or as a mental health professional phrased it in a qualitative study by Bucci, Berry, et al. (2019): "They are not hard-to-reach clients. We have just got hard-to-reach services" (p.1).

Third, digital delivery formats of interventions may have other advantages for mental health services besides potential positive implications for reach. Most importantly, participants acknowledged and appreciated key components of the rationale of using an app to deliver the intervention: The app was reported to facilitate the translation of strategies into participants' daily life and to offer intervention when it was needed most. Participants perceived the delivery

format with daily consolidating tasks and on-demand content as helpful to train strategies acquired previously. Interestingly, evidence from Part 3 indicated that appreciation of digital tools may not be limited to especially "technophile" service users but was shared by the majority of young participants. This indicates that EMIs may be promising tools for prevention and intervention and may be implemented in different settings, as low-intensity approaches or as add-ons to standard care. In addition, other applications for digital mental health interventions, such as promotion of shared decision making informed by ESM data (Reininghaus & Schick, 2022), are currently investigated. Moreover, the delivery of sessions via video-conferencing was highly appreciated by the EMIcompass sample. Although many clinicians familiarised with video therapy during the pandemic, changing the medium for therapy should not be considered a side issue (Aafjes-van Doorn et al., 2021). If video therapy is to be implemented as an ubiquitous alternative to sessions in person, adequate training of staff is necessary to address stakeholders' concerns, improve user experience and foster successful use of video therapy in the future (Aafjes-van Doorn et al., 2021).

Fourth, evidence generated in Part 3 highlights the relevance of tailored and personalised interventions. Findings suggest that individual differences in needs and personality are important context factors for prevention and intervention approaches. Increasing flexibility in all parts of prevention and intervention may therefore be the way to go for optimizing services. Echoing suggestions of 'stepped-care' models of services (Bower & Gilbody, 2005; Kaltenthaler et al., 2002; Marks et al., 2003; Scogin et al., 2003), individualised intensity, frequency and scope of treatment as well as personalised intervention content and delivery formats (group vs. individual sessions, video-conferencing vs. face-to-face sessions) may be promising. Future services may move from 'one size fits all' to gradable hybrid approaches in which all aspects of care may be personalised to the needs and preferences of an individual service user.

8.4. Concluding remark

Overall, the findings presented in this thesis provide a transdiagnostic perspective on early mental health problems and link adversity, digital markers, putative mechanisms in the development of psychopathology and a novel, hybrid compassion-focused intervention approach. From the thesis, six central conclusions can be drawn:

First, the thesis highlighted the **potential of digital markers** in the prediction of clinical outcomes using the experience sampling method. This approach acknowledges the importance of social interactions and contextual factors as well as participants' expertise for their own experiences (Myin-Germeys et al., 2018). Experience sampling may therefore be a promising diagnostic tool over and above traditional clinical measures of symptoms that has the potential to significantly advance research and practice. For example, findings on the predictive value of momentary manifestations of negative symptoms as digital markers may – if replicated – provide a new perspective on negative symptoms in UHR and inform new intervention approaches that are urgently needed to improve service users' outcomes.

Second, the thesis showed that **putative mechanisms may combine with early adversity in complex ways** in the development of psychopathology and may be **promising targets for prevention and intervention**. In line with previous research highlighting early adversity as an important transdiagnostic risk factor and a major public health challenge (Committee on Psychosocial Aspects of Child and Family Health et al., 2012; Dube, 2018; Juwariah et al., 2022; LeMoult et al., 2020; Morgan & Gayer-Anderson, 2016; Palmier-Claus et al., 2016; Sara & Lappin, 2017; Selous et al., 2020; Varese et al., 2012), the thesis provided evidence for associations of early adversity and psychopathology. An expansion of resolute countermeasures comprising screening, prevention, and intervention approaches for individuals at risk or already afflicted by early adversity is urgently needed as efforts to protect children can save lives, prevent illness, enhance life expectancy and quality of life and decrease the financial burden on social systems (Ottley et al., 2022; Symonds, 2020). In addition, the thesis was one of first in the field of psychosis research to generate evidence for the mediated synergy model. It provided evidence suggesting that socio-environmental risk factors may both modify putative mechanisms and exert detrimental effects via putative mechanisms to push individuals along more severe clinical trajectories (Hafeman, 2008; Hafeman & Schwartz, 2009). Moreover, findings were suggestive of stress reactivity and threat anticipation as putative transdiagnostic mechanisms in the development of psychopathology and highlighted them as promising targets for prevention and intervention approaches. Future research may extend these findings (e.g. by

investigating how various risk factors and putative mechanisms combine in large and transdiagnostic samples to test the mediated synergy model) and thereby further elucidate the complex interplay of various factors contributing to the development of mental health problems.

Third, **digital prevention and intervention approaches have the potential to significantly advance existing services.** I developed a structured intervention manual for a hybrid CFI combining face-to-face sessions and an EMI (i.e., EMIcompass), for which promising initial evidence was observed in quantitative and qualitative analyses presented in this thesis and elsewhere (Reininghaus et al., under review). EMIs were perceived to enhance ecological translation of intervention strategies into daily life and to lower barriers to, and burden of, treatment. To my knowledge, the thesis is the first to provide qualitative evidence for a core claim of the ecological momentary intervention literature (Heron & Smyth, 2010; Myin-Germeys et al., 2018; Myin-Germeys et al., 2016) suggesting EMIs may offer support in "moments when intervention is most needed" (Myin-Germeys et al., 2018, p. 127).

Taken together, findings can be seen as an encouragement for future versions of EMIcompass and digital mental health interventions in general. Digital intervention approaches may be a useful extension of services potentially increasing their reach and addressing the existing treatment gap. Recently, effort is made to increase the availability of evidence-based digital interventions and integrate them into services, for example by the Platform for Digital Health Applications (DiGA) in Germany. Future research may follow-up on this by developing, evaluating and implementing new, and further improve existing, evidence-based digital prevention and intervention approaches.

Fourth, scrutinising **reach** and increasing **tailoring and personalisation** will further improve digital prevention and intervention approaches. Against the background of marked health inequalities and the inequality paradox suggesting that health gains associated with innovative approaches are likely to further amplify social inequalities in health (Frohlich & Potvin, 2008; Link & Phelan, 1995; Marmot, 2005, 2020; Phelan et al., 2010), reach needs to be considered at all stages in the 'life' of prevention and intervention approaches. For the EMIcompass intervention, findings indicated that reach of participants by the intervention was largely independent from their sociodemographic, clinical, and functional characteristics. In addition, evidence generate in this thesis suggests that, echoing 'stepped-care' models of services (Bower & Gilbody, 2005; Kaltenthaler et al., 2002; Marks et al., 2003; Scogin et al., 2003), increasing tailoring and flexibility may be the way to go for optimizing services. Prioritizing reach may contribute to build up 'easy-to-reach services', which may have the potential to prevent young

individuals from getting entangled in a downward spiral of disadvantage and missed opportunities (Malla et al., 2018). This may be facilitated by adopting participative approaches such as co-design and co-production (Dockweiler & Razum, 2016; David C. Mohr et al., 2017) especially considering minoritized and underserved populations (Friis-Healy et al., 2021).

Fifth, the thesis highlighted the **potential of multimethod examinations** to provide a more comprehensive understanding of prevention and intervention approaches. Quantitative and qualitative methods are not mutually exclusive, on the contrary, they provide complementing perspectives. It is therefore urgently necessary for future research to conduct process evaluations considering both quantitative and qualitative data (G. F. Moore et al., 2015).

Sixth, the thesis' findings encourage a shift to more **transdiagnostic and continuous conceptualisations of mental health**. The thesis provided evidence on a transdiagnostic risk factor, on transdiagnostic putative mechanisms and presented a transdiagnostic prevention and intervention approach based on compassion-focused principles. Future research may benefit from adopting a transdiagnostic perspective and may thereby contribute to overcome the traditional conceptualisation of mental health problems in the prevailing medical model (Craddock & Owen, 2010; Kendler, 2012; van Os et al., 2019).

SUMMARY

In this thesis, I adopted a transdiagnostic perspective on early mental health problems and pursued three overarching goals. First, I aimed to investigate digital markers in the prediction of clinical outcomes. Second, I aimed to examine how early adversity may combine and interact with putative candidate mechanisms in the development of psychopathology. Third, I aimed at the development of a hybrid transdiagnostic intervention for enhancing resilience in youth with early mental health problems. I aimed to explore its reach, putative mechanisms of change involved, and personalised intervention trajectories including context factors (i.e., what works for whom under which circumstances?).

In line with the first goal, *Chapter II* presented the first study, which examined the predictive value of momentary manifestations of negative symptoms as digital markers for clinical outcomes in individuals at ultra-high risk for psychosis using an experience sampling design. I found evidence for momentary manifestations of negative symptoms, especially social anhedonia, to predict clinical outcomes. Higher levels of momentary manifestations of negative symptoms were associated with higher levels of illness severity and poorer functioning at 1- and 2-year follow-up. This approach offers important insights into service users' symptoms in the context of their daily life, which are relevant for research and practice. Moreover, subjective experiences of negative symptoms, especially social anhedonia, in daily life may be a promising target for future intervention approaches in the early stages of psychosis.

Addressing the second aim, *Chapters III* and *IV* presented investigations of stress reactivity and threat anticipation as putative mechanisms linking early adversity with psychopathology. In Chapter *III*, I examined stress reactivity as a putative mechanism linking childhood trauma with clinical outcomes in individuals at ultra-high risk for psychosis. Replicating previous findings, childhood trauma modified the effect of daily stressors on negative affect and psychotic experiences. Individuals exposed to higher levels of childhood trauma showed more intense psychotic experiences and stronger increases in negative affect in response to minor daily stressors. In addition, there was some evidence suggestive of the predictive value of stress reactivity for clinical outcomes at follow-up. Some evidence for partial mediation of the association of childhood trauma and clinical outcomes via stress reactivity emerged. Taken together, these findings added evidence to the mediated synergy model and highlighted stress reactivity as a promising target mechanism for ecological momentary interventions. In *Chapter IV*, I investigated the role of threat anticipation in the development of psychopathology. I found evidence that threat anticipation and experiences of early adversity were associated with psychopathology. In addition,

I observed mediation effects for the association between early adversity and psychopathology via pathways through threat anticipation. This suggests the relevance of threat anticipation as a putative transdiagnostic mechanism linking early adversity with psychopathology that may be targeted by prevention and intervention approaches.

In line with the third goal, *Chapter V* presented an intervention manual for a hybrid compassion-focused intervention targeting putative transdiagnostic candidate mechanisms such as stress reactivity and threat anticipation in youth with early mental health problems (i.e., EMIcompass) and provided promising initial evidence on the intervention's reach. In *Chapter VI,* I explored putative therapeutic mechanisms of change in the EMIcompass intervention. I did not detect initial signals of a mediation of the effect of experimental condition on clinical outcomes at follow-up via putative therapeutic mechanisms. However, results show that, if targeted successfully, change in self-compassion and emotion regulation may be promising targets for intervention and prevention approaches. To explore personalised intervention trajectories including context factors, *Chapter VII* presented a realist evaluation of the implementation of EMIcompass. Qualitative results indicated that the EMIcompass intervention worked by strengthening participants' soothing system and improved their well-being. In addition, there was evidence indicating that the intervention may even improve the functioning of participants' drive system. The digital delivery format was perceived as facilitating the translation into daily life and lowering the burden of, and barriers to, treatment. The findings may inform the development and implementation of future digital mental health interventions in general and future versions of EMIcompass in particular.

ZUSAMMENFASSUNG

In dieser Dissertation betrachtete ich frühe psychische Probleme aus einer transdiagnostischen Perspektive und verfolgte drei zentrale Ziele: Erstens sollten digitale Marker für die Vorhersage klinischer Variablen untersucht werden. Zweitens hatte die Dissertation zum Ziel, zu untersuchen, wie frühe belastende Erfahrungen und mutmaßliche Mechanismen in der Entwicklung psychopathologischer Symptome miteinander interagieren. Das dritte Ziel der Dissertation war es, eine hybride, transdiagnostische Intervention zur Resilienzförderung bei Jugendlichen und jungen Erwachsenen zu entwickeln und ihre Reichweite, mutmaßliche therapeutische Mechanismen der Veränderung sowie individuelle Interventionsverläufe einschließlich relevanter Kontextfaktoren (d.h. was funktioniert für wen unter welchen Umständen?) zu untersuchen.

Im Einklang mit dem ersten Ziel stellte *Kapitel II* die erste Studie dar, die den prädiktiven Wert momentaner Manifestationen von Negativsymptomen als digitale Marker für klinische Outcomes bei Personen mit Psychoserisikosyndrom unter Nutzung der Experience Sampling Methode untersuchte. Dabei zeigte sich, dass momentane Manifestationen von Negativsymptomen, insbesondere soziale Anhedonie, klinische Variablen vorhersagten. Höhere Ausprägungen momentaner Manifestationen von Negativsymptomen gingen dabei mit einem ausgeprägteren Schweregrad der Symptomatik und einem niedrigeren Funktionsniveau zum Zeitpunkt der Nachuntersuchungen nach einem und zwei Jahren einher. Der Ansatz digitaler Marker kann wichtige Einblicke in das subjektive Erleben von Patient*innen im Kontext ihres Alltags bieten, die für Forschung und Praxis gleichermaßen relevant sind. Darüber hinaus könnte das subjektive Erleben von Negativsymptomen, insbesondere von sozialer Anhedonie, ein vielversprechendes Ziel für zukünftige Interventionsansätze in frühen Stadien psychotischer Störungen sein.

Im Einklang mit dem zweiten Ziel stellten *Kapitel III* und *IV* Untersuchungen von Stressreaktivität und Bedrohungserwartung als potentielle Mechanismen dar, die frühe belastende Erfahrungen und psychopathologische Symptome miteinander verbinden könnten. In *Kapitel III* untersuchte ich Stressreaktivität als potentiellen Mechanismus, der traumatische Erlebnisse in der Kindheit und Jugend mit klinischen Variablen bei Personen mit Psychoserisikosyndrom verbinden könnte. In Übereinstimmung mit bisherigen Forschungsergebnissen zeigten Personen, die einem höheren Maß an Trauma ausgesetzt waren, intensivere psychotische Erlebnisse und einen stärkeren Anstieg des negativen Affekts als Reaktion auf geringfügige alltägliche Stressoren. Darüber hinaus zeigten sich Hinweise für den prädiktiven Wert von Stressreaktivität für klinische Variablen zum Zeitpunkt der Nachuntersuchungen. Es gab Hinweise auf eine partielle

Mediation des Zusammenhangs zwischen Trauma und klinischen Variablen durch Stressreaktivität. Insgesamt unterstützten die Ergebnisse das Modell der mediierten Synergie und deuteten darauf hin, dass Stressreaktivität ein vielsprechendes Ziel für ambulatorische Interventionen sein könnte. *Kapitel IV* untersuchte die Rolle von Bedrohungserwartung in der Entwicklung psychopathologischer Symptome. Dabei zeigten sich positive Zusammenhänge von Bedrohungserwartung und frühen belastenden Erfahrungen mit psychopathologischen Symptomen. Außerdem beobachtete ich, dass die Bedrohungserwartung die Assoziation früher belastender Erfahrungen mit psychopathologischen Symptomen mediierte. Die Ergebnisse unterstreichen die Bedeutung von Bedrohungserwartung als potentiellen transdiagnostischen Mechanismus, der frühe belastende Erfahrungen mit psychopathologischen Symptomen verbindet und einen relevanter Zielmechanismus für Präventions- und Interventionsansätze darstellen könnte.

Im Einklang mit dem dritten Ziel der Dissertation stellte ich in *Kapitel V* ein Interventionsmanual für eine hybride, mitgefühlsbasierte Intervention vor, die die Modifikation mutmaßlicher Mechanismen, wie Stressreaktivität und Bedrohungserwartung, bei Jugendlichen und jungen Erwachsen mit frühen psychischen Problemen zum Ziel hatte (EMIcompass). Dabei zeigten sich vielversprechende erste Befunde für die Reichweite der Intervention in *Kapitel V*. In *Kapitel VI* wurden mutmaßliche therapeutische Mechanismen der Veränderung im Rahmen der EMIcompass Intervention untersucht. Dabei fand ich keine Hinweise für eine Mediation des Zusammenhangs zwischen experimenteller Bedingung und klinischen Variablen zum Zeitpunkt der Nachuntersuchung durch potentielle therapeutische Mechanismen der Veränderung. Die Ergebnisse deuteten jedoch an, dass Selbstmitgefühl und Emotionsregulation vielversprechende Ziele für Interventions- und Präventionsansätze sein könnten. Um individuelle Interventionsverläufe unter Einbezug von Kontextfaktoren zu untersuchen, wurden in *Kapitel VII* die Ergebnisse einer Realist Evaluation der Implementierung der EMIcompass Intervention vorgestellt. Die qualitativen Ergebnisse wiesen darauf hin, dass die EMIcompass Intervention durch die Stärkung des Geborgenheitssystems der Teilnehmenden wirkte und ihr Wohlbefinden verbesserte. Darüber hinaus ergaben sich Hinweise darauf, dass die Intervention auch die Funktion des Antriebssystems der Teilnehmenden verbessern könnte. Es zeigte sich, dass das digitale Format als Unterstützung der Translation von Interventionsinhalten in den Alltag wahrgenommen wurde, wahrgenommene Behandlungshindernisse abbaute und die erlebte Belastung durch die Intervention verringerte. Die Ergebnisse bieten Orientierung für die Entwicklung und Implementation künftiger digitaler Anwendungen für psychische Gesundheit und die Weiterentwicklung der EMIcompass Intervention.

SUPPLEMENTARY MATERIALS

Supplementary materials Chapter II

Supplementary material 1: Convergent validity of momentary manifestations of negative symptoms and interviewer-rated measures of negative symptoms

The association of momentary manifestations of negative symptoms and observer-rated measures of negative symptoms at baseline was examined to evaluate convergent validity of the measures (Table S1). In addition, we used observer-rated measures of negative symptoms to predict momentary manifestations of negative symptoms measured with ESM in a multilevel model (Table S2).

Table S1. *Correlation matrix of momentary manifestations of negative symptoms and observer-rated negative symptoms.*

	BPRS total score	BPRS neg. symptom score	Inten-sity NA	Inten-sity PA	Varia-bility NA	Varia-bility PA	Insta-bility NA	Insta-bility PA	Anhedonia	Social an-hedonia	Amount of time spent alone	Preference to be alone when in company	Pleasantness of being alone
BPRS total score	1.00												
BPRS neg. symptom score	0.54 *p*<.001	1.00											
Intensity NA	0.28 *p*=.017	0.13 *p*=.285	1.00										
Intensity PA	-0.34 *p*=.004	-0.21 *p*=.081	-0.60 *p*<.001	1.00									
Variability NA	0.26 *p*=.025	0.03 *p*=.777	0.28 *p*=.012	-0.06 *p*=.590	1.00								
Variability PA	-0.06 *p*=.595	-0.10 *p*=.418	0.03 *p*=.823	0.18 *p*=.112	0.67 *p*<.001	1.00							
Instability NA	0.18 *p*=.123	0.09 *p*=.420	0.09 *p*=.420	0.06 *p*=.621	0.85 *p*<.001	0.62 *p*<.001	1.00						
Instability PA	0.00 *p*=.982	-0.13 *p*=.270	-0.08 *p*=.497	.23 *p*=.038	0.61 *p*<.001	0.80 *p*<.001	0.78 *p*<.001	1.00					
Anhedonia	-0.34 *p*=.003	-0.19 *p*=.100	-0.57 *p*<.001	0.99 *p*<.001	-0.01 *p*=.908	0.25 *p*=.028	0.09 *p*=.427	0.28 *p*=.012	1.00				
Social anhedonia	-0.31 *p*=.008	-0.17 *p*=.142	-0.53 *p*<.001	0.95 *p*<.001	-0.07 *p*=.541	0.20 *p*=.07	0.03 *p*=.781	0.21 *p*=.060	0.95 *p*<.001	1.00			
Amount of time spent alone	-0.13 *p*=.266	-0.12 *p*=.327	-0.05 *p*=.687	0.08 *p*=.458	0.01 *p*=.944	0.12 *p*=.283	0.11 *p*=.320	0.16 *p*=.155	0.11 *p*=.314	0.12 *p*=.309	1.00		
Preference to be alone when in company	0.10 *p*=.412	0.16 *p*=.183	.049 *p*<.001	-0.46 *p*<.001	0.06 *p*=.576	-0.12 *p*=.294	-0.02 *p*=.880	-0.11 *p*=.342	-0.470 *p*<.001	-0.50 *p*<.001	-0.20 *p*=.074	1.00	
Pleasantness of being alone	-0.08 *p*=.489	-0.03 *p*=.789	0.02 *p*=.894	0.06 *p*=.613	0.15 *p*=.184	0.00 *p*=.999	0.14 *p*=.232	0.04 *p*=.714	0.04 *p*=.752	-0.03 *p*=.786	-0.05 *p*=.661	0.42 *p*=.002	1.00

Note. BRPS=Brief Psychiatric Rating Scale (Ventura et al., 1993). NA=negative affect. PA=positive affect.

Table S2. *Momentary manifestations of negative symptoms predicted by observer-rated negative symptoms.*

	Predictors			
	BPRS total score		**BPRS negative symptom score**	
	b (95% CI)	*p*	*b* (95% CI)	*p*
Outcome: Blunted affective experience				
Intensity NA	0.04 (0.01 – 0.06)	.013	0.08 (-0.07 – 0.23)	.292
Intensity PA	-0.04 (-0.06 – -0.02)	<.001	-0.11 (-0.23 – 0.01)	.063
Instability NA	0.04 (0.00 – 0.08)	.029	0.01 (-0.18 – 0.20)	.905
Instability PA	0.00 (-0.02 – 0.03)	.965	-0.06 (-0.19 – 0.06)	.332
Variability NA	0.03 (0.01 – 0.04)	.003	0.02 (-0.08 – 0.11)	.731
Variability PA	0.00 (-0.02 – 0.01.)	.639	-0.03 (-0.12 – 0.05)	.471
Outcome: Lack of social drive				
Preference to be alone when in company	0.01 (-0.02 – 0.04)	.450	0.12 (-0.05 – 0.28)	.165
Pleasantness of being alone	-0.01 (-0.05 – 0.02)	.480	-0.02 (-0.20 – 0.16)	.800
Outcome: Anhedonia	-0.04 (-0.06 – -0.02)	<.001	-0.09 (-0.20 – 0.02)	.095
Outcome: Social anhedonia	-0.04 (-0.06 – -0.01)	.001	-0.08 (-0.19 – 0.03)	.134

Note. BRPS=Brief Psychiatric Rating Scale (Ventura et al., 1993). CI=confidence interval. NA=negative affect. PA=positive affect.

Supplementary material 2: Data quality of clinical outcome measures

To ensure data quality, extensive training on instruments and interview skills was provided. Initial assessments were reviewed, and possible difficulties were anticipated. In addition to the EU-GEI web-based training designed to control and increase inter-rater reliability, regular meetings were held to discuss case vignettes. Site visits were held in order to evaluate and standardize interviews. In addition, extensive, repetitious training procedures and reliability checks were conducted. Training videos of the most advanced instruments were updated regularly. For each of the training videos, a 'gold standard score' was determined through independent rating of the training videos by independent experienced researchers. In case of disagreement, the head of the training work package was consulted. Per instrument, we subsequently determined the maximum number of errors/deviation from the gold standard score the researcher was allowed, in order to 'pass' the video.

Supplementary material 3: Unadjusted analyses

Table S3. *Clinical outcomes at 1- and 2-year follow-up predicted by blunted affective experience at baseline (i.e., intensity, instability, and variability of negative and positive affect) and clinical outcome at baseline – unadjusted analyses.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Intensity NA								
Outcome at baseline	0.25 (-0.03 – 0.54)	.077	0.26 (-0.23 – 0.75)	.285	0.42 (0.15 – 0.70)	.003	0.49 (0.11 – 0.87)	.013
Intensity NA	-3.31 (-6.47 – -1.41)	.041	-2.94 (-6.69 – 0.80)	.119	-3.81 (-7.85 – 0.04)	.048	0.80 (-3.44 – 5.04)	.701
Predictor: Intensity PA								
Outcome at baseline	0.26 (-0.03 – 0.55)	.075	0.29 (-0.20 – 0.79)	.240	0.39 (0.12 – 0.66)	.006	0.50 (0.12 – 0.87)	.011
Intensity PA	3.03 (-0.62 – 6.67)	.101	2.08 (-2.46 – 6.63)	.385	5.48 (1.34 – 9.62)	.011	1.46 (-3.64 – 6.55)	.562
Predictor: Instability NA								
Outcome at baseline	0.30 (0.00 – 0.60)	.052	0.22 (-0.28 – 0.72)	.374	0.40 (0.11 – 0.68)	.008	0.38 (0.01 – 0.75)	.045
Instability NA	-0.02 (-1.84 – 1.81)	.986	-2.55 (-5.95 – 0.85)	.136	-0.87 (-3.01 – 1.27)	.417	-3.01 (-6.70 – 0.69)	.107
Predictor: Instability PA								
Outcome at baseline	0.28 (-0.01 – 0.58)	.061	0.17 (-0.31 – 0.66)	.471	0.41 (0.12 – 0.70)	.006	0.38 (0.02 – 0.74)	.039
Instability PA	-1.24 (-4.19 – 1.70)	.400	-5.40 (-10.65 – -0.16)	.044	-0.95 (-4.46 – 2.56)	.588	-6.40 (-12.01 – -0.79)	.027
Predictor: Variability NA								
Outcome at baseline	0.29 (-0.01 – 0.58)	.059	0.21 (-0.27 – 0.69)	.376	0.40 (0.11 – 0.69)	.007	0.41 (0.04 – 0.77)	.032
Variability NA	-0.92 (-4.70 – 2.78)	.628	-5.50 (-10.96 – -0.05)	.048	-1.97 (-6.41 – 2.48)	.378	-5.67 (-11.74 – 0.40)	.066
Predictor: Variability PA								
Outcome at baseline	0.29 (0.00 – 0.58)	.049	0.26 (-0.21 – 0.74)	.266	0.41 (0.12 – 0.70)	.007	0.37 (0.00 – 0.75)	.051
Variability PA	-1.68 (-6.01 – 2.65)	.438	-5.86 (-11.79 – 0.08)	.053	-0.62 (-5.83 – 4.60)	.813	-5.13 (-11.91 – 1.65)	.134

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	p	b (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Predictor: Intensity NA								
Outcome at baseline	0.62 (0.37 – 0.88)	<.001	0.46 (0.11 – 0.80)	.011				
Intensity NA	0.36 (0.02 – 0.69)	.036	0.00 (-0.38 – 0.37)	.992	0.33 (0.17 – 0.63)	.001	1.73 (0.94 – 3.21)	.080

Predictor: Intensity PA

Outcome at baseline	0.62 (0.35 – 0.89)	.<001	0.36 (0.02 – 0.71)	.039				
Intensity PA	-0.31 (-0.68 – 0.06)	.103	-0.40 (-0.85 – 0.06)	.083	2.40 (1.16 – 4.98)	.018	0.61 (0.27 – 1.40)	.245

Predictor: Instability NA

Outcome at baseline	0.68 (0.42 – 0.94)	<.001	0.46 (0.12 – 0.81)	.010				
Instability NA	-0.04 (-0.22 – 0.14)	.648	0.03 (-0.31 – 0.37)	.853	0.87 (0.44 – 1.72)	.678	1.10 (0.78 – 1.55)	.594

Predictor: Instability PA

Outcome at baseline	0.68 (0.42 – 0.95)	<.001	0.48 (0.14 – 0.82)	.007				
Instability PA	-0.04 (-0.33 – 0.26)	.797	0.23 (-0.28 – 0.74)	.366	1.37 (0.70 – 2.68)	.353	1.25 (0.69 – 2.24)	.465

Predictor: Variability NA

Outcome at baseline	0.68 (0.42 – 0.95)	<.001	0.47 (0.11 – 0.82)	.011				
Variability NA	-0.03 (-0.40 – 0.35)	.882	0.06 (-0.53 – 0.64)	.840	0.62 (0.16 – 2.35)	.485	1.43 (0.77 – 2.64)	.258

Predictor: Variability PA

Outcome at baseline	0.72 (0.45 – 0.98)	<.001	0.55 (0.20 – 0.89)	.003				
Variability PA	0.20 (-0.24 – 0.64)	.371	0.52 (-0.10 – 1.15)	.098	2.10 (0.98 – 4.50)	.058	1.84 (0.83 – 4.08)	.136

Note. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. NA=negative affect. PA=positive affect. HR=hazard ratio.

Table S4. *Clinical outcomes at 1- and 2-year follow-up predicted by lack of social drive (i.e., amount of time spent alone, preference to be alone when in company, and experienced pleasantness of being alone) and clinical outcome at baseline – unadjusted analyses.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Amount of time spent alone								
Outcome at baseline	0.30 (0.00 – 0.59)	.046	0.26 (-0.23 – 0.75)	.282	0.39 (0.13 – 0.65)	.004	0.31 (-0.06 – 0.68)	.097
Amount of time spent alone	2.51 (-9.29 – 14.31)	.670	12.06 (-4.51 – 28.63)	.148	4.32 (-9.03 – 17.67)	.519	19.01 (0.87 – 37.15)	.041
Predictor: Preference to be alone when in company								
Outcome at baseline	0.27 (-0.02 – 0.56)	.064	0.34 (-0.15 – 0.83)	.168	0.40 (0.12 – 0.68)	.006	0.38 (-0.01 – 0.76)	.055
Preference to be alone	-1.95 (-4.37 – 0.47)	.112	-2.66 (-6.29 – 0.97)	.146	-2.33 (-5.22 – 0.56)	.111	-1.04 (-5.20 – 3.12)	.616
Predictor: Pleasantness of being alone								
Outcome at baseline	0.29 (-0.02 – 0.60)	.062	0.32 (-0.18 – 0.81)	.203	0.44 (0.15 – 0.73)	.004	0.35 (-0.03 – 0.73)	.067
Pleasantness of being alone	-0.49 (-2.92 – 1.94)	.688	-1.68 (-4.82 – 1.46)	.284	-1.78 (-4.60 – 1.04)	.209	-2.54 (-6.02 – 0.94)	.147

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*HR* (95% CI)	*p*	*HR* (95% CI)	*p*
Predictor: Amount of time spent alone								
Outcome at baseline	0.70 (0.43 – 0.96)	<.001	0.45 (0.11 – 0.79)	.011				
Amount of time spent alone	0.33 (-0.85 – 1.52)	.573	-0.60 (-2.23 – 1.04)	.464	1.77 (0.14 – 21.90)	.658	0.10 (0.01 – 1.28)	.076
Predictor: Preference to be alone when in company								
Outcome at baseline	0.65 (0.38 – 0.92)	<.001	0.45 (0.11 – 0.78)	.011				
Preference to be alone	0.14 (-0.11 – 0.40)	.267	0.16 (-0.19 – 0.51)	.366	0.89 (0.51 – 1.53)	.665	1.26 (0.72 – 2.21)	.423
Predictor: Pleasantness of being alone								
Outcome at baseline	0.67 (0.40 – 0.94)	<.001	0.46 (0.13 – 0.80)	.009				
Pleasantness of being alone	0.14 (-0.10 – 0.38)	.234	0.13 (-0.16 – 0.43)	.361	1.89 (0.55 – 1.73)	.940	1.06 (0.61 – 1.84)	.840

Note. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Symptom severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. HR=hazard ratio.

Table S5. *Clinical outcomes at 1- and 2-year follow-up predicted by anhedonia, social anhedonia and outcome at baseline – unadjusted analyses.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Anhedonia								
Outcome at baseline	0.27 (-0.02 – 0.56)	.056	0.30 (-0.20 – 0.80)	.238	0.38 (0.12 – 0.65)	.006	0.38 (0.00 – 0.76)	.052
Anhedonia	2.73 (-1.02 – 6.48)	.150	1.29 (-3.45 – 6.03)	.585	5.80 (1.57 – 10.03)	.008	2.06 (-3.22 – 7.34)	.433
Predictor: Social anhedonia								
Outcome at baseline	0.27 (-0.02 – 0.55)	.064	0.30 (-0.19 – 0.79)	.226	0.35 (0.09 – 0.62)	.009	0.36 (0.00 – 0.73)	.053
Social anhedonia	3.36 (-0.31 – 7.03)	.072	2.79 (-1.94 – 7.51)	.239	6.59 (2.47 – 10.72)	.002	4.74 (-0.41 – 9.88)	.070

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*HR* (95% CI)	*p*	*HR* (95% CI)	*p*
Predictor: Anhedonia								
Outcome at baseline	0.62 (0.34 – 0.89)	<.001	0.36 (0.01 – 0.71)	.044				
Anhedonia	-0.30 (-0.69 – 0.09)	.0123	-0.37 (-0.85 – 0.10)	.121	2.40 (1.09 – 5.27)	.029	0.67 (0.29 – 1.54)	.343
Predictor: Social anhedonia								
Outcome at baseline	0.63 (0.36 – 0.89)	<.001	0.34 (0.01 – 0.66)	.044				
Social anhedonia	-0.32 (-0.70 – 0.05)	.091	-0.56 (-1.02 – -0.11)	.017	2.08 (1.01 – 4.28)	.046	0.75 (0.32 – 1.76)	.507

Note. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Symptom severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. HR=hazard ratio.

Supplementary material 4: Sensitivity analysis with current depressive episode as an additional independent variable to control for potential confounding

Table S6. *Clinical outcomes at 1- and 2-year follow-up predicted by blunted affective experience at baseline (i.e., intensity, instability, and variability of negative and positive affect) and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Intensity NA								
Outcome at baseline	0.15 (-0.21 – 0.51)	.411	0.05 (-0.60 – 0.70)	.865	0.30 (-0.05 – 0.65)	.091	0.56 (0.05 – 1.07)	.033
Intensity NA	-2.18 (-6.46 – 2.10)	.309	-1.67 (-7.37 – 4.04)	.553	-1.73 (-6.54 – 3.08)	.471	1.17 (-5.19 – 7.54)	.708
Predictor: Intensity PA								
Outcome at baseline	0.14 (-0.21 – 0.50)	.422	0.05 (-0.59 – 0.69)	.869	0.30 (-0.04 – 0.65)	.079	0.57 (0.05 – 1.08)	.031
Intensity PA	3.70 (-0.59 – 7.99)	.089	1.74 (-4.34 – 7.82)	.561	3.68 (-1.15 – 8.50)	.131	0.30 (-6.48 – 7.09)	.927
Predictor: Instability NA								
Outcome at baseline	0.18 (-0.19 – 0.54)	.337	0.05 (-0.58 – 0.68)	.869	0.31 (-0.05 – 0.66)	.089	0.59 (0.11 – 1.07)	.018
Instability NA	0.91 (-1.33 – 3.16)	.417	-2.43 (-6.98 – 2.13)	.283	-0.01 (-2.55 – 2.52)	.991	-4.44 (-9.32 – 0.45)	.073
Predictor: Instability PA								
Outcome at baseline	0.16 (-0.21 – 0.53)	.400	-0.01 (-0.62 – 0.60)	.973	0.30 (-0.05 – 0.65)	.090	0.57 (0.12 – 1.03)	.016
Instability PA	-0.45 (-4.01 – 3.11)	.801	-4.81 (-10.65 – 1.03)	.102	-0.88 (-4.82 – 3.06)	.652	-7.66 (-13.80 – -1.52)	.017
Predictor: Variability NA								
Outcome at baseline	0.16 (-0.21 – 0.52)	.384	0.09 (-0.54 – 0.72)	.765	0.31 (-0.04 – 0.66)	.084	0.56 (0.10 – 1.03)	.020
Variability NA	2.15 (-2.87 – 7.17)	.391	-5.23 (-13.56 – 3.09)	.207	1.37 (-4.29 – 7.02)	.627	-9.32 (-18.01 – -0.63)	.037
Predictor: Variability PA								
Outcome at baseline	0.16 (-0.21 – 0.52)	.397	0.07 (-0.54 – 0.68)	.816	0.31 (-0.04 – 0.66)	.083	0.48 (-0.02 – 0.98)	.057
Variability PA	1.00 (-4.69 – 6.70)	.724	-5.59 (-12.66 – 1.48)	.116	1.58 (-4.74 – 7.90)	.615	-6.27 (-14.38 – 1.84)	.124

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*HR* (95% CI)	*p*	*HR* (95% CI)	*p*
Predictor: Intensity NA								
Outcome at baseline	0.40 (0.08 – 0.73)	.017	0.27 (-0.23 – 0.78)	.276				
Intensity NA	0.29 (-0.13 – 0.70)	.167	-0.03 (-0.61 – 0.55)	.911	0.28 (0.09 – 0.89)	.031	1.44 (0.67 – 3.07)	.347

Predictor: Intensity PA

Outcome at baseline	0.42 (0.09 – 0.74)	.013	0.19 (-0.31 – 0.69)	.447				
Intensity PA	-0.28 (-0.69 – 0.13)	.176	-0.37 (-1.03 – 0.29)	.262	2.08 (0.88 – 4.94)	.096	0.44 (0.15 – 1.33)	.146

Predictor: Instability NA

Outcome at baseline	0.45 (0.12 – 0.78)	.009	0.26 (-0.23 – 0.76)	.285				
Instability NA	-0.03 (-0.24 – 0.17)	.744	-0.02 (-0.49 – 0.45)	.936	1.21 (0.58 – 2.55)	.611	1.04 (0.68 – 1.59)	.857

Predictor: Instability PA

Outcome at baseline	0.45 (0.12 – 0.78)	.009	0.29 (-0.20 – 0.78)	.237				
Instability PA	-0.05 (-0.37 – 0.28)	.775	0.25 (-0.39 – 0.88)	.434	1.77 (0.70 – 4.48)	.230	0.82 (0.33 – 2.04)	.667

Predictor: Variability NA

Outcome at baseline	0.44 (0.12 – 0.77)	.009	0.25 (-0.27 – 0.77)	.327				
Variability NA	-0.14 (-0.58 – 0.30)	.519	-0.09 (-0.97 – 0.79)	.839	1.28 (0.29 – 5.57)	.741	1.37 (0.61 – 3.09)	.447

Predictor: Variability PA

Outcome at baseline	0.45 (0.12 – 0.78)	.010	0.38 (-0.13 – 0.89)	.138				
Variability PA	0.04 (-0.46 – 0.55)	.860	0.50 (-0.30 – 1.30)	.212	4.85 (1.59 – 14.81)	.006	1.29 (0.42 – 3.99)	.654

Note. Results adjusted for age, gender, ethnicity, centre, time to follow-up, and current depressive episode. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. NA=negative affect. PA=positive affect. HR=hazard ratio.

Table S7. *Clinical outcomes at 1- and 2-year follow-up predicted by lack of social drive (i.e., amount of time spent alone, preference to be alone when in company, and experienced pleasantness of being alone) and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Amount of time spent alone								
Outcome at baseline	0.16 (-0.21 – 0.53)	.378	-0.12 (-0.76 – 0.53)	.714	0.30 (-0.05 – 0.65)	.086	0.47 (-0.02 – 0.96)	.061
Amount of time spent alone	2.03 (-11.94 – 15.99)	.771	14.02 (-5.64 – 33.68)	.154	5.41 (-10.11 – 20.91)	.485	19.48 (-1.49 – 40.45)	.067
Predictor: Preference to be alone when in company								
Outcome at baseline	0.17 (-0.19 – 0.53)	.347	0.10 (-0.56 – 0.77)	.755	0.31 (-0.04 – 0.66)	.080	0.55 (0.04 – 1.07)	.034
Preference to be alone	-1.40 (-4.15 – 1.34)	.307	-1.54 (-5.66 – 2.58)	.448	-0.97 (-4.07 – 2.13)	.529	-1.13 (-5.56 – 3.30)	.604
Predictor: Pleasantness of being alone								
Outcome at baseline	0.16 (-0.21 – 0.54)	.391	0.17 (-0.46 – 0.79)	.558	0.34 (-0.03 – 0.70)	.070	0.53 (0.08 – 0.98)	.023
Pleasantness of being alone	0.17 (-2.78 – 3.11)	.909	-3.18 (-6.76 – 0.40)	.079	-0.99 (-4.33 – 2.34)	.550	-4.74 (-8.39 – -1.09)	.013

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*HR* (95% CI)	*p*	*HR* (95% CI)	*p*
Predictor: Amount of time spent alone								
Outcome at baseline	0.41 (0.06 – 0.75)	.023	0.14 (-0.36 – 0.64)	.571				
Amount of time spent alone	-0.44 (-1.77 – 0.90)	.512	-1.54 (-3.67 – 0.58)	.147	5.58 (0.28 – 11.20)	.260	0.05 (0.00 – 2.07)	.116
Predictor: Preference to be alone when in company								
Outcome at baseline	0.43 (0.11 – 0.76)	.011	0.24 (-0.24 – 0.73)	.310				
Preference to be alone	0.09 (-0.17 – 0.35)	.505	0.23 (-0.17 – 0.64)	.252	0.97 (0.51 – 1.86)	.929	1.17 (0.61 – 2.23)	.635
Predictor: Pleasantness of being alone								
Outcome at baseline	0.45 (0.11 – 0.78)	.011	0.34 (-0.16 – 0.83)	.179				
Pleasantness of being alone	0.04 (-0.21 – 0.29)	.730	0.19 (-0.17 – 0.56)	.285	0.82 (0.44 – 1.54)	.540	1.47 (0.76 – 2.87)	.255

Note. Results adjusted for age, gender, ethnicity, centre, time to follow-up, and current depressive episode. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. HR=hazard ratio.

Table S8. *Clinical outcomes at 1- and 2-year follow-up predicted by anhedonia, social anhedonia, and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Anhedonia								
Outcome at baseline	0.15 (-0.17 – 0.49)	.394	-0.04 (-0.61 – 0.68)	.907	0.30 (-0.03 – 0.64)	.076	0.57 (0.05 – 1.08)	.031
Anhedonia events	3.56 (-0.86 – 7.98)	.111	0.78 (-5.24 – 6.80)	.791	4.31 (-0.59 – 9.21)	.083	-0.22 (-6.90 – 6.46)	.946
Predictor: Social anhedonia								
Outcome at baseline	0.16 (-0.19 – 0.50)	.362	0.08 (-0.56 – 0.72)	.807	0.30 (-0.03 – 0.62)	.074	0.54 (0.04 – 1.05)	.035
Social anhedonia	4.47 (0.38 – 8.56)	.033	2.80 (-3.38 – 8.98)	.359	5.35 (0.83 – 9.88)	.022	3.34 (-3.49 – 10.16)	.324

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*HR* (95% CI)	*p*	*HR* (95% CI)	*p*
Predictor: Anhedonia								
Outcome at baseline	0.42 (0.09 – 0.74)	.013	0.20 (-0.30 – 0.71)	.415				
Anhedonia	-0.26 (-0.68 – 0.15)	.206	-0.31 (-0.96 – 0.34)	.334	2.02 (0.82 – 4.97)	.125	0.49 (0.16 – 1.52)	.217
Predictor: Social anhedonia								
Outcome at baseline	0.41 (0.09 – 0.72)	.013	0.16 (-0.32 – 0.64)	.505				
Social anhedonia	-0.35 (-0.73 – 0.03)	.069	-0.58 (-1.21 – 0.05)	.072	2.26 (0.84 – 6.04)	.105	0.57 (0.21 – 1.59)	.286

Note. Results adjusted for age, gender, ethnicity, centre, time to follow-up, and current depressive episode. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. HR=hazard ratio.

Supplementary material 5: Sensitivity analysis with comorbid axis-I disorder as an additional independent variable to control for potential confounding

Table S9. *Clinical outcomes at 1- and 2-year follow-up predicted by blunted affective experience at baseline (i.e., intensity, instability, and variability of negative and positive affect) and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Intensity NA								
Outcome	0.21	.247	0.15	.647	0.35	.059	0.55	.029
at baseline	(-0.15 – 0.57)		(-0.52 – 0.82)		(-0.01 – 0.71)		(0.06 – 1.04)	
Intensity NA	-2.43	.236	-1.75	.523	-3.17	.181	1.01	.738
	(-6.51 – 1.65)		(-7.33 – 3.82)		(-7.88 – 1.55)		(-5.13 – 7.15)	
Predictor: Intensity PA								
Outcome	0.20	.254	0.18	.594	0.34	.049	0.55	.029
at baseline	(-0.15 – 0.54)		(-0.50 – 0.85)		(0.00 – 0.69)		(0.06 – 1.03)	
Intensity PA	4.12	.043	2.45	.413	5.38	.022	1.26	.699
	(0.14 – 8.10)		(-3.62 – 8.52)		(0.81 – 9.96)		(-5.37 – 7.90)	
Predictor: Instability NA								
Outcome	0.31	.099	0.09	.787	0.37	.053	0.55	.025
at baseline	(-0.06 – 0.68)		(-0.58 – 0.76)		(-0.01 – 0.74)		(0.07 – 1.02)	
Instability NA	1.32	.283	-1.14	.608	-0.27	.851	-3.12	.193
	(-1.13 – 3.76)		(-5.66 – 3.38)		(-3.12 – 2.59)		(-7.92 – 1.69)	
Predictor: Instability PA								
Outcome	0.26	.166	0.00	.992	0.37	.049	0.55	.018
at baseline	(-0.11 – 0.63)		(-0.66 – 0.67)		(0.00 – 0.74)		(0.10 – 1.00)	
Instability PA	0.18	.923	-4.15	.194	-0.32	.882	-7.00	.036
	(-3.62 – 3.99)		(-10.56 – 2.26)		(-4.71 – 4.06)		(-13.48 – -0.51)	
Predictor: Variability NA								
Outcome	0.30	.106	0.10	.765	0.37	.047	0.53	.028
at baseline	(-0.07 – 0.66)		(-0.54 – 0.76)		(0.00 – 0.74)		(0.06 – 0.99)	
Variability NA	2.99	.283	-2.77	.502	0.44	.892	-7.04	.115
	(-2.57 – 8.55)		(-11.13 – 5.59)		(-6.08 – 6.96)		(-15.92 – 1.84)	
Predictor: Variability PA								
Outcome	0.25	.159	0.09	.769	0.38	.043	0.49	.050
at baseline	(-0.10 – 0.61)		(-0.55 – 0.74)		(0.01 – 0.74)		(0.00 – 0.97)	
Variability PA	2.12	.490	-4.89	.192	3.09	.394	-5.26	.218
	(-4.05 – 8.30)		(-12.40 – 2.63)		(-4.17 – 10.35)		(-13.82 – 3.31)	

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	p	b (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Predictor: Intensity NA								
Outcome	0.45	.008	0.36	.181				
at baseline	(0.12 – 0.78)		(-0.18 – 0.89)					
Intensity NA	0.31	.133	-0.06	.831	0.31	.025	1.44	.364
	(-0.10 – 0.71)		(-0.64 – 0.52)		(0.11 – 0.86)		(0.66 – 3.15)	

Predictor: Intensity PA

Outcome at baseline	0.48 (0.17 – 0.79)	.004	0.25 (-0.27 – 0.77)	.337				
Intensity PA	-0.32 (-0.70 – 0.07)	.101	-0.37 (-1.00 – 0.27)	.247	2.73 (1.02 – 7.33)	.046	0.60 (0.22 – 1.66)	.324

Predictor: Instability NA

Outcome At baseline	0.56 (0.23 – 0.89)	.001	0.34 (-0.17 – 0.85)	.178				
Instability NA	-0.05 (-0.27 – 0.16)	.631	-0.04 (-0.48 – 0.41)	.873	1.25 (0.50 – 3.17)	.639	1.01 (0.65 – 1.56)	.982

Predictor: Instability PA

Outcome at baseline	0.56 (0.24 – 0.87)	.001	0.33 (-0.17 – 0.84)	.184				
Instability PA	-0.11 (-0.45 – 0.24)	.535	0.21 (-0.44 – 0.86)	.520	1.89 (0.62 – 5.68)	.257	0.95 (0.46 – 1.98)	.899

Predictor: Variability NA

Outcome at baseline	0.56 (0.25 – 0.88)	.001	0.33 (-0.18 – 0.84)	.191				
Variability NA	-0.18 (-0.65 – 0.29)	.447	-0.12 (-0.96 – 0.71)	.763	1.28 (0.24 – 6.94)	.773	1.19 (0.52 – 2.74)	.679

Predictor: Variability PA

Outcome at baseline	0.54 (0.22 – 0.86)	.001	0.41 (-0.10 – 0.92)	.110				
Variability PA	-0.02 (-0.57 – 0.53)	.944	0.46 (-0.35 – 1.27)	.252	9.13 (2.02 – 41.30)	.004	1.48 (0.49 – 4.45)	.489

Note. Results adjusted for age, gender, ethnicity, centre, time to follow-up, and comorbid disorders. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. NA=negative affect. PA=positive affect. HR=hazard ratio.

Table S10. *Clinical outcomes at 1- and 2-year follow-up predicted by lack of social drive (i.e., amount of time spent alone, preference to be alone when in company, and experienced pleasantness of being alone) and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Amount of time spent alone								
Outcome at baseline	0.26 (-0.10 – 0.62)	.154	0.07 (-0.56 – 0.69)	.832	0.37 (0.01 – 0.74)	.046	0.47 (0.03 – 0.92)	.037
Amount of time spent alone	2.80 (-11.56 – 17.51)	.695	16.24 (-1.43 – 33.91)	.070	5.17 (-11.65 – 21.99)	.537	22.59 (3.66 – 41.52)	.021
Predictor: Preference to be alone when in company								
Outcome at baseline	0.24 (-0.11 – 0.59)	.172	0.29 (-0.43 – 1.00)	.419	0.37 (0.01 – 0.73)	.043	0.53 (0.05 – 1.02)	.032
Preference to be alone	-1.69 (-4.30 – 0.92)	.197	-2.41 (-6.66 – 1.84)	.254	-1.94 (-5.02 – 1.14)	.210	-1.66 (-6.03 – 2.70)	.440
Predictor: Pleasantness of being alone								
Outcome at baseline	0.25 (-0.11 – 0.62)	.169	0.17 (-0.47 – 0.82)	.585	0.41 (0.03 – 0.79)	.035	0.51 (0.07 – 0.95)	.026
Pleasantness of being alone	0.15 (-2.82 – 3.12)	.918	-2.62 (-6.21 – 0.97)	.145	-1.36 (-4.93 – 2.21)	.445	-4.30 (-8.04 – -0.55)	.026

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	p	b (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Predictor: Amount of time spent alone								
Outcome at baseline	0.52 (0.20 – 0.84)	.002	0.32 (-0.16 – 0.81)	.185				
Amount of time spent alone	-0.35 (-1.68 – 0.98)	.600	-1.35 (-3.23 – 0.53)	.152	4.35 (0.32 – 59.89)	.272	0.02 (0.00 – 1.12)	.056
Predictor: Preference to be alone when in company								
Outcome at baseline	0.51 (0.19 – 0.83)	.002	0.32 (-0.17 – 0.81)	.192				
Preference to be alone	0.11 (-0.14 – 0.36)	.368	0.24 (-0.16 – 0.64)	.226	0.85 (0.43 – 1.67)	.632	1.21 (0.64 – 2.27)	.555
Predictor: Pleasantness of being alone								
Outcome at baseline	0.54 (0.22 – 0.86)	.002	0.37 (-0.13 – 0.87)	.139				
Pleasantness of being alone	0.05 (-0.20 – 0.29)	.715	0.18 (-0.19 – 0.54)	.329	0.89 (0.48 – 1.66)	.716	1.38 (0.73 – 2.59)	.316

Note. Results adjusted for age, gender, ethnicity, centre, time to follow-up, and comorbid disorders. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. HR=hazard ratio.

Table S11. *Clinical outcomes at 1- and 2-year follow-up predicted by anhedonia, social anhedonia, and clinical outcome at baseline.*

	Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		36		48		36	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Anhedonia								
Outcome at baseline	0.21 (-0.13 – 0.56)	.221	0.15 (-0.53 – 0.84)	.645	0.34 (0.00 – 0.68)	.047	0.55 (0.06 – 1.04)	.029
Anhedonia events	4.12 (-0.01 – 8.24)	.050	1.46 (-4.56 – 7.48)	.621	6.08 (1.40 – 10.75)	.012	0.75 (-5.79 – 7.29)	.815
Predictor: Social anhedonia								
Outcome at baseline	0.22 (-0.11 – 0.55)	.186	0.24 (-0.43 – 0.91)	.471	0.334 (0.01 – 0.67)	.045	0.51 (0.03 – 0.98)	.037
Social anhedonia	4.90 (0.98 – 8.91)	.016	4.05 (-2.27 – 10.36)	.199	6.67 (2.19 – 11.14)	.005	4.70 (-2.02 – 11.44)	.162

	Illness severity				Remission from UHR status		Transition status	
	1-year follow-up		2-year follow-up					
N	47		37		54		57	
	b (95% CI)	p	*b* (95% CI)	p	*HR* (95% CI)	p	*HR* (95% CI)	p
Predictor: Anhedonia								
Outcome at baseline	0.48 (0.17 – 0.80)	.004	0.26 (-0.25 – 0.78)	.305				
Anhedonia	-0.32 (-0.71 – 0.08)	.116	-0.32 (-0.95 – 0.31)	.305	2.68 (0.94 – 7.60)	.064	0.64 (0.22 – 1.89)	.418
Predictor: Social anhedonia								
Outcome at baseline	0.48 (0.17 – 0.78)	.003	0.23 (-0.25 – 0.72)	.338				
Social anhedonia	-0.39 (-0.76 – -0.02)	.039	-0.61 (-1.23 – 0.02)	.056	4.71 (1.07 – 20.73)	.041	0.68 (0.25 – 1.83)	.449

Note. Results adjusted for age, gender, ethnicity, centre, time to follow-up, and comorbid disorders. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). CI=confidence interval. HR=hazard ratio.

Supplementary material 6: Comorbid axis-I diagnoses at baseline

Table S12. *Comorbid axis-I diagnoses at baseline.*

| | ESM sample | | | No ESM sample | Comparison ESM vs. no ESM |
	Baseline	1-year follow-up	2-year follow-up	Baseline	Baseline
N	79	48	36	266	
Comorbidity at baseline, *N* (%)	60 (76%)	37 (77%)	28 (78%)	220 (83%)	χ^2=1.82, *p*=.177
Major depressive disorder, *N* (%)	29 (37%)	14 (31%)	11 (31%)	123 (51%)	χ^2=4.67, *p*=.031
Current depressive episode, *N* (%)	22 (28%)	11 (24%)	8 (22%)	88 (35%)	χ^2=1.26, *p*=.262
Bipolar disorder, *N* (%)	7 (9%)	4 (9%)	5 (14%)	17 (6%)	χ^2=0.57, *p*=.449
Any anxiety disorder, *N* (%)	42 (53%)	26 (57%)	17 (47%)	117 (44%)	χ^2=2.06, *p*=.151
Panic disorder, *N* (%)	19 (24%)	12 (27%)	6 (17%)	52 (21%)	χ^2=0.30, *p*=.584
Panic disorder + agoraphobia, *N* (%)	6 (8%)	4 (9%)	1 (3%)	25 (11%)	χ^2=0.46, *p*=.496
Agoraphobia only, *N* (%)	2 (3%)	0	0	4 (2%)	χ^2=0.26, *p*=.607
Social phobia, *N* (%)	19 (24%)	14 (30%)	9 (25%)	42 (17%)	χ^2=1.87, *p*=.172
Specific phobia, *N* (%)	14 (18%)	9 (20%)	5 (14%)	22 (9%)	χ^2=4.86, *p*=.027
Generalised anxiety disorder, *N* (%)	11 (14%)	7 (15%)	5 (14%)	26 (11%)	χ^2=0.67, *p*=.413
Not otherwise specified anxiety disorder, *N* (%)	3 (4%)	1 (2%)	0	14 (6%)	χ^2=0.49, *p*=.485
Obsessive-compulsive disorder, *N* (%)	3 (4%)	2 (4%)	3 (9%)	26 (12%)	χ^2=3.41, *p*=.065
Posttraumatic stress disorder, *N* (%)	11 (14%)	4 (9%)	0	23 (6%)	χ^2=1.40, *p*=.237
Any eating disorder, *N* (%)	10 (13%)	7 (15%)	6 (17%)	22 (8%)	χ^2=1.39, *p*=.238
Anorexia nervosa, *N* (%)	5 (6%)	3 (7%)	3 (8%)	10 (4%)	χ^2=0.69, *p*=.408
Bulimia nervosa, *N* (%)	5 (6%)	3 (7%)	2 (6%)	10 (4%)	χ^2=0.66, *p*=.417
Binge eating disorder, *N* (%)	1 (1%)	1 (2%)	1 (3%)	6 (3%)	χ^2=0.44, *p*=.508
Any somatoform disorder, *N* (%)	2 (3%)	1 (2%)	1 (3%)	9 (3%)	χ^2=0.14, *p*=.705
Somatization disorder, *N* (%)	1 (1%)	0	0	4 (2%)	χ^2=0.06, *p*=.812
Chronic pain, *N* (%)	1 (1%)	0	0	1 (<1%)	χ^2=0.70, *p*=.403
Hypochondriasis, *N* (%)	1 (1%)	1 (2%)	1 (3%)	4 (2%)	χ^2=0.07, *p*=.789
Body dismorph disorder, *N* (%)	0	0	0	2 (1%)	χ^2=0.67, *p*=.412

Note. ESM=experience sampling method.

Supplementary material 7: Restricted analyses

The restricted sample only comprises participants, who returned within a +/- 6 month time interval around the expected follow-up time points. The analyses were conducted with varying sample sizes for illness severity and level of functioning.

Table S13. *Clinical outcomes at 1- and 2-year follow-up predicted by blunted affective experience at baseline (i.e., intensity, instability, and variability of negative and positive affect) and clinical outcome at baseline – restricted analyses.*

	Illness severity				Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	42		32		46		31		46		31	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Intensity NA												
Outcome at baseline	0.57 (0.31 – 0.84)	<.001	0.47 (-0.06 – 1.01)	.082	0.28 (-0.03 – 0.60)	.078	0.10 (-0.54 – 0.74)	.745	0.41 (0.07 – 0.76)	.021	0.57 (0.08 – 1.06)	.024
Intensity NA	0.23 (-0.11 – 0.56)	.174	-0.22 (-0.79 – 0.35)	.439	-2.68 (-6.41 – 1.05)	.155	1.53 (-3.57 – 6.64)	.540	-2.70 (-7.21 – 1.81)	.233	4.22 (-1.80 – 10.23)	.160
Predictor: Intensity PA												
Outcome at baseline	0.60 (0.34 – 0.86)	<.001	0.33 (-0.26 – 0.91)	.260	0.29 (-0.02 – 0.62)	.065	0.14 (-0.49 – 0.78)	.643	0.42 (0.09 – 0.75)	.014	0.56 (0.04 – 1.07)	.035
Intensity PA	-0.18 (-0.54 – 0.18)	.315	-0.23 (-0.90 – 0.44)	.485	3.02 (-0.91 – 6.95)	.128	0.60 (-4.47 – 5.67)	.808	4.63 (0.02 – 9.25)	.049	-0.88 (-7.15 – 5.40)	.775
Predictor: Instability NA												
Outcome at baseline	0.65 (0.40 – 0.90)	<.001	0.42 (-0.11 – 0.94)	.114	0.36 (0.04 – 0.68)	.028	0.14 (-0.49 – 0.76)	.657	0.43 (0.08 – 0.79)	.018	0.56 (0.08 – 1.05)	.024
Instability NA	-0.02 (-0.19 – 0.15)	.838	-0.05 (-0.49 – 0.39)	.809	0.78 (-1.36 – 2.92)	.464	-1.06 (-4.75 – 2.64)	.558	-0.44 (-3.08 – 2.20)	.737	-3.51 (-7.86 – 0.84)	.109
Predictor: Instability PA												
Outcome at baseline	0.65 (0.40 – 0.90)	<.001	0.43 (-0.09 – 0.96)	.101	0.33 (0.01 – 0.65)	.042	0.06 (-0.57 – 0.68)	.851	0.44 (0.09 – 0.79)	.015	0.55 (0.08 – 1.02)	.023
Instability PA	-0.06 (-0.33 – 0.21)	.672	0.15 (-0.49 – 0.79)	.632	-0.19 (-3.62 – 3.24)	.910	-3.10 (-8.44 – 2.24)	.241	-0.64 (-4.77 – 3.49)	.755	-6.02 (-12.15 – 0.10)	.053
Predictor: Variability NA												
Outcome at baseline	0.65 (0.40 – 0.90)	<.001	0.41 (-0.12 – 0.94)	.121	0.36 (0.05 – 0.68)	.026	0.14 (-0.47 – 0.76)	.635	0.45 (0.09 – 0.81)	.015	0.58 (0.11 – 1.04)	.017
Variability NA	-0.12 (-0.48 – 0.25)	.514	-0.15 (-0.95 – 0.65)	.706	2.05 (-2.64 – 6.74)	.382	-3.29 (-10.04 – 3.45)	.323	0.12 (-5.64 – 5.88)	.967	-8.14 (-15.92 – -0.37)	.041

Predictor: Variability PA

Outcome at baseline	0.64 (0.39 – 0.89)	<.001	0.48 (-0.04 – 1.01)	.071	0.34 (0.03 – 0.66)	.031	0.09 (-0.49 – 0.68)	.751	0.46 (0.12 – 0.81)	.010	0.50 (0.02 – 0.99)	.043
Variability PA	-0.12 (-0.58 – 0.35)	.606	0.41 (-0.37 – 1.18)	.289	2.93 (-2.89 – 8.75)	.314	-5.77 (-11.91 – 0.37)	.064	3.09 (-4.01 – 10.20)	.384	-6.20 (-14.01 – 1.60)	.114

Note. Results adjusted for age, gender, ethnicity, and centre. Symptom severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). CI=Confidence interval. NA=negative affect. PA=positive affect.

Table S14. *Clinical outcomes at 1- and 2-year follow-up predicted by lack of social drive (i.e., amount of time spent alone, preference to be alone when in company, and experienced pleasantness of being alone) and clinical outcome at baseline – restricted analyses.*

	Illness severity				Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	42		32		46		31		46		31	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Amount of time spent alone												
Outcome at baseline	0.69 (0.43 – 0.95)	<.001	0.35 (-0.17 – 0.86)	.178	0.33 (0.02 – 0.65)	.039	0.04 (-0.56 – 0.63)	.900	0.44 (0.09 – 0.79)	.014	0.46 (-0.02 – 0.94)	.057
Amount of time spent alone	0.65 (-0.57 – 1.87)	.288	-1.22 (-3.03 – 0.59)	.177	0.63 (-12.47 – 13.72)	.923	13.74 (-1.04 – 28.52)	.067	5.18 (-10.66 – 21.03)	.512	17.72 (-0.52 – 35.95)	.056
Predictor: Preference to be alone when in company												
Outcome at baseline	0.61 (0.36 – 0.87)	<.001	0.37 (-0.15 – 0.90)	.156	0.30 (-0.01 – 0.61)	.058	0.16 (-0.50 – 0.81)	.622	0.41 (0.07 – 0.76)	.020	0.56 (0.03 – 1.08)	.039
Preference to be alone	0.12 (-0.10 – 0.33)	.274	0.18 (-0.24 – 0.61)	.381	-1.74 (-4.30 – 0.82)	.177	-0.48 (-4.21 – 3.25)	.792	-1.80 (-4.94 – 1.33)	.251	0.24 (-4.34 – 4.82)	.914
Predictor: Pleasantness of being alone												
Outcome at baseline	0.65 (0.38 – 0.91)	<.001	0.43 (-0.09 – 0.95)	.099	0.33 (0.00 – 0.65)	.050	0.20 (-0.42 – 0.81)	.516	0.48 (0.13 – 0.84)	.009	0.47 (-0.02 – 0.96)	.058
Pleasantness of being alone	0.04 (-0.18 – 0.26)	.712	0.14 (-0.25 – 0.53)	.461	-0.38 (-2.95 – 2.19)	.764	-2.09 (-5.37 – 1.18)	.199	-1.52 (-4.61 – 1.57)	.325	-3.44 (-7.41 – 0.53)	.086

Note. Results adjusted for age, gender, ethnicity, and centre. Symptom severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). CI=Confidence interval.

Table S15. *Clinical outcomes at 1- and 2-year follow-up predicted by anhedonia, social anhedonia and outcome at baseline – restricted analyses.*

	Illness severity				Level of functioning: Symptoms				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	42		32		46		31		46		31	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Anhedonia												
Outcome at baseline	0.60 (0.34 – 0.86)	<.001	0.35 (-0.23 – 0.93)	.230	0.30 (-0.01 – 0.61)	.057	0.13 (-0.50 – 0.77)	.674	0.42 (0.09 – 0.74)	.014	0.56 (0.05 – 1.08)	.033
Anhedonia	-0.19 (-0.55 – 0.17)	.294	-0.19 (-0.84 – 0.46)	.554	3.08 (-0.89 – 7.05)	.124	-0.30 (-5.29 – 4.68)	.901	5.35 (0.74 – 9.97)	.024	-1.39 (-7.54 – 4.76)	.644
Predictor: Social anhedonia												
Outcome at baseline	0.60 (0.34 – 0.85)	<.001	0.29 (-0.27 – 0.85)	.301	0.29 (-0.01 – 0.59)	.059	0.14 (-0.49 – 0.78)	.642	0.39 (0.07 – 0.71)	.018	0.54 (0.02 – 1.06)	.043
Social anhedonia	-0.22 (-0.57 – 0.14)	.220	-0.38 (-1.05 – 0.29)	.248	3.92 (0.00 – 7.85)	.050	0.59 (-4.87 – 6.05)	.824	6.18 (1.60 – 10.75)	.010	0.69 (-6.14 – 7.52)	.836

Note. Results adjusted for age, gender, ethnicity, and centre. Symptom severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). CI=Confidence interval.

Supplementary material 8: Graphic illustration of the hypotheses tested in the current study
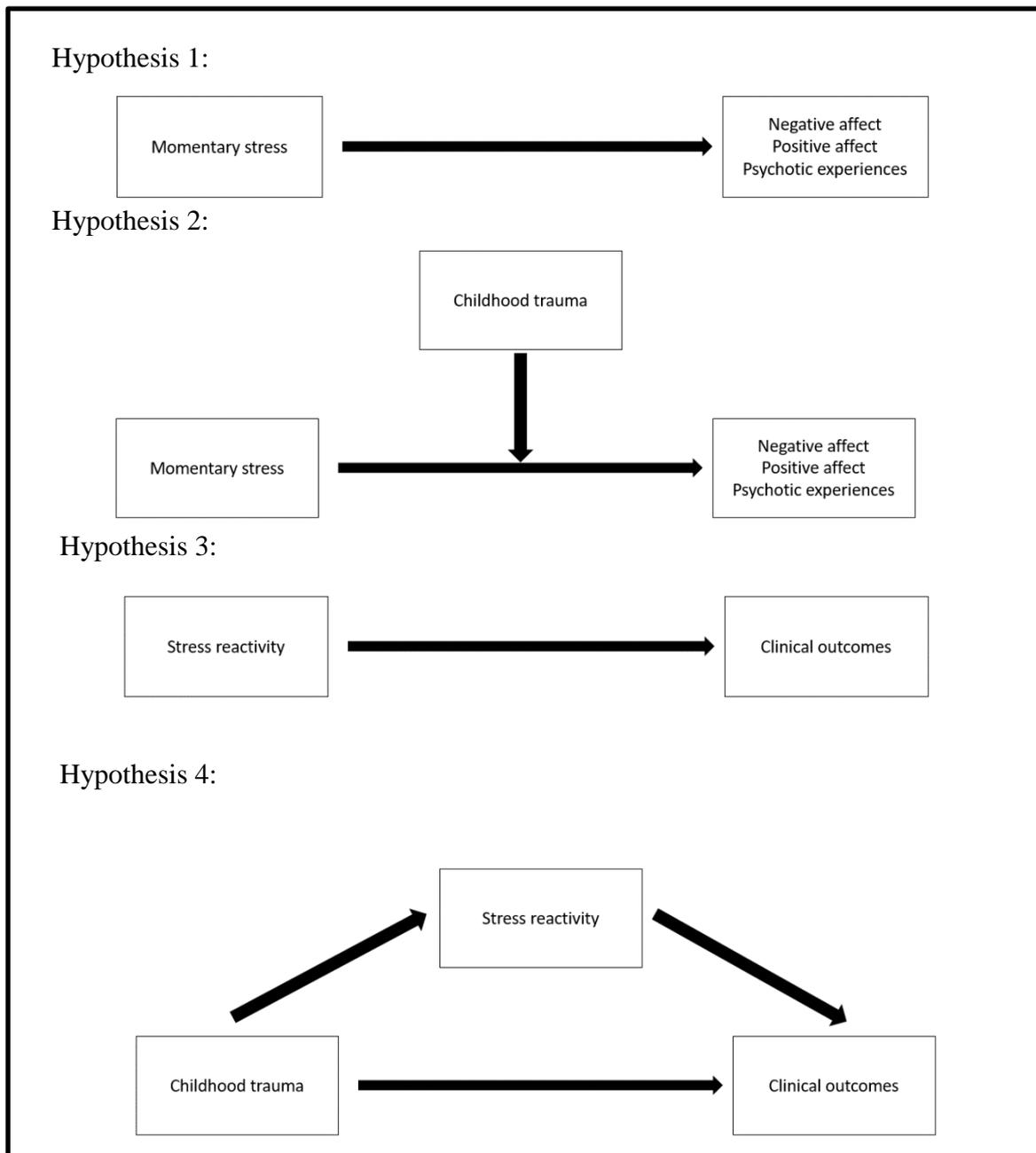
Figure S1. *Graphic illustration of the hypotheses tested in the current study.*

Supplementary material 9: Overview of the measures used in the current study

Table S16. *Data collection.*

Experience sampling	
Momentary stress	Momentary stress was defined as minor disturbances occurring throughout the day based on previous ESM studies (Myin-Germeys et al., 2001; Palmier-Claus et al., 2012). We used a composite stress measure (row mean) consisting of items assessing event-related, activity-related and social stress to avoid multiple testing (Klippel et al., 2021; Pries et al., 2020). *Event-related stress:* Participants were asked to rate the most important event since the last beep on a 7-point Likert scale ranging from -3 (very unpleasant) to 3 (very pleasant). We recoded this item so that higher ratings indicate higher levels of stress (-3 recoded as 7 and 3 recoded as 1). *Activity-related stress:* Participants were asked to indicate what they were doing just before the beep and answer three follow-up questions ('I would prefer doing something else', 'This activity is difficult for me', 'I can do this well' [reversed]) with a 7-point Likert scale ranging from 1 (not at all) to 7 (very much). *Social stress:* Participants were asked to specify categorically with whom they were spending time and then rated the following items on a 7-point Likert scale ranging from 1 (not at all) to 7 (very much): 'I would prefer to be alone [if in company]/I would prefer to have company [if alone, reversed]' and 'I find being with these people pleasant [if in company]/I find it pleasant to be alone [if alone]'. Previous research demonstrated good feasibility and reliability for the ESM items in UHR individuals and good concurrent validity with other stress measures (Myin-Germeys et al., 2003; Palmier-Claus et al., 2012).
Positive affect	Positive affect was measured by asking participants to rate how cheerful, relaxed, satisfied and enthusiastic they felt, rated on a Likert scale ranging from 1 (not at all) to 7 (very much). We found satisfying internal consistency (Cronbach's α=.73). Mean scores were computed as overall measure of positive affect.
Negative affect	Negative affect was measured by asking participants to rate the extent to which they felt insecure, down, lonely, anxious and irritated on a Likert scale ranging from 1 (not at all) to 7 (very much). We found satisfying internal consistency (Cronbach's α=.73). Mean scores were computed as overall measure of negative affect.
Psychotic experiences	The ESM psychosis measure was used to assess intensity of psychotic experiences. It consisted of 7 items (e.g. 'I feel paranoid', 'I hear things that aren't really there') rated on a 7-point Likert scale ranging from 1 (not at all) to 7 (very much). Previous studies reported high levels of internal consistency and good concurrent validity with interviewer-rated measures of psychotic experiences (Myin-Germeys et al., 2005; Reininghaus, Gayer-Anderson, et al., 2016). In the current study, the ESM items for psychotic experiences showed satisfying internal consistency (Cronbach's α=.72).
Childhood trauma	
CTQ	The Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998) assesses five types of childhood maltreatment (emotional, physical and sexual abuse, emotional and physical neglect) on a 5-point Likert scale (1=never true, 5=very often true). As the utility of a CTQ total score for clinical research and practice has been demonstrated, we calculated the sum of answers to all 25 questions (potential range 25-125) as a general measure of childhood trauma (Scher et al., 2001). Good psychometric properties have been reported (Bernstein et al., 1997; Bernstein et al., 2003; Scher et al., 2001; Wingenfeld et al., 2010). In the current study, the CTQ total score showed excellent internal consistency (Cronbach's α=.92).

Clinical outcome measures

CGI	The Clinical Global Impression Scale (CGI) illness severity subscale is an expert rating of average illness severity during the last week ranging from 1 (normal, not at all ill) to 7 (among the most extremely ill patients; Guy, 1976).
GAF	The Global Assessment of Functioning (GAF) obtains ratings of burdening symptoms and disabilities in the last month on a scale from 100 (no symptoms/superior functioning in a wide range of activities) to 1 (persistent danger of severely hurting self or others or serious suicidal act with clear expectation of death/persistent inability to maintain minimal personal hygiene; American Psychiatric Association, 2002).

Note. Experience sampling procedure: During an initial briefing, participants were asked to stop their activity and answer the questions each time the device emitted the beep signal. The experience sampling questionnaire was available to participants for the duration of 10 min after emission of the beep signal. Participants were contacted at least once during the assessment period to assess their adherence to instructions, identify any potential distress associated with the method, and maximize the number of observations per participant. At the end of the assessment period, participants' reactivity to, and compliance with, the method was examined in a debriefing session. Participants were required to provide valid responses to at least one-third (i.e., 20 valid answers) of the emitted beeps to be included in the analysis (Delespaul et al., 2002).

Supplementary material 10: Data quality of clinical outcome measures

To ensure data quality, extensive training on instruments and interview skills was provided. Initial assessments were reviewed, and possible difficulties were anticipated. In addition to the EU-GEI web-based training designed to control and increase inter-rater reliability, regular meetings were held to discuss case vignettes. Site visits were held in order to evaluate and standardize interviews. In addition, extensive, repetitious training procedures and reliability checks were conducted. Training videos of the most advanced instruments were updated regularly. For each of the training videos, a 'golden standard score' was determined through independent rating of the training videos by independent experienced researchers. In case of disagreement, the head of the training work package was consulted. Per instrument, we subsequently determined the maximum amount of errors/deviation from the gold standard score the researcher was allowed, in order 'pass' the video.

Supplementary material 11: Restricted sample – unadjusted analyses

Method

In Supplementary material 11, we present unadjusted analyses in the restricted sample. The restricted sample only comprises participants, who returned within a +/- 6 month time interval around the expected follow-up time points. The analyses were conducted with varying sample sizes for illness severity, level of functioning and symptom burden.

Results

Basic sample and clinical characteristics

Table S17 gives an overview of relevant basic sample and clinical characteristics of the restricted sample at 1- (*N*=46) and 2-year follow-up (*N*=31).

Table S17. *Basic sample and clinical characteristics for the restricted sample.*

	1-year follow-up	*2-year follow-up*
N	46	31
Age at baseline (years), mean (*SD*)	23.9 (5.51)	24.06 (5.25)
Gender, *N* (%)		
Male, *N* (%)	21 (46%)	12 (39%)
Female, *N* (%)	25 (54%)	19 61%)
Ethnicity, *N* (%)		
White, *N* (%)	31 (67%)	23 (74%)
Black, *N* (%)	9 (20%)	4 (13%)
Other, *N* (%)	6 (13%)	4 (13%)
Comorbidity at baseline, *N* (%)		
Major depressive disorder, *N* (%)	14 (31%)	11 (37%)
Current depressive episode, *N* (%)	11 (24%)	8 (26%)
Bipolar disorder, *N* (%)	4 (9%)	4 (13%)
Any anxiety disorder, *N* (%)	26 (57%)	16 (52%)
Panic disorder, *N* (%)	12 (27%)	6 (19%)
Panic disorder + agoraphobia, *N* (%)	4 (9%)	1 (4%)
Agoraphobia only, *N* (%)	0	0
Social phobia, *N* (%)	14 (30%)	8 (26%)
Specific phobia, *N* (%)	9 (20%)	5 (17%)
Generalised anxiety disorder, *N* (%)	7 (15%)	5 (16%)
Not otherwise specified anxiety disorder, *N* (%)	1 (2%)	0
Obsessive-compulsive disorder, *N* (%)	2 (4%)	3 (10%)
Posttraumatic stress disorder, *N* (%)	4 (9%)	0
Any eating disorder, *N* (%)	7 (15%)	6 (19%)
Anorexia nervosa, *N* (%)	3 (7%)	3 (10%)
Bulimia nervosa, *N* (%)	3 (7%)	2 (6%)
Binge eating disorder, *N* (%)	1 (2%)	1 (3%)
Any somatoform disorder, *N* (%)	1 (2%)	1 (3%)
Somatization disorder, *N* (%)	0	0
Chronic pain, *N* (%)	0	0
Hypochondriasis, *N* (%)	1 (2%)	1 (3%)
Body dismorph disorder, *N* (%)	0	1
Childhood trauma questionnaire		
Total score at baseline, mean (*SD*)	49.70 (16.63)	47.74 (13.41)

Clinical global impression	3.73 (1.16)	3.87 (1.22)
Illness severity, mean (*SD*)		
Global assessment of functioning		
Disability, mean (*SD*)	56.15 (12.65)	57.00 (12.09)
Comprehensive Assessment of At Risk Mental States		
Unusual thought content, mean (*SD*)	2.91 (1.94)	2.58 (1.77)
Perceptual abnormalities, mean (*SD*)	3.13 (1.75)	3.03 (1.54)
Anxiety, mean (*SD*)	3.43 (1.00)	3.45 (0.62)
Tolerance to normal stress, mean (*SD*)	2.22 (1.87)	2.29 (1.66)

Note. ESM=experience sampling method. Comorbidity: Participants were diagnosed with a comorbid disorder, if classification criteria were fulfilled. Thus, one participant can be diagnosed with multiple comorbid disorders. Sample sizes based on valid restricted Global Assessment of Functioning Scale at follow-up.

<u>Stress reactivity and clinical outcomes at follow-up (H3)</u>

As displayed in Table S18, in the restricted sample, illness severity at follow-up was not predicted by emotional or psychotic stress reactivity. However, decreased positive affect in response to stress predicted level of functioning at 1-year follow-up (b=7.16, 95% CI 1.22 – 13.10, p=.019). Increased negative affect (b=1.45, 95% CI 0.75 – 2.14, p<.001) and increased psychotic experiences in response to stress (b=1.11, 95% CI 0.35 – 1.88, p=.006) predicted perceptual abnormalities at 1-year follow-up. In addition, decreased positive affect in response to stress predicted anxiety at 1-year follow-up (b=-0.83, 95% CI -1.59 – -0.07, p=.032).

Table S18. *Restricted sample: Clinical outcomes at 1- and 2-year follow-up predicted by emotional and psychotic stress reactivity at baseline and clinical outcome at baseline.*

	Clinical Outcomes							
	Illness severity				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	42		32		46		31	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.74 (0.50 – 0.97)	<.001	0.45 (0.08 – 0.82)	.020	0.40 (0.12 – 0.69)	.007	0.49 (0.11 – 0.87)	.013
Emotional reactivity	0.28 (-0.19 – 0.74)	.234	-0.08 (-0.71 – 0.54)	.793	-5.30 (-10.97 – 0.37)	.066	1.24 (-5.32 – 7.79)	.701
Predictor: Emotional reactivity (decreased positive affect in response to stress)								
Outcome at baseline	0.74 (0.49 – 0.99)	<.001	0.38 (0.01 – 0.74)	.045	0.36 (0.08 – 0.63)	.013	0.50 (0.12 – 0.87)	.011
Emotional reactivity	-0.21 (-0.74 – 0.31)	.418	-0.48 (-1.18 – 0.21)	.162	7.16 (1.22 – 13.10)	.019	2.01 (-5.15 – 9.16)	.571
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)								
Outcome at baseline	0.78 (0.54 – 1.01)	<.001	0.44 (0.08 – 0.81)	.019	0.42 (0.12 – 0.71)	.007	0.48 (0.09 – 0.87)	.018
Psychotic reactivity	0.01 (-0.44 – 0.45)	.980	-0.16 (-0.77 – 0.45)	.588	-3.28 (-9.00 – 2.43)	.253	1.62 (-5.29 – 8.53)	.635

	Unusual thought content				Perceptual abnormalities			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	40		30		40		30	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.46 (0.16 – 0.76)	.004	0.25 (-0.17 – 0.67)	.231	0.42 (0.18 – 0.67)	.001	0.43 (0.00 – 0.87)	.052
Emotional reactivity	0.66 (-0.27 – 1.59)	.160	0.45 (-0.81 – 1.70)	.474	1.45 (0.75 – 2.14)	<.001	-0.20 (-1.32 – 0.92)	.720
Predictor: Emotional reactivity (decreased positive affect in response to stress)								
Outcome at baseline	0.49 (0.19 – 0.79)	.002	0.30 (-0.11 – 0.70)	.146	0.48 (0.20 – 0.77)	.002	0.47 (0.03 – 0.91)	.039
Emotional reactivity	-0.70 (-1.69 – 0.29)	.161	-0.18 (-1.44 – 1.09)	.778	-0.68 (-1.55 – 0.19)	.124	-0.45 (-1.63 – 0.73)	.438
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)								
Outcome at baseline	0.43 (0.12 – 0.74)	.008	0.20 (-0.23 – 0.64)	.351	0.36 (0.09 – 0.63)	.011	0.41 (-0.03 – 0.84)	.066
Psychotic reactivity	0.60 (-0.34 – 1.54)	.206	0.70 (-0.62 – 2.02)	.285	1.11 (0.35 – 1.88)	.006	0.39 (-0.74 – 1.52)	.488

	Anxiety				Tolerance to normal stress			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	40		30		40		30	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.32 (-0.09 – 0.73)	.122	0.90 (0.08 – 1.73)	.033	0.31 (0.05 – 0.56)	0.18	0.18 (-0.20 – 0.55)	.343
Emotional reactivity	0.51 (-0.27 – 1.28)	.194	-0.72 (1.87 – 0.44)	.216	-0.08 (-0.84 – 0.68)	.833	-0.04 (-1.51 – 1.07)	.942

Predictor: Emotional reactivity (decreased positive affect in response to stress)							
Outcome	0.33	.084	0.70	.077	0.30	.019	0.14	.412
at baseline	(-0.05 – 0.71)		(-0.08 – 1.48)		(0.05 – 0.55)		(-0.21 – 0.49)	
Emotional	-0.83	.032	-0.08	.893	0.22	.580	-0.54	.316
reactivity	(-1.59 – -0.07)		(-1.22 – 1.07)		(-0.58 – 1.02)		(-1.62 – 0.54)	
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)							
Outcome	0.38	.058	0.76	.045	0.31	.019	0.22	.209
at baseline	(-0.01 – 0.77)		(0.02 – 1.51)		(0.05 – 0.56)		(-0.13 – 0.58)	
Psychotic	0.43	.234	-0.86	.106	-0.06	.365	-0.54	.312
reactivity	(-0.29 – 1.16)		(-1.93 – 0.20)		(-0.38 – 1.00)		(-1.62 – 0.54)	

Note. Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Unusual thought content, perceptual abnormalities, anxiety, and tolerance to normal stress assessed with the Comprehensive Assessment of At-Risk Mental States (Yung et al., 2005). CI=confidence interval.

<u>Emotional and psychotic stress reactivity as mediators of the association of childhood trauma and clinical outcomes (H4)</u>

Table S19 shows the unadjusted results on emotional and psychotic stress reactivity as mediators of the association of childhood trauma and clinical outcomes in the restricted sample. It displays total, direct and indirect effects of childhood trauma, emotional and psychotic stress reactivity on illness severity, level of functioning and CAARMS symptoms at follow-up. The association of illness severity at 1-year follow-up and childhood trauma was mediated by decreased positive affect in response to stress (indirect effect: *b*=0.16, 95% CI 0.00 – 0.32, *p*=.049). The association of childhood trauma and unusual thought content at 1-year follow-up was mediated by psychotic reactivity (indirect effect: *b*=0.34, 95% CI 0.01 – 0.67, *p*=.046). Furthermore, the association of childhood trauma and perceptual abnormalities at 1-year follow-up was mediated by increase negative affect (indirect effect: *b*=0.46, 95% CI 0.14 – 0.78, *p*=.005) and increase psychotic experiences in response to stress (indirect effect: *b*=0.47, 95% CI 0.15 – 0.79, *p*=.004).

Table S19. *Restricted sample: Emotional and psychotic stress reactivity as mediators of the association of childhood trauma and clinical outcomes.*

	Clinical Outcomes							
	Illness severity				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	43		33		46		31	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	0.43 (0.05 – 0.81)	.027	-0.11 (-0.59 – 0.37)	.645	-3.40 (-7.13 – 0.33)	.074	1.36 (-4.06 – 6.78)	.623
Direct effect	0.24 (-0.12 – 0.60)	.191	-0.15 (-0.66 – 0.36)	.570	-2.34 (-6.09 – 1.41)	.222	0.85 (-4.93 – 6.63)	.773
Indirect effect	0.19 (-0.01 – 0.38)	.059	0.03 (-0.15 – 0.22)	.709	-1.06 (-2.81 – 0.69)	.235	0.51 (-1.50 – 2.52)	.618
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	0.40 (0.03 – 0.77)	.032	-0.12 (-0.57 – 0.34)	.619	-3.49 (-7.12 – 0.15)	.060	1.50 (-3.90 – 6.91)	.586
Direct effect	0.24 (-0.11 – 0.59)	.178	-0.27 (-0.73 – 0.19)	.254	-2.13 (-5.69 – 1.43)	.241	2.13 (-3.54 – 7.79)	.462
Indirect effect	0.16 (0.00 – 0.32)	.049	0.15 (-0.01 – 0.31)	.064	-1.36 (-2.82 – 0.11)	.069	-0.62 (-2.15 – 0.90)	.422
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	0.37 (-0.02 – 0.75)	.061	-0.12 (-0.60 – 0.36)	.624	-3.00 (-6.74 – 0.74)	.116	1.89 (-3.58 – 7.35)	.499
Direct effect	0.28 (-0.10 – 0.66)	.145	-0.10 (-0.60 – 0.40)	.692	-2.57 (-6.75 – 1.01)	.147	0.77 (-4.70 – .624)	.782
Indirect effect	0.08 (-0.11 – 0.27)	.394	-0.02 (-0.22 – 0.18)	.840	-0.13 (-1.98 – 1.71)	.888	1.11 (-1.08 – 3.31)	.320

	Unusual thought content				Perceptual abnormalities			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	40		31		40		31	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	-0.12 (-0.72 – 0.48)	.697	0.54 (-0.37 – 1.45)	.242	0.16 (-0.35 – 0.67)	.549	-0.14 (-1.02 – 0.74)	.755
Direct effect	-0.37 (-0.96 – 0.22)	.220	-0.37 (-0.52 – 1.25)	.416	-0.30 (-0.75 – 0.15)	.186	-0.09 (-0.95 – 0.77)	.838
Indirect effect	0.24 (-0.06 – 0.55)	.110	0.18 (-0.15 – 0.50)	.287	0.46 (0.14 – 0.78)	.005	-0.05 (-0.36 – 0.26)	.746
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	-0.19 (-0.79 – 0.41)	.532	0.43 (-0.47 – 1.34)	.348	-0.03 (-0.57 – 0.50)	.899	-0.08 (-0.95 – 0.78)	.850
Direct effect	-0.31 (-0.91 – 0.28)	.299	0.40 (-0.50 – 1.30)	.379	-0.14 (-0.67 – 0.39)	.612	-0.12 (-0.98 – 0.74)	.785
Indirect effect	0.12 (-0.09 – 0.34)	.265	0.03 (-0.20 – 0.26)	.801	0.10 (-0.09 – 0.30)	.296	0.04 (-0.18 – 0.26)	.746
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	-0.09 (-0.69 – 0.50)	.762	0.68 (-0.24 – 1.60)	.147	0.13 (-0.38 – 0.64)	.610	0.05 (-0.84 – 0.95)	.906
Direct effect	-0.43 (-1.01 – 0.15)	.147	0.39 (-0.47 – 1.25)	.373	-0.33 (-0.81 – 0.14)	.164	-0.12 (-0.96 – 0.72)	.784
Indirect effect	0.34 (0.01 – 0.67)	.046	0.29 (-0.07 – 0.66)	.118	0.47 (0.15 – 0.79)	.004	0.17 (-0.17 – 0.52)	.327

	Anxiety				Tolerance to normal stress			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	40		31		40		31	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	0.25 (-0.19 – 0.70)	.268	-0.24 (-1.10 – 0.62)	.580	-0.07 (-0.53 – 0.40)	.778	0.12 (-0.66 – 0.91)	.756
Direct effect	.006 (-0.37 – 0.49)	.792	-0.19 (-1.02 – 0.65)	.657	-0.08 (-0.55 – 0.38)	.727	0.09 (-0.68 – 0.85)	.826
Indirect effect	0.19 (-0.03 – 0.42)	.093	-0.05 (-0.35 – 0.24)	.725	0.02 (-0.20 – 0.23)	.888	0.04 (-0.23 – 0.31)	.778
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	0.24 (-0.19 – 0.66)	.283	-0.19 (-1.03 – 0.65)	.660	-0.10 (-0.55 – 0.36)	.679	0.17 (-.09 – 0.92)	.668
Direct effect	0.05 (-0.36 – 0.47)	.796	-0.21 (-1.05 – 0.62)	.616	-0.05 (-0.51 – 0.41)	.828	0.05 (-0.70 – 0.80)	.899
Indirect effect	0.18 (0.00 – 0.37)	.055	0.03 (-0.19 – 0.24)	.817	-0.05 (-0.20 – 0.11)	.572	0.12 (-0.09 – 0.32)	.263
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	0.22 (-0.22 – 0.67)	.329	-0.41 (-1.28 – 0.45)	.347	-0.06 (-0.53 – 0.40)	.790	0.00 (-0.81 – 0.80)	.996
Direct effect	0.07 (-0.38 – 0.51)	.767	-0.18 (-0.99 – 0.62)	.656	-0.09 (-0.56 – 0.38)	.710	0.11 (-0.65 – 0.86)	.784
Indirect effect	0.16 (-0.08 – 0.39)	.200	-0.23 (-0.57 – 0.11)	.179	0.03 (-0.21 – 0.27)	.831	-0.11 (-0.41 – 0.20)	.488

Note. Childhood trauma assessed with the Childhood Trauma Questionnaire (Bernstein & Fink, 1998; Wingenfeld et al., 2010). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Unusual thought content, perceptual abnormalities, anxiety and tolerance to normal stress assessed with the Comprehensive Assessment of At-Risk Mental State (Yung et al., 2005). CI=confidence interval.

Supplementary material 12: Restricted sample – adjusted analyses

Method

In Supplementary material 12, we present adjusted analyses in the restricted sample. The restricted sample only comprises participants, who returned within a +/- 6 month time interval around the expected follow-up time points. The analyses were conducted with varying sample sizes for illness severity, level of functioning and symptom burden. The analyses are adjusted for age, gender, ethnicity, centre, comorbid major depressive, and anxiety disorders and time to follow-up.

Results

<u>Stress reactivity and clinical outcomes at follow-up (H3)</u>

As displayed in Table S20, in the restricted sample, illness severity at follow-up was not predicted by emotional or psychotic stress reactivity. However, decreased positive affect in response to stress predicted level of functioning at 1-year follow-up (b=6.64, 95% CI 0.14 – 13.13, p=.046). Increased negative affect in response to stress predicted unusual thought content at 2-year follow-up (b=1.83, 95% CI 0.17 – 3.48, p=.033). In addition, perceptual abnormalities at 1-year follow-up were predicted by emotional (negative affect: b=1.31, 95% CI 0.49 – 2.13, p=.003; positive affect: b=-1.09, 95% CI -1.96 – -0.23, p=.015) and psychotic stress reactivity (b=1.09, 95% CI 0.18 – 2.00, p=.020). More intense emotional and psychotic reactivity was associated with higher symptom burden and lower level of functioning.

Table S20. *Restricted sample: Clinical outcomes at 1- and 2-year follow-up predicted by emotional and psychotic stress reactivity at baseline and clinical outcome at baseline.*

	Clinical Outcomes							
	Illness severity				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	41		31		45		30	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.71 (0.46 – 0.96)	<.001	0.46 (-0.07 – 0.98)	.085	0.42 (0.07 – 0.76)	.019	0.56 (0.03 – 1.08)	.040
Emotional reactivity	0.36 (-0.08 – 0.80)	.105	-0.34 (-1.28 – 1.83)	.338	-3.89 (-10.86 – 3.08)	.265	5.60 (-4.36 – 15.57)	.255
Predictor: Emotional reactivity (decreased positive affect in response to stress)								
Outcome at baseline	0.73 (0.49 – 0.97)	<.001	0.29 (-0.26 – 0.83)	.284	0.41 (0.09 – 0.74)	.015	0.48 (-0.05 – 1.02)	.075
Emotional reactivity	-0.42 (-0.86 – 0.02)	.061	-0.34 (-1.30 – 0.62)	.474	6.64 (0.14 – 13.13)	.046	-1.22 (-10.45 – 7.99)	.784
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)								
Outcome at baseline	0.75 (0.47 – 1.03)	<.001	0.44 (-0.06 – 0.95)	.083	0.45 (0.11 – 0.79)	.012	0.51 (0.01 – 1.00)	.046
Psychotic reactivity	0.13 (-0.36 – 0.61)	.598	-0.37 (-1.33 – 0.60)	.440	-1.11 (-8.21 – 5.99)	.753	7.39 (-3.20 – 17.98)	.161

	Unusual thought content				Perceptual abnormalities			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	39		30		39		29	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.53 (0.19 – 0.86)	.004	-0.16 (-0.65 – 0.32)	.483	0.41 (0.14 – 0.67)	.004	0.54 (-0.04 – 1.12)	.066
Emotional reactivity	1.06 (0.03 – 2.09)	.044	1.83 (0.17 – 3.48)	.033	1.31 (0.49 – 2.13)	.003	0.22 (-1.56 – 2.01)	.798
Predictor: Emotional reactivity (decreased positive affect in response to stress)								
Outcome at baseline	0.50 (0.15 – 0.85)	.005	-0.13 (0.65 – 0.39)	.601	0.45 (0.18 – 0.73)	.002	0.56 (0.01 – 1.11)	.048
Emotional reactivity	-0.97 (-2.01 – 0.07)	.065	-0.99 (-2.38 – 0.40)	.152	-1.09 (-1.96 – -0.23)	.015	-0.48 (-1.79 – 0.84)	.457
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)								
Outcome at baseline	0.45 (0.09 – 0.82)	.016	-0.20 (-0.73 – 0.34)	.450	0.34 (0.05 – 0.63)	.021	0.57 (0.05 – 1.09)	.033
Psychotic reactivity	0.80 (-0.31 – 1.92)	.150	1.41 (-0.35 – 3.17)	.111	1.09 (0.18 – 2.00)	.020	1.19 (-0.37 – 2.74)	.125

	Anxiety				Tolerance to normal stress			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	39		30		39		30	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.31 (-0.19 – 0.81)	.222	0.85 (-0.31 – 2.02)	.141	0.29 (0.00 – 0.57)	.054	0.22 (-0.19 – 0.63)	.270
Emotional reactivity	0.030 (-0.56 – 1.17)	.478	-0.73 (-2.52 – 1.06)	.404	-0.03 (-0.97 – 0.91)	.950	-0.20 (-1.80 – 1.39)	.794

Predictor: Emotional reactivity (decreased positive affect in response to stress)								
Outcome at baseline	0.27 (-0.18 – 0.71)	.230	0.071 (-0.42 – 1.83)	.204	0.28 (-0.01 – 0.56)	.058	0.21 (-0.19 – 0.60)	.286
Emotional reactivity	-0.81 (-1.58 – -0.03)	.041	0.10 (-1.24 – 1.45)	.873	0.36 (0.56 – 1.29)	.428	0.02 (-1.16 – 1.21)	.967
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)								
Outcome at baseline	0.35 (-0.14 – 0.83)	.155	0.75 (-0.34 – 1.84)	.168	0.28 (-0.01 – 0.58)	.057	0.23 (-0.18 – 0.65)	.252
Psychotic reactivity	0.17 (-0.68 – 1.02)	.689	-0.84 (-2.45 – 0.77)	.288	0.01 (-0.95 – 0.97)	.985	-0.29 (-1.83 – 1.25)	.701

Note. Results adjusted for age, gender, ethnicity, centre, comorbid major depressive and anxiety disorders, and time to follow-up. Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002).Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). Unusual thought content, perceptual abnormalities, anxiety and tolerance to normal stress assessed with the Comprehensive Assessment of At-Risk Mental State (Yung et al., 2005). CI=confidence interval.

<u>Emotional and psychotic stress reactivity as mediators of the association of childhood trauma and clinical outcomes (H4)</u>

As displayed in Table S21, the adjusted analysis in the restricted sample showed similar results compared to the main analysis. Increased negative affect in response to stress mediated the association of childhood trauma and illness severity at 1-year follow-up (indirect effect: *b*=0.19, 95% CI 0.02 – 0.37, *p*=.030). Moreover, increased psychotic experiences in response to stress mediated the association of childhood trauma and unusual thought content at 1-year follow-up (indirect effect: *b*=0.36, 95% CI 0.02 – 0.70, *p*=.037). In addition, the association of childhood trauma and perceptual abnormalities at 1-year follow-up was mediated by increased negative affect (indirect effect: *b*=0.40, 95% CI 0.08 – 0.72, *p*=.013) and increased psychotic experiences in response to stress (indirect effect: *b*=0.43, 95% CI 0.11 – 0.75, *p*=.008).

Table S21. *Restricted sample: Emotional and psychotic stress reactivity as mediators of the association of childhood trauma and clinical outcomes.*

	Clinical Outcomes							
	Illness severity				**Level of functioning: Disability**			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	42		32		46		30	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	0.49 (0.15 – 0.83)	.004	-0.48 (-0.95 – 0.00)	.052	-3.00 (-7.12 – 1.12)	.153	2.93 (-2.55 – 8.40)	.295
Direct effect	0.30 (-0.02 – 0.62)	.068	-0.58 (-1.12 – -0.04)	.034	-1.80 (-6.02 – 2.42)	.403	2.89 (-3.38 – 9.17)	.366
Indirect effect	0.19 (0.02 – 0.37)	.030	0.11 (-0.10 – 0.31)	.305	-1.20 (-3.02 – 0.61)	.195	0.03 (-2.31 – 2.38)	.978
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	0.44 (0.12 – 0.77)	.007	-0.45 (-0.90 – 0.01)	.054	-2.82 (-6.83 – 1.20)	.169	2.99 (-2.42 – 8.39)	.279
Direct effect	0.35 (0.05 – 0.66)	.024	-0.53 (-0.98 – -0.08)	.021	-1.99 (-5.92 – 1.94)	.321	3.19 (-2.31 – 8.69)	.637
Indirect effect	0.09 (-0.03 – 0.22)	.148	0.08 (-0.04 – 0.21)	.182	-0.83 (-2.04 – 0.39)	.182	-0.20 (-1.08 – 0.68)	.651
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	0.41 (0.07 – 0.75)	.018	-0.43 (-0.91 – 0.05)	.078	-2.73 (-6.88 – 1.43)	.198	3.41 (-2.03 – 8.86)	.219
Direct effect	0.30 (-0.03 – 0.64)	.075	-0.49 (-1.01 – 0.02)	.059	-2.61 (-6.96 – 1.74)	.240	2.03 (-3.55 – 7.61)	.476
Indirect effect	0.11 (-0.04 – 0.26)	.149	0.06 (-0.15 – 0.28)	.562	-0.12 (-2.03 – 1.80)	.903	1.38 (-1.30 – 4.07)	.313

	Unusual thought content				**Perceptual abnormalities**			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	39		30		39		29	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	0.04 (-0.61 – 0.69)	.909	0.45 (-0.38 – 1.27)	.287	-0.03 (-0.58 – 0.51)	.900	0.00 (-0.90 – 0.91)	.993
Direct effect	-0.26 (-0.92 – 0.39)	.430	0.17 (-0.73 – 1.06)	.717	-0.44 (-0.94 – 0.07)	.090	0.25 (-0.75 – 1.24)	.628
Indirect effect	0.30 (-0.02 – 0.62)	.063	0.28 (-0.09 – 0.65)	.136	0.40 (0.08 – 0.72)	.013	-0.24 (-0.64 – 0.15)	.229
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	0.04 (-0.61 – 0.68)	.908	0.49 (-0.32 – 1.30)	.240	-0.06 (-0.31 – 0.50)	.844	-0.05 (-0.96 – 0.86)	.910
Direct effect	-0.07 (-0.70 – 0.56)	.816	0.39 (-0.42 – 1.20)	.349	-0.17 (-0.70 – 0.37)	.541	-0.09 (-1.02 – 0.83)	.841
Indirect effect	0.11 (-0.06 – 0.29)	.209	0.10 (-0.07 – 0.26)	.245	0.11 (-0.05 – 0.28)	.184	0.04 (-0.10 – 0.18)	.553
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	0.09 (-0.55 – 0.74)	.780	0.60 (-0.23 – 1.44)	.157	0.02 (-0.52 – 0.56)	.936	0.03 (-0.90 – 0.96)	.950
Direct effect	-0.27 (-0.91 -0.37)	.408	0.37 (-0.46 – 1.21)	.381	-0.41 (-0.92 – 0.10)	.112	-0.13 (-.106 – 0.80)	.782
Indirect effect	0.36 (0.02 – 0.70)	0.37	0.23 (-0.13 – 0.59)	.213	0.43 (0.11 – 0.75)	.008	0.16 (-0.23 – 0.56)	.426

	Anxiety				Tolerance to normal stress			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	39		30		39		30	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	-0.19 (-0.63 – 0.25)	.389	-0.29 (-1.14 – 0.56)	.499	-0.15 (-0.68 – 0.38)	.576	-0.11 (-0.83 – 0.61)	.767
Direct effect	-0.38 (-0.82 – 0.07)	.099	-0.20 (-1.15 – 0.74)	.670	-0.18 (-0.74 – 0.37)	.513	-0.14 (-0.94 – 0.66)	.730
Indirect effect	0.18 (-0.03 – 0.39)	.087	-0.09 (-0.44 – 0.26)	.620	0.03 (-0.18 – 0.25)	.759	0.03 (-0.26 – 0.33)	.830
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	-0.18 (-0.61 – 0.25)	.415	-0.31 (-1.16 – 0.54)	.472	-0.18 (-0.70 – 0.35)	.509	-0.11 (-0.83 – 0.61)	.774
Direct effect	-0.28 (-0.69 – 0.14)	.190	-0.32 (-1.18 – 0.54)	.470	-0.14 (-0.66 – 0.38)	.602	-0.12 (-0.85 – 0.61)	.742
Indirect effect	0.10 (-0.04 – 0.24)	.168	0.01 (-0.11 – 0.13)	.921	-0.04 (0.14 – 0.06)	.472	0.02 (-0.09 – 0.12)	.752
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	-0.19 (-0.63 – 0.26)	.414	-0.41 (-1.26 – 0.44)	.349	-0.13 (-0.66 – 0.39)	.618	-0.10 (-0.83 – 0.64)	.794
Direct effect	-0.32 (-0.78 – 0.13)	.164	-0.19 (-1.04 – 0.66)	.661	-0.21 (-0.75 – 0.34)	.462	-0.11 (-0.85 – 0.63)	.772
Indirect effect	0.14 (-0.07 – 0.35)	.204	-0.22 (-0.58 – 0.15)	.246	0.07 (-0.17 – 0.31)	.568	0.01 (-0.29 – 0.31)	.937

Note. Results adjusted for age, gender, ethnicity, centre, comorbid major depressive and anxiety disorders, and time to follow-up. Childhood trauma assessed with the Childhood Trauma Questionnaire (Bernstein & Fink, 1998; Wingenfeld et al., 2010). Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Unusual thought content, perceptual abnormalities, anxiety and tolerance to normal stress assessed with the Comprehensive Assessment of At-Risk Mental State (Yung et al., 2005). CI=confidence interval.

Supplementary material 13: Unadjusted analysis in the full sample

Method

In Supplementary material 13, we report the results of the unadjusted analyses in the full sample.

Results

<u>Association between momentary stress, affect and psychotic experiences (H1)</u>

Momentary stress was associated with small to moderate increases in negative affect (negative affect; $\beta=0.31$, 95% CI $0.27 - 0.36$, $p<.001$) and psychotic experiences (psychotic experiences; $\beta=0.16$, 95% CI $0.13 - 0.19$, $p<.001$) as well as with a moderate decrease in positive affect (positive affect; $\beta=-0.39$, 95% CI $-0.43 - -0.34$, $p<.001$).

<u>Association between momentary stress, affect and psychotic experiences by childhood trauma (H2)</u>

As displayed in Table S22, childhood trauma modified the associations of momentary stress and negative affect (stress × childhood trauma: $\beta=0.03$, 95% CI $0.01 - 0.06$, $p=.018$) and psychotic experiences (stress × childhood trauma: $\beta=0.02$, 95% CI $0.00 - 0.05$, $p=.037$). These associations were greater in individuals with high levels of childhood trauma (outcome negative affect: high vs. low childhood trauma: $\beta=0.06$, 95% CI $0.01 - 0.11$, $p=.018$; outcome psychotic experiences: high vs. low childhood trauma: $\beta=0.05$, 95% CI $0.00 - 0.09$, $p=.037$). The results are congruent with the adjusted analysis.

Table S22. *Modification of the association between momentary stress and affect/psychotic experiences by childhood trauma.*

	β	95% CI	SE	p
Effect modification by childhood trauma				
Outcome: Negative affect				
Stress	0.31	0.28 – 0.34	0.01	<.001
Childhood trauma	0.26	0.12 – 0.40	0.07	<.001
Stress × childhood trauma	0.03	0.01 – 0.06	0.01	.018
High childhood trauma	0.34	0.31 – 0.37	0.02	<.001
Low childhood trauma	0.28	0.24 – 0.32	0.02	<.001
High vs. low childhood trauma	0.06	0.01 – 0.11	0.03	.018
Outcome: Positive affect				
Stress	-0.39	-0.42 – -0.36	0.02	<.001
Childhood trauma	-0.16	-0.28 – -0.03	0.07	.014
Stress × childhood trauma	0.03	0.00 – 0.06	0.01	.084
Outcome: Psychotic experiences				
Stress	0.15	0.13 – 0.17	0.01	<.001
Childhood trauma	0.31	0.17 – 0.46	0.07	<.001
Stress × childhood trauma	0.02	0.00 – 0.05	0.01	.037
High childhood trauma	0.17	0.14 – 0.20	0.02	<.001
Low childhood trauma	0.12	0.09 – 0.16	0.02	<.001
High vs. low childhood trauma	0.05	0.00 – 0.09	0.02	.037

Note. Childhood trauma assessed with the Childhood Trauma Questionnaire (Bernstein & Fink, 1998; Wingenfeld et al., 2010).

CI=confidence interval. SE=standard error.

Table S23 shows the unadjusted results on the association of emotional and psychotic stress reactivity with illness severity and level of functioning at 1- and 2-year follow-up. Illness severity at 1-year follow-up was predicted by increased negative affect in response to stress (b=0.55, 95% CI 0.03 – 1.06, p=.037). Level of functioning at 1-year follow-up was predicted by decreased positive affect in response to stress (b=7.64, 95% CI 1.82 – 13.46, p=.011). In addition, increased negative affect (b=1.31, 95% CI 0.72 – 1.90, p<.001) and increased psychotic experiences (b=1.00, 95% CI 0.35 – 1.66, p=.004) in response to stress predicted perceptual abnormalities at 1-year follow-up. There was no evidence that emotional or psychotic stress reactivity predicted unusual thought content, anxiety or tolerance to normal stress at follow-up.

Table S23. *Clinical outcomes at 1- and 2-year follow-up predicted by emotional and psychotic stress reactivity at baseline and clinical outcome at baseline.*

	Clinical Outcomes						
	Illness severity				Level of functioning: Disability		
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	47		36		48		36	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.63 (0.37 – 0.88)	<.001	0.46 (0.11 – 0.81)	.012	0.42 (0.15 – 0.70)	.003	0.37 (-0.02 – 0.76)	.059
Emotional reactivity	0.55 (0.03 – 1.06)	.037	-0.01 (-0.61 – 0.59)	.981	-5.82 (-11.64 – -0.01)	.050	0.66 (-6.07 – 7.39)	.844
Predictor: Emotional reactivity (decreased positive affect in response to stress)								
Outcome at baseline	0.62 (0.35 – 0.89)	<.001	0.36 (0.01 – 0.71)	.043	0.39 (0.12 – 0.66)	.006	0.39 (0.01 – 0.77)	.045
Emotional reactivity	-0.43 (-0.95 – -0.10)	.108	-0.56 (-1.21 – 0.10)	.092	7.64 (1.82 – 13.46)	.011	3.61 (-3.53 – 10.75)	.311
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)								
Outcome at baseline	0.67 (0.40 – 0.93)	<.001	0.47 (0.12 – 0.81)	.010	0.44 (0.15 – 0.72)	.003	0.35 (-0.05 – 0.75)	.080
Psychotic reactivity	0.22 (-0.28 – 0.73)	.377	-0.17 (-0.80 – 0.45)	.578	-4.11 (-9.81 – 1.60)	.154	1.60 (-5.62 – 8.81)	.655

	Unusual thought content				Perceptual abnormalities			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	44		34		44		34	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.48 (0.19 – 0.77)	.002	0.14 (-0.26 – 0.54)	.477	0.42 (0.18 – 0.65)	.001	0.36 (-0.05 – 0.77)	.082
Emotional reactivity	0.49 (-0.32 – 1.30)	.229	0.43 (-0.76 – 1.61)	.470	1.31 (0.72 – 1.90)	<.001	-0.18 (-1.24 – 0.87)	.724
Predictor: Emotional reactivity (decreased positive affect in response to stress)								
Outcome at baseline	0.50 (0.22 – 0.79)	.001	0.19 (-0.19 – 0.73)	.320	0.48 (0.20 – 0.75)	.001	0.44 (-0.02 – 0.86)	.042
Emotional reactivity	-0.64 (-1.52 – 0.24)	.152	-0.46 (-1.65 – 0.73)	.435	-0.74 (-1.50 – -0.01)	.054	-0.65 (-1.76 – 0.47)	.248
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)								
Outcome at baseline	0.45 (0.16 – 0.74)	.003	0.07 (-0.32 – 0.47)	.703	0.36 (0.10 – 0.62)	.009	0.34 (-0.07 – 0.74)	.101
Psychotic reactivity	0.46 (-0.35 – 1.28)	.257	0.98 (-0.26 – 2.21)	.116	1.00 (0.35 – 1.66)	.004	0.53 (-0.56 – 1.63)	.328

	Anxiety				Tolerance to normal stress			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	44		34		44		34	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Predictor: Emotional reactivity (increased negative affect in response to stress)								
Outcome at baseline	0.38 (-0.02 – 0.79)	.063	0.72 (-0.07 – 1.52)	.074	0.34 (0.10 – 0.58)	.007	0.10 (-0.24 – 0.44)	.555
Emotional reactivity	0.30 (-0.38 – 0.97)	.384	-0.39 (-1.53 – 0.75)	.494	0.00 (-0.67 – 0.66)	.995	-0.02 (-1.05 – 1.01)	.974
Predictor: Emotional reactivity (decreased positive affect in response to stress)								
Outcome at baseline	0.37 (-0.01 – 0.76)	.057	0.61 (-0.12 – 1.34)	.097	0.34 (0.10 – 0.58)	.007	0.08 (-0.23 – 0.39)	.606
Emotional reactivity	-0.61 (-1.31 – 0.10)	.090	-0.20 (-1.29 – 0.88)	.706	0.01 (-0.71 – 0.73)	.971	-0.67 (-1.64 – 0.30)	.168
Predictor: Psychotic reactivity (increased psychotic experiences in response to stress)								
Outcome at baseline	0.41 (0.02 – 0.80)	.039	0.63 (-0.07 – 1.33)	.078	0.34 (0.10 – 0.59)	.007	0.12 (-0.20 – 0.45)	.454
Psychotic reactivity	0.37 (-0.28 – 1.01)	.255	-0.81 (-1.86 – 0.25)	.129	-0.03 (-0.69 – 0.63)	.932	-0.32 (-1.35 – 0.70)	.522

Note. Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Unusual thought content, perceptual abnormalities, anxiety and tolerance to normal stress assessed with the Comprehensive Assessment of At-Risk Mental State (Yung et al., 2005). CI=confidence interval.

Emotional and psychotic stress reactivity as mediators of the association of childhood trauma and clinical outcomes (H4)

Table S24 shows unadjusted findings on total, direct, and indirect effects of childhood trauma, emotional and psychotic stress reactivity on illness severity and level of functioning at follow-up. Increased negative affect in response to stress mediated the effect of childhood trauma on illness severity at 1-year follow-up (indirect effect: $b=0.23$, 95% CI $0.02 – 0.31$, $p=.030$). Decreased positive affect in response to stress mediated the effect of childhood trauma on illness severity at 2-year follow-up (indirect effect: $b=0.17$, 95% CI $0.01 – 0.34$, $p=.039$). Higher levels of childhood trauma were associated with more intense emotional stress reactivity in form of a stronger reduction of positive affect and an increase of negative affect when exposed to momentary stress. Stronger reduction of positive affect and stronger increase of negative affect in response to stress, in turn, were associated with higher ratings of illness severity at follow-up. Furthermore, psychotic reactivity to stress mediated the effect of childhood trauma on unusual thought content at 1-year follow-up (indirect effect: $b=0.32$, 95% CI $0.02 – 0.62$, $p=.037$). In addition, the association of childhood trauma and perceptual abnormalities at 1-year follow-up was mediated by increased negative affect up (indirect effect: $b=0.44$, 95% CI $0.15 – 0.73$, $p=.003$) and increased psychotic experiences up (indirect effect: $b=0.44$, 95% CI $0.16 – 0.73$, $p=.002$) in response to stress.

Table S24. *Emotional and psychotic stress reactivity as mediators of the association of child-hood trauma and clinical outcomes.*

	Clinical Outcomes							
	Illness severity				Level of functioning: Disability			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	48		37		48		35	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	0.45 (0.07 – 0.83)	.022	-0.11 (-0.59 – 0.37)	.644	-3.83 (-7.56 – -0.09)	.045	1.65 (3.58 – 6.88)	.536
Direct effect	0.22 (-0.13 – 0.57)	.222	-0.16 (-0.64 – -0.33)	.527	-2.64 (-6.39 – 1.10)	.166	1.38 (-3.99 – 6.74)	.615
Indirect effect	0.23 (0.02 – 0.43)	.030	0.04 (-0.13 – 0.22)	.622	-1.19 (-3.02 – 0.64)	.202	0.28 (-1.62 – 2.17)	.776
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	0.36 (0.00 – 0.73)	.051	-0.13 (-0.57 – 0.32)	.575	-3.82 (-7.45 – -0.19)	.039	1.65 (-3.50 – 6.79)	.531
Direct effect	0.22 (-0.14 – -0.57)	.234	-0.30 (-0.74 – -0.15)	.187	-2.41 (-5.97 – 1.14)	.184	2.43 (-2.91 – 7.77)	.373
Indirect effect	0.15 (0.00 – 0.30)	.052	0.17 (0.01 – 0.34)	.039	-1.41 (-2.89 – 0.08)	.063	-0.78 (-2.26 – 0.70)	.302
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	0.37 (-0.01 – 0.75)	.060	-0.13 (-0.62 – 0.35)	.091	-3.45 (-7.18 – 0.28)	.070	1.89 (-3.34 – 7.11)	.479
Direct effect	0.24 (-0.14 – 0.62)	.214	-0.12 (-0.62 – 0.37)	.619	-2.72 (-6.92 – 1.48)	.205	0.97 (-4.38 – 6.32)	.723
Indirect effect	0.13 (-0.07 – 0.32)	.211	-0.01 (-0.21 – 0.19)	.928	-0.43 (-2.33 – 1.47)	.658	0.92 (-1.29 – 3.13)	.415

	Unusual thought content				Perceptual abnormalities			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	45		34		45		33	
	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p	b (95% CI)	p
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	-0.17 (-0.70 – 0.36)	.534	0.65 (-0.22 – 1.52)	.146	0.11 (-0.33 – 0.55)	.621	-0.09 (-0.94 – 0.75)	.830
Direct effect	-0.38 (-0.93 – 0.18)	.181	0.50 (-0.32 – 1.31)	.235	-0.33 (0.73 – 0.08)	.116	-0.03 (-0.82 – 0.77)	.951
Indirect effect	0.21 (-0.06 – 0.48)	.123	0.15 (-0.15 – 0.46)	.318	0.44 (0.15 – 0.73)	.003	-0.07 (-0.36 – 0.22)	.645
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	-0.17 (-0.70 – 0.36)	.539	0.53 (-0.30 – 1.37)	.210	0.07 (-0.39 – 0.54)	.754	-0.01 (-0.79 – 0.81)	.980
Direct effect	-0.28 (-0.82 – 0.26)	.305	0.47 (-0.36 – 1.30)	.272	-0.04 (-0.51 – 0.43)	.875	-0.05 (-0.85 – 0.75)	.907
Indirect effect	0.11 (-0.08 – 0.31)	.255	0.07 (-0.15 – 0.28)	.526	0.11 (-0.06 – 0.29)	.211	0.06 (-0.15 – 0.26)	.582
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	-0.17 (-0.69 – 0.35)	.523	0.75 (-0.10 – 1.59)	.084	0.08 (-0.36 – 0.53)	.709	0.14 (-0.68 – 0.97)	.734
Direct effect	-0.49 (-1.04 – 0.07)	.084	0.43 (-0.36 – 1.22)	.287	-0.36 (-0.79 – 0.07)	.106	-0.06 (-0.85 – 0.72)	.872
Indirect effect	0.32 (0.02 – 0.62)	.037	0.31 (-0.04 – 0.67)	.084	0.44 (0.16 – 0.73)	.002	0.21 (-0.13 – 0.54)	.228

	Anxiety				Tolerance to normal stress			
	1-year follow-up		2-year follow-up		1-year follow-up		2-year follow-up	
N	45		34		45		34	
	b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Mediator: Emotional reactivity (increased negative affect in response to stress)								
Total effect	-0.16 (-0.24 – 0.56)	.432	-0.36 (-1.20 – 0.47)	.391	0.04 (-0.40 – 0.47)	.873	0.19 (-0.55 – 0.93)	.618
Direct effect	-0.04 (-0.38 – 0.46)	.860	-0.38 (-1.16 – 0.41)	.345	-0.05 (-0.51 – 0.41)	.840	0.16 (-0.54 – 0.86)	.649
Indirect effect	0.12 (-0.07 – 0.32)	.224	0.01 (-0.27 – 0.29)	.930	0.08 (-0.13 – 0.29)	.435	0.03 (-0.22 – 0.28)	.830
Mediator: Emotional reactivity (decreased positive affect in response to stress)								
Total effect	0.19 (-0.21 – 0.56)	.366	-0.35 (-1.14 – 0.44)	.388	0.02 (-0.41 – 0.45)	.928	0.24 (-0.45 – 0.93)	.494
Direct effect	0.05 (-0.35 – 0.44)	.821	-0.40 (-1.18 – 0.39)	.322	0.03 (-0.42 – 0.47)	.911	0.11 (-0.57 – 0.79)	.751
Indirect effect	0.14 (-0.02 – 0.30)	.096	0.05 (-0.15 – 0.25)	.639	-0.01 (-0.16 – 0.15)	.944	0.13 (-0.06 – 0.32)	.184
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)								
Total effect	0.15 (-0.25 – 0.55)	.332	-0.56 (-1.37 – 0.25)	.176	0.03 (-0.40 – 0.46)	.884	0.10 (-0.64 – 0.83)	.799
Direct effect	0.03 (-0.40 – 0.47)	.887	-0.33 (-1.09 – 0.43)	.394	-0.07 (-0.55 – 0.40)	.763	0.18 (-0.52 – 0.87)	.618
Indirect effect	0.12 (-0.09 – 0.33)	.269	-0.23 (-0.56 – 0.10)	.173	0.10 (-0.12 – 0.33)	.370	-0.08 (-0.37 – 0.21)	.581

Note. Illness severity assessed with the Clinical Global Impression Scale (Guy, 1976). Level of functioning assessed with the Global Assessment of Functioning Scale (American Psychiatric Association, 2002). Unusual thought content, perceptual abnormalities, anxiety and tolerance to normal stress assessed with the Comprehensive Assessment of At-Risk Mental State (Yung et al., 2005). CI=confidence interval.

Supplementary material 14: Exploring the role of transition

Does transition moderate the effect of momentary stress on affect and psychotic experiences?

Method

As ESM data have a multilevel structure with multiple observations (level-1) nested within participants (level-2), the 'mixed' command in Stata 15 was used to fit two-level, linear mixed models (StataCorp, 2017). The composite stress measure and transition status were included as independent variables, and negative affect, positive affect, and psychotic experiences as outcome variables. To examine effect modification by transition, we included two-way interaction-terms for stress × transition. Analyses were performed twice, once unadjusted, once while controlling for potential confounders (i.e., age, gender, centre, ethnicity, comorbid major depressive and anxiety disorders).

Results

Table S25 shows the results of the adjusted analyses. Transition status modified the associations of momentary stress with negative affect (stress × transition: $\beta=0.11$, 95% CI 0.02 – 0.20, $p=.021$) and positive affect (stress × transition: $\beta=-0.14$, 95% CI -0.25 – -0.03, $p=.010$). These associations were greater in individuals who transitioned to psychosis (outcome negative affect: transition vs. non-transition: $\beta=0.11$, 95% CI 0.02 – 0.20, $p=.021$; outcome positive affect: transition vs. non-transition: $\beta=-0.14$, 95% CI -0.24 – -0.03, $p=.010$). However, transition status did not modify the effect of momentary stress on psychotic experiences (stress × transition: $\beta=0.01$, 95% CI -0.07 – 0.09, $p=.814$).

Table S26 shows the results of the unadjusted analyses. Transition modified the associations of momentary stress with negative affect (stress × transition: $\beta=0.11$, 95% CI 0.02 – 0.20, $p=.021$) and positive affect (stress × transition: $\beta=-0.14$, 95% CI -0.24 – -0.03, $p=.011$). The associations

were greater in individuals, who transitioned to psychosis compared to those who did not transition (outcome negative affect: transition vs. non-transition: β=0.11, 95% CI 0.02 – 0.20, *p*=.021; outcome positive affect: transition vs. non-transition: β=-0.14, 95% CI -0.24 – -0.03, *p*=.011). Adjusted and unadjusted results converge.

Table S25. *Modification of the association between momentary stress and affect/psychotic experiences by transition status.*

	β	95% CI	SE	*p*
Effect modification by transition status				
Outcome: Negative affect				
Stress	0.30	0.28 – 0.33	0.01	<.001
Transition status	0.19	-0.27 – 0.64	0.23	.422
Stress × transition status	0.11	0.02 – 0.20	0.05	.021
Transition	0.41	0.32 – 0.50	0.04	<.001
Non-transition	0.30	0.28 – 0.33	0.01	<.001
Transition vs. non-transition	0.11	0.02 – 0.20	0.05	.021
Outcome: Positive affect				
Stress	-0.37	-0.40 – -0.34	0.02	<.001
Transition status	-0.05	-0.44 – 0.33	0.20	.784
Stress × transition status	-0.14	-0.25 – -0.03	0.05	.010
Transition	-0.51	-0.61 – -0.41	0.05	<.001
Non-transition	-0.37	-0.40 – -0.34	0.02	<.001
Transition vs. non-transition	-0.14	-0.24 – -0.03	0.05	.010
Outcome: Psychotic experiences				
Stress	0.16	0.13 – 0.18	0.01	<.001
Transition status	-0.11	-0.63 – 0.40	0.26	.668
Stress × transition status	0.01	-0.07 – 0.09	0.04	.814

Note. Results adjusted for age, gender, ethnicity, centre, comorbid major depressive and anxiety disorders. CI=confidence interval. SE=standard error.

Table S26. *Modification of the association between momentary stress and affect/psychotic experiences by transition status (unadjusted).*

Effect modification by transition status				
	β	95% CI	SE	p
Outcome: Negative affect				
Stress	0.30	0.28 – 0.33	0.01	<.001
Transition status	0.30	-0.16 – 0.77	0.24	.204
Stress × transition status	0.11	0.02 – 0.20	0.05	.021
Transition	0.41	0.32 – 0.50	0.04	<.001
Non-transition	0.30	0.28 – 0.33	0.01	<.001
Transition vs. non-transition	0.11	0.02 – 0.20	0.05	.021
Outcome: Positive affect				
Stress	-0.37	-0.40 – -0.34	0.02	<.001
Transition status	-0.12	-0.52 – 0.28	0.21	.552
Stress × transition status	-0.14	-0.25 – -0.03	0.05	.011
Transition	-0.51	-0.61 – -0.41	0.05	<.001
Non-transition	-0.37	-0.40 – -0.34	0.02	<.001
Transition vs. non-transition	-0.14	-0.24 – -0.03	0.05	.011
Outcome: Psychotic experiences				
Stress	0.15	0.13 – 0.18	0.01	<.001
Transition status	0.16	-0.37 – 0.70	0.27	.549
Stress × transition status	0.01	-0.07 – 0.09	0.04	.790

Note. CI=confidence interval. SE=standard error.

Do emotional and psychotic stress reactivity mediate the association of childhood trauma and transition?

Method

To examine whether emotional and psychotic stress reactivity mediate the association of childhood trauma and transition, we used fitted values of psychotic experiences and affect predicted by the composite stress measure. We performed mediation analyses using the 'gsem' command. The total effect of childhood trauma on transition was apportioned into a direct effect and an indirect effect through stress reactivity. The indirect effect was computed using the product of coefficients strategy. The indirect and the total effect were computed and tested on significance using the 'nlcom' command. For transition, a Weibull distribution was assumed. Again, analyses were performed with and without adjusting for potential confounders.

Results

As displayed in Tables S27 and S28, we found no evidence for direct effects of childhood trauma on time to transition and no evidence for mediation via emotional or psychotic stress reactivity.

Table S27. *Emotional and psychotic stress reactivity as mediators of the association of childhood trauma and time to transition.*

	Transition	
N	56	
	b (95% CI)	*p*
Mediator: Emotional reactivity (increased negative affect in response to stress)		
Total effect	0.90 (-0.21 – 2.01)	.112
Direct effect	0.84 (-0.34 – 2.02)	.165
Indirect effect	0.07 (-0.21 – 0.45)	.731
Mediator: Emotional reactivity (decreased positive affect in response to stress)		
Total effect	0.94 (-0.16 – 2.04)	.093
Direct effect	0.88 (-0.21 – 1.09)	.529
Indirect effect	0.06 (-0.14 – 0.27)	.554
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)		
Total effect	1.19 (-0.13 – 2.51)	.077
Direct effect	-0.76 (-2.56 – 1.04)	.408
Indirect effect	-0.22 (-0.76 – 0.32)	.418

Note. Results adjusted for age, gender, ethnicity, centre, comorbid major depressive and anxiety disorders, and time to follow-up. Childhood trauma assessed with the Childhood Trauma Questionnaire (Bernstein & Fink, 1998; Wingenfeld et al., 2010). CI=confidence interval.

Table S28. *Emotional and psychotic stress reactivity as mediators of the association of childhood trauma and time to transition (unadjusted analyses).*

	Transition	
N	56	
	b (95% CI)	*p*
Mediator: Emotional reactivity (increased negative affect in response to stress)		
Total effect	0.90 (-0.21 – 2.01)	.112
Direct effect	0.84 (-0.34 – 2.02)	.165
Indirect effect	0.07 (-0.21 – 0.45)	.731
Mediator: Emotional reactivity (decreased positive affect in response to stress)		
Total effect	0.94 (-0.16 – 2.04)	.093
Direct effect	0.88 (-0.21 – 1.09)	.529
Indirect effect	0.06 (-0.14 – 0.27)	.554
Mediator: Psychotic reactivity (increased psychotic experiences in response to stress)		
Total effect	1.19 (-0.13 – 2.51)	.077
Direct effect	-0.76 (-2.56 – 1.04)	.408
Indirect effect	-0.22 (-0.76 – 0.32)	.418

Note. Childhood trauma assessed with the Childhood Trauma Questionnaire (Bernstein & Fink, 1998; Wingenfeld et al., 2010). CI=confidence interval.

Supplementary material 15: Examining the structural validity of the ESM items

Method

To examine the structural validity of the ESM items, we conducted multilevel confirmatory factor analysis in R (R Core Team, 2019). We compared two models:

1) a model with a single ESM factor (Model A)

2) a model with correlated factors for negative affect, positive affect, psychotic experiences stress (Model B)

We compared the extent to which these models match the data using indicators of comparative model fit (information criteria, log-likelihood; (Brown & Moore, 2012; Dziak, Coffman, Lanza, Li, & Jermiin, 2020).

Results

Table S29 gives an overview of the relevant indicators of comparative model fit. We found a better model fit for Model B, suggesting that this model with correlated factors of negative affect, positive affect and psychotic experiences matches the data better than a single ESM factor (Model A). Figures S2-S5 display detailed results of the multilevel confirmatory factor analyses.

Table S29. *Model fit criteria.*

Model	AIC	BIC	ABIC	Log Likelihood
A	154432.611	154911.231	154657.042	-77136.305
B	151928.040	152442.557	152169.303	-75878.020

Note. AIC=Akaike Information Criterion. BIC=Bayesian Information Criterion. ABIC=sample-size adjusted Bayesian Information Criterion.
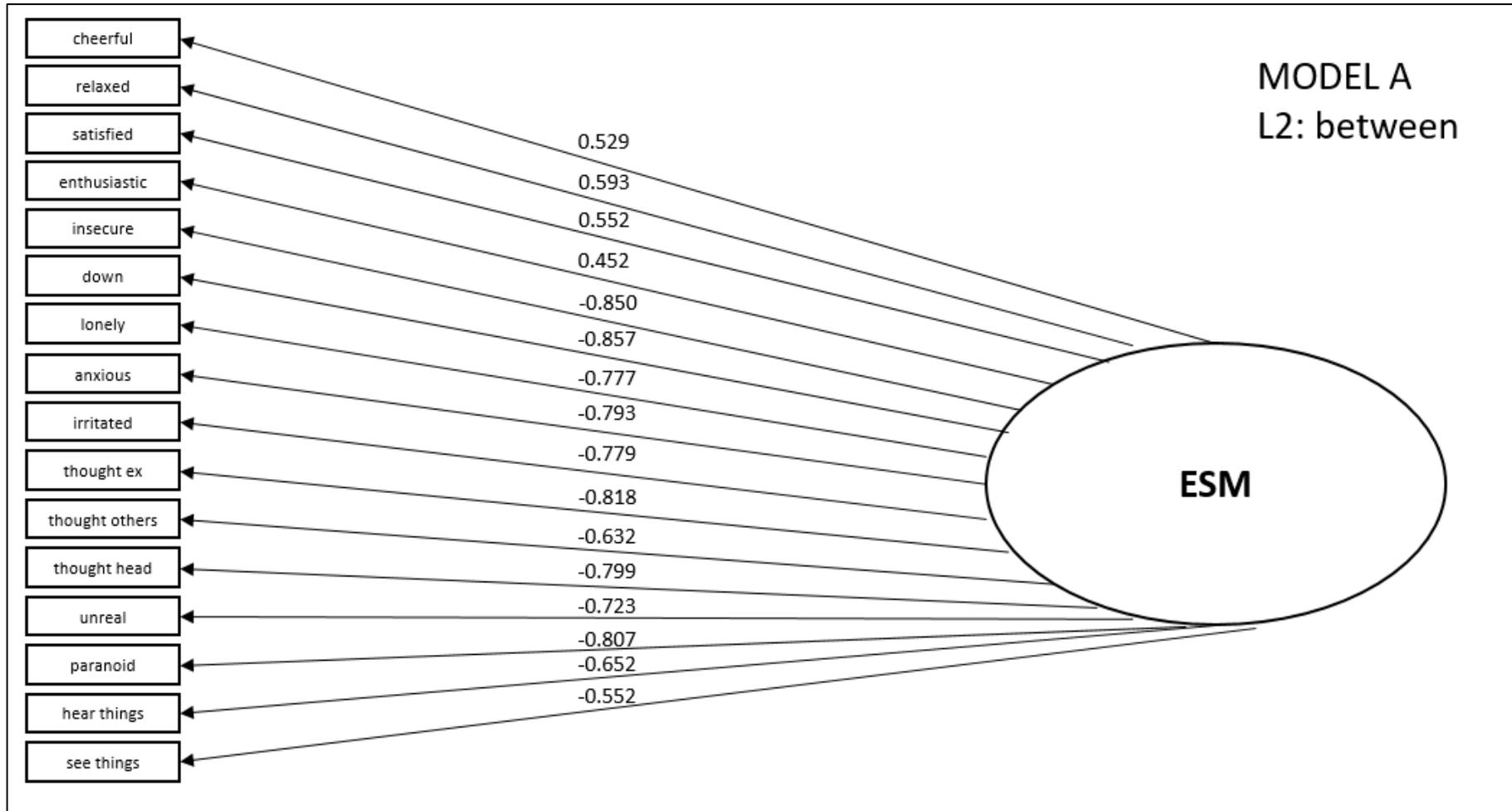
Figure S2. *Model A, Level 2: between.*
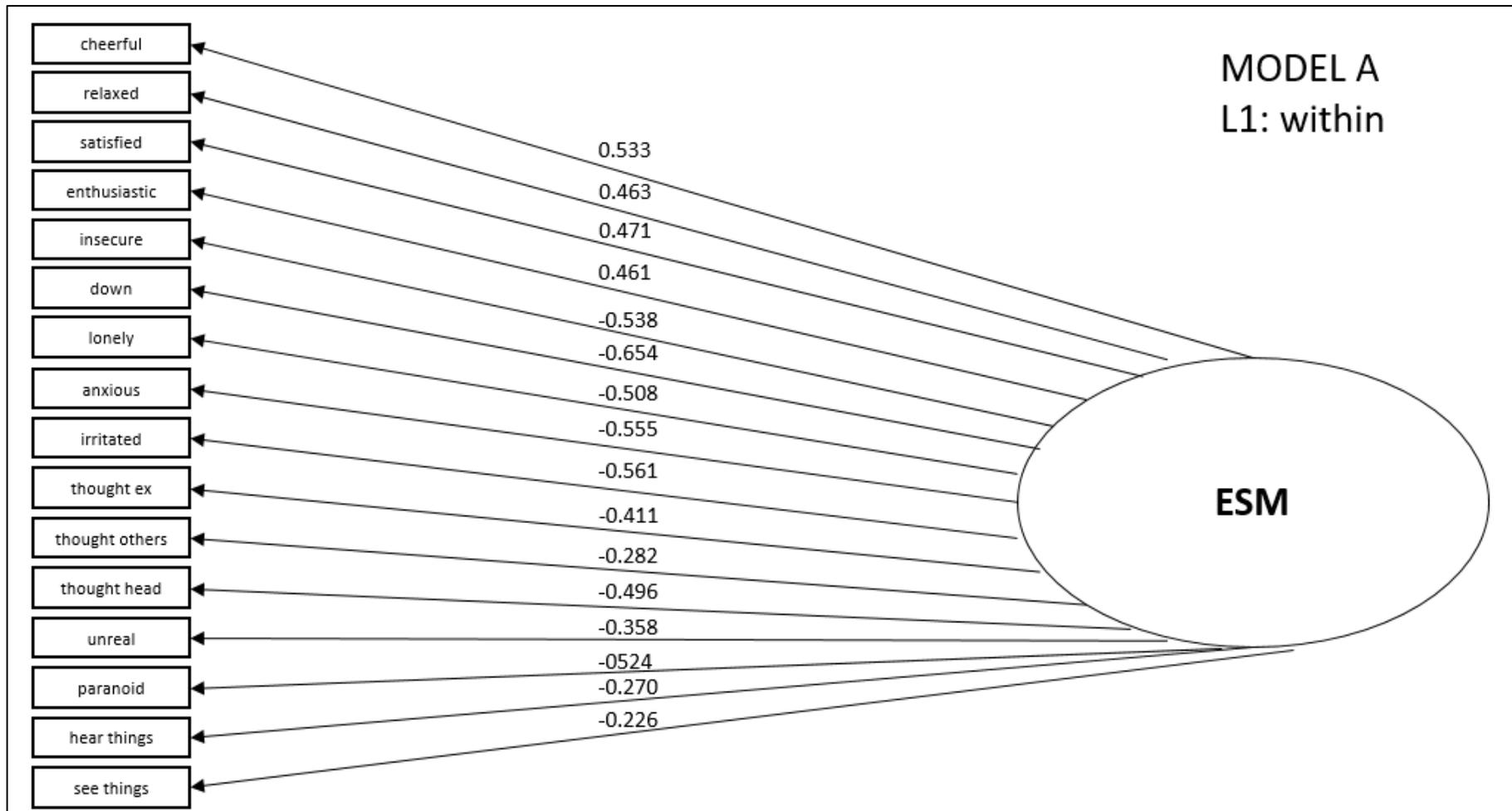
Figure S3. *Model A, Level 1: within.*
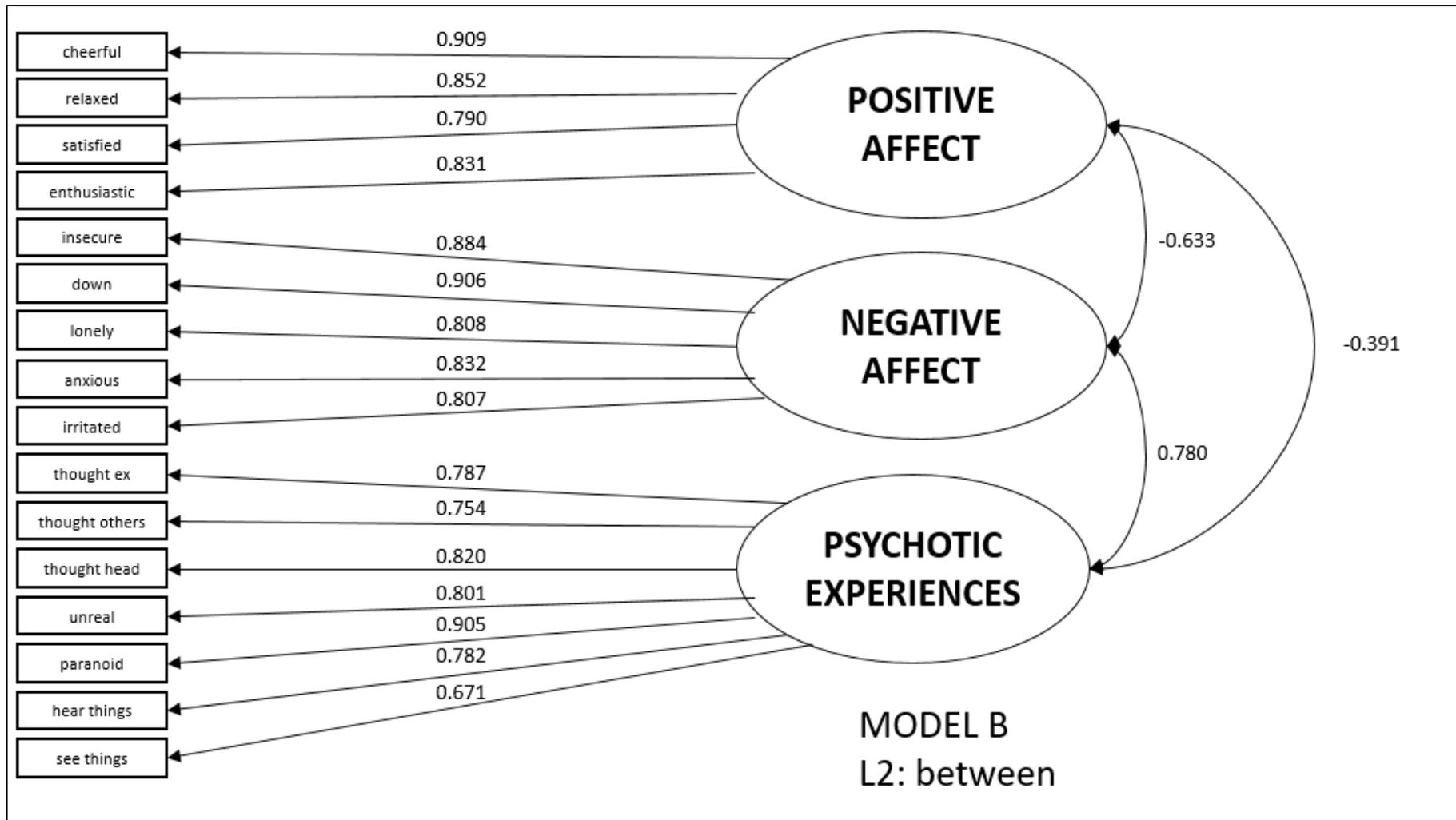
Figure S4. *Model B, Level 2: between.*
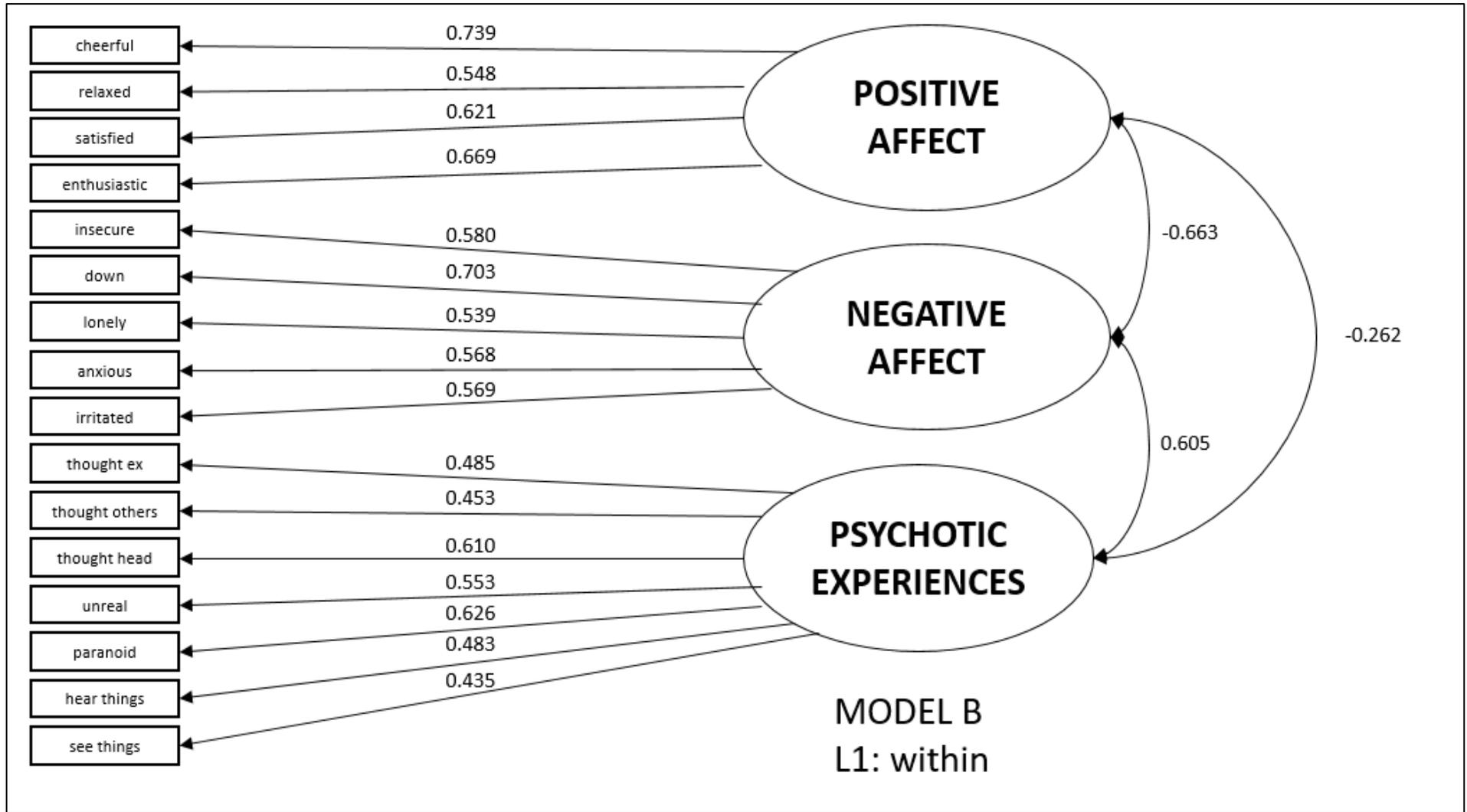
Figure S5. *Model B, Level 1: within.*

Supplementary material 16: Graphic illustration of the hypotheses
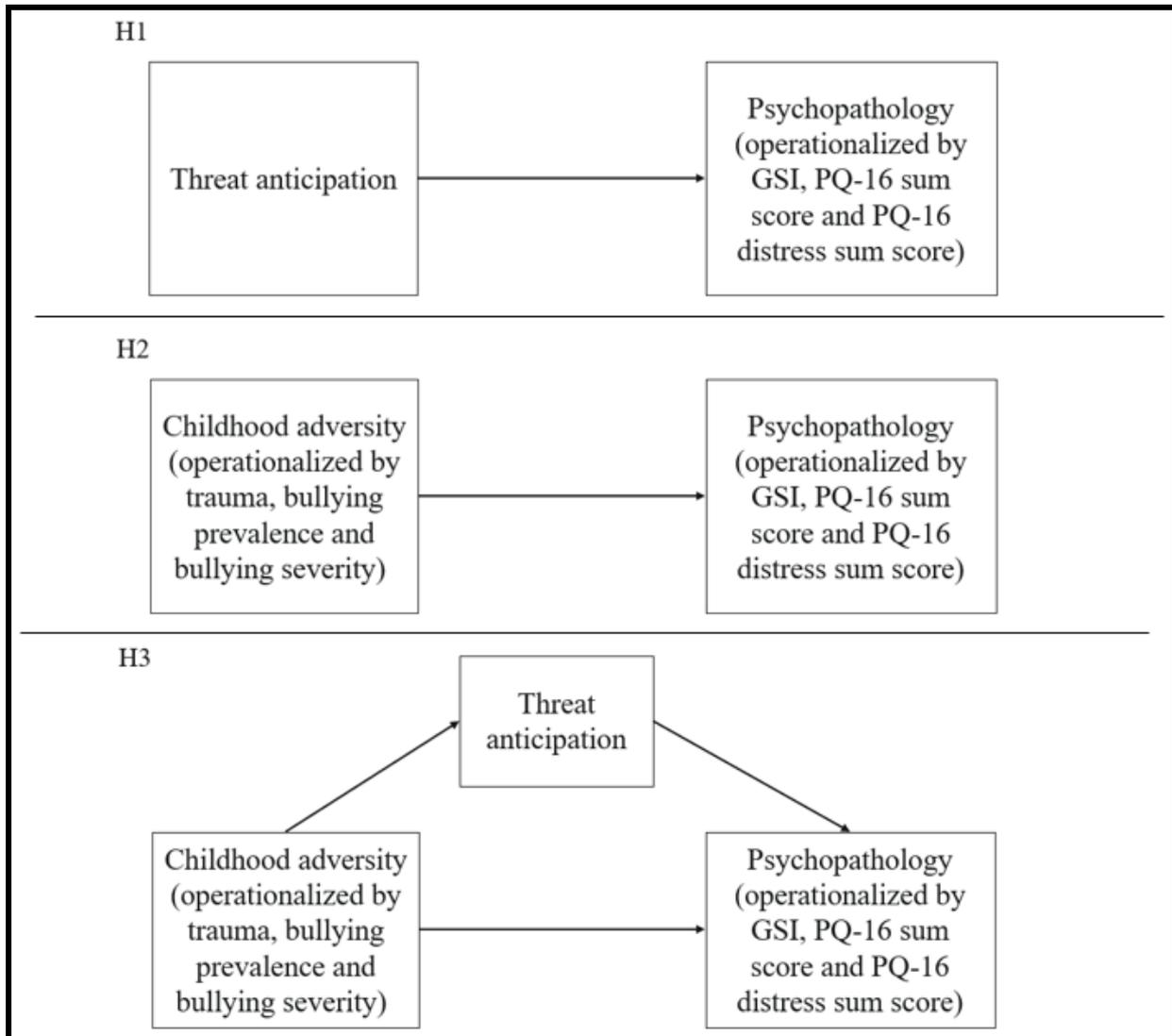
Figure S6. *Graphic illustration of the hypotheses tested.*

Supplementary material 17: Transparent changes document

This study was registered at the OSF website before accessing the data (https://osf.io/92e3w). we made to following deviations:

- We performed multilevel analyses taking into account schools as a variable of higher level.
- We calculated a proportion mediated
- Caregivers' reports were strongly affected by missing values. Therefore, we were not able to compute an index of social disadvantage. Instead, we adjusted for known a priori confounders (age, gender, self-reported ethnicity, and deviations in cognitive functioning).
- To adjust for multiple testing, we used Simes correction (Simes, 1986).
- We performed additional exploratory analyses exploring differential effects on hallucinations and delusions.

Supplementary material 18: Exploratory analyses

The association of the specific types of childhood trauma with general psychopathology and prodromal symptoms

Table S30. *Exploratory analyses of the association of the different trauma subscales with general psychopathology and prodromal symptoms.*

| | General psychopathology | | | Prodromal symptoms | | | | | |
| | | | | Anomalous experiences | | | Perceived distress | | |
	β (95% CI)	p	N	β (95% CI)	p	N	β (95% CI)	p	N
Childhood trauma									
Conventional crime	0.39 (0.30 – 0.48)	<.001	530	0.28 (0.16 – 0.39)	<.001	530	0.29 (0.18 – 0.39)	<.001	530
Indirect victimisation	0.26 (0.19 – 0.34)	<.001	530	0.22 (0.14 – 0.30)	<.001	530	0.20 (0.11 – 0.30)	<.001	530
Child maltreatment	0.31 (0.23 – 0.38)	<.001	530	0.23 (0.14 – 0.33)	<.001	530	0.25 (0.14 – 0.35)	<.001	530
Peer or sibling victimisation	0.49 (0.39 – 0.59)	<.001	530	0.30 (0.18 – 0.43)	<.001	530	0.30 (0.19 – 0.42)	<.001	530
Sexual victimisation	0.27 (0.20 – 0.34)	<.001	530	0.21 (0.11 – 0.31)	<.001	530	0.26 (0.14 – 0.38)	<.001	530

Note. Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). To ensure comparability, a constant sample size was used for all analyses displayed. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. CI=confidence interval. For the association of child maltreatment and general psychopathology, the random intercept and random slope model cloud not be estimated, so the values are estimated with a random intercept model for this test.

The association of specific types of bullying with general psychopathology and prodromal symptoms

Table S31. *Exploratory analyses of the association of physical vs. cyber bullying with general psychopathology and prodromal symptoms.*

	General psychopathology			Prodromal symptoms					
				Anomalous experiences			Perceived distress		
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Physical bullying	0.38 (0.26 – 0.49)	<.001	408	0.28 (0.13 – 0.42)	<.001	408	0.29 (0.15 – 0.43)	<.001	408
Cyber bullying	0.33 (0.25 – 0.42)	<.001	408	0.20 (0.10 – 0.30)	<.001	408	0.22 (0.13 – 0.31)	<.001	408

Note. General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). To ensure comparability, a constant sample size was used for all analyses displayed. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. CI=confidence interval.

The association of early adversity with different dimensions of psychopathology

Table S32. *Exploratory analyses of the association of early adversity (i.e., childhood trauma, bullying prevalence and bullying severity) with the different dimensions of psychopathology.*

	Somatisation	Obsession-compulsion	Interpersonal sensitivity	Depression	Anxiety	Hostility	Phobic anxiety	Paranoid ideation	Psychoti-cism
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Childhood trauma	0.40 (0.33 – 0.46)[a]	0.42 (0.35 – 0.49)	0.37 (0.29 – 0.44)	0.44 (0.35 – 0.53)	0.43 (0.37 – 0.50)	0.47 (0.41 – 0.53)	0.32 (0.24 – 0.39)	0.55 (0.49 – 0.61)	0.44 (0.36 – 0.51)
Bullying prevalence	0.27 (0.20 – 0.34)	0.29 (0.21 – 0.36)	0.31 (0.24 – 0.38)	0.36 (0.30 – 0.42)[a]	0.28 (0.21 – 0.35)	0.24 (0.17 – 0.30)	0.20 (0.13 – 0.27)	0.32 (0.25 – 0.39)	0.30 (0.21 – 0.39)
Bullying severity	0.33 (0.24 – 0.41)	0.33 (0.25 – 0.42)	0.37 (0.29 – 0.44)	0.42 (0.33 – 0.51)	0.36 (0.28 – 0.43)	0.28 (0.21 – 0.34)	0.27 (0.19 – 0.35)	0.37 (0.30 – 0.43)	0.36 (0.30 – 0.43)[a]

Note. Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). Dimensions of psychopathology assessed with the BSI-53(Derogatis, 1993; Derogatis & Fitzpatrick, 2004). To ensure comparability, a constant sample size was used for all analyses displayed, *N* for all tests=928. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. CI=confidence interval. All *p*-values<.001. For the association of childhood trauma and somatisation and the association of bullying severity and psychoticism, the random intercept and random slope model cloud not be estimated, so the values are estimated with a random intercept model for this test.

The indirect effect of early adversity on dimensions of prodromal symptoms via pathways through threat anticipation

Table S33. *Exploratory analyses of the indirect effect of early adversity on dimensions of prodromal symptoms (hallucinations vs. delusions) via pathways through threat anticipation.*

	Prodromal symptoms							
	Hallucinations				**Delusions**			
	β (95% CI)	*p*	N_{min}	P_M	β (95% CI)	*p*	N_{min}	P_M
Childhood trauma			563				563	
Total effect	0.31 (0.24 – 0.38)	<.001			0.26 (0.19 – 0.33)	<.001		
Direct effect	0.27 (0.20 – 0.35)	<.001			0.20 (0.12 – 0.28)	<.001		
Indirect effect	0.04 (0.00 – 0.07)	.063		0.13	0.06 (0.02 – 0.09)	.004		0.23
Bullying prevalence			449				449	
Total effect	0.23 (0.15 – 0.32)	<.001			0.22 (0.13 – 0.31)	<.001		
Direct effect	0.20 (0.11 – 0.28)	<.001			0.19 (0.10 – 0.28)	<.001		
Indirect effect	0.04 (0.02 – 0.06)	<.001		0.17	0.03 (0.01 – 0.05)	.001		0.14
Bullying severity			452				452	
Total effect	0.28 (0.19 – 0.37)	<.001			0.24 (0.15 – 0.33)	<.001		
Direct effect	0.25 (0.16 – 0.33)	<.001			0.21 (0.12 – 0.30)	<.001		
Indirect effect	0.03 (0.01 – 0.05)	.001		0.11	0.03 (0.01 – 0.05)	.002		0.13

Note. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). Subscales of prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. CI=confidence interval. N_{min}=due to varying numbers of missing values, different paths of the mediation analyses comprised varying sample sizes. Therefore, the minimum sample size is displayed here. P_M=proportion mediated.

Supplementary material 19: Overview of missing values

Table S34. *Distribution of missing values across scales.*

	Missing values per scale
Variables reported by adolescents	
Age	0
Gender	4
Ethnicity	1,231
Self-reported ethnicity	0
Early adversity	
Conventional crime	1,077
Indirect victimisation	425
Child maltreatment	369
Peer or sibling victimisation	370
Sexual victimisation	376
Bullying prevalence	441
Cyber bullying prevalence	449
Physical bullying prevalence	455
Threat anticipation	0
Lifetime prevalence of prodromal symptoms	1,024
General psychopathology	326
Variables reported by parents/caregivers	
Cohabitation	1,237
Income	1,267
Ethnicity	
Educator 1	1,239
Educator 2	1,269
Education	
Educator 1	1,236
Educator 2	1,252
Employment	
Educator 1	1,237
Educator 2	1,253

Note. The conventional crime subscale and the assessment of prodromal symptoms were omitted for 12-year-olds, resulting in missing values.

Supplementary material 20: Sensitivity analyses

Sensitivity analyses with restrictions on missing values

In line with the manuals (Derogatis, 1993; Ising et al., 2012; Loewy, Bearden, Johnson, Raine, & Cannon, 2005), we allowed for one missing value per scale for the BSI and one missing on the PQ-16. The PQ-16 perceived distress variable had to be omitted as there were too many missing values as perceived distress was assessed only if the participant indicates that he or she has already experienced the symptom. No missing values allowed for threat anticipation.

Hypothesis 1: The association of threat anticipation and psychopathology – with restrictions on missing values

Table S35. *Sensitivity analysis: The association of threat anticipation and psychopathology – with restrictions on missing values.*

	General psychopathology			**Prodromal symptoms** Anomalous experiences		
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Threat anticipation	0.49 (0.43 – 0.56)	<.001	1,112	0.53 (0.36 – 0.69)	<.001	399

Note. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. CI=confidence interval.

Hypothesis 2: The association of early adversity and psychopathology – with restrictions on missing values

Table S36. *Sensitivity analysis: The association of early adversity (i.e., childhood trauma, bullying prevalence, and bullying severity) and psychopathology – with restrictions on missing values.*

	General psychopathology			Prodromal symptoms Anomalous experiences		
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Childhood trauma	0.52 (0.46 – 0.58)	<.001	834	0.47 (0.38 – 0.57)	<.001	322
Bullying prevalence	0.36 (0.29 – 0.43)	<.001	971	0.26 (0.16 – 0.36)	<.001	356
Bullying severity	0.43 (0.36 – 0.50)	<.001	981	0.29 (0.19 – 0.39)	<.001	358

Note. Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. CI = confidence interval.

Hypothesis 3: The indirect effect of early adversity on psychopathology via pathways through threat anticipation – with restrictions on missing values

Table S37. *Sensitivity analysis: The indirect effect of early adversity on psychopathology via pathways through threat anticipation – with restrictions on missing values.*

	General psychopathology				Prodromal symptoms Anomalous experiences			
	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M
Childhood trauma			820				316	
Total effect	0.52 (0.46 – 0.58)	<.001			0.48 (0.39 – 0.57)	<.001		
Direct effect	0.40 (0.34 – 0.46)	<.001			0.38 (0.28 – 0.47)	<.001		
Indirect effect	0.13 (0.10 – 0.16)	<.001		0.25	0.10 (0.05 – 0.15)	<.001		0.21
Bullying prevalence			870				337	
Total effect	0.37 (0.31 – 0.43)	<.001			0.28 (0.18 – 0.37)	<.001		
Direct effect	0.28 (0.23 – 0.34)	<.001			0.17 (0.08 – 0.27)	<.001		
Indirect effect	0.09 (0.06 – 0.11)	<.001		0.24	0.10 (0.06 – 0.14)	<.001		0.36
Bullying severity			882				339	
Total effect	0.44 (0.38 – 0.50)	<.001			0.32 (0.22 – 0.41)	<.001		
Direct effect	0.35 (0.29 – 0.40)	<.001			0.21 (0.11 – 0.30)	<.001		0.34
Indirect effect	0.09 (0.06 – 0.12)	<.001		0.21	0.11 (0.07 – 0.15)	<.001		

Note. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. CI=confidence interval. N_{min}=due to varying numbers of missing values, different paths of the mediation analyses comprised varying sample sizes. Therefore, the minimum sample size is displayed here. P_M=proportion mediated.

Sensitivity analyses after exclusion of outliers

We identified 103 outliers based on an outlier analysis for skewed data (Hubert & Van der Veeken, 2008) and excluded them for this sensitivity analysis.

Hypothesis 1: The association of threat anticipation and psychopathology – after exclusion of outliers

Table S38. *Sensitivity analysis: The association of threat anticipation and psychopathology – after exclusion of outliers.*

	General psychopathology			Prodromal symptoms					
				Anomalous experiences			Perceived distress		
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*	β (CI)	*p*	*N*
Threat anticipation	0.35 (0.28 – 0.42)	<.001	1,300	0.31 (0.18 – 0.43)	<.001	567	0.39 (0.25 – 0.54)	<.001	567

Note. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval.

Hypothesis 2: The association of early adversity and psychopathology – after exclusion of outliers

Table S39. *Sensitivity analysis: The association of early adversity (i.e., childhood trauma, bullying prevalence, and bullying severity) and psycho-pathology – after exclusion of outliers.*

| | General psychopathology | | | Prodromal symptoms | | | | | |
| | | | | Anomalous experiences | | | Perceived distress | | |
	β (95% CI)	p	N	β (95% CI)	p	N	β (95% CI)	p	N
Childhood trauma	0.52 (0.45 – 0.59)	<.001	1,163	0.33 (0.23 – 0.44)	<.001	525	0.34 (0.24 – 0.44)	<.001	525
Bullying prevalence	0.31 (0.24 – 0.38)	<.001	971	0.27 (0.17 – 0.37)	<.001	416	0.27 (0.16 – 0.37)	<.001	416
Bullying severity	0.42 (0.34 – 0.50)	<.001	980	0.35 (0.24 – 0.47)	<.001	415	0.34 (0.22 – 0.46)	<.001	415

Note. Results adjusted for age, gender, cognitive deviance, and self-reported ethnicity. Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval.

Hypothesis 3: Threat anticipation as a mediator of the association between early adversity and psychopathology – after exclusion of outliers

Table S40. *Sensitivity analysis: The indirect effect of early adversity on psychopathology via pathways through threat anticipation – after exclusion of outliers.*

| | General psychopathology | | | | Prodromal symptoms | | | | | | | |
| | | | | | Anomalous experiences | | | | Perceived distress | | | |
	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M
Childhood trauma			1,163				525				525	
Total effect	0.52 (0.47 – 0.57)	<.001			0.34 (0.27 – 0.42)	<.001			0.35 (0.28 – 0.43)	<.001		
Direct effect	0.40 (0.34 – 0.45)	<.001			0.27 (0.19 – 0.36)	<.001			0.25 (0.17 – 0.33)	<.001		
Indirect effect	0.12 (0.10 – 0.15)	<.001		0.23	0.07 (0.03 – 0.11)	<.001		0.21	0.10 (0.06 – 0.14)	<.001		0.29
Bullying prevalence			971				416				416	
Total effect	0.31 (0.25 – 0.37)	<.001			0.27 (0.17 – 0.37)	<.001			0.27 (0.17 – 0.37)	<.001		
Direct effect	0.26 (0.21 – 0.32)	<.001			0.22 (0.13 – 0.32)	<.001			0.21 (0.12 – 0.31)	<.001		
Indirect effect	0.05 (0.03 – 0.07)	<.001		0.16	0.05 (0.02 – 0.07)	<.001		0.19	0.06 (0.03 – 0.08)	<.001		0.22
Bullying severity			980				415				415	
Total effect	0.42 (0.35 – 0.49)	<.001			0.36 (0.25 – 0.46)	<.001			0.36 (0.25 – 0.47)	<.001		
Direct effect	0.36 (0.30 – 0.42)	<.001			0.30 (0.20 – 0.41)	<.001			0.29 (0.18 – 0.40)	<.001		
Indirect effect	0.06 (0.04 – 0.09)	<.001		0.14	0.05 (0.02 – 0.08)	<.001		0.14	0.06 (0.03 – 010)	<.001		0.17

Note. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval. N_{min}=due to varying numbers of missing values, different paths of the mediation analyses comprised varying sample sizes. Therefore, the minimum sample size is displayed here. P_M=proportion mediated.

Sensitivity analyses with restriction on missing values and after exclusion of outliers

In line with the manuals (Derogatis, 1993; Ising et al., 2012; Loewy et al., 2005), we allowed for one missing value per scale for the BSI and one missing on the PQ-16. The PQ-16 perceived distress variable had to be omitted as there were too many missing values as perceived distress was assessed only if the participant indicates that he or she has already experienced the symptom. No missing values allowed for threat anticipation. We identified 103 outliers based on an outlier analysis for skewed data (Hubert & Van der Veeken, 2008) and excluded them for this sensitivity analysis.

Hypothesis 1: The association of threat anticipation and psychopathology – with restrictions on missing values and after exclusion of outliers

Table S41. *Sensitivity analysis: The association of threat anticipation and psychopathology – with restrictions on missing values and after exclusion of outliers.*

	General psychopathology			**Prodromal symptoms** Anomalous experiences		
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Threat anticipation	0.51 (0.45 – 0.56)	<.001	1,045	0.52 (0.36 – 0.69)	<.001	373

Note. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval.

Hypothesis 2: The association of early adversity and psychopathology – with restrictions on missing values and after exclusion of outliers

Table S42. *Sensitivity analysis: The association of early adversity (i.e., childhood trauma, bullying prevalence, and bullying severity) and psychopathology – with restrictions on missing values and after exclusion of outliers.*

	General psychopathology			Prodromal symptoms Anomalous experiences		
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Childhood trauma	0.52 (0.45 – 0.58)	<.001	790	0.47 (0.38 – 0.57)	<.001	302
Bullying prevalence	0.33 (0.25 – 0.40)	<.001	904	0.29 (0.18 – 0.40)	<.001	330
Bullying severity	0.44 (0.36 – 0.52)	<.001	909	0.41 (0.29 – 0.53)	<.001	329

Note. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval.

Hypothesis 3: The indirect effect of early adversity on psychopathology via pathways through threat anticipation – with restrictions on missing values and after exclusion of outliers

Table S43. *Sensitivity analysis: The indirect effect of early adversity on psychopathology via pathways through threat anticipation – with restrictions on missing values and after exclusion of outliers.*

	General psychopathology				Prodromal symptoms Anomalous experiences			
	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M
Childhood trauma			777				297	
Total effect	0.51 (0.46 – 0.57)	<.001			0.48 (0.39 – 0.57)	<.001		
Direct effect	0.39 (0.33 – 0.45)	<.001			0.38 (0.28 – 0.47)	<.001		
Indirect effect	0.13 (0.10 – 0.16)	<.001		0.25	0.10 (0.05 – 0.15)	<.001		0.21
Bullying prevalence			810				314	
Total effect	0.34 (0.27 – 0.40)	<.001			0.31 (0.20 – 0.41)	<.001		
Direct effect	0.25 (0.19 – 0.31)	<.001			0.21 (0.11 – 0.31)	<.001		
Indirect effect	0.09 (0.06 – 0.12)	<.001		0.26	0.10 (0.06 – 0.13)	<.001		0.32
Bullying severity			818				313	
Total effect	0.46 (0.39 – 0.53)	<.001			0.43 (0.31 – 0.54)	<.001		
Direct effect	0.35 (0.28 – 0.42)	<.001			0.31 (0.19 – 43)	<.001		
Indirect effect	0.11 (0.07 – 0.14)	<.001		0.24	0.11 (0.07 – 0.16)	<.001		0.26

Note. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval. N_{min}=Due to varying numbers of missing values, different paths of the mediation analyses comprised varying sample sizes. Therefore, the minimum sample size is displayed here. P_M=proportion mediated.

Sensitivity analyses with robust standard errors

To account for heteroscedasticity in the computation of standard errors, we conducted sensitivity analyses with robust standard errors using the Huber/White/sandwich estimator (Freedman, 2006; Huber, 1967; White, 1980).

Hypothesis 1: The association of early adversity and psychopathology – with robust standard errors

Table S44. *Sensitivity analysis: The association of early adversity and psychopathology – with robust standard errors.*

| | **General psychopathology** | | | **Prodromal symptoms** | | | | | |
| | | | | Anomalous experiences | | | Perceived distress | | |
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Threat anticipation	0.36 (0.30 – 0.41)	<.001	1,384	0.28 (0.14 – 0.42)	<.001	607	0.35 (0.20 – 0.51)	<.001	607

Note. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval.

Hypothesis 2: The association of early adversity and psychopathology – with robust standard errors

Table S45. *Sensitivity analysis: The association of early adversity (i.e., childhood trauma, bullying prevalence, and bullying severity) and psychopathology – with robust standard errors.*

| | General psychopathology | | | Prodromal symptoms | | | | | |
| | | | | Anomalous experiences | | | Perceived distress | | |
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Childhood trauma	0.54 (0.47 – 0.61)	<.001	1,239	0.32 (0.22 – 0.43)	<.001	563	0.34 (0.24 – 0.44)	<.001	563
Bullying prevalence	0.35 (0.28 – 0.42)	<.001	1,045	0.23 (0.17 – 0.29)	<.001	449	0.24 (0.18 – 0.30)	<.001	449
Bullying severity	0.42 (0.35 – 0.49)	<.001	1,059	0.26 (0.17 – 0.35)	<.001	452	0.28 (0.20 – 0.36)	<.001	452

Note. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval. For the association of bullying prevalence and general psychopathology and the association of bullying severity and anomalous experiences, the random intercept and random slope model cloud not be estimated, so the values are estimated with a random intercept model for this test.

Hypothesis 3: The indirect effect of early adversity on psychopathology via pathways through threat anticipation

Table S46. *Sensitivity analysis: The indirect effects of early adversity (i.e., childhood trauma, bullying prevalence, and bullying severity) on psychopathology (i.e., general psychopathology, prodromal symptoms) via pathways through threat anticipation – with robust standard errors.*

| | General psychopathology | | | | Prodromal symptoms | | | | | | | |
| | | | | | Anomalous experiences | | | | Perceived distress | | | |
	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M
Childhood trauma			1,239				563				563	
Total effect	0.55(0.48 – 0.61)	<.001			0.31 (0.21 – 0.42)	<.001			0.33 (0.23 – 0.44)	<.001		
Direct effect	0.42 (0.35 – 0.49)	<.001			0.26 (0.17 – 0.36)	<.001			0.25 (0.16 – 0.34)	<.001		
Indirect effect	0.13 (0.10 – 0.15)	<.001		0.24	0.05 (-0.00 – 0.10)	.071		0.16	0.08 (0.02 – 0.14)	.008		0.24
Bullying prevalence			1,045				449				449	
Total effect	0.35 (0.28 – 0.42)	<.001			0.24 (0.17 – 0.30)	<.001			0.25 (0.19 – 0.31)	<.001		
Direct effect	0.30 (0.23 – 0.37)	<.001			0.20 (0.14 – 0.26)	<.001			0.20 (0.13 – 0.27)	<.001		
Indirect effect	0.05 (0.02 – 0.07)	<.001		0.14	0.04 (0.02 – 0.06)	.011		0.17	0.05 (0.02 – 0.07)	<.001		0.20
Bullying severity			1,059				452				452	
Total effect	0.41 (0.34 – 0.48)	<.001			0.27 (0.18 – 0.36)	<.001			0.29 (0.22 – 0.37)	<.001		
Direct effect	0.36 (0.29 – 0.44)	<.001			0.24 (0.15 – 0.33)	<.001			0.25 (0.17 – 0.33)	<.001		
Indirect effect	0.05 (0.03 – 0.07)	<.001		0.12	0.04 (-0.00 – 0.8)	.081		0.15	0.05 (0.02 – 0.07)	.001		0.17

Note. Results adjusted for age, gender, self-reported ethnicity, and cognitive deviance. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006). Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval. N_{min}=due to varying numbers of missing values, different paths of the mediation analyses comprised varying sample sizes. Therefore, the minimum sample size is displayed here. P_M=proportion mediated.

Supplementary material 21: Unadjusted analyses

Hypothesis 1: The association of threat anticipation and psychopathology – unadjusted

Table S47. *The association of threat anticipation and psychopathology – unadjusted.*

| | General psychopathology | | | Prodromal symptoms | | | | | |
| | | | | Anomalous experiences | | | Perceived distress | | |
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Threat anticipation	0.39 (0.33 – 0.45)	<.001	1,476	0.32 (0.19 – 0.44)	<.001	658	0.39 (0.25 – 0.53)	<.001	658

Note. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval.

Hypothesis 2: The association of early adversity and psychopathology – unadjusted

Table S48. *The association of early adversity (i.e., childhood trauma, bullying prevalence, and bullying severity) and psychopathology– unadjusted.*

| | General psychopathology | | | Prodromal symptoms | | | | | |
| | | | | Anomalous experiences | | | Perceived distress | | |
	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*	β (95% CI)	*p*	*N*
Childhood trauma	0.54 (0.46 – 0.61)	<.001	1,319	0.35 (0.25 – 0.46)	<.001	607	0.36 (0.26 – 0.47)	<.001	607
Bullying prevalence	0.37 (0.31 – 0.44)	<.001	1,112	0.26 (0.18 – 0.35)	<.001	484	0.27 (0.18 – 0.36)	<.001	484
Bullying severity	0.43 (0.36 – 0.49)	<.001	1,128	0.29 (0.20 – 0.39)	<.001	488	0.31 (0.21 – 0.41)	<.001	488

Note. Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval.

Hypothesis 3: The indirect effect of early adversity on psychopathology via pathways through threat anticipation

Table S49. *The indirect effect of early adversity (i.e., childhood trauma, bullying prevalence, and bullying severity) on psychopathology (i.e., general psychopathology, prodromal symptoms) via pathways through threat anticipation– unadjusted.*

| | General psychopathology | | | | Prodromal symptoms | | | | | | | |
| | | | | | Anomalous experiences | | | | Perceived distress | | | |
	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M	β (95% CI)	p	N_{min}	P_M
Childhood trauma			1,319				607				607	
Total effect	0.53 (0.49 – 0.58)	<.001			0.34 (0.27 – 0.40)	<.001			0.35 (0.28 – 0.41)	<.001		
Direct effect	0.41 (0.36 – 0.46)	<.001			0.29 (0.22 – 0.36)	<.001			0.27 (0.20 – 0.34)	<.001		
Indirect effect	0.12 (0.10 – 0.15)	<.001		0.23	0.05 (0.01 – 0.08)	.007		0.15	0.07 (0.04 – 0.11)	<.001		0.20
Bullying prevalence			1,112				484				482	
Total effect	0.41 (0.34 – 0.48)	<.001			0.27 (0.19 – 0.35)	<.001			0.28 (0.20 – 0.36)	<.001		
Direct effect	0.31 (0.26 – 0.36)	<.001			0.23 (0.15 – 0.31)	<.001			0.23 (0.15 – 0.31)	<.001		
Indirect effect	0.06 (0.04 – 0.08)	<.001		0.15	0.05 (0.03 – 0.07)	<.001		0.19	0.05 (0.03 – 0.08)	<.001		0.18
Bullying severity			1,128				488				488	
Total effect	0.41 (0.36 – 0.46)	<.001			0.30 (0.22 – 0.38)	<.001			0.32 (0.24 – 0.40)	<.001		
Direct effect	0.36 (0.31 – 0.41)	<.001			0.26 (0.18 – 0.34)	<.001			0.27 (0.19 – 0.35)	<.001		
Indirect effect	0.05 (0.03 – 0.07)	<.001		0.12	0.04 (0.02 – 0.06)	<.001		0.13	0.05 (0.03 – 0.07)	<.001		0.16

Note. Threat anticipation assessed with the availability test (R. Corcoran et al., 2006; Freeman et al., 2013). Childhood trauma assessed with the Juvenile Victimisation Questionnaire (Finkelhor et al., 2005). General psychopathology assessed with the BSI-53 (Derogatis, 1993; Derogatis & Fitzpatrick, 2004). Prodromal symptoms assessed with the PQ-16 (Ising et al., 2012). CI=confidence interval. N_{min}=due to varying numbers of missing values, different paths of the mediation analyses comprised varying sample sizes. Therefore, the minimum sample size is displayed here. P_M=proportion mediated.

Supplementary material 22: Changes to the pilot version

- Extended intervention period from 3 to 6 weeks, more strategies/tasks presented
- Two intervention tracks with varying foci and demand levels
- Sessions delivered in face-to-face contact or via video calls
- To lower the burden: reduced number of interactive questionnaires, morning and evening questionnaire omitted
- Gamification elements
- Moved from Psymate to movisensXS
- Translation from Dutch to German

Supplementary material 23: EMIcompass intervention manual

Introduction

EMIcompass is an intervention that targets adolescents and young adults with multiple mental health difficulties. The target group includes adolescents and young adults seeking help with unspecific distress, individuals at CHARMS, and patients with a first episode of severe mental disorder. EMIcompass comprises a guided, application-based (app), mHealth self-help intervention that lasts a total of six weeks and includes three psychological sessions and a closing session. The app provides therapeutic content during and between intervention sessions. In addition, daily exercises to train what has been learned are offered via the app between sessions. Optionally, there is also the possibility to assess participants' mood and symptoms in everyday life, in order to offer helpful exercises, if needed.

EMIcompass is based on the rationale of Compassion Focused Therapy (P. Gilbert, 2009, 2014)) and aims to promote a compassion-based, benevolent self-image and to strengthen the capacity for self-care in everyday life. CFT techniques, such as various breathing and imagination exercises, are used.

Core principles of Compassion Focused Therapy (P. Gilbert, 2009, 2014)

P. Gilbert (2013), based on a quote from the Dalai Lama, refers to compassion as "sensitivity to one's own suffering and that of others, with a deep dedication to alleviating it" (p.16). CFT aims to foster this compassion for the self and others. Self-compassion is referred to in the intervention as "self-care" or "compassionate or benevolent treatment of oneself" to make the terminology simpler and easier to understand for youth (P. Gilbert, 2013).

Findings from evolutionary biology show that various psychological phenomena arose at different times in evolution. Competencies such as sexuality, fighting, defending oneself and one's territory, etc. emerged early. Humans share these basal survival skills with many animals. Abilities such as complex thinking and reasoning, reflection, theory of mind, and sense of self-identity emerged much later. Consequently, the human brain combines a variety of different motives and emotions, which can conflict with each other. Thus, according to P. Gilbert (2013), many psychological problems can be seen as unhelpful, conflicting loops between old and newer systems.

Physical symptoms, for example, in combination with the newer skills of thinking, reasoning, and explaining, can lead to the conclusion "my racing heart means I'm going to have a heart

attack and die" which in turn can trigger a panic attack. P. Gilbert (2013) thus describes the human brain as a "*tricky brain*."

CFT assumes three basic emotional systems in which emotions can be grouped according to their function (P. Gilbert, 2009, 2014). The three emotional systems are:

- threat (danger): the threat system includes emotions such as anger, fear, and disgust, functions that help us recognize danger and protect ourselves.

- drive (goals and needs): The drive system includes emotions such as excitement and joy, functions that motivate us to move toward helpful goals and resources.

- soothing (calm and security): The soothing system includes emotions such as satisfaction and security, functions that motivate us to take care of ourselves and others and to allow others to take care of us.

Many participants have a very active threat system and are therefore often and strongly confronted with emotions such as anger and fear. The therapeutic elements of CFT (Gilbert, 2009, 2013) strengthen the calm and security system to mitigate negative emotions from the threat system and form a basis for emotions rooted in the drive system.

The basic therapeutic attitude of EMIcompass

The basic therapeutic attitude of the EMIcompass sessions is also based on the therapeutic rationale of CFT (P. Gilbert, 2009, 2013, 2014). Thus, a warm, unconditionally appreciative, and empathic attitude of the therapist is of utmost relevance. This is expressed in the following principles according to which sessions should be delivered:

- Take time to listen to participants' concerns and problems, make them feel that you are listening with genuine interest

- Address all participants' reactions compassionately ("leading by example")

- A focus of the intervention is "de-shaming," so validate participants' individual emotional experiences sincerely

- Understand safety strategies and symptoms as the participant's best effort to deal with difficult situations

- Be careful to show compassion but not pity

- Be patient and do not try to force anything

- Exude warmth and friendliness

- Anticipate and validate participant resistance and acknowledge that it can be very difficult for participants

- Make participants feel that there is no pressure. Convey the feeling that it is perfectly okay, and you understand if they have difficulty doing the exercises

<u>Instructions for the use of the manual for study therapists</u>

All sessions in the EMIcompass intervention are described and explained in this manual. The manual contains example phrases that you can use in your sessions.

The manual is structured to provide a brief overview at the beginning of each session, summarizing the planned structure and time estimates. The individual sessions are divided into subsections. In addition to the introduction and conclusion of the sessions, there will be phases of information transfer - hereafter referred to as **info** and marked with this symbol ⓘ .

In addition, the intervention includes concrete **exercises** that are performed together in the sessions, marked below with this symbol 🏋. During the sessions, we first discuss the small information section with the participants and then jointly perform the associated exercise on the smartphone. It is important that the participants work through the exercises on the smartphone themselves, while we guide them in the therapeutic conversation.

EMIcompass aims to provide optimal support for all participants, which is why the intervention is divided into two study tracks. Track 1 comprises basic exercises and is aimed at participants who experience imagination exercises as difficult (the exercises are marked with X.1). The elaborate track 2 is aimed at participants who can imagination exercises easily (the exercises are marked with X.2). The assignment to the study arms will be made in the second intervention session and will be based on the participants' report and psychologists' clinical impression.

For participants to progress to the next week of intervention and learn a new exercise, it is necessary that the last enhancing task has been performed and a previously acquired strategy has been practiced at least once during the week. If this is not the case, participants remain in the week and repeat it, which is set by the study psychologist (see technique guide for instructions).

Overview of the intervention

Table S50 provides an overview of the EMIcompass intervention

Table S50. *Overview of the intervention.*

Week	Level 1	Level 2
1	1. Emotional compass	
	2. Count the breath	
2	3. Find a soothing colour	
3	4.1 Find a calm and safe place	4.2 Compassionate companion
4	5.1 Breathing with pauses	5.2 Find a calm and safe place
5	6.1 Surf the waves of your feelings	6.2 My compassionate self
6	7.1 My toolbox	7.2 My compassionate message

EMIcompass intervention – a guide through all sessions

First session (1. week)

Table S 51 provides an overview of the first session.

Table S51. *Overview of the first session.*

Topic	Time
Introduction	5 min
Getting to know, overview of complaints	10 min
ⓘ Information: Emotional compass	10 min
⫶⊩ Exercise: Emotional compass	10 min
ⓘ Information: Count the breath	5 min
⫶⊩ Exercise: Count the breath	5 min
Closing of the session	5 min

Introduction

- Greeting, briefly introducing yourself
    - "My name is XXX, I am a psychologist. Nice to meet you!"
- Give a brief overview of the process

- "I would like to use the session today to get to know you and to discuss what EMIcompass involves and how the treatment will proceed within the framework of EMIcompass. In addition, we can already start with some exercises today."
- Study information:
  - "As you heard in the previous appointments with my colleagues, in this smartphone-assisted intervention, I would like to offer to work on improving your self-care in dealing with feelings in everyday life over the next 6 weeks. Or perhaps to put it another way, I would like to offer that we practice together how to look at yourself a little more benevolently - just as a friend may do. This will help you go through everyday life with a better emotional compass - which is why we call the intervention "EMIcompass". Through specific exercises, we will work on strengthening your self-care, sense of self-acceptance, and positive feelings in general. By self-care, I mean the ability to empathize with, understand and accept your own situation from your unique life story - so you learn to be more compassionate with yourself. For this, firstly, we will meet here every 2 weeks for a face-to-face session. I will also provide you with an app that can help you develop your emotional compass. The app will use signals to prompt you to do exercises and answer short mood queries, like the ones you already know from the last few days. If you want, you can also do more exercises on your own at any time or repeat exercises you have already done, you don't have to wait specifically for the app to prompt you through a signal. So, you can work on improving your self-care in dealing with feelings at any time (use DEMO expression to explain the different categories of exercises). Please do not turn off your study smartphone and charge it regularly. In the time between our appointments, I will support you by calling or emailing you. Do you agree with this? Do you have any questions?"

Getting to know, overview of complaints

- Getting to know each other and building relationships
  - "Before we start with the exercises, I'd like to get to know you a bit first. Perhaps you would like to just briefly introduce yourself?"

- Provide overview of life situation: student/apprentice/working? Leisure activities/hobbies? Who are important people in life, friends, family, partnership, etc.? Ask interested follow-up questions, active listening!
  - "Thank you for telling me a little bit about yourself, I look forward to working with you over the next few weeks."
- Overview of the complaints
  - "How did it come about that you contacted us here at CIMH? What was the reason?" → Record reason for call and complaints so they can be used as examples later in the process. Validate remarks.
  - "It is important for us that you please do not use illegal drugs during the study, as they have a negative impact on your well-being and mental health."

Emotional compass

ⓘ**Information: Emotional compass**
- Exercise Introduction:
  - "Do you have any questions so far? (If yes, answer questions, If no continue). Then let's start with the exercises now!"
  - "For this we will first familiarize with the app! (Participant uses the smartphone him/herself, study psychologist explains → DEMO printout can also be used). When you open the app, you will immediately see the home screen. New exercises always appear here on the home screen of the app. Look, here is the first exercise we will do together. It's called "New: Emotional compass. Please click on the exercise!" Once the exercise is open, on the first page, briefly explain the structure of the exercises in the app: "Here you can see the first screen of the first exercise, it is called "Emotional compass". At the top right you will see a small arrow, you can use it to go to the next page. Sometimes you can scroll down the pages, you'll see that later."
- Getting started with providing information, clicking through the app together with the participant while discussing the content:
  - "The exercise is about improving our understanding of emotions. Therefore, it's worth taking a brief look at our brain. As you know, humans have evolved over many thousands of years. From our ancestors, we have inherited an old brain, which is how other animals, even crocodiles, have it." (click to continue)

- "What can our old brain do now? The old brain has many important tasks, it is responsible for our emotions, such as fear, anger, or joy. It is also important for our behaviour, for example whether we flee when it becomes dangerous. In addition, the old brain is responsible for our basic needs, for example eating or avoiding injury. These are all abilities that not only humans have, but also crocodiles." (click to continue)

- "Unlike the crocodile, we also have a new brain in addition, which developed much later in evolution. This distinguishes us from other animals. So, what can our new brain do? The new brain is responsible for our complex thinking, planning, and thinking about our thinking. It is through these abilities that the many great inventions that humans have made have come into being. However, worries and self-criticism also arise in the new brain. The crocodile can't build rockets to fly into space and it didn't invent the Internet, but it probably doesn't worry about the future either and probably doesn't suffer from self-doubt." (click to continue)

- "Between our old brain and our new brain, there are helpful loops. But there are also unhelpful loops. We call these 'tricky brain loops.' We just have a tricky brain." (click to continue)

- "Look at an example of a tricky brain loop: Julia sees a photo on Facebook of several good friends having fun at another friend's party. The comment on the photo reads, 'All best friends together - what a party!!!' Upon seeing the photo, Julia begins to feel tense and anxious. A loop develops between Julia's old brain and her new brain' → Click through and discuss loop

- "Now you may wonder why we have these unhelpful loops between the old brain and the new brain in the first place. The old brain wants to protect us from danger. That doesn't always fit well with what's going on in our new brain, which is what we think about situations in everyday life, for example. This creates unhelpful brain loops."

- "Perhaps you also know such or similar loops from yourself? It's not your fault at all if you sometimes have similar thoughts and feelings as Julia in the example. We just have a tricky brain, a complicated brain." (click to continue)

- "The emotions that arise in our "tricky brain" can be thought of as a compass. Our emotional compass consists of three emotional systems: threat, soothing,

and drive, which influence each other. Let's take a closer look at these emotional systems together!"

- Introducing emotional systems (see Figure S7)
    - "Do you have any questions about the emotional systems so far?" (Answer questions, then click on next)
    - "Our emotion areas are interrelated and influence each other." (click on next)
    - "Often, our emotional compass is not very balanced. Red is often strongest and dominates our other emotion areas. Perhaps you can relate to this?" (click to continue)
    - "The red emotional system influences our thinking and behaviour. It affects our attention, motivation and imagination. Red can often determine how our entire emotional compass works!"
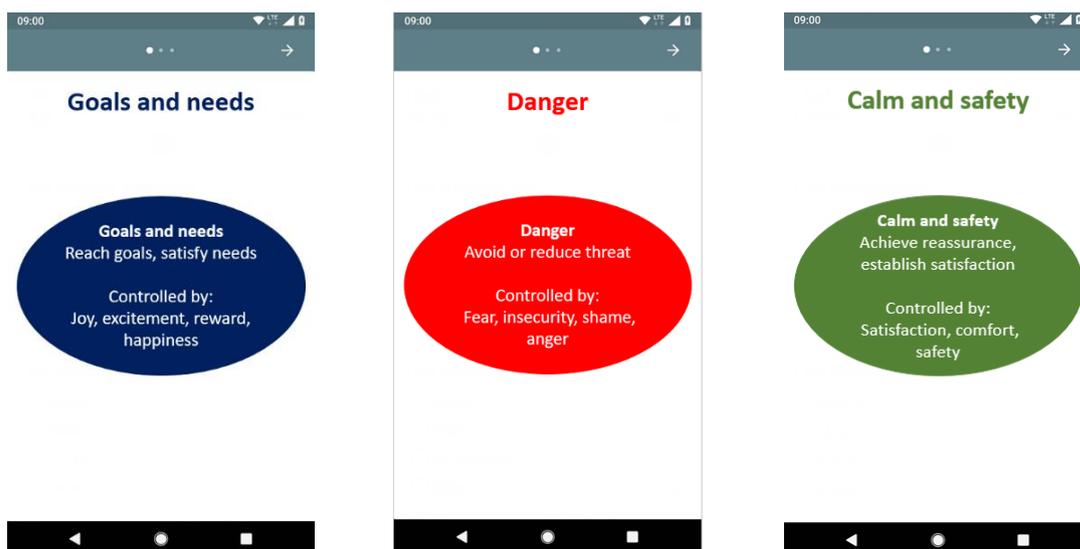
Figure S7. *Emotional systems.*

🏋 *Exercise: Emotional compass*
- "Let's start with the emotional system of threat. How does this emotional system work for you? What triggers unpleasant emotions in you, such as fear, insecurity, shame, or anger? (Validate answer) Let's fill that in, too! To do so, click on the text box and a keyboard will open. Next, please rate how strong these feelings are at such moments. On a scale from 1 (= very weak) to 7 (= very strong), how strong are your feelings then? (Validate answer) You can also enter this in the app - just select the number that suits best for you. Now let's consider how you think about these feelings. You remember that

earlier we talked about the new brain, which is responsible for complex thinking and planning but also for self-criticism and worry. What does your new brain say in situations where you have these feelings? (Validate answer) Let's put that in too! Okay, done, now let's look at the next emotional system, please click on for that."

- Work on the other two emotional systems in the same way, validate answers. If the participant cannot think of anything at first, make it clear that this is not a bad thing. Offer help, for example, think about the last time you had this feeling to get an example situation. Finally: „Great, we've been thinking about your Emotional Compass together! It's absolutely okay if you found the exercise difficult or exhausting - a lot of people do."

- "With our Emotional Compass, when **RED** takes control, our goal is to strengthen **GREEN! GREEN** calms **RED** and is a safe foundation for **BLUE**." (click to continue)

- "There are several ways to strengthen green to calm down and feel secure. One way is to learn to pay attention to your own breath. Shall we look at that together right now, too? All right, click the "Proceed to the Breathing Exercise!" button for that."

Count the breath

ⓘ **Information: Count the breath**

- "Great that you want to do a breathing exercise while you're at it! The breathing exercise can help you calm down. The goal of the exercise is for you to learn a way to find a **calming and soothing** breathing rhythm." (click to continue)

- "That means we focus on the green emotional area, the calm and security system, and aim to strengthen it." (click to continue)

- "There are two options for the exercise now: You can listen to an audio file to guide you through the exercise, or you can read the exercise on your own. Please select which you prefer on the screen." If audio is selected, the next instructions will be omitted and you will not restart until you complete the exercise.

- "All right, you've decided to read the exercise with me. As a first step, before we begin the breathing exercise, take some time to assume a **comfortable and upright posture**. You may choose to lie down, stand, or sit, whichever seems most comfortable for you at the time." (If the participant wishes to sit, the therapist will also assume an upright and relaxed posture to set an example for the participant) (click to continue).

- "Try to find a posture that makes you feel **confident and open**. If you choose to sit or stand, it may be helpful to stand with both soles of your feet flat on the floor and you try to straighten your shoulders and back at the same time." (Therapist should demonstrate)

- "Have you found a comfortable posture?" (Assist as needed, emphasizing that any posture is okay as long as the person finds it comfortable. If the person can't decide, suggest if necessary that they try one posture, but of course can change it as the exercise progresses if it feels better another way) "First take a few **deep, slow breaths**. Perhaps as you breathe in and out deeply, you will already recognize a rhythm that is comfortable for you?" (short pause to breathe, click on).

- "Try to notice how the **air slowly flows into and out of your body**. Here, it can be helpful to focus on your nose to feel the air flowing through your nose." (pause briefly to breathe, continue clicking)

- "This can be **very difficult**! So it's perfectly okay if you find that your mind wanders off during the exercise. Then simply return your attention to the breath and **try not to view the wandering as a mistake or judge it negatively.**" (click to continue)

- "Conscious breathing is like a muscle that you have to train. It is therefore perfectly normal if you may find the exercise difficult at first. You're going to practice counting your breath right now. In doing so, you will learn to focus on your breath." (click to continue)

⫩ Exercise: Count the breath

- "Now let's begin the breathing exercise. Please close your eyes right away and with each inhale and each exhale count to 5 silently, with a pause in between that is comfortable for you. The entire exercise will take **3 minutes** and you will be notified about the beginning and the end of the exercise with a gong. Do you have any questions? (Answer questions) When you are ready to begin the exercise, press the button on the screen!"

- "Great, you tried out the breathing exercise. That's how you practice **calming yourself down**. If that hasn't worked out so well yet, that's not a problem, most people feel that way! Since our **everyday life** is usually **very hectic**, it is very difficult for us to stop for a few minutes and focus "only" on our breath." (click more)

- "No matter how it just worked out, you are on a good path. Through practice you will improve this technique! With practice, your breath can become your own personal **anchor of calm** that you always have with you in everyday life. How did you feel about the exercise?" (Validate experiences of the participants, click on)

- Explain gamification
  - "You will earn points from now on! You will get points when you think about your feelings in everyday life and when you do exercises. When your EMIcompass score is high enough, you will move up to the next level. So the more points you earn, the higher your EMIcompass level will be at the end."

Closing of the session

- Praise for effort in lesson, clarify questions, summarize
  - "We really got a lot done today, that was certainly exhausting for you! You are on a very good path and have already worked a lot today on your self-care in dealing with emotions in everyday life. Do you have any questions about the exercises? What would be your conclusion to our session today, what is your take away message?"

Discuss organizational issues

- "Finally, I would like to discuss with you what will happen next: You will take the study phone home/to the ward today. So that you can consolidate what we have practiced together today, please practice independently over the next few days. The smartphone will remind you to practice once a day. However, you do not have to do the exercise from memory. The app will guide you, just as you have seen today. If you ever don't have time when the app offers you your daily exercise, the app will remind you again at a later point in time. We can set here in the app when it is best for the smartphone to offer you a task. This setting will remain the same throughout the course of the study. What time would be good on most days, when would you like to practice?" (Open initial questionnaire in the app and select time - See DEMO printout for illustration).
- "In addition, you can allow us to ask you questions three days a week about your mood and situations you experience in your daily life. The app will then prompt you six times

a day to briefly answer some questions about what you're doing and how you're feeling. This would have the advantage of allowing the app to provide you with an exercise when it is needed. Based on our clinical experience and previous research findings, we believe that these small mood queries contribute to better treatment outcomes. You yourself get to decide whether or not you want us to set this option for you. Would you like to use the option?" → If the TN allows the queries: from when and until when may we send you the mood queries? (enter the times in the initial questionnaire, enter them in the Mutable Value Editor at Interactive 1→ see Technology Guide, use DEMO printout for illustration).

- "If you want, you can also do additional exercises on your own at any time; you don't have to wait specifically for the app to prompt you. So if you want to do additional exercises in between, open the app and select "Perform exercise", for example. There you can select which of the previously learned exercises you would like to train. Clicking on "What have I learned so far?", you can look at all exercises previously presented again in detail with all the explanations." (Make sure participants understand the difference, use DEMO printout for illustration)

- "In one week, something will change in your app. In addition to the exercises you already know, a new task will appear in the main menu of the app. The exercise will be explained to you via your smartphone. We won't see each other next week, so we will call you to hear how the exercises are going and to let you know that there is a new exercise. Or we can e-mail you, in which case I would need an e-mail address where I can reach you. What would you prefer?"

- It is important that you do this exercise as soon as possible then. At what time can we reach you well? If you have any questions or any other difficulties, you can also contact me or my colleagues on your own initiative. You can reach us by e-mail. You can also reach us by phone, we have set up an answering machine, where you can leave us a message. We will then call you back as soon as possible".

- Make new appointment in two weeks, discuss procedure for cancelling appointments

Between sessions (2nd week)

There will be no intervention session during this week, the participants will learn a new exercise on their own guided by the EMIcompass app. Exactly one week after the first session, the study

psychologists or the support staff (please make arrangements!) will contact the participants by phone at the agreed time or send an email. Beforehand, the participants' data must be downloaded and reviewed so that you can give the participants feedback in this regard.

How do I see what participants have completed and how many exercises they have done?
Feedback on adherence should be provided by the support staff as a printout before the session - should be in the participant's folder, please check before the session!

Topics for the telephone call

-   How the participant is feeling?
-   Previous experience with the app, questions and difficulties
-   Feedback on participant's adherence (positively reinforce good adherence; do not reprimand low adherence, emphasise importance and consider together how it could be better next week). To progress to the next week of intervention, participants must at least complete the newly introduced exercise and one consolidating exercise during the week. If these requirements are not met, participants remain in that week of intervention. If participants express great difficulty or desire to do so on their own, a week of intervention may also be repeated based on clinical impression. (For settings, see technique guide).
-   Note that a new exercise (see EMICOMPASS Intervention - Overview) should now appear in the app and that it should be done promptly.
-   Remind of appointment in the following week

Second session – Track 1 (3rd week)

Table S 52 provides an overview of the second session in the basic intervention track.

Table S52. *Overview of the second session in the basic intervention track.*

Topic	Time
Introduction	5 min
Debriefing of last week, decision for intervention arm	10 min
ⓘInformation: My calm, safe place	5 min
⫸Exercise: My calm, safe place	20 min
Closing of the session	10 min

<u>Introduction</u>

- Welcome participants, express joy about second appointment
- Ask how they are feeling
- Discuss agenda: "First, I would like to know how the time has been for you since our last session and hear how the exercises are going. Also, I would love to do a new exercise with you so that you have even more tools in your daily life to help you feel calm and secure. Do you agree with this plan for our session today?"

<u>Debriefing of last week, decision for intervention track</u>

- Last week's debrief: "In our last session, you first practiced counting your breath and thought about your emotional compass. Then last week you learned a new exercise, you practiced imagining your one soothing colour. How was it going with the exercises? (Ask more questions if needed for understanding until you feel you have a good impression of which intervention track participants benefit more from Include your impression from first contact. (For overview of all exercises still to come, see EMICOMPASS Intervention - Overview) What did you find easy, did you experience difficulties? Did you find the exercises helpful, which one helped you most? Were you able to visualize your colour? Were there any difficulties with the smartphone?"
- Provide adherence feedback (adherence feedback should be provided as a printout by the support staff before the session - should be in the participant's folder, please check before the session!): "I saw that you were very committed and practiced a lot since our last session! That's great!" If not practicing as much: "I saw that unfortunately you haven't practiced very much since our last meeting. What was the reason for that? (Showing understanding) It would be important to practice a little more often next week, let's figure out together how to make that happen!"
- If ESM was allowed, provide feedback on adherence here as well: "I also noticed that you answered a lot of mood queries, great!" for low adherence: "I've seen that it's been difficult for you to answer the mood queries lately."
- Decide in which intervention track participants will benefit more, set appropriate exercise on smartphone (see technology guide)

<u>My calm, safe place</u>

ⓘ Information: My calm, safe place

- Introduce new exercise:
    - "Today we want to learn a new exercise! The exercise is called "Finding a calm and safe place". Let's look at the exercise together! The exercise can help you calm down and feel more secure - much like the exercises before. In this exercise, you have the task of finding a place that is calm and safe for you. As you'll notice, this exercise is very similar to last week's exercise in which you practiced imagining a very personal colour." (click to continue)
    - "But before you find a calm, safe place for yourself, it can be helpful to adopt a comfortable posture and find a breathing rhythm that is comfortable for you. Try to find a posture that makes you feel confident and open. Again, you can choose to sit, lie down or stand. If you choose to sit or stand, it may again be helpful for you to stand with both soles of your feet flat on the floor and you simultaneously try to straighten your shoulders and back." (click to continue)

🏋 **Exercise: My calm, safe place**

- "Let's start the exercise! Imagine a place that calms you down and seems peaceful to you. Remember that there is no right or wrong place - it's your own personal choice." (click to continue)
- "Take your time to decide and try to consciously observe what place or places come to mind. For example, it could be a place you have visited many times in the past. But you also have the possibility to imagine a completely new place. To do this, close your eyes for a moment!" (Pause. Wait to see what comes to mind and encourage participants.) "Have you thought of a place yet?" (click to continue)
- If at first nothing comes to mind for the participant: "Please don't be frustrated if you don't come up with a place right away - that's normal! Take as much time as you need to search and decide." (click to continue)
- If they think of several places: "It is also no problem if you think of several places at once and you can't decide directly which place you want to choose. Take as much time as you need to search and decide." (click to continue)
- "If you have already decided on a place, you can now select "I have found my place". If you haven't found a place for yourself yet, that's no big deal at all. Just choose "I can't

think of a place" and we'll think about it again together!" (participants make their selection)

- If "I can't think of a place" was selected: "It's not problem that you haven't thought of a place yet, a lot of people feel that way. Feel free to take more time. It may help you to focus on your breath again. Maybe a short breathing exercise will help you to relax a bit before you start to search for your calm and safe place again without rushing. To do this, simply breathe in and out calmly, counting to 5 with a comfortable pause in between - just as you've been practicing for the past few weeks." (do breathing exercise for 1-2 minutes, then click on next)

- "If you have already thought of a place now, you can just keep clicking. If not, the next page offers some examples and you can select the place that is most closely associated with calm and safety for you. That place will then be your very own calm and safe place starting today!" (click to continue)

- If no place has been found yet: "Just choose the place here that is most likely to represent peace and security for you. Which one would you like to take? (validate answer TN) Okay, then click to continue." (click to continue)

- "Very nice, you have found your personal calm and safe place! In the exercise, you are to try to explore the place in your imagination. In doing so, try to imagine the place as vividly as possible." (click to continue)

- "It is perfectly okay if your place appears less clear in your mind's eye or disappears altogether. That is completely normal! Then simply return with your attention to your personal place, completely without negative evaluation." (click to continue)

- "Do you have any questions up to this point? If you are ready, we will then start with the actual imagery exercise! Go to your place in your mind right away. Try to focus on what you can see when you are at your personal place. This part of the exercise will take two minutes. As you know it from previous exercises, a gong will signal you the beginning and the end of the exercise. When you are ready, please click the button and close your eyes to begin the exercise!"

- "Great, you've explored your place for the first time! Now try to focus on other features of your place. Maybe you hear something, you see other people, or maybe you notice a sensation on your body, such as the warmth of the sun or a slight breeze. Let's take another two minutes so you can explore your personal place further! When you are ready, please start the exercise again with the button"

- "Very nice, you have found a calm and safe place for yourself today. You pictured the place in your mind and explored it! On a scale of 1 (very bad) to 7 (very good), how well were you able to imagine your safe place? (Record on paper sheet) How did you feel about the exercise? (Praise, validate experience. If difficult, emphasise that many people have a hard time at first, that this is normal, etc.) Your safe place can also become your own personal anchor of calm and security with a little practice. Just like your breath, you always have your imagination with you. So you can always call your place to mind - wherever you are and no matter how you're feeling right now." (click to continue)
- "Your EMICOMPASS score has continued to rise - great how many points you've already earned!"

Closing of the session

- Praise for the effort in the lesson, clarify questions, summary
    - "We really got a lot done again today, which was certainly exhausting for you! You are on a very good path and have already worked a lot on your self-care in dealing with feelings in everyday life in the last few weeks. Do you have any questions about the exercises? What would be your conclusion to our session today, what do you take away? "

Discuss organizational matters

- "Finally, I would like to discuss with you again how to proceed. We will have our next appointment in two weeks (make appointment). In the meantime, you will again be reminded daily by the smartphone about your exercise - was the time okay, or should we change something here? (Make changes? See tech guide) If you ever don't have time when the app reminds you of your daily exercise, the app will remind you again at a later time. Of course, you can continue to do exercises on your own and don't have to wait for the signal from the app. A week from today, just like last week, you will again learn a new exercise on your own via the smartphone. It would be important that you then do this exercise again promptly. Again, we will call or mail you to let you know that there is a new exercise.

- "You can continue to allow us to ask you questions three days a week about your mood and situations you experience in your daily life. The app would then prompt you six times a day to briefly answer some questions about what you're doing and how you're doing. If participants have had this in the last few weeks: it would continue exactly as you are used to. Would you be okay with that? If participants have not had it in the last few weeks: The app would then prompt you six times a day, three days a week, to briefly answer some questions about what you are doing and how you are doing. This would have the advantage that the app could offer you an exercise exactly when there is a need. In addition, it would also help researchers better understand what stresses young people in their daily lives. Based on our clinical experience and previous research findings, we believe that these small mood queries will help improve treatment outcomes. You yourself get to decide whether or not you want us to discontinue this option for you. Would you like to use the option?" If yes: "From when and until when may we send you mood surveys?" (if participated in advance) "Should we stay with the times we discussed?" (change if sentiment queries are allowed or times → see tech guide)
- "Is there anything else to discuss from your side, do you have any questions?"
- Farewell

Second session – elaborate intervention track (3rd week)

Table S 53 provides an overview of the second session in the elaborate study track.

Table S53. *Overview of the second session in the elaborate study track.*

Topic	Time
Introduction	5 min
Debriefing of last week, decision for intervention arm	10 min
ⓘInformation: Compassionate companion	10 min
Exercise: Compassionate companion	15 min
Closing of the session	10 min

Introduction

- Welcome participant, express joy about second appointment

- Ask how they are feeling
- Discuss agenda for session: *"First, I would like to know how the time has been for you since our last session and hear how the exercises are going. Also, I would love to do a new exercise with you so that you have even more tools in your daily life to help you feel calm and secure. Do you agree with this plan for our session today?"*

Debriefing of last week, decision for intervention arm

- Debriefing from last week: "In our last session, you first learned counting your breath and thought about your emotional compass. Then last week you learned a new exercise. You practiced imagining your one calming colour. How did it go with the exercises? (If needed for understanding, ask more questions until you feel you have a good gauge of which intervention arm participants would benefit better in. Include impression from first contact). What did you find easy, did you experience difficulties? Did you find the exercises helpful, which one helped you the most? Were you able to visualize your colour well? Were there any difficulties with the smartphone?"
- Provide adherence feedback (adherence feedback should be provided as a printout by the support staff before the session - should be in the participant's folder, please check before the session!): "I saw that you were very committed and practiced a lot since our last meeting! That's great!" If not practicing as much: "I saw that unfortunately you haven't practiced very much since our last meeting. What was the reason for that? (Showing understanding) It would be important to practice a little more often next week, let's figure out together how to make that happen!"
- If ESM was allowed, provide feedback on adherence here as well: "I also noticed that you answered a lot of mood queries, great!" for low adherence: "I've seen that it's been difficult for you to answer the mood queries lately."

Compassionate companion

ⓘ**Information: Compassionate companion**
- Guide to the exercise:
    - "Today we want to learn a new exercise! The exercise is called "My compassionate companion". Let's look at the exercise together! The exercise can help

you be more compassionate with yourself and feel secure in your everyday life-much like the exercises before." (click to continue)

- "But before we start the exercise, it can be helpful to adopt a comfortable posture and find a breathing rhythm that is comfortable for you. Try to find a posture that makes you feel confident and open. Again, you can choose to sit, lie down or stand. If you choose to sit or stand, it may again be helpful for you to stand with both soles of your feet flat on the floor and you simultaneously try to straighten your shoulders and back." (click to continue)

⫶⫶ Exercise: Compassionate companion

- "Let's begin with the exercise! You now have the tasks of picturing a personal companion who conveys compassion to you. Your compassionate companion knows you and knows what you have been through in life." (click to continue)
- "Your companion has certain characteristics: it is only there for you and wants to take care of you so that you feel good and have no worries. It does not judge you no matter what you think or feel. Your compassionate companion understands your problems and accepts you as you are." (click to continue)
- "Your compassionate companion may be anything you can think of. It can be an animal, a fantasy creature, or even the sun. It can be a person you know or someone completely foreign." (click to continue)
- "You can choose your compassionate companion freely. Your compassionate companion can be old or young, male or female. Perhaps your compassionate companion has experienced something similar to you?" (click to continue)
- "Please close your eyes now and search for your compassionate companion. Take your time in doing so. If you cannot think of a companion, you could also focus on your breath again for a short time. Then turn back to the task of finding your compassionate companion in a relaxed and non-judgmental way." (Wait, give participants time to find a compassionate companion). (click to continue)
- Have you found your compassionate companion?
    - YES: "Great, then please select "I have found my compassionate companion" here" (keep clicking)
    - NO: „It's no problem if you haven't thought of a compassionate companion yet. Feel free to take your time with this and choose what feels good to you." (click to continue)

- Only if NO was answered, "When choosing your compassionate companion, it may help to think of someone you feel comfortable with. There is no right or wrong with this exercise either, just choose what comes to mind." (Repeat compassionate companion characteristics again if needed.) (click to continue)
- "Great, you have found your compassionate companion! It's perfectly okay if your compassionate companion appears less clearly in your mind's eye or disappears completely during the following exercise. Then simply imagine you companion again without immediately judging this negatively." (click to continue)
- "Now please close your eyes and take 2 minutes to picture your compassionate companion. The beginning and the end of the exercise will again be signalled to you with a gong. When you are ready, please click the button and close your eyes to begin the exercise!" (wait for exercise) (click on next)
- "Very well done! Your compassionate companion can help you in difficult situations, strengthening your soothing system." (click to continue)
- "Now, to practice doing just that, recall a situation that you experienced as unpleasant. To make it easier for you to remember, it is best to choose a current situation with other people in which you felt ashamed or anxious. Please do not choose a situation that is too bad. Can you think of a situation?" (click YES or NO)
    - YES: (have the situation told). "How would you rate the situation on a scale from 1(= not bad at all) to 7 (= very bad)?" (Make sure that participants choose unpleasant but not traumatic situations! Optimal difficulty between 3 and 6)
    - NO: "It's no problem if you can't think of a situation right away. Maybe you can remember a situation where you felt rejected or excluded or a thing that embarrassed you. Maybe you can think of a situation where you were disappointed or other people were unkind to you. Can you think of anything?" If NO: "Feel free to take some more time and think about the last few days and weeks. If you thought of something, please select "I thought of a situation"! How would you rate the situation on a scale of 1(= not bad at all) to 7 (= very bad)?" (Make sure that participants choose unpleasant but not traumatic situations, optimal difficulty between 3 and 6)
- "Now please imagine this unpleasant situation for 2 minutes. The beginning and the end of the exercise will again be signalled to you with a gong. Please remember: Where are you? What can you see or hear? Who else is there? What has happened? When you are

ready, start the exercise by pressing the button. Then close your eyes and imagine the situation."

- "Very nice! It must not have been easy to imagine this unpleasant situation again. On a scale of 1 (very low) to 7 (very high), how high is your tension right now (1-7)?" (Write down on paper sheet)

- "Your compassionate companion can now help you calm down after imagining this uncomfortable situation. Now take another 2 minutes to imagine your compassionate companion with your eyes closed. When you are ready, start the exercise by clicking the button!"

- "On a scale of 1(very poor) to 7 (very good), how well were you able to visualize your compassionate companion? (Write down on paper sheet) How did you feel about the exercise? (Praise, validate experience. If difficult, emphasise that many people find it difficult at first, that this is quite normal, etc.) Your compassionate companion can also, with practice, become your own personal anchor of calm and security. Just like your breath, you always have your imagination with you. So you can always call your compassionate companion to mind - wherever you are and no matter how you're feeling right now." (click to continue)

- "Your EMICOMPASS score has continued to rise - great how many points you've already earned!"

Closing of the session

- Praise for the effort in the lesson, clarify questions, summary
    - "We really got a lot done again today, that was certainly exhausting for you! You are on a very good path and have already worked a lot on your self-care in dealing with feelings in everyday life in the last few weeks. Do you have any questions about the exercises? What would be your conclusion to our session today, what is your take away message? "

Discuss organizational matters

- "Finally, I would like to discuss with you again how to proceed. We will have our next session in two weeks (schedule appointment). In the meantime, you will again be reminded daily by the smartphone about your exercise - was the time okay, or should we

change something here? (Make changes? See tech guide). If you ever don't have time when the app reminds you of your daily exercise, the app will remind you again at a second time. Of course, you can continue to do exercises on your own and don't have to wait for the signal from the app. One week from today, just like last week, you will again learn a new exercise on your own via the smartphone. It would be important that you then do this exercise again promptly. Again, we will call or mail you to let you know that there is a new exercise."

- "Also, you can continue to allow us to ask you questions three days a week about your mood and situations you experience in your daily life. The app would then prompt you six times a day to briefly answer some questions about what you're doing and how you're doing." If participants have had this in the last few weeks: it would continue exactly as you are used to. Would you be okay with that? If participants haven't had it in the last few weeks: The app would then prompt you six times a day, three days a week, to briefly answer some questions about what you are doing and how you are doing. This would have the advantage of allowing the app to provide you with an exercise exactly when there is a need. In addition, it would also help researchers better understand what stresses young people in their daily lives. Based on our clinical experience and previous research findings, we believe that these small mood queries will help improve treatment outcomes. You yourself get to decide whether or not you want us to discontinue this option for you. Would you like to use the option?" If yes: "From when and until when may we send you mood surveys?" (if participated in advance) "Should we stay with the times we discussed?" (change if sentiment queries are allowed or times → see tech guide).
- „Is there anything else to discuss from your side, do you have any questions?"
- Farewell

Between sessions (week 4)

See above.

Third session – Basic intervention track (5th week)

Table S54 provides an overview of the third session in the basic intervention track.

Table S54. *Overview of the third session in the basic intervention track.*

Topic	Time
Introduction	5 min
Debriefing of the last week	10 min
ⓘ Information: Surf the waves of your feelings	5 min
🏋 Exercise: Surf the waves of your feelings	20 min
Closure of the session	10 min

Introduction

- Greet participants, express joy about third appointment
- Ask how you are feeling
- Discuss agenda for session: "First, I would like to hear again how the time has been for you since our last meeting and hear how the exercises are going. Also, I would love to do a new exercise with you so that you have even more tools in your daily life to calm down and feel safe. Do you agree with this plan for our session today?"

Debriefing of the last week

- Last week's debrief: "Since our last session, you practiced imagining and exploring your calm and safe place. Then last week you learned a new breathing exercise where you practiced breathing with pauses. How did you experience the exercises? (Ask more questions for understanding if needed until you feel you have a good understanding of how the participant was doing and how to best support him/her). What did you find easy, did you experience difficulties? Did you find the exercises helpful, which one helped you the most? Do you have any questions about the exercises? Were there any difficulties with the smartphone?"
- Provide adherence feedback (adherence feedback should be provided as a printout by the support staff prior to the session - should be in the TN's folder, please review prior to the session!): "I saw that you were very committed and practiced a lot since our last meeting! That's great!" If not practicing as much: "I saw that unfortunately you haven't practiced very much since our last meeting. What was the reason for that? (Showing understanding) It would be important to practice a little more often next week, let's figure out together how to make that happen!"

- If ESM was allowed, give feedback on adherence here too: "I also noticed that you answered a lot of mood queries, great!" if adherence is low: "I've seen that it's been difficult for you to answer the mood queries lately."

Emotion as a wave

ⓘ**Information: Emotion as a wave**
- Guide to the exercise:
    - "Today we want to learn a new exercise! The exercise is called "Emotion as a wave". Let's look at the exercise together! The exercise can help you be more compassionate with yourself and feel more secure in your everyday life - much like the exercises before." (click to continue)
    - Inform about rational behind the exercise: "You can think about emotions in many different ways. One way would be to think of them as waves in the sea. In moments when we feel good, relaxed, and have little stress, our emotions resemble an ocean with shallow, small waves."
    - Before clicking on, excursus on emotions: Sometimes it's not so easy to identify what emotion you're experiencing. Often we mix our emotions with what we feel in our body or with our thoughts. Sometimes we can tell if we are having a pleasant or unpleasant emotion but have difficulties naming it. What pleasant and unpleasant emotions do you know? (Validate participant's answer, add if necessary if important feelings are missing. If the patient is very undifferentiated, spend a little more time here to differentiate this more precisely, then click on).
    - "Perhaps you have experienced it yourself, or maybe seen it in a movie or heard that the sea can change constantly? In a similar way, our emotions can change quickly." (click to continue)
    - "The sea can change greatly with an oncoming storm and suddenly have bigger waves. In our lives, too, many things can influence our emotions. For example, we may have problems at school, college, or work, or conflicts with family members, making us feel upset or angry." (click to continue)
    - "In the process, it can happen that we get carried away by the rising waves of emotions, they take us over completely and wash us to a place we didn't really want to be - we may even do or say things we don't mean to say or do. It's also

possible that we run away from our emotions, ignore them, and don't take them seriously. Do you recognize anything of this?"

- "Today we are going to learn a new exercise that can help you perceive and feel emerging emotions more clearly. The goal is not to simply be carried away by the strong waves of emotions, but to surf on the waves that arise in life!"

⫿▬⫿ Exercise: Emotion as a wave

- "To practice surfing your emotions, please recall a situation that you experienced as unpleasant. To make it easier for you to remember, it is best to choose a recent situation with other people in which you felt ashamed or anxious. Please do not choose a situation that is too bad. Can you think of a situation yet?" (click YES or NO)
  - YES: (have the situation told). "How would you rate the situation on a scale from 1(=not at all bad) to 7 (=very bad)?" (Make sure participants choose unpleasant but not traumatic situations! Optimal difficulty between 3 and 6)
  - NO: "It's not bad if you can't think of a situation right away. Maybe you can remember a situation where you felt rejected or excluded or a thing that embarrassed you. Maybe you can think of a situation where you were disappointed or other people were unkind to you. Can you think of anything?" If NO: "Feel free to take some more time and think about the last few days and weeks. If you thought of something, please select "I thought of a situation"! How would you rate the situation on a scale of 1(= not bad at all) to 7 (= very bad)?" (Make sure that participants choose unpleasant but not traumatic situations!!! Optimal difficulty between 3 and 6)
- "Now please imagine this unpleasant situation for 2 minutes. The beginning and the end of the exercise will again be signalled to you with a gong. Please remember: Where are you? What can you see or hear? Who else is there? What has happened? When you are ready, start the exercise by pressing the button. Then close your eyes and picture the situation." (click to continue)
- "On a scale from 1 (very low) to 7 (very high), how high is your tension right now (1-7)? (Write down on a sheet of paper) Now try to perceive the emotions that have arisen while imagining the situation as clearly as possible and look at them closely. In doing so, try not to directly get rid of the emotions, block them, ignore them, or evaluate them negatively." (Participants should be given the opportunity here to express their observations and be validated for them).

- "Now try to look at your emotion like a wave that quickly gets bigger, has a peak, and then subsides. Allow yourself two minutes. The beginning and end of the exercise will again be signalled to you by a gong. When you are ready, start the exercise by pressing the button. Then close your eyes and imagine your emotions as waves in the ocean."

- After the exercise: "Very well done, that may not have been easy! It is no problem if you experienced this exercise as difficult. Many people feel that way. On a scale of 1 (very low) to 7 (very high), how high is your tension right now (1-7)? (Write it down on a sheet of paper)" (click to continue)

- "Remember, just like a wave, the emotions you are feeling right now, and have felt in the past, can also become less strong after a while - so they can come quickly and abruptly, but they can also go away." (click to continue)

- "Sometimes it can be helpful to accept the emotions you feel as they are. While our emotions are important, they don't define us as a person - so we are not our emotions." (click to continue)

- "That's why it's important to try not to hold on to our emotions for too long, but also to let them go in order to realign our emotional compass." (click to continue)

- "Very nice, you imagined your emotions as waves for the first time today! On a scale from 1 (very bad) to 7 (very good), how well were you able to imagine your emotions as waves? (Write down on paper sheet) How did you do with the exercise? (Praise, validate experience. If difficult, emphasise that many people have a hard time at first, that this is normal, etc.) This exercise can also help you calm down and deal better with your feelings. Like all the previous exercises, you can do this exercise anytime in your daily life, no matter where you are!" (click to continue)

- "Your EMICOMPASS score has continued to rise - great how many points you've already earned!"

Closing of the session

- Praise for effort in lesson, clarify questions, summarize.
    - "We really got a lot done today, that was certainly exhausting for you! You are on a very good path and have already worked a lot today on your self-care in dealing with feelings in everyday life. Do you have any questions about the exercises? What would be your conclusion to our session today, what do you take away?"

<u>Discuss organizational matters</u>

- "In conclusion, I would like to discuss with you again how to proceed. This was the last appointment we had together to do exercises. In two weeks I would like to meet you again for a short final discussion to look back on the treatment together with you. After that you will also meet my colleague for an assessment. Following this, you will then receive questions about your mood and situations you experience in everyday life via smartphone for another 5 days. The app will again prompt you six times a day to briefly answer some questions about what you are doing and how you are feeling. After these 5 days, please return the phone to us or send it to us with the return envelope, an agreement on this will be made in the final meeting with my colleague. (An agreement should be made in the final diagnostic meeting and, if necessary, a return date should be agreed upon)."

- "In the next two weeks, everything will proceed as usual: You will again be reminded of your exercise every day by the smartphone - was the time okay, or should we change something here? (Make changes? → see Technology guide) If you sometimes don't have time when the app reminds you of your daily exercise, the app will remind you again at a second time. Of course, you can continue to do exercises on your own and don't have to wait for the signal from the app. One week from today, just like last week, something will change again on your smartphone. Something new will appear again. It would be important for you to do this exercise promptly again then. Again, we will call or email you to let you know that there is a new exercise now."

- "Also, you can continue to allow us to ask you questions three days a week about your mood and situations you experience in your daily life. The app would then prompt you six times a day to briefly answer some questions about what you're doing and how you're doing." If participants have had this in the last few weeks: it would continue exactly as you are used to. Would you be okay with that? If participants haven't had it in the last few weeks: The app would then ask you six times a day, three days a week, to briefly answer some questions about what you are doing and how you are doing. This would have the advantage that the app can offer you an exercise exactly when there is a need. In addition, it would also help researchers better understand what stresses young people in their daily lives. Based on our clinical experience and previous research findings, we

believe that these small mood queries will help improve treatment outcomes. You yourself get to decide whether or not you want us to discontinue this option for you. Would you like to use the option?" If yes: "From when and until when may we send you mood surveys?" (if participated in advance) "Should we stay with the times we discussed?" (change if sentiment queries are allowed or times → see tech guide).

- "Is there anything else to discuss from your side, do you have any questions?"
- Farewell

Third session – elaborate intervention track (5th week)

Table S55 provides an overview of the third session in the elaborate intervention track.

Table S55. *Overview of the third session in the elaborate intervention track.*

Topic	Time
Introduction	5 min
Debriefing of the last week	10 min
ⓘ Information: My compassionate Self	5 min
❚█❚ Exercise: My Compassionate Self	20 min
Closing of the session	10 min

Introduction

- Greet participants, express joy about third appointment
- Ask how you are feeling
- Discuss agenda for session: "First, I would like to hear again how the time has been for you since our last meeting and hear how the exercises are going. Also, I would love to do a new exercise with you so that you have even more tools in your daily life to calm down and feel safe. Do you agree with this plan for our session today?"

Debriefing of the last week

- Debriefing from last week: "Since our last session, you first practiced imagining your compassionate companion with its different characteristics. Then last week you learned a new exercise where you found a safe place for yourself and explored it. How did you feel about the exercises? (Ask more questions for understanding if needed, until you

feel you have a good understanding of how the participant was doing and how he/she can be optimally supported). What did you find easy, did you experience any difficulties? Did you find the exercises helpful, which one helped you the most? Do you have any questions about the exercises? Were there any difficulties with the smartphone?"

- Provide adherence feedback (adherence feedback should be provided as a printout by the support staff prior to the session - should be in the TN's folder, please review prior to the session!): "I saw that you were very committed and practiced a lot since our last meeting! That's great!" If not practicing as much: "I saw that unfortunately you haven't practiced very much since our last meeting. What was the reason for that? (Showing understanding) It would be important for them to practice a little more often next week, let's figure out together how to make that happen!"

- If ESM was allowed, give feedback on adherence here too: "I also noticed that you answered a lot of mood queries, great!" if adherence is low: "I've seen that it's been difficult for you to answer the mood queries lately."

My compassionate self

ⓘ**Information: My compassionate self**

- Guide to the exercise:
    - "Today we want to learn a new exercise again! The exercise is called "My compassionate self". Let's look at the exercise together! The exercise can help you be more compassionate with yourself and feel secure in your everyday life - much like the exercises before." (click to continue)
    - "Over the past few weeks, you have practiced using your imagination to access your compassionate companion in everyday life and to imagine your safe place. Although this has definitely been difficult and possibly exhausting for you at times, you have done everything very well so far! Keep it up!" (click to continue)
    - Inform about rational behind the exercise
    - "Today you will learn a new exercise that can help you calm yourself down and be more caring with yourself. In this way, we will again strengthen the green system of your emotional compass, the soothing system." (click to continue)

- "In the next exercise, you will learn to imagine your compassionate self. This will give you the opportunity to learn, step by step, to be more caring and compassionate with yourself. Your compassionate self can help you feel more secure in your everyday life." (click to continue)
- "But before we begin the exercise, it may be helpful to return to a comfortable posture and find a breathing rhythm that is comfortable for you. Try to find a posture that makes you feel confident and open. Again, you can choose to sit, lie down or stand. If you choose to sit or stand, it may again be helpful for you to stand with both soles of your feet flat on the floor and you simultaneously try to straighten your shoulders and back." (click to continue)

⫘ Exercise: My compassionate self

- "The exercise has similarities to your compassionate companion. Your compassionate self has certain characteristics: just like your compassionate companion, your compassionate self does not judge you. It is loving, warm and understands you. It is full of warmth and understanding." (click to continue)
- "Your compassionate self can look like your reflection, or it can look like you in the future or in the past." (click to continue)
- "As you already know, there is no right or wrong in this exercise. It's your own personal choice how you want to envision your compassionate self." (click to continue)
- "As you do the exercise, imagine right now how you walk step by step toward your compassionate self and you become one. Imagine seeing the world through the eyes of your compassionate self and also seeing yourself compassionately. You do not judge and are loving and benevolent. You are full of warmth and understanding." (click to continue)
- "It's perfectly okay if you don't always have a clear picture in your mind's eye during the following exercise, or if the image sometimes disappears altogether. Then simply return to the exercise, without any negative evaluation at all!" (click to continue)
- "Please close your eyes right now and take two minutes to imagine looking at the world and yourself through the eyes of your compassionate self. As usual, the beginning and end of the exercise will be signalled with a gong. When you are ready, start the exercise by pressing the button."

- After the exercise: "Very nice! Your compassionate self can help you calm down in everyday life. The exercise can support you in becoming more caring and compassionate with yourself step by step in your everyday life as well. It's absolutely okay if you've sometimes had a hard time picturing your compassionate self and its compassionate view of the world - many people do!" (click to continue)
- "You always have the opportunity to think of your compassionate self wherever you are and no matter how you are feeling. Your compassionate self can be your personal anchor of peace and security." (click to continue)
- "Very nice, you have imagined your compassionate self for the first time today! On a scale of 1 (very bad) to 7 (very good), how well were you able to imagine your compassionate companion? (Record on paper sheet) How did you feel about the exercise? (Praise, validate experience. If difficult, emphasise that many people have a hard time at first, that this is normal, etc.).
- "Your EMICOMPASS score has continued to rise - great how many points you've already earned!"

Closing of the session

- Praise for effort in lesson, clarify questions, summarize.
    - "We really got a lot done again today, that was certainly exhausting for you! You are on a very good path and have already worked a lot today on your self-care in dealing with feelings in everyday life. Do you have any questions about the exercises? What would be your conclusion to our session today, what do you take away? "

Discuss organizational matters

- "In conclusion, I would like to discuss with you again how to proceed. This was the last appointment we had together to do exercises. In two weeks I would like to meet you again for a short final discussion to look back on the treatment together with you. After that you will also meet my colleague for an assessment. Following this, you will then receive questions about your mood and situations you experience in everyday life via smartphone for another 5 days. The app will again prompt you six times a day to briefly

answer some questions about what you are doing and how you are feeling. After these 5 days, please return the cell phone to us or send it to us with the return envelope, an agreement on this will be made in the final meeting with my colleague. (An agreement should be made in the final diagnostic meeting and, if necessary, a return date should be agreed upon).

- "In the next two weeks, everything will proceed as usual: You will again be reminded of your exercise every day by the smartphone - was the time okay, or should we change something here? (Make changes? → see tech guide). If you sometimes don't have time when the app reminds you of your daily exercise, the app will remind you again at a second time. Of course, you can continue to do exercises on your own and don't have to wait for the signal from the app. A week from today, just like last week, something will change again on your smartphone. A new task will appear, building on today's exercise. It is important for you to do this exercise then as soon as possible. Again, we will call or email you to let you know that there is now a new exercise - was the time okay last time, or should we change something here?"

- "Also, you can continue to allow us to ask you questions three days a week about your mood and situations you experience in your daily life. The app would then prompt you six times a day to briefly answer some questions about what you're doing and how you're doing." If participants have had this in the last few weeks: it would continue exactly as you are used to. Would you be okay with that? If participants haven't had it in the last few weeks: The app would then prompt you six times a day, three days a week, to briefly answer some questions about what you are doing and how you are doing. This would have the advantage that the app could offer you an exercise exactly when there is a need. In addition, it would also help researchers better understand what stresses young people in their daily lives. Based on our clinical experience and previous research findings, we believe that these small mood queries will help improve treatment outcomes. You yourself get to decide whether or not you want us to discontinue this option for you. Would you like to use the option?" If yes: "From when and until when may we send you mood surveys?" (if participated in advance) "Should we stay with the times we discussed?" (change if sentiment queries are allowed or times → see tech guide).

- "Is there anything else to discuss from your side, do you have any questions?"
- Farewell
-

Between sessions (6th week)

See above.

Review session

Table S56 provides an overview of the review session in both intervention tracks.

Table S56. *Overview of the review session.*

Topic	Time
Introduction	5 min
Debriefing of the last week	10 min
Review of the intervention	10 min

Introduction

- Greet participants, express joy about last appointment
- Ask how you are feeling
- Discuss agenda for session: "First, I would like to hear again how the time has been for you since our last meeting and hear how the exercises are going. Also, I would very much like to review the treatment with you today and end by giving you an overview of the exercises you learned during treatment. Do you agree with this plan for our session today?"

Debriefing of the last week

- Debriefing of last week for Level 1: "In our last meeting, you first practiced imagining your emotions as a wave and surfing on it, so to speak. Then last week, a summary of the exercises you learned during the treatment was added, you took a closer look at your toolbox, and continued to practice these exercises. How did you experience the exercises? (Ask more questions for understanding if needed, until you feel you have a good understanding of how the participant was doing and how he/she can be optimally supported).What did you find easy, did you experience difficulties? Did you find the exercises helpful, which one helped you the most? Do you have any questions about the exercises? Were there any difficulties with the smartphone?"

- Last week's debrief for Level 2: "In our last session, you first practiced imagining your compassionate self and looking at the world and yourself through its eyes. Then, last week, you practiced writing a compassionate message for yourself. How did you experience the exercises? (ask more questions for understanding if needed, until you feel you have a good understanding of how the participant was doing and how he/she can be optimally supported) What did you find easy, did you experience difficulties? Did you find the exercises helpful, which one helped you the most? Do you have any questions about the exercises? Were there any difficulties with the smartphone?"
- Provide adherence feedback (adherence feedback should be provided as a printout by the support staff before the session - should be in the participant's folder, please check before the session!): "I saw that you were very committed and practiced a lot since our last meeting! That's great!"
- If ESM was allowed, provide feedback on adherence here as well: "I also noticed that you answered a lot of mood queries, great!" for low adherence: "I've seen that it's been difficult for you to answer the mood queries lately."

Review of the intervention

- "To conclude, I think it would be nice if we could take a look back together! How was the intervention for you? Do you have any questions? What exercises did you find helpful? What do you take away?"

- Finally, say goodbye to participants, give them the participant manual and remind them of the diagnostic appointments!

Potential difficulties during the intervention

Potential difficulties in the intervention may be low adherence and participants not showing up for appointments. It is important that the therapeutic attitude remains approachable, empathetic and compassionate. Together with the participants, it should then be worked out how adherence or compliance can be improved. If necessary, there is also the possibility of remaining in one week of the intervention and repeating it rather than progressing to the next week of intervention if, for example, the new exercise has not been done at all. This should be decided on a case-by-case basis and together with the participants.

It is also conceivable that participants may devalue themselves during the session, for example, because they found it difficult to perform an exercise. At this point it is important to normalize difficulties with the exercises and to activate the participants' soothing system by dealing with their problems in an empathic and compassionate way.

In addition, self-compassion could be experienced as aversive, here especially information from the biographical anamnesis should be considered, as this is often necessary to be able to correctly understand the current behaviour of the participants.

All difficulties can and should be discussed in the supervision sessions.

Deviations from the protocol:

Appointment with participants takes place a few days after the actual appointment:
- Participants can continue to follow the intervention process. Work on a new exercise in the session. If this has already been done independently by the participants, it can be called up again via "What I have learned so far".

Dates are delayed longer (e.g. because participants want to travel spontaneously).
- The start of the intervention can be up to 4 weeks after randomization, so one option is to start the intervention after the trip. The intervention can also be paused for the time of the trip. Participants should hand in the smartphone in the meantime. After the break, a session takes place in which the participants receive the smartphone and re-join the intervention; if necessary, the session duration can be extended somewhat in order to refresh the content previously worked on. In such cases, please consult with the study team!

Supplementary material 24: Modified criteria of the clinical staging model

Table S57. *Inclusion criteria and transdiagnostic sample characteristics based on a modified version of the clinical staging model (Hartmann et al., 2019) as published in Schick et al. (2021).*

Stage	Criteria	Measure
1a (Distressed individuals)	Psychological distress (K10 score ≥ 20), but not fulfilling criteria of stage 1b or 2	K10
1b (CHARMS)		
Psychosis Trait Vulnerability	1st degree relative with psychosis *and* SOFAS < 50 in the last 12 months *or* SOFAS 30% below past level	Family risk SOFAS
Psychosis Trait Vulnerability	Schizotypal personality *and* SOFAS < 50 in the last 12 months *or* SOFAS 30% below past level	SCID II SOFAS
Bipolar Trait Vulnerability	Depressed mood or diminished interest or pleasure for at least 1 week as well as 2 additional criteria of depression: • weight loss, • sleep disorder, • psychomotor disturbances, • loss of energy, • feelings of worthlessness or guilt, • diminished ability to think or concentrate or indecisiveness, • suicidality *And* mood swings for at least 6 months in the lifetime (not symptom-free for a longer time period than 2 months consecutively) and at least 3 symptoms: • decreased need for sleep, • increased energy, • inflated self-esteem or grandiosity, • increase in goal-directed activity, • restlessness, • increased talkativeness, • unusual ideas, • risky behaviour, • inappropriate humour (does not have to equal loss of function!) *Or* 1st degree relative with bipolar disorder	SCID-5 Family risk
Attenuated Psychotic Symptoms	CAARMS global rating 3-6 *and* frequency of 3-6 on the subscales: • unusual thought content, • non bizarre ideas, • perceptual abnormalities, • disorganised speech *Or:* global rating score of 6 *and* frequency of 3 on the subscales: • unusual thought content, • non bizarre ideas, • perceptual abnormalities, • disorganised speech	CAARMS
Attenuated Hypomanic Symptoms	Elevated, expansive or unusually irritable mood on at least 2 consecutive days *and* 2 (or in case of only irritable mood 3) additional criteria: • inflated self-esteem or grandiosity, • decreased need for sleep, • increased talkativeness, • flight of ideas or subjective experience that thoughts are racing, • distractibility, • increase in goal-directed activity or psychomotor agitation, • unusual ideas,	SCID-5

	• increased involvement in activities, that are pleasurable in short-time but have a high potential for long-term damage for a duration of max. 3 days, if 3 or more (or in case of only irritable mood 4 or more) additional criteria are met *and* there are functional disturbances *or* others notice the mood or functional disturbances for a duration of max. 6 days, if 3 or more (or in case of only irritable mood 4 or more) additional criteria are met *or* there are functional disturbances or others notice the mood or functional disturbances Exclusion: hospitalization, severe impairment in social or professional functioning, no psychotic elements	
Moderate (attenuated) depression	SKID: mild or moderate depression (current or lifetime) At least 1 cardinal symptom, 5 additional symptoms *And* HAM-D > 17 (cut-off)	SCID-5 HAM-D
BLIPS	Global rating of 6 on the subscales • unusual thought content • non bizarre ideas Global rating of 5 or 6 on the subscale perceptual abnormalities *And/or* global rating of 6 on the subscale disorganised speech present for less than a week *And* frequency: 4 - 6 on all above-named scales	CAARMS
Anxiety	SKID: mild - moderate panic disorder/agoraphobia (current or lifetime) *or* SKID: not meeting criteria for GAS[i], i.e., symptoms for less than 6 months or less than 4 symptoms met <u>or</u> Diagnosis of a mild -moderate social phobia (current or lifetime) *And* HAM-A > 9 (cut-off)	SCID-5 HAM-A
2 (first treated episode)		
	Psychosis	CAARMS
	Severe major depression (current or lifetime)	SCID-5
	Mania/Hypomania	SCID-5
	Severe anxiety disorder (current or lifetime) e.g. agoraphobia, GAS	SCID-5

Note. K10=Kessler Distress Scale (Kessler et al., 2002). CHARMS=Clinical High At-Risk Mental State (Hartmann et al., 2019). SOFAS=Social and Occupational Functioning Assessment Scale (Goldman et al., 1992). SCID-5=Structured Clinical Interview for DSM-5 (First, Williams, Karg, & Spitzer, 2015). CAARMS=Comprehensive Assessment of At-Risk Mental State (Yung et al., 2005). HAM-D=Hamilton Depression Rating Scale (M. Hamilton, 1960). BLIPS=Brief Limited Intermittent Psychotic Symptoms. HAM-A=Hamilton Anxiety Rating Scale (M. Hamilton, 1959). GAD=Generalised Anxiety Disorder.

In deviation to the clinical staging model proposed by Hartmann et al. (2019), we did not include participants from attenuated symptoms (stage 1b) or a first treated episode of borderline personality disorder. We added participants with stage 1b or stage 2 of anxiety disorders. In addition, we used a different clinician rated instrument to assess attenuated depression.

Supplementary material 25: Correlation table

Table S58. *Correlation table.*

	Clinical stage	Age	Gender	Minority status	K10	BSI	SOFAS	Momentary SC	Overall SC	Adaptive emotion regulation	Maladaptive emotion regulation	Training frequency	WAI-P	WAI-T
Clinical stage	1.00													
Age	0.00	1.00												
	p=.988													
Gender	0.18	-0.04	1.00											
	p=.244	*p=.778*												
Minority status	0.17	0.01	0.07	1.00										
	p=.097	*p=.935*	*p=.633*											
K10	0.38	-0.16	0.21	0.07	1.00									
	p=.009	*p=.293*	*p=.159*	*p=.655*										
BSI	0.14	-0.23	0.07	-0.13	0.77	1.00								
	p=.356	*p=.117*	*p=.634*	*p=.377*	*P<.001*									
SOFAS	-0.39	-0.06	-0.01	-0.15	-0.37	-0.17	1.00							
	p=.008	*p=.693*	*p=.943*	*p=.312*	*p=.011*	*p=.271*								
Momentary SC	-0.36	0.06	-0.24	-0.13	-0.51	-0.43	0.40	1.00						
	p=.015	*p=.681*	*p=.106*	*p=.390*	*P<.001*	*p=.002*	*p=.006*							
Overall SC	0.04	0.11	-0.12	-0.01	0.22	0.21	-0.13	-0.06	1.00					
	p=.808	*p=.457*	*p=.421*	*p=.958*	*p=.155*	*p=.173*	*p=.397*	*p=.700*						
Adaptive emotion regulation	-0.25	0.42	-0.10	0.03	-0.07	0.02	0.09	0.25	0.30	1.00				
	p=.091	*p=.004*	*p=.506*	*p=.831*	*p=.641*	*p=.899*	*p=.578*	*p=.099*	*p=.047*					
Maladaptive emotion regulation	0.06	-0.06	0.02	0.09	0.33	0.09	-0.12	0.03	0.46	-0.04	1.00			
	p=.718	*p=.681*	*p=.886*	*p=.553*	*p=.027*	*p=.578*	*p=.427*	*p=.831*	*p=.002*	*p=.768*				
Training frequency	-0.03	0.06	-0.13	-0.12	0.04	0.00	-0.03	-0.22	0.14	-0.13	0.17	1.00		
	p=.864	*p=.680*	*p=.384*	*p=.432*	*p=.819*	*p=.993*	*p=.847*	*p=.145*	*p=.378*	*p=.385*	*p=.263*			

WAI-P	0.27	0.07	0.09	0.14	0.40	0.28	-0.16	-0.24	-0.03	-0.07	0.16	0.08	1.00	
	$p=.078$	$p=.667$	$p=.556$	$p=.368$	$p=.007$	$p=.069$	$p=.290$	$p=.111$	$p=.838$	$p=.652$	$p=.293$	$p=.622$		
WAI-T	0.14	0.06	0.25	0.18	0.07	-0.08	0.10	-0.10	-0.24	-0.15	0.06	0.13	0.46	1.00
	$p=.385$	$p=.695$	$p=.102$	$p=.257$	$p=.673$	$p=.606$	$p=.522$	$p=.505$	$p=.123$	$p=.351$	$p=.702$	$p=.420$	$p=.002$	

Note. K10=Psychological distress at baseline (Kessler et al., 2002). BSI=General psychopathology at baseline (Derogatis & Fitzpatrick, 2004). SOFAS=Level of functioning at baseline (Goldman et al., 1992). SC=Self-compassion at baseline, assessed with ESM and the Self-Compassion Scale (Hupfeld & Ruffieux, 2011; Neff, 2003). WAI-P=Patient ratings of working alliance (Horvath & Greenberg, 1989). WAI-T=Therapist ratings of working alliance (Horvath & Greenberg, 1989).

Supplementary material 26: Variance inflation factors and tolerance

Table S59. *Variance inflation factors/tolerance for the results displayed in table 20.*

	Putative mechanisms and processes of change							
	Change in overall self-rated self-compassion		Change in momentary self-compassion		Change in adaptive emotion regulation		Change in maladaptive emotion regulation	
	VIF	*Tolerance*	*VIF*	*Tolerance*	*VIF*	*Tolerance*	*VIF*	*Tolerance*
Age	1.09	0.92	1.11	0.90	1.09	0.92	1.09	0.92
Gender	1.22	0.82	1.16	0.86	1.22	0.82	1.22	0.82
Ethnic minority status	1.07	0.94	1.12	0.89	1.07	0.94	1.07	0.94
Clinical stage								
stage 1b	1.11	0.90	1.15	0.87	1.11	0.90	1.11	0.90
stage 2	1.44	0.69	1.48	0.67	1.44	0.69	1.44	0.69
Psychological distress	3.35	0.30	3.33	0.30	3.35	0.30	3.35	0.30
General psychopathology	2.96	0.34	2.92	0.34	2.96	0.34	2.96	0.34
Level of functioning	1.26	0.79	1.33	0.75	1.26	0.79	1.26	0.79

Note. VIF=Variance Inflation Factor. Stage 1a was used as a reference group. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002). General psychopathology assessed with the Brief Symptom Inventory (Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Social and Occupational Functioning Assessment Scale (Goldman et al., 1992).

Table S60. *Variance inflation factors/tolerance for the results displayed in table 21.*

	Putative mechanisms and processes of change					
	Working alliance – participant rating		Working alliance – therapist rating		Training frequency	
	VIF	*Tolerance*	*VIF*	*Tolerance*	*VIF*	*Tolerance*
Age	1.10	0.91	1.11	0.90	1.14	0.87
Gender	1.23	0.81	1.17	0.86	1.18	0.84
Ethnic minority status	1.08	0.92	1.09	0.92	1.15	0.87
Clinical stage						
stage 1b	1.17	0.86	1.16	0.86	1.15	0.87
stage 2	1.79	0.56	1.65	0.61	1.42	0.70
Psychological distress	3.90	0.26	3.50	0.29	3.30	0.30
General psychopathology	3.26	0.31	3.06	0.33	3.04	0.33
Level of functioning	1.34	0.74	1.33	0.75	1.26	0.80

Note. VIF=Variance Inflation Factor. Stage 1a was used as a reference group. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002). General psychopathology assessed with the Brief Symptom Inventory (Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Social and Occupational Functioning Assessment Scale (Goldman et al., 1992).

Table S61. *Variance inflation factors/tolerance for the results displayed in tables 22 and 23.*

	Psychological distress		General psychopathology	
	VIF	*Tolerance*	*VIF*	*Tolerance*
Time	1.00	1.00	1.00	1.00
Age	1.45	0.69	1.45	0.69
Gender	1.19	0.84	1.19	0.84
Ethnic minority status	1.28	0.78	1.28	0.78
Clinical stage	1.37	0.73	1.37	0.73
General psychopathology at baseline	4.45	0.22	4.45	0.22
Level of functioning at baseline	1.38	0.72	1.38	0.72
Overall self-rated self-compassion at baseline	2.01	0.50	2.01	0.50
Momentary self-compassion at baseline	1.89	0.53	1.89	0.53
Adaptive emotion regulation at baseline	1.80	0.56	1.80	0.56
Maladaptive emotion regulation at baseline	2.19	0.46	2.19	0.46

Note. VIF=Variance Inflation Factor. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002). General psychopathology assessed with the Brief Symptom Inventory (Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Social and Occupational Functioning Assessment Scale (Goldman et al., 1992). Self-compassion assesses with the experience sampling method and the Self-Compassion Scale (Hupfeld & Ruffieux, 2011; Neff, 2003). Emotion regulation assessed with the Cognitive Emotion Regulation Questionnaire (Garnefski & Kraaij, 2006; Garnefski et al., 2002).

Supplementary material 27: Cross differences

Method

I computed cross differences to compare developments in psychological distress and general psychopathology from post-intervention to follow-up for different levels of baseline characteristics. Cross differences can be understood as the difference of differences (Puhani, 2012).

Results

Table S62 displays the cross differences for psychological distress and general psychopathology.

Table S62. *Cross differences.*

	Cross differences in psychological distress	Cross differences in general psychopathology
Age		
Low vs. high	2.82	0.10
Gender		
Female vs. male	-4.94	-3.81
Ethnic minority status		
White majority vs. minority	-2.99	3.01
Clinical stage		
Stage 1a vs. stage 1b	0.04	-1.94
Stage 1a vs. stage 2	2.38	-0.70
General psychopathology at baseline		
Low vs. high	6.71	-
Psychological distress at baseline		
Low vs. high	-	-4.10
Level of functioning at baseline		
Low vs. high	2.66	4.67
Overall self-rated self-compassion at baseline		
Low vs. high	2.06	6.96
Momentary self-compassion at baseline		
Low vs. high	4.12	7.14
Adaptive emotion regulation at baseline		
Low vs. high	-1.66	-7.59
Maladaptive emotion regulation at baseline		
Low vs. high	4.16	0.52

Note. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002). General psychopathology assessed with the Brief Symptom Inventory (Derogatis & Fitzpatrick, 2004). Level of functioning assessed with the Social and Occupational Functioning Assessment Scale (Goldman et al., 1992). Self-compassion assesses with the experience sampling method and the Self-Compassion Scale (Hupfeld & Ruffieux, 2011; Neff, 2003). Emotion regulation assessed with the Cognitive Emotion Regulation Questionnaire (Garnefski & Kraaij, 2006; Garnefski et al., 2002).

Psychological distress

Comparing post-intervention and follow-up assessments of psychological distress, we observed positive cross differences for younger vs. older participants and negative cross differences for females vs. males and majority vs. minority participants. This descriptively indicates that being older, male and from an ethnic minority group was associated with more positive developments from post-intervention to follow-up. Regarding clinical characteristics, we observed positive cross differences for stage 1a vs. stage 2 participants und low vs. high general psychopathology. Descriptively, this indicates a less severe clinical stage and lower level of general psychopathology were associated with more positive developments from post-intervention to follow-up. For level of functioning, however, we observed opposing cross differences, suggesting that a lower level of functioning was associated with more positive developments from post-intervention to follow-up. In addition, we observed positive cross differences for baseline levels of self-compassion and maladaptive emotion regulation and a negative cross difference for adaptive emotion regulation. This descriptively indicates that low overall and momentary self-compassion, low levels of maladaptive and high levels of adaptive emotion regulation associated with more positive developments from post-intervention to follow-up.

General psychopathology

Comparing post-intervention and follow-up assessments of, we observed a negative cross difference for gender, a positive cross difference for ethnic minority status and no large values for age. This descriptively indicates that developments between post-intervention and follow-up did not differ between older and younger participants, whereas being male and from the ethnic majority was associated with more positive developments from post-intervention to follow-up. For clinical characteristics, we descriptively observed more positive developments from post-intervention to follow-up for participants from stage 1b vs. stage 1a and stage 2 vs. 1a, participants with higher level of psychological distress at baseline, and lower levels of functioning. In addition, we observed positive cross differences for baseline levels of self-compassion and maladaptive emotion regulation and a negative cross difference for adaptive emotion regulation. This descriptively indicates that low overall and momentary self-compassion, low levels of maladaptive and high levels of adaptive emotion regulation associated with more positive developments from post-intervention to follow-up.

Supplementary material 28: Sensitivity analyses controlled for group status

Table S63 shows the main effects of putative mechanisms and processes of change and time on psychological distress whilst controlling for sociodemographic characteristics (age, gender, ethnic minority status) and clinical stage. Consistent with the main analyses, there was evidence for an association of greater differences in adaptive emotion regulation after the intervention with lower psychological distress (b=-1.09, 95% CI -1.90 – -0.35).

Main effects of effects of putative mechanisms and processes of change and time on general psychopathology whilst controlling for sociodemographic characteristics (age, gender, ethnic minority status) and clinical stage are displayed in Table S64. In line with findings from the main analyses, there was evidence for an association of general psychopathology with change in adaptive emotion regulation such that greater differences in emotion regulation after the intervention were associated with lower general psychopathology (b=-2.59, 95% CI -3.75 – -1.44). There was no evidence of initial signals of associations of general psychopathology with overall self-rated and momentary self-compassion, maladaptive emotion regulation, training frequency or working alliance in the sensitivity analyses.

Table S65 shows findings on total, direct, and indirect effects of experimental condition and change in self-compassion and change in emotion regulation on psychological distress and general psychopathology at four-week follow-up. There was no evidence for signals of indirect effects via pathways through change in self-compassion or change in emotion regulation. Consistent with the main analyses, I observed associations of change in momentary self-compassion with psychological distress (β=-0.27, 95% CI -0.50 – -0.08) and general psychopathology (β=-0.28, 95% CI -0.48 – -0.08). In addition, I observed an association of change adaptive emotion regulation with psychological distress (β=-0.33, 95 %CI -0.52 – -0.12) and general psychopathology (β=-0.33, 95% CI=-0.54 – -0.11).

Table S63. *Psychological distress predicted by putative mechanisms and processes of change (controlled for clinical stage).*

	Post-intervention		Follow-Up			
	Marginal mean (95% CI)	SE	Marginal mean (95% CI)	SE	b (95% CI)	Effect size
Change in overall self-rated self-compassion					-0.19 (-0.50 – 0.29)	-0.03
Time					-1.38 (-3.08 – -0.04)	-0.23
Low change in overall self-rated self-compassion	24.57 (22.11 – 27.02)	1.25	23.52 (21.04 – 26.00)	1.26		
Mean change in overall self-rated self-compassion	23.74 (22.47 – 25.00)	0.65	22.65 (21.37 – 23.93)	0.65		
High change in overall self-rated self-compassion	22.91 (20.75 – 25.07)	1.10	21.77 (19.61 – 23.94)	1.10		
Change in momentary self-compassion					-1.12 (-2.54 – 0.49)	-0.19
Time					-0.89 (-2.47 – 0.63)	-0.15
Low change in momentary self-compassion	24.69 (22.96 – 26.42)	0.88	24.45 (22.70 – 26.20)	0.89		
Mean change in momentary self-compassion	23.72 (22.53 – 24.92)	0.61	22.47 (21.26 – 23.68)	0.62		
High change in momentary self-compassion	22.76 (21.02 – 24.49)	0.89	20.49 (18.75 – 22.24)	0.89		
Change in adaptive emotion regulation at baseline					-1.09 (-1.90 – -0.35)	-0.18
Time					-1.09 (-2.61 – 0.43)	-0.18
Low change in adaptive emotion regulation	25.02 (23.25 – 26.79)	0.90	24.53 (22.75 – 26.30)	0.91		
Mean change in adaptive emotion regulation	23.66 (22.45 – 24.87)	0.62	22.55 (21.33 – 23.78)	0.62		
High change in adaptive emotion regulation	22.30 (20.53 – 24.08)	0.90	20.58 (18.80 – 22.36)	0.91		
Change in maladaptive emotion regulation at baseline					0.69 (-0.04 – 1.67)	0.11
Time					-1.19 (-2.92 – 0.15)	-0.20
Low change in maladaptive emotion regulation	22.73 (20.95 - 24.51)	0.91	21.88 (20.08 – 23.68)	0.92		
Mean change in maladaptive emotion regulation	23.66 (22.41 – 24.91)	0.64	22.56 (21.31 – 23.82)	0.64		
High change in maladaptive emotion regulation	24.59 (22.81 – 26.36)	0.91	23.24 (21.44 – 25.05)	0.92		
Training frequency					0.01 (-0.04 – 0.05)	0.00
Time					-0.66 (-6.07 – 5.00)	-0.11
Low training frequency	23.33 (20.64 – 26.01)	1.37	22.90 (20.21 – 25.59)	1.37		
Mean training frequency	24.04 (22.19 – 25.89)	0.94	22.68 (20.83 – 24.53)	0.94		
High training frequency	24.76 (22.08 – 27.44)	1.37	22.46 (19.79 – 25.14)	1.37		
Working alliance – participant ratings					0.09 (-0.18 – 0.30)	0.01
Time					1.94 (-16.32 – 14.43)	0.32
Low working alliance	23.28 (20.49 – 26.06)	1.42	22.49 (19.70 – (25.27)	1.42		
Mean working alliance	24.05 (22.20 – 25.89)	0.94	22.68 (20.83 – 24.53)	0.94		
High working alliance	24.81 (22.03 – 27.60)	1.42	22.88 (20.09 – 25.67)	1.42		

					0.17 (-0.05 – 0.39)	0.03
Working alliance – psychologist ratings						
Time					10.85 (-4.17 – 25.67)	1.81
Low working alliance	22.63 (20.01 – 25.25)	1.34	23.40 (20.78 – 25.02)	1.34		
Mean working alliance	23.70 (21.91 – 25.49)	0.91	22.86 (21.07 – 24.65)	0.91		
High working alliance	24.76 (22.14 – 27.39)	1.34	22.32 (19.70 – 24.94)	1.34		

Note. Continuous variables z-standardised (M=0, SD=1). Adjusted for age, gender, ethnic minority status, and baseline levels of psychological distress, and clinical stage. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002). Self-compassion assesses with the experience sampling method and the Self-Compassion Scale (Hupfeld & Ruffieux, 2011; Neff, 2003). Emotion regulation assessed with the Cognitive Emotion Regulation Questionnaire (Garnefski & Kraaij, 2006; Garnefski et al., 2002). Working alliance assessed with the Working Alliance Inventory (Horvath & Greenberg, 1989).

Table S64. *General psychopathology predicted by putative mechanisms and processes of change (controlled for clinical stage).*

	Post-intervention		Follow-Up			
	Marginal mean (95% CI)	*SE*	Marginal mean (95% CI)	*SE*	*b* (95% CI)	Effect size
Change in overall self-rated self-compassion					-0.24 (-0.63 – 0.35)	-0.03
Time					-1.48 (-3.75 – 0.57)	-0.16
Low change in overall self-rated self-compassion	17.69 (13.76 – 21.61)	2.00	16.39 (12.44 – 20.34)	2.02		
Mean change in overall self-rated self-compassion	17.20 (15.18 – 19.21)	1.03	15.90 (13.87 – 17.93)	1.04		
High change in overall self-rated self-compassion	16.71 (13.25 – 20.16)	1.76	15.40 (11.95 – 18.85)	1.76		
Change in momentary self-compassion					-1.55 (-3.53 – 0.62)	-0.16
Time					-0.87 (-3.13 – 1.26)	-0.09
Low change in momentary self-compassion	18.83 (16.02 – 21.63)	1.43	19.11 (16.28 – 21.93)	1.44		
Mean change in momentary self-compassion	17.48 (15.55 – 19.42)	0.99	15.71 (13.76 – 17.66)	1.00		
High change in momentary self-compassion	16.14 (13.33 – 18.95)	1.44	12.31 (9.49 – 15.13)	1.44		
Change in adaptive emotion regulation at baseline					-2.59 (-3.75 – -1.44)	-0.27
Time					-1.22 (-3.75 – 0.84)	-0.13
Low change in adaptive emotion regulation	20.36 (17.61 – 23.12)	1.40	19.34 (16.58 – 22.10)	1.41		
Mean change in adaptive emotion regulation	17.15 (15.27 – 19.02)	0.96	15.83 (13.94 – 17.72)	0.96		
High change in adaptive emotion regulation	13.93 (11.17 – 16.69)	1.41	12.32 (9.56 – 15.09)	1.41		
Change in maladaptive emotion regulation at baseline					0.61 (-0.52 – 2.20)	0.06
Time					-1.34 (-3.36 – 0.97)	-0.14
Low change in maladaptive emotion regulation	16.32 (13.47 – 19.17)	1.45	15.63 (12.76 – 18.51)	1.47		
Mean change in maladaptive emotion regulation	17.15 (15.16 – 19.14)	1.02	15.85 (13.84 – 17.85)	1.02		
High change in maladaptive emotion regulation	17.98 (15.14 – 20.82)	1.45	16.06 (13.19 – 18.93)	1.47		
Training frequency					0.01 (-0.10 – 0.08)	0.00
Time					-1.57 (-8.40 – 5.77)	-0.17
Low training frequency	17.11 (12.65 – 21.56)	2.27	15.76 (11.31 – 20.22)	2.27		
Mean training frequency	18.06 (15.00 – 21.13)	1.56	16.27 (13.21 – 19.33)	1.56		
High training frequency	19.02 (14.59 – 23.46)	2.26	16.78 (12.34 – 21.21)	2.26		

Working alliance – participant ratings						0.07 (-0.19 – 0.38)	0.01
Time						6.17 (-11.66 – 28.88)	0.65
Low working alliance	18.28 (13.72 – 22.83)	2.32	17.86 (13.31 – 22.42)	2.32			
Mean working alliance	18.07 (14.96 – 21.18)	1.59	16.27 (13.16 – 19.38)	1.59			
High working alliance	17.86 (13.30 – 22.41)	2.32	14.68 (10.13 – 19.24)	2.32			
Working alliance – psychologist ratings						0.00 (-0.38 – 0.35)	0.00
Time						0.49 (-20.81 – 29.48)	0.05
Low working alliance	17.57 (13.14 – 21.99)	2.26	16.67 (12.24 – 21.10)	2.26			
Mean working alliance	17.56 (14.54 – 20.57)	1.54	16.44 (13.43 – 19.46)	1.54			
High working alliance	17.55 (13.12 – 21.98)	2.26	16.21 (11.79 – 20.64)	2.26			

Note. Continuous variables z-standardised (M=0, SD=1). Adjusted for age, gender, ethnic minority status, baseline level of general psychopathology, and clinical stage. General psychopathology assessed with the Brief Symptom Inventory (Derogatis & Fitzpatrick, 2004). Self-compassion assesses with the experience sampling method and the Self-Compassion Scale (Hupfeld & Ruffieux, 2011; Neff, 2003). Emotion regulation assessed with the Cognitive Emotion Regulation Questionnaire (Garnefski & Kraaij, 2006; Garnefski et al., 2002). Working alliance assessed with the Working Alliance Inventory (Horvath & Greenberg, 1989).

Table S65. The *indirect effects of experimental condition on psychological distress, and general psychopathology at 4-week follow-up via pathways through change in self-compassion and emotion regulation (controlled for clinical stage).*

	Psychological distress			General psychopathology		
	β	95% CI	P_M	β	95% CI	P_M
Pathways through change in overall self-rated self-compassion						
Total effect	-0.04	-0.45 – 0.33		-0.06	-0.46 – 0.36	
Direct effect of condition on outcome	-0.06	-0.51 – 0.33		-0.06	-0.48 – 0.36	
Effect of condition on mediator	-0.08	-0.38 – 0.19		-0.07	-0.39 – 0.20	
Effect of mediator on outcome	-0.16	-0.39 – 0.24		-0.08	-0.32 – 0.31	
Indirect effect	0.01	-0.03 – 0.14	0.25	0.01	-0.03 – 0.10	0.17
Pathways through change in self-compassion in daily life						
Total effect	0.00	-0.38 – 0.41		-0.05	-0.43 – 0.35	
Direct effect of condition on outcome	0.03	-0.34 – 0.43		-0.01	-0.40 – 0.37	
Effect of condition on mediator	0.13	-0.29 – 0.52		0.13	-0.28– 0.57	
Effect of mediator on outcome	-0.27	-0.50 – -0.08		-0.28	-0.48 – -0.08	
Indirect effect	-0.03	-0.19 – 0.06	-	-0.04	-0.21 – 0.08	0.80
Pathways through change in adaptive emotion regulation						
Total effect	-0.04	-0.42 – 0.37		-0.05	-0.42 – 0.37	
Direct effect of condition on outcome	-0.08	-0.43 – 0.31		-0.08	-0.41 – 0.32	
Effect of condition on mediator	-0.09	-0.56 – 0.34		-0.09	-0.56 – 0.31	
Effect of mediator on outcome	-0.33	-0.52 – -0.12		-0.33	-0.54 – 0.11	
Indirect effect	0.03	-0.09 – 0.25	0.75	0.03	-0.10 – 0.23	0.60
Pathways through change in maladaptive emotion regulation						
Total effect	-0.04	-0.42 – 0.37		-0.06	-0.44 – 0.36	
Direct effect of condition on outcome	-0.03	-0.40 – 0.39		0.06	-0.41 – 0.36	
Effect of condition on mediator	-0.17	-0.66 – 0.27		-0.17	-0.62 – 0.27	
Effect of mediator on outcome	0.10	-0.08 – 0.32		0.02	-0.18 – 0.22	
Indirect effect	-0.02	-0.17 – 0.01	0.50	0.00	-0.12 – 0.03	0.00

Note. Continuous variables z-standardised (*M*=0, *SD*=1). Adjusted for age, gender, ethnic minority status, baseline levels of outcomes, and clinical stage. Psychological distress assessed with the Kessler Psychological Distress Scale (Kessler et al., 2002). General psychopathology assessed with the Brief Symptom Inventory (Derogatis & Fitzpatrick, 2004). P_M=proportion mediated. For pathways through change in self-compassion in daily life, no proportion mediated could be computed as the total effect was 0.00. Self-compassion assesses with the experience sampling method and the Self-Compassion Scale (Hupfeld & Ruffieux, 2011; Neff, 2003). Emotion regulation assessed with the Cognitive Emotion Regulation Questionnaire (Garnefski & Kraaij, 2006; Garnefski et al., 2002).

Supplementary material 29: Topic guide – expert focus group

(Introductory) Thank you for taking the time to participate in this focus group to help us explore how the EMIcompass intervention works. Our main goal is to develop one or more theories about how exactly EMIcompass works, for whom, and under what circumstances. To do this, I will ask you a few questions.

1. Outcomes

- What changes should EMIcompass produce in participants?
- What are appropriate outcomes for EMIcompass intervention participants?

2. Context

(Introductory) There are different ideas about how, for whom, and in what circumstances our intervention works. The context includes material resources and social structures such as conventions, rules, and systems.

- What individual contextual variables do you think might help participants benefit from EMIcompass?
    - Do you see an association between certain contexts and certain outcomes? (...) If so, between which ones?
    - Are there characteristics of participants that might help in achieving the outcomes you mentioned? (If yes, which ones and how exactly?) (Collect).
- Could external factors in participants' lives also influence the intervention process in some way or interact with other impact factors? If so, which ones and how exactly?
- If not mentioned: For example, could personality variables, needs, or attitudes contribute?
- If not mentioned: In your view, what role does the study psychologist play in achieving the desired outcomes? Are there characteristics or attitudes that might be conducive to this on the part of the therapist?

3. Mechanisms

General:

- In your view, what elements of the intervention itself contribute decisively to the desired outcomes?

Content of the intervention:

- How can EMIcompass influence how participants deal with their difficulties? (Collect).
- What content of the CFT do you find beneficial here and why?

→ Address different strategies or groups of strategies provided in the intervention (e.g. positive imagery, breathing exercises)

Presentation of the intervention:

- Aside from the specific content of the app such as the exercises, do you think the presentation format may influence participants' outcomes?
- If yes. What elements of the presentation as an Ecological Momentary Intervention/ the hybrid format do you think have an impact on the outcomes?

→ **Besides what we've already discussed, is there anything we should know to understand how EMIcompass works?**

Supplementary material 30: Topic guide – participant interviews

(Introductory) Thank you for taking the time to do this interview. We are interested in learning what exactly about the EMIcompass intervention might be helpful to our participants. Therefore, I would like to ask you a few questions today (address how the interview will proceed).

1. Outcomes

- What do you see as the goal of your participation in the EMIcompass study?
- Do you think you came closer to achieving this goal by participating in EMIcompass?
- What changes in your everyday life have you experienced since participating in the study?
  - o For example, in the way you treat yourself, cope with stressful situations, your perspective on difficulties, symptoms, sense of well-being, …
- Have people around you (friends, family etc.) noticed changes in you since you started participating in EMIcompass?

2. Context

- Do you have any idea what might have influenced the outcome of EMIcompass for you?
- What factors played a role in you being able to achieve goal XX/ change XX?
  - o Did any of your personal characteristics play a role in goal XX?
  - o Did your personal situation play a role?
  - o Your personality, what you are like as a person?
  - o Previous experiences/ what you have been through in life so far?
- Do you think you would have had different outcomes from participating at a different time in your life?
  - o Why/what was different (e.g. better or worse)?
  - o Can you tell me what made you x (more open or similar)?
- Do you think others might have the same results if they participated in EMIcompass?
- How did you experience the reaction of people around you (e.g. family and friends) when you participated in EMIcompass? Did this influence your participation?

3. Mechanisms

The EMIcompass intervention consisted of different parts. You attended sessions with the study psychologist and you used the smartphone to learn new exercises and practice the previously acquired techniques.

Let's start with the sessions.

- Were the sessions helpful to achieve "goal XX"?
    - o If so, what exactly did you find helpful about them?
    - o What did you take home from the sessions and how did that come about?

Additionally, you learned about certain exercises and strategies in the study.

- Do you feel that the exercises (or maybe just one in particular?) helped you achieve "Goal XX"?
    - o If so, how?
- Name strategies, participants were presented in the intervention. How did you feel the exercises was related to "goal XX"?
    - o What exactly did you find helpful about "exercise X"?
    - o What was helpful? Challenging or difficult?
    - o What does this do to you then?

One aspect of EMIcompass, in addition to the sessions and the specific content of the exercises, was, that you learned about the exercises via smartphone and practiced them autonomously.

- How did you experience that?
- Do you think that the app was supportive in achieving "goal XX"?
- How did you experience working out and practicing on your own?

If interactives on**:** In addition, you did have the option with the mood questionnaires activated, right? In this case, the smartphone sent mood questionnaires a few days a week and then offered you exercises if you were not feeling well or were in an unpleasant situation.

- How did you experience that?
- Did you find that this contributed to the achievement of "goal XX"?

You also received feedback once a week and had brief contact with the study team.

- How did you experience that? Did that have an impact? Was this helpful in any way?
- If so, can you describe how that was helpful?

→ **What do you think we, the research team, would need to know to understand how EMIcompass worked for you? Something I may not have asked about yet?**

Supplementary material 31: Topic guide – revised participant interviews

(Introductory) Thank you for taking the time to do this interview. We are interested in learning what exactly about the EMIcompass intervention might be helpful for participants. Therefore, I would like to ask you a few questions today (address how the interview will proceed).

💡 "zooming in": What is it about X that helps? Insight into thought processes "let's look at such a thought process in a stressful situation, how and what exactly are you thinking in those moments?"

💡 Focus more on exploring the connection between mechanisms and outcomes.

We have already conducted a few interviews with other participants and have been able to develop a rough idea of what about EMIcompass worked, how, for whom, and under what circumstances. In the interview with you today, I want to check if we understood things correctly. However, it may also be that you see something completely different than other participants - that is also really interesting for us and we are grateful to hear that. Please keep an open mind, I welcome your feedback.

1. Outcomes

- What do you see as the goal of your participation in the EMIcompass study?
- Do you feel you have come closer to achieving this goal by participating in EMIcompass?
- We have heard A, B, C from other participants so far. In your opinion, would you say this also fits with what you have experienced? Is there any important aspect missing?
    - o Increase in well-being
    - o More understanding/knowledge
    - o Increase self-compassion
    - o Increase mindfulness
    - o New perspective
- What changes in your daily life have you experienced since participating in the study?
    - o In how you treat yourself, cope with stressful situations, your perspective on things, symptoms, well-being, ...
    - o How would you describe your approach to yourself before study participation (= pre-intervention self-compassion).
    - o How would you describe the way you deal with yourself after study participation? (= post-intervention self-compassion)

- o If different: How did this change occur?
- Do you feel you can cope with unpleasant situations, or do you often feel helpless and powerless? Has this feeling changed since the beginning of the study? If yes: how did the change occur? (→ explore potential change in self-efficacy further)

2. Context

I would now like to go into a little more detail about the factors that influenced the outcome of the study for you. I have already been able to conduct a few interviews with participants and various factors have been mentioned very frequently, so I would like to hear your opinion on those factors.

But: note that alternative explanations/opinions are also important and significant "All opinions are significant and provide important insights."

Active reflection part (explicit hypothesis testing)**:**
- Personality (esp. openness, determined, etc.) increases commitment/ positive outcomes
- Interest in topic increases willingness/motivation to achieve positive results
- Positive attitude towards study/meditation exercises increases commitment/ positive results
- Positive previous experience (yoga, meditation etc.) increases commitment/ positive results
- Life situation (stressful situation/"difficult situation" increases commitment/willingness to change)
- Symptomatology
  - o I have now heard from some participants that because they were not doing so well at the time of the study, they were particularly motivated. But on the other hand, other participants have also reported that they think they would have practiced less if they had been too bad, because then they can't get up for anything...so we think that maybe the interventions are particularly helpful in a moderate-severe area...what do you think about that?
- How did you experience the reaction of those around you (e.g. family and friends) when you participated in EMIcompass? Did their reaction influence your participation?
- Technology: We have the idea that a certain closeness to technology is necessary for people to even consider participating in the study. Would you say that's true?

3. Mechanisms

The EMIcompass intervention consisted of different parts. You attended sessions with the study psychologist and you used the smartphone to learn new exercises and to practice those previously learned.

Let's maybe start with the sessions.

- First, in general; were the sessions helpful in achieving "goal XX"?

Again, I want to refer to the aspects that were mentioned very often in the interviews already conducted and would like to know if this also applies to you or if you have other aspects that helped you at the sessions. (Pointing out that other opinions are also very significant and relevant).

For each aspect, ask: what about it helped, how did it help?

- Psychoeducation/knowledge (better understanding about inner processes etc.)
- Positive atmosphere (CFT Spirit: security, trust)
- Positive bonding experience
- Self-opening/talking about problems
- Study psychologists (CFT Spirit; understanding, friendly, validating)
    - How did you feel about the contact with study psychologist? How would you describe the attitude of the study psychologist? (explore potential modelling of CFT principles)
    - What did it feel like for you to be treated in this way? What did that do to you?
    - Would you say that the way the study psychologist talked to you (if mentioned before: compassionate, understanding?) also made you x (more compassionate, understanding) with themselves? (explore potential taking over of CFT attitude)

Additionally, you learned about certain exercises and strategies in the study.

- Do you feel that the exercises (or maybe just one in particular?) helped you achieve "goal XX"? If so, how?

I would now like to go into the individual exercises and there again discuss with you what has come out so far in the interviews, what has helped about each exercise and of course get your opinion on it. Let's start with exercise X... (Highlight relevance of opposing views again) → for each exercise:

- Was it helpful? What was helpful? What was challenging or difficult? Wat did this do to you then?)

- Why or what exactly helps about the exercise, breathing, etc.? What did you get from using the strategy?

Active reflection, explicit hypotheses testing from information acquired from previous interviews:

- **Emotional compass**: Understanding/knowledge, increase Reflection
- **Breathing exercises:** Calming down, distancing from the situation leading to new perspective, relaxation
- **Soothing colour imagery:** Here we heard from many participants that they found it very challenging to focus on the colour if they succeeded, then also calming but by "pausing for a moment" rather than by exercise per se.
- **Calm and safe place:** Calming down, feeling of security, relaxation
- **Emotions as a wave**: Understanding/knowledge, new perspective on emotional states
- **Toolbox**: Overview of developed resources
- **Compassionate companion**: increased compassion, security (CFT Spirit), new perspective, calming down, enhancement of well-being
- **Compassionate self:** increased self-compassion, new Perspective, calming down
- **Compassionate message**: increased self-compassion, new perspective, calming down
  - How would you describe the attitudes and values of the intervention exercises if they were a person? (e.g. compassionate, accepting, understanding, etc.? (explore transfer self-compassion attitude via exercises).

One component of EMIcompass besides the sessions and the specific content of the exercises was, after all, that you learned about the exercises through your cell phone and practiced there on your own.

- We were told a lot that this independent work was found to be very pleasant, how do you see that?

Also go into the aspects that were mentioned a lot in earlier interviews:

- Reminder function
- Motivation function
- Free availability of the exercises
- But also: annoying/stressful?

If interactives on: You had additionally activated the option with the mood questionnaires, right? Here the smartphone sent mood questionnaires a few days a week and then offered you exercises when you were not feeling well or were in an unpleasant situation.

- How did you experience that?

- Did you find that this contributed to the achievement of "Goal XX"?

- We would have the idea here that....

    o Stress reduction through application in acute situation

    o Better handling of stressful situation

    o Emotion change (pre, post)

    o Mindfulness

We were told a lot that the weekly feedback was perceived as very positive (feeling connected, "people care about you" etc.)

- How do you see this?

- Did it have an impact on your participation? (Willingness to learn, etc.)

- Who would you say is responsible for your personal success in the study? You or the study therapist (in percent)? → explore self-efficacy

What do you think we, the research team, would need to know to understand how EMIcompass worked/was working for you? Something I may not have asked about yet?

Supplementary material 32: Further components of the programme

Between-session telephone or e-mail contact

Between the sessions, participants were contacted via telephone or e-mail once a week. This contact was used to provide feedback on compliance, to address questions and problems and to remind them of their next appointment. Participants appreciated this service, however most reported no impact. If a positive effect was reported, increased commitment to the intervention, increased focus on own needs and help to keep structure was mentioned. For some participants, receiving positive feedback led to higher motivation, others mostly benefitted from a feeling of connectedness and being cared for.

Gamification elements were perceived as a motivating factor by some participants.

> *Yes, I actually thought the score-system was quite good. I'm a gamer, so I always strive to get nice level-ups [...] because you think to yourself "if I do this, I'll get points, then I can even get level-ups" and something like that - that's a bit of an incentive. (EMI0097, 105)*

Structure provided by the intervention

Some participants reported a high need for external structure and therefore perceived the structure provided by the intervention (e.g. appointments, prompts on the study smartphone, etc.) as helpful and motivating.

> *As soon as I have to do things on my own, I find it harder and the cell phone has helped me a lot to stay on it and keep up with the exercises. (EMI0164, 232)*

> *Because I always knew that the next appointment would be in two weeks and that definitely helped me to motivate myself more, because then I knew that we would talk about it in two weeks. (EMI0125, 63)*

Daily prompts in the intervention period were perceived as reliable "fix points throughout the day" (EMI0134) that helped to structure everyday life and to engage with other tasks after completing the training task.

> *Again, due to the COVID pandemic, I'm somehow a bit stuck in my daily life, so somehow, sometimes I get up at eight, sometimes at ten, and somehow I had no rhythm at all. And I once again started to set up such a rhythm (EMI0122, 19)*

Then, I always ensured, that when I was procrastinating on something, I said 'okay, at 3pm I'll do my exercise and then after that the thing". So it was then few fix points on the day that I set myself through these exercises. (EMI0134, 25)

However, participants with a high need for autonomy or a very structured and busy everyday life with many obligations (e.g. meetings, lectures, etc.) expressed more critical thoughts about the structure provided in the intervention, mostly regarding the prompts on the smartphone.

I just think, if I had had a really tough learning phase and was sitting in the library all the time – even if that is not possible right now - I would definitely not do the exercises. Then somehow, so it's also not possible when you're on the road a lot, then you can't look at your cell phone all the time. (EMI0115, 41)

Guided self-help

Participants embraced the guided self-help character of the EMIcompass intervention and gained the feeling of empowerment, competence and self-efficacy by successfully applying the techniques acquired in the intervention.

I also feel like every time panic comes up, I can handle it better, because I use the exercise. (EMI0162, 15)

I can be more relaxed now, because I know that if something comes up, I'll deal with it - I'll be able to handle it. (EMI0162, 45)

It was highlighted that this was mainly attributed to the self-directed application of the strategies and the guided self-help character of the intervention.

The independent working was then primarily the trigger or the effect. (EMI0117, 125)

Some reported that the gradually made themselves independent from the guidance on the smartphone and were able to transfer the strategies into their daily life without external cues.

It was just nice, that I realised 'okay, I can also do without the cell phone'. (EMI0112, 227)

This may be further enhanced by context factors such as personality traits, for example being determined and goal-oriented, which the participants described as beneficial for self-directed training of strategies.

You should know that I am very determined and because I have set myself the goal of learning to deal better with myself and my emotions, I think it was quite easy for me. (EMI0125, 175)

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09/2022	**Center for Psychological Psychotherapy Mannheim**
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2018 - 2020	**Central Institute of Mental Health, Mannheim**
	- Clinical internships I & II, track for affective disorders

♦ Teaching experience

2021	**Central Institute of Mental Health, Mannheim**
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2020-2022	**Central Institute of Mental Health, Mannheim**
	- Supervision of interns (Bachelor and Master students) at the Department of Public Mental Health
2020 & 2021	**University of Applied Sciences Mannheim**
	- Guest lecturer in the seminar Digital Health

LIST OF PUBLICATIONS

Gayer-Anderson, C., Reininghaus, U., **Paetzold, I.**, Hubbard, K., Beards, S., Mondelli, V., ... & Morgan, C. (2020). A comparison between self-report and interviewer-rated retrospective reports of childhood abuse among individuals with first-episode psychosis and population-based controls. *Journal of Psychiatric Research, 123*, 145-150. doi: https://doi.org/10.1016/j.jpsychires.2020.02.002

Paetzold, I., Gugel, J., Schick, A., Kirtley, O. J., Achterhof, R., Hagemann, N., ... & Reininghaus, U. (2022). The role of threat anticipation in the development of psychopathology in adolescence: Findings from the SIGMA Study. *European Child & Adolescent Psychiatry,* 1-9. doi: https://doi.org/10.1007/s00787-022-02048-w

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Paetzold, I., Myin-Germeys, I., Schick, A., Nelson, B., Velthorst, E., Schirmbeck, F., ... & Reininghaus, U. (2021). Stress reactivity as a putative mechanism linking childhood trauma with clinical outcomes in individuals at ultra-high-risk for psychosis: Findings from the EU-GEI High Risk Study. *Epidemiology and Psychiatric Sciences, 30*, e40, 1–13. doi: https://doi.org/10.1017/ S2045796021000251

Paetzold I., Schick A., Rauschenberg C., Hirjak D., Banaschewski T., Meyer-Lindenberg A., … & Reininghaus U. (in preparation). Exploring the implementation of a novel, transdiagnostic, hybrid ecological momentary intervention for improving resilience in youth (EMIcompass): A realist evaluation.

Paetzold I., Schick A., Rauschenberg C., Hirjak D., Banaschewski T., Meyer-Lindenberg A., …& Reininghaus U. (under review). Exploring putative therapeutic mechanisms of change in a hybrid compassion-focused, ecological momentary intervention: Findings from the EMIcompass trial.

Paetzold, I., Schick, A., Rauschenberg, C., Hirjak, D., Banaschewski, T., Meyer-Lindenberg, A., ... & Reininghaus, U. (2022). A hybrid ecological momentary compassion–focused

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Rauschenberg, C., Schick, A., Hirjak, D., Seidler, A., **Paetzold, I.**, Apfelbacher, C., ... & Reininghaus, U. (2021). Evidence synthesis of digital interventions to mitigate the negative impact of the COVID-19 pandemic on public mental health: rapid meta-review. *Journal of Medical Internet Research, 23*(3), e23365. doi: https://doi.org/10.2196/23365

Reininghaus U.A., **Paetzold I.**, Rauschenberg C., Hirjak D., Banaschewski T., Meyer-Lindenberg A, … Schick, A. (under review). Effects of a Novel, Transdiagnostic, Hybrid Ecological Momentary Intervention for Improving Resilience in Youth (EMIcompass).

Schick, A., **Paetzold, I.**, Rauschenberg, C., Hirjak, D., Banaschewski, T., Meyer-Lindenberg, A., ... & Reininghaus, U. (2021). Effects of a novel, transdiagnostic, hybrid ecological momentary intervention for improving resilience in youth (EMIcompass): Protocol for an exploratory randomized controlled trial. *JMIR Research Protocols, 10*(12), e27462. doi: https://doi.org/10.2196/27462

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Zemp, M., **Paetzold, I.,** & Milek, A. (2021). The impact of interparental conflict on children's attention and memory performance. *Family Relations, 70*(2), 587-602. doi: https://doi.org/10.1111/fare.12481

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