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Ambulatory assessment of antecedents and consequences of non-suicidal self-injury

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# Preface

All three publications are based on a project funded by the "CIMH Young Investigator Award", awarded to Prof. (apl.) Dr. Inga Niedtfeld.

*Publication 1*: Salivary beta-endorphin in non-suicidal self-injury: an ambulatory assessment study (Chapter II). Conceptualization: Under supervision of I. Niedtfeld and A. Karabatsiakis, I conceptualized the study design (80%). I set up the methods of the study (e.g., study flow, recruitment of participants, collection of saliva samples, questionnaires, participant information, and consent) and programmed and tested the app for the assessment in daily life in Movisens XS (100%). Literature search: I did all relevant literature search for this publication (100%). Ethics approval: Under supervision of I. Niedtfeld, I wrote the ethics application (90%). Data collection: I performed recruitment and diagnostic interviews for all study participants and the administration (100%). Examination of study data: I analyzed the data of the study under supervision and with support of J. Hepp (70%). The analysis of the saliva samples was done by A. Karabatsiakis (with me supporting him in the laboratory, 10%). Interpretation of the data: Biological data were interpreted by A. Karabatsiakis. I interpreted the results of the multi-level models under supervision of I. Niedtfeld and J. Hepp (80%). Manuscript writing: I wrote the first draft of the paper manuscript (80%), and the co-authors were involved in editing of the manuscript text. Revision of the manuscript: I completed the main part of the revision for publication (90%), and the co-authors were involved in editing the revised manuscript. Tables and figures: I created all tables and figures of this publication (100%).

Publication 2: Does self-harm have the desired effect? Comparing non-suicidal selfinjury to high-urge moments in an ambulatory assessment design (Chapter III). *Conceptualization:* Under supervision of I. Niedtfeld, I conceptualized the study design (80%). I set up the methods of the study (e.g., study flow, recruitment of participants, questionnaires, participant information, and consent) and programmed and tested the app for the assessment in daily life in Movisens XS (100%). Additionally, I conducted a pilot study to evaluate the affect items (80%). Literature search: I did all relevant literature search for this publication (100%). Ethics approval: Under supervision of I. Niedtfeld, I wrote the ethics application (90%). Data collection: I performed recruitment and diagnostic of all study participants and the administration (100%). Examination of study data: I analyzed the data of the study under supervision and with support of J. Hepp (70%). Interpretation of the data: I interpreted the results of the multi-level models under supervision of I. Niedtfeld and J. Hepp (80%). Manuscript writing: I wrote the first draft of the manuscript (80%), and the co-authors were involved in *editing of the manuscript* text. *Revision of the manuscript*: I did the main part of the revision for publication (90%), and the co-authors were involved in editing the revised manuscript. Tables and figures: I created all tables and figures of this publication (100%).

*Publication 3*: A test of the interpersonal function of non-suicidal self-injury in daily life (Chapter IV). *Conceptualization:* Under supervision of I. Niedtfeld, I conceptualized the study design (80%). I set up the methods of the study (e.g., study flow, recruitment of participants, questionnaires, participant information, and consent) and programmed and tested the app for the assessment in daily life in Movisens XS (100%). Additionally, I conducted a pilot study to evaluate the presented set of interpersonal events (80%). *Literature search:* I was only marginally involved in the literature search of this publication (10%). *Ethics approval:* Under supervision of I. Niedtfeld, I wrote the ethics application (90%). *Data collection:* I performed recruitment and diagnostic of all study participants and the administration (100%). *Examination of study data:* J. Hepp and the other co-authors performed the analysis of this data. *Interpretation of the data:* I gave feedback on the interpretation of the data done by the analysts and added ideas for further analyses included in the article (20%). *Manuscript writing:* I was mainly involved in editing the first written draft by J. Hepp (20%). *Revision of the manuscript:* As the second author, I edited the revised manuscript (20%). *Tables and figures*: I was involved in creating and editing tables and figures (15%).

# Abbreviations

AA	Ambulatory Assessment
ACE	Adverse childhood experiences
ANS	Autonomic nervous system
APD	Avoidant Personality Disorder
BPD	Borderline Personality Disorder
CIMH	Central Institute for Mental Health Mannheim
DD	Daily diary study
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5 <sup>th</sup> edition
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
EOS	Endogenous opioid system
ECS	Endocannabinoid system
Est.	Model estimate
HPA-Axis	Hypothalamic-Pituitary-Adrenal Axis
НС	Healthy controls
IPDE	International Personality Disorder Examination
IPE	Interpersonal event
MLM	Multi-level model
NA	Negative affect
NSSI	Non-suicidal self-injury
PA	Positive affect
PANAS-X	Positive and negative affect scale
SCID-I	Structured Clinical Interview for DSM-IV
SITBI-G	Self-Injurious Thoughts and Behavior Interview

# **Theoretical Background**

# **CHAPTER I**

Parts of this chapter have been published in 'Hepp, J., Carpenter, R. W., Störkel, L. M., Schmitz, S. E., Schmahl, C., & Niedtfeld, I. (2020). A systematic review of daily life studies on non-suicidal self-injury based on the four-function model. *Clinical Psychology Review*, 82, 101888. doi.org/10.1016/j.cpr.2020.101888'

To introduce this work, I aim to provide an overview of different facets and frameworks of non-suicidal self-injury (NSSI). First, I focus on the extant literature in the field of ambulatory assessment (AA), as my thesis comprises three publications based on an AA study. There are various theoretical models, which aim to describe the triggers, consequences, and functions of NSSI. The current literature review concentrates on the intra- and interpersonal functions of NSSI as conceptualized in the *Four-function Model* (Nock, 2009; Nock & Prinstein, 2004) Thereby, the study designs, sample characteristics and phenomenology of NSSI assessed in previous AA studies are discussed. Here I focus on potential shortcomings of those studies and derive methodological improvements, which I tried to implement in the design of my dissertation project. Additionally, I summarize findings regarding the biological mechanism of NSSI based on the *model of distal and proximal trait biology as well as biological states around NSSI* (Kaess et al., 2021). To end this chapter, I discuss current research gaps and formulate research questions.

# 1.1 Non-suicidal self-injury

Non-suicidal self-injury (NSSI) is defined as deliberate, self-inflicted damage of body tissue without suicidal intent (e.g., Klonsky, 2011) and has a lifetime prevalence of approximately 5% in the general population (Swannell et al., 2014). Individuals with and

without additional psychopathology engage in NSSI, but NSSI is more prevalent within clinical populations (e.g., Briere & Gil, 1998). NSSI appears to be largely trans-diagnostic, affecting individuals with a range of psychopathology, including anxiety and mood disorders, psychosis, eating disorders, and personality disorders (Bentley et al., 2015; Nock et al., 2006). Importantly, NSSI not only correlates with suicidal behavior, but is also a specific risk factor for suicide attempts (Klonsky et al., 2013; Ribeiro et al., 2016; Victor & Klonsky, 2014). Beyond the personal burden, self-harm, including NSSI and that with suicidal intent, entails substantial health care and economic costs due to increased morbidity and mortality (Kinchin et al., 2017; Tsiachristas et al., 2017), which further underlines the need for research on why and how people self-injure.

In an effort to explain why people self-injure, multiple theoretical models of NSSI have been proposed over the past two decades. One of the earliest models is the Experiential Avoidance Model (Chapman et al., 2006), which proposes that NSSI is primarily performed to avoid aversive emotional experiences (i.e., negative reinforcement). Extending this, the Emotional Cascade Model (Selby et al., 2013) proposes that individuals engage in NSSI to distract themselves from positive feedback loops of negative affect (NA) and rumination (i.e., emotional cascades). Thus, this model incorporates negative thoughts in addition to NA, but still posits negative reinforcement as a central component. In addition to negative reinforcement, the Four-function Model (Nock, 2009; Nock & Prinstein, 2004) includes a positive reinforcement component, suggesting NSSI can also serve to induce positive states. It further distinguishes between interpersonal and intrapersonal functions. Some factor-analytic work suggests that individuals who engage in NSSI may more clearly distinguish between intraand interpersonal functions than between positive and negative reinforcement functions (Klonsky et al., 2015). This may suggest that a simpler two-factor model may be sufficient for understanding why individuals self-injure. However, there are theoretical grounds for distinguishing positive and negative reinforcement (Nock & Prinstein, 2004) and, although individuals may not as readily distinguish between positive and negative reinforcement, they may still experience effects from NSSI that can be meaningfully categorized along this dimension.

Extending this previous work, two recent models have additionally focused on understanding why individuals first decide to engage in NSSI. Both the Cognitive-Emotional Model of NSSI (Hasking et al., 2017) and the Benefits and Barriers Model (Hooley & Franklin, 2018) propose that positive and negative reinforcement (i.e. the 'benefits' of NSSI) primarily explain the maintenance of NSSI, but not why individuals first decide to engage in this selfdestructive behavior. To fill this gap, the Cognitive-Emotional Model describes how cognitions, specifically cognitive representations of NSSI, expectations about the outcome of NSSI, and self-related cognitions such as self-efficacy expectations predict who initiates NSSI. Similarly, Hooley and Franklin suggest in their model that most people have innate barriers that keep them from engaging in NSSI, such as an innate aversion to pain, and that these barriers must be lowered before someone engages in NSSI for the first time. While the attention to barriers of NSSI is likely important, the majority of existing empirical studies have focused on testing the 'benefits' of NSSI, which are most comprehensively summarized in the Four-function Model of NSSI (Nock, 2009). Thus, I chose this model as the focus for this introduction, while acknowledging that several components are also integrated within other models and that barriers are not represented.

The Four-function Model (Nock, 2009) proposes that NSSI serves four functions that can be either *intrapersonal* or *interpersonal*, and that are either *negatively* or *positively reinforcing*. Intrapersonal negative reinforcement suggests that NSSI serves to alleviate aversive intrapersonal states, such as NA. The counterpart, intrapersonal positive reinforcement, suggests that NSSI serves to generate positive internal states, for instance a sense of euphoria or thrill. The two interpersonal functions comprise NSSI that is performed to influence the behavior of others, or the individual's relationship with others. Interpersonal negative

reinforcement comprises NSSI with the intent to reduce undesired behavior from another person or undesired interactions with them, such as ending a conflict or avoiding being confronted for a mistake. Interpersonal positive reinforcement, in contrast, suggests that individuals engage in NSSI to elicit positive behavior from others or positive interactions with them, such as gaining attention or comfort. Past studies have extensively tested the model in a *cross-sectional* framework and this evidence has been summarized in several reviews and meta-analyses (e.g., Bentley et al., 2014). Adding to this, an increasing number of recent studies have tested components of the model in *intensive longitudinal* designs, which overcome several of the limitations of cross-sectional work. Below, I summarize advantages of intensive longitudinal studies and argue why these are ideally suited to test models of NSSI.

Intensive longitudinal designs comprise an assessment of NSSI in the context of daily life and in near real-time via methods such as Ambulatory Assessment (AA, Trull & Ebner-Priemer, 2013). In AA, participants report on constructs of interest (e.g., NSSI events, affect) via smartphone several times a day over a period of days or weeks. Daily diary (DD) studies are a specific type of AA wherein participants report on their experiences once daily. Using AA and DD to capture NSSI overcomes a number of limitations associated with laboratory or crosssectional self-report methods. First, most laboratory studies have used experimenter- and not self-administered pain stimuli as proxies for NSSI. The few studies that have used selfadministered pain stimuli employed electric shock or cold stimuli, which do not closely match the methods typically used by those who self-harm (see Ammerman et al., 2018 for a review of laboratory studies on NSSI). AA and DD studies overcome this problem by capturing NSSI as it occurs in real life. Second, the ability of daily life studies to reduce memory biases is particularly relevant in the case of NSSI, because memory biases are intensified when participants report on highly emotional events (e.g., Blaney, 1986), and this likely reduces the accuracy of cross-sectional self-report of past NSSI episodes. Third, theoretical models of NSSI make relatively fine-grained assumptions about the effects NSSI has over time and these can be ideally tested in an AA framework. For instance, most models propose that some individuals use NSSI to alleviate NA. To test this, NA must be assessed before, during, and after NSSI, as well as at comparison occasions without NSSI. In conclusion, AA and DD are uniquely suited for testing theoretical models of NSSI and I therefore summarize the available AA and DD evidence.

# 1.2 Study designs, sample characteristics and phenomenology of NSSI

# Sample size and sampling frequency

For the current introduction, I reviewed in total 35 articles. Ten studies used DD and 26 studies used AA methods. Although each study addressed different research questions, several studies used the same sample or a subsample of another study. Taken together, 24 independent samples are reviewed and sample overlap is indicated in the tables (see appendix chapter I, Table A3 and A4). The total number of participants included in all reviewed studies combined was 1,727. Sample sizes ranged from 21 to 255 with an average sample size of M = 71.9 participants (SD = 54.1), and a median sample size of Md = 52.5. The duration of AA and DD studies was similar, with both types of studies ranging between 5 and 21 days; on average 13.4 days in AA studies (SD = 5.9), and 17.5 days in DD studies (SD = 5.9). The median study duration was 14 days in both cases.

In DD studies, participants typically provided only one diary report at the end of the day, whereas AA studies differed in both the number of assessments, as well as the type of prompts included. Seventeen out of 18 AA samples included prompts that were presented at random time-points throughout the day, or semi-random prompts that were presented within prespecified time-frames. The number of random prompts within a day ranged between four and 10 prompts with an average of M = 6.14 random prompts per day (SD = 1.75). Other than random prompts, seven out of 18 samples used fixed prompts that were presented at specific times throughout the day (e.g., morning reports directly after wake-up) and seven samples

included event-contingent prompts that participants self-initiated to provide reports right after an NSSI act or urge.

The total number of included study days (across all participants) in the reviewed DD studies was an average 623.6 days (SD = 74.6, Md = 613 days). The total number of prompts that was included in the reviewed AA studies varied significantly depending on sample size and sampling scheme, with longer study periods and more frequent within-day sampling leading to a higher number of included prompts. Only 10 of 18 unique AA samples reported the total number of included prompts (for details, see Table A3 presented in the appendix for chapter I). For the studies that reported this number, included prompts ranged from 428 to 11,172 prompts with an average completed 3,434.4 prompts (Md = 2,429.5, SD = 3,431.5).

# Mental health status

Nine out of the reviewed 24 unique samples recruited participants with a specific type of psychopathology. Six samples comprised participants with a formal borderline personality disorder (BPD) diagnosis and three samples comprised individuals with bulimia nervosa. Participants in the remaining 15 samples were selected for having a history of NSSI. However, this does not mean that participants could not also meet criteria for mental disorders. Eight of the 15 samples that did not explicitly recruit participants with a formal diagnosis conducted clinical interviews and reported diagnoses for their participants (diagnostic information was unavailable for participants in the remaining seven samples). Pooling these with the above described nine studies that recruited participants with BPD and bulimia nervosa allowed us to review the distribution of diagnostic categories across studies.

BPD was assessed in 10 samples and on average 61.5% (*SD* = 35.1) of participants met criteria for BPD in these samples (28.0% in the studies that did not specifically recruit BPD). Mood disorders (predominantly major depressive disorders) were assessed in 12 samples and affected on average 53.5% (*SD* = 23.1) of the sample. Anxiety disorders were assessed in 10 samples and affected on average 47.5% (*SD* = 20.8) of the sample, though the type of anxiety

disorder assessed, and the prevalence of specific anxiety disorders differed substantially. Similarly, eating disorders were also assessed in 10 samples and affected 48.9% (SD = 47.9) of participants in these samples. Lastly, substance use disorder diagnoses were established in eight samples and showed a prevalence of 17.5% (SD = 12.1), on average. Thus, while the majority of included samples did not recruit participants with a specific diagnosis, most samples comprised participants with substantial amounts of psychopathology beyond NSSI (for the most prevalent diagnostic categories see Table A3 in the appendix).

The inclusion of individuals with psychopathology in some but not in other samples is also reflected by the studies' different recruitment strategies. Overall, 27.27% of studies recruited their participants only in clinical settings such as outpatient clinics, 36.36% of studies recruited their participants only from the community, and 40.91% recruited participants from both clinical and community settings (see Table A4 presented in the appendix). Thus, more than two thirds of studies recruited at least some proportion of their participants in clinical settings, which likely accounts for the high prevalence of psychopathology in the reviewed samples.

# NSSI history

In addition to the nine samples that recruited individuals with a formal diagnosis that incurs risk for NSSI (i.e., BPD, bulimia nervosa), the remaining samples recruited individuals based on a history of NSSI. One set of samples included individuals with recent NSSI thoughts or behaviors. Specifically, three samples included participants with NSSI in the past two weeks, and four samples included participants with NSSI urges in the past two weeks or last month. Of the latter four samples, two also required lifetime history of NSSI or past year acts. A second set of samples required NSSI thoughts or behaviors in the past year (three samples), and a third set recruited participants based on a lifetime history of NSSI (two samples, see Table A3 for details).

# Phenomenology of NSSI acts

Table A1 (see appendix chapter I) provides detailed descriptive information for NSSI acts and their daily life context. The majority of studies assessed NSSI acts dichotomously, as present or absent. The number of observed NSSI acts varied considerably across studies. To obtain a fuller picture of how prevalent acts were, I reviewed the percentage of participants in each study that reported any acts, the average number of acts per participant when considering all included participants in each study, and the average number of acts per participant when considering only participants that showed at least one act during the study period. The percentage of participants that showed at least one act ranged from 14.3% to 93.8% and, on average, 46.1% of participants in each sample reported NSSI (Md = 42.5, SD = 25.6). Thus, the majority of all assessed participants did *not* report any NSSI acts. The average number of acts across all participants was 1.60 (Md = 1.23, SD = 1.06) and this number increased to 2.82 (Md= 2.93, SD = 1.23), when considering only participants that reported any act.

Eleven samples assessed which NSSI method participants used for each specific NSSI act. However, only seven samples reported this data. The method with the highest endorsement rate across studies was skin picking or wound manipulation. This was endorsed for an average 41.8% of NSSI acts and was the most commonly endorsed method in two samples (Armey et al., 2011; Lear et al., 2019), but was only assessed in three samples. Cutting, in contrast, was assessed in all seven samples and endorsed for an average 37.4% of NSSI acts. It was also the most commonly endorsed method in three samples (Andrewes et al., 2016; Armey et al., 2011; Kranzler et al., 2018). The next most common method was hitting oneself (incl. head banging), which was endorsed for 23.8% of acts and was the most common method in one sample (Ammerman et al., 2017). Scratching was assessed in six samples and endorsed for an average of 22.9% of acts and was the most endorsed method in also one sample (Turner, Cobb, et al., 2016). Lastly, biting was assessed in five samples and was endorsed for an average 17.7% of

acts across studies, followed by burning the skin, which was endorsed in 8.3% of acts across four samples.

Other aspects of NSSI acts, such as how severe or painful the injury was, were infrequently assessed. Only three samples assessed the experience of pain during NSSI (Kranzler et al., 2018; Lear et al., 2019; Selby et al., 2013). This is of particular interest because pain is assumed to be a central component of NSSI and a number of experimental studies find that individuals with a history of NSSI report reduced pain experience on pain induction tasks (Ammerman et al., 2018). The reviewed studies found that most individuals report some pain (vs. complete analgesia) during NSSI, but that the pain intensity was generally mild (i.e. ranging around three on a 0 - 10 scale).

# 1.3 Evidence for intrapersonal and interpersonal functions of NSSI

# Evidence for intrapersonal negative reinforcement

Participants in eight unique samples self-reported that they engaged in NSSI to reduce aversive internal states, which describes negative intrapersonal reinforcement. In all but one of these samples, this was the most commonly endorsed function. Specifically, participants indicated they performed NSSI to regulate their affect, 'get rid of negative feelings', or obtain 'emotion relief' for, on average, 44.8% of NSSI acts (SD = 22.4). Notably, this includes the study by Shingleton et al. (2013), which was an outlier reporting only 4% endorsement of intrapersonal negative reinforcement. Nock et al. (2010) further assessed self-reported intrapersonal negative reinforcement for specific types of NA and found that adolescents with mood, anxiety, and substance use disorders most commonly endorsed wanting to reduce anxiety (34.8% of acts), followed by sadness (24.2%), and anger (19.7%). Additionally, participants in their study specifically endorsed the goal of reducing negative thoughts (28.8%) and bad memories (13.6%). Two further studies coupled the question about NA reduction with negative thoughts (Shingleton et al., 2013; Turner, Cobb, et al., 2016). Adults with anxiety and mood

disorders or BPD in the study by Turner and colleagues (2016) reported NSSI with the goal to 'get rid of thoughts or feelings' in 67.3% of events, but adolescents with depression or generalized anxiety disorder in the study by Shingleton and colleagues (2013) endorsed this in only 4% of cases. Lastly, youth with BPD in the study by Andrewes et al. (2016) endorsed NSSI with the goal to end dissociation in 5% of cases (for an overview see Table A2 presented in the appendix).

Beyond self-reported functions, several studies also assessed the association between daily life NSSI and aversive inner states. Predominantly, these studies focused on the association between NSSI and momentary or daily NA. Intrapersonal negative reinforcement in this case would imply that a) NA is elevated prior to NSSI, and that it b) decreases from pre to post NSSI, which c) increases the probability of individuals using NSSI to reduce NA in the future. While no AA study has directly assessed component c), both increased levels of NA prior to NSSI and decreased NA post NSSI have been observed. Increased NA prior to NSSI acts was found in eight out of 10 studies. Most studies examined general NA (Andrewes et al., 2016; Armey et al., 2011; Houben et al., 2017; Hughes et al., 2019; Kranzler et al., 2018; Muehlenkamp et al., 2009). With regard to specific types of NA, one study found elevated levels prior to NSSI for a 'negative complex emotions' index, which comprised the number of NA items that were rated above 2 on a 1 to 5 scale (Andrewes et al., 2017), for the PANAS-X guilt scale (Armey et al., 2011), and for a number of individual NA items, including 'distressed' (Andrewes et al., 2017), 'angry' (Armey et al., 2011), 'overwhelmed' and 'anxious/afraid' (Hughes et al., 2019) and 'feeling rejected or hurt' (Turner, Yiu, et al., 2016)<sup>1</sup>. In contrast, Law et al. (2015) and Snir et al. (2015) examined whether NA at one report was associated with NSSI acts at the next report and found no significant association.

<sup>&</sup>lt;sup>1</sup> I note that feeling rejected or hurt can also be seen as evidence for the interpersonal function, because it refers to rejection as an interpersonal event. However, the authors of the study assessed it within their affect scale and therefore I have included it with the intrapersonal function here.

A decrease in NA post NSSI was observed in four out of seven studies. Specifically, Andrewes and colleagues (2016, 2017) found a decrease in mean NA following NSSI, as well as a decrease in negative complex emotions and 'distressed' affect. Armey et al. (2011) observed decreases in NA and guilt, as well as 'angry' affect post NSSI, as did Kranzler et al. (2018) for general NA and the specific items 'sad, angry, overwhelmed, lonely, frustrated, hurt, anxious'. In contrast, Houben et al. (2017) did not observe a decrease post NSSI, but rather found that NA continued to *increase* after the NSSI event. Muchlenkamp et al. (2009) and Snir et al. (2015) both found no change in NA following NSSI.

Two important methodological aspects to consider when interpreting these findings are the time-frame for which change in affect was measured and the number of NSSI acts that were observed. Regarding time-frames, samples can be split into those that assessed affect proximal to the NSSI act and studies that considered affect across the whole day or even across days. Of the latter, four of the reviewed studies modelled change in NA for time-frames of 10 hours or more. Andrewes et al. (2016, 2017) modelled NA 15 hours prior to and following NSSI, and observed both increases of NA prior to and decreases post NSSI that followed a quadratic pattern in youth with BPD. Similarly, Armey et al. (2011) modelled NA up to 20 hours prior to and 20 hours post NSSI and also found the predicted quadratic trajectory in a sample of college students with lifetime NSSI history. Contrasting this, Snir et al. (2015), modelled changes in affect up to 10 hours before and after NSSI and found no discernable pattern for NA surrounding NSSI acts in participants with BPD or APD. Andrewes et al. (2016) observed 52 NSSI acts in their sample, Armey et al. (2011) observed 22 events, and Snir et al. (2015) observed 110 events. Thus, while findings for longer time frames from two samples support negative intrapersonal reinforcement, the negative findings by Snir et al. (2015) are based on a larger number of acts than both other studies combined, and should therefore be weighed equally. Looking at short time periods, Kranzler et al. (2018) found that NA levels 2-3 hours prior to NSSI predict NSSI engagement, and that NSSI predicts NA decrease at the next prompt

(again around 2-3 hours later) in youth with depression or BPD. Importantly, these findings are based on a large number of 143 individual NSSI episodes and thus provide strong evidence for intrapersonal negative reinforcement. This is contrasted by Muehlenkamp et al. (2009), who observed a linear trend for increased NA pre NSSI, but no changes in NA in the 4 hours following NSSI, based on 55 acts and in adult women with bulimia nervosa. Likewise, Houben et al. (2017) found *increased* rather than decreased NA approximately 1.5 hours following 88 NSSI acts in inpatients with high BPD features and depression scores.

# Evidence for intrapersonal positive reinforcement

Participants self-endorsed performing NSSI to increase desired internal states in a number of studies, but overall this function was less commonly endorsed than intrapersonal negative reinforcement (see also Table A2 in the appendix). Performing NSSI with the desired effect of 'feeling something' was endorsed by participants in three studies, specifically in 14.3% of NSSI events in the study by Turner, Yiu, et al. (2016), in 25% of events in the sample reported by Nock et al. (2010) and in 35% in Selby et al. (2013). Turner and colleagues (2016) as well as Selby and colleagues (2013) assessed adults with mixed psychopathology, whereas Nock et al. (2010) assessed adolescents, also with different types of psychopathology. Participants in the sample collected by Selby et al. (2013) also reported NSSI with the motivation to 'feel satisfaction' (20%) or 'feel stimulation' (16%). Additionally youth with BPD endorsed 'sensation seeking' for 5% of acts (Andrewes et al., 2016) and adults with BPD or APD endorsed 'feeling generation' as a motive in 32.5% of events across groups (Snir et al., 2015).

Beyond self-reported motives, five studies tested whether PA decreased prior to and increased post NSSI. Two studies found decreased levels of PA pre NSSI and an increase post NSSI that followed a quadratic trend (15 hour time-frame in youth with BPD: Andrewes et al., 2016; 4 hour time-frame in adult women with bulimia nervosa: Muehlenkamp et al., 2009). Partly corroborating this, Kranzler et al. (2018) also observed an increase in PA 2-3 hours following NSSI, but did not find decreased PA prior to NSSI in youth with depression or BPD.

Not supporting positive reinforcement, Armey et al. (2011) did not find a significant pattern of PA in the 20 hours pre and post NSSI in college students and Houben et al. (2017) found *decreased* PA approx. 1.5 hours following NSSI in inpatients with BPD features.

# Evidence for the interpersonal function of NSSI

The interpersonal function of NSSI suggests individuals engage in NSSI to influence others or to create desired outcomes in interactions with others (see Table A2 in the appendix for an overview). Four of the reviewed studies assessed self-reported functions of interpersonal *negative* reinforcement<sup>2</sup>. Participants endorsed the function 'To escape a task or people' in approximately 15% of NSSI events in two studies (adolescents with mixed psychopathology: Nock et al., 2010; adults with mixed psychopathology, including BPD: Turner, Yiu, et al., 2016), and the function 'interpersonal avoidance' in around 8% of NSSI events across a BPD and an APD group (Snir et al., 2015). The same studies also assessed self-reported functions pertaining to interpersonal *positive* reinforcement. Endorsement rates for the function 'interpersonal communication' ranged from 2% and 4% in studies by Nock et al. (2010) and Turner, Yiu, et al. (2016), to 12% in the BPD group and 17% in the APD group in the study by Snir et al. (2015). Lastly, Horowitz and Stermac (2018) assessed the functions 'influencing others', 'getting revenge', 'establishing autonomy', and 'setting interpersonal boundaries', in community individuals with NSSI history, which all showed a close to zero endorsement.

Beyond self-reported interpersonal functions, only two of the reviewed 35 studies assessed interpersonal constructs and how they relate to NSSI in daily life. Snir et al. (2015) assessed perceived rejection/isolation from others at each assessment and found that it increased prior to NSSI and decreased post NSSI in a quadratic trend. This was observed for both the BPD group and the APD group in their sample, and provides evidence for interpersonal negative reinforcement. Adding to this, Turner, Cobb, et al. (2016) assessed how conflict and

 $<sup>^{2}</sup>$  Andrewes et al. (2016, 2017) asked participants to indicate the desired function in an open response format and did not categorize any of the responses as reflecting intrapersonal functions.

social support related to NSSI on a daily basis in adults with anxiety and mood disorders or BPD. They hypothesized that interpersonal conflict would decrease on days following NSSI that was revealed to others, thus eliciting the desired interpersonal negative reinforcement of NSSI. However, while interpersonal conflict was elevated on days with NSSI, conflict did not decrease on days following revealed NSSI. The authors further tested the association between social support and NSSI. They found that social support increased on days following NSSI that was revealed to others, which supports the notion that NSSI can elicit interpersonal positive reinforcement.

# **1.4 Biological parameters of NSSI**

NSSI emerges as a result of the combination of inter- and intrapersonal stressors as well as biological mechanisms. As described above, inter- and intrapersonal stressors are relatively well studied, when looking at the combination of studies conducted in the laboratory and in daily life. In contrast, evidence for specific biological mechanisms underlying NSSI is still sparse. Until now, most studies assessing biological parameters surrounding NSSI were conducted in the laboratory. Frequently, those studies compare individuals with NSSI to those without the behavior. Kaess et al. (2021) have formulated a *model of distal and proximal trait biology as well as biological states around NSSI* that distinguishes between *trait* and *state* markers. Furthermore, these authors differentiate the biological mechanisms associated with NSSI into *distal* and *proximal* risk factors (Kaess et al., 2021). *Trait markers* in general describe stable, underlying processes (e.g., behavior patterns, alterations in biological functioning), which normally do not change within days or weeks. *States* are described as temporal, fluctuating markers, reflecting the current status of the individual and changing across an episode of NSSI (Kaess et al., 2021).

*Distal traits* are defined as global risk factors, formed through stressors during pregnancy or in early childhood (Kaess et al., 2021). Specifically, distal traits are functional

abnormalities, for instance, in brain functioning or genetic/ epigenetic expressions, probably leading to a predisposition or vulnerability for the engagement in NSSI (Kaess et al., 2021). Results concerning distal traits of NSSI show that the heritability of NSSI is estimated to be 40 - 60% in twin studies (Maciejewski et al., 2014), but there are no clearly identifiable genetic factors explaining engagement in NSSI until now (Kaess et al., 2021). Furthermore, results of different studies give a first hint that adverse childhood experiences (ACEs; or other forms of chronic stress) could be understood as a specific stressor forming distal traits for NSSI. Studies assessing the impact of ACEs on epigenetics and different neurobiological systems show that ACEs may cause epigenetic alternations (Martín-Blanco et al., 2014) and could lead to abnormalities in the Hypothalamic-Pituitary-Adrenal Axis (HPA; see Kuhlman et al., 2017 for an overview), brain structure, and function (Teicher et al., 2016), and that these abnormalities increase the risk for NSSI engagement.

*Proximal traits* (in comparison to distal traits which globally increase the risk for NSSI engagement) are described as *direct* correlates between biological mechanisms and NSSI in the model by Kaess et al. (2021). Whereas distal traits describe functional abnormalities between individuals with and without NSSI engagement, proximal traits are characterized by alterations in activation patterns in the concerned brain areas and endocrine and physiological systems. Findings regarding proximal traits of NSSI include, for instance, the brain circuitry, reward system, peripheral stress-response systems, and pain system (Kaess et al., 2021). *Biological states* of NSSI were directly related to proximal traits, as they affect the same systems and, therefore, findings are summarized together in the following sections. Biological states directly precede or follow NSSI, describing the associations between biological systems and NSSI on a micro-level, reflecting the current status of the individual (e.g., biological components of feelings, reactivity of endocrine of physiological systems) across an episode of NSSI (Kaess et al., 2021). Overall, findings for biological states of NSSI were very sparse, due to ethical and feasibility reasons (Kaess et al., 2021).

#### Central activation patterns

Studies assessing activation patterns in the brain (proximal traits) in the context of NSSI often focus on areas associated with affect regulation, since engagement in NSSI is related to problems in dealing with overwhelming affect or aversive tension (Nock, 2009; Taylor et al., 2018). Consequently, NSSI engagement is often linked to problems with affect perception, regulation, and expression. In line with this, different studies found evidence for alterations in activation patterns in the fronto-limbic neural systems (involved in affect regulation and expression) in individuals with NSSI (Ando et al., 2018; Phillips et al., 2003; Schreiner et al., 2017). Additionally, brain areas associated with social interaction and affect regulation showed an over-activation in response to social exclusion in individuals with NSSI compared to individuals without NSSI (Brown et al., 2017; Groschwitz et al., 2016; Malejko et al., 2020). This was interpreted by the authors as indicating higher rejection sensitivity in individuals with NSSI compared to individuals without NSSI. In line with this, several studies focus on the state *level* of brain activation during NSSI-like stimulation (e.g. heat stimulation) in the laboratory, as a proxy for NSSI engagement (Kaess et al., 2021). Overall, those studies found an altered activation of fronto-limbic and somatosensory neural systems in response to painful stimulation in individuals with NSSI compared to healthy controls (Kraus et al., 2010; Niedtfeld et al., 2012; Niedtfeld et al., 2010; Schmahl et al., 2006). Thus, similarly altered activation patterns were found on a state as well as on a broader proximal trait level for individuals suffering from NSSI.

# Reward system

Another central component in the research surrounding NSSI is the reward system, also categorized as a proximal trait for NSSI. The question whether NSSI is maintained via positive or negative reinforcing processes is central for understanding the underlying mechanism of NSSI and to develop helpful interventions to overcome this behavior. Therefore, several studies assessed different brain regions associated with reward. The assessments led to mixed results with some studies showing that NSSI is associated with altered activation in the reward systems whereas other studies did not find an association between NSSI and the reward system (see Kaess et al., 2021 for a detailed overview).

# Stress-response systems

Beyond the central processes in the brain, surrounding the affect regulation motive, social interaction, and rewarding stimuli in the context of NSSI, evidence emerges that also the peripheral stress-response systems (autonomic nervous system (ANS) and HPA-Axis) play a crucial role for the development and maintenance of NSSI on a proximal trait level. Regarding the ANS, which regulates organ functions during rest (parasympathetic activity) and stress (sympathetic activity), data suggest that individuals with NSSI seem to have an over-active sympathetic system (with studies primary focusing on heart rate variability) compared to individuals without NSSI, possibly due to personality pathology (e.g., deficits in affect regulation; Kaess et al., 2021). HPA-Axis activity is also an indicator for increased intraindividual stress (current as well as chronic stress), with cortisol as the most prominent marker. Most studies assessing cortisol in the context of NSSI found a blunted cortisol response after psychological stress induction in individuals with NSSI compared to those without (Kaess et al., 2012; Klimes-Dougan et al., 2019; Plener et al., 2017).

# Pain system

NSSI is by definition associated with pain, since the behavior is considered to be harmful to oneself. Therefore, the activation, processing, and perception of pain is an important area in the research of NSSI, also summarized as proximal trait for NSSI by Kaess and colleagues (2021). There are many studies in the laboratory assessing pain perception in individuals with NSSI using thermal pain (Franklin et al., 2012; Koenig et al., 2017), electrical pain (Weinberg & Klonsky, 2012), pain through mechanical pressure (Glenn et al., 2014; McCoy et al., 2010) or a blade (indroducing sharp, non-injurious pain; Shabes et al., 2016) as pain induction. Findings indicate that individuals with NSSI show reduced pain sensitivity (the

individual way a painful stimulus is perceived, defined by pain threshold, tolerance and intensity; Koenig et al., 2016) during pain induction compared to individuals without NSSI. In line with this, Koenig et al. (2016) summarized results of 32 studies in a meta-analysis and concluded that adolescents with NSSI reported overall greater pain threshold (i.e., amount of time/ intensity a stimulus needs to be rated as painful), pain tolerance (i.e., max. endurance of painful stimulation) and lower self-reported pain intensity compared to individuals without NSSI. The results showed medium to large effects and indicated a general decreased sensitivity for painful stimulation in individuals with NSSI.

While the majority of laboratory studies found decreased sensitivity to pain or even analgesia during pain induction, the same is not necessarily true for AA findings (Carpenter & Hepp, 2021). Studies assessing pain during NSSI in an AA design in which individuals decide when they engage in the behavior, which method they use, and how severe the injury is, report more heterogeneity in pain ratings (Carpenter & Hepp, 2021; Hepp et al., 2020). While these results do not negate that individuals with NSSI have altered pain-processing mechanisms in comparison to individuals without NSSI, they nonetheless underline the importance of research under real-life conditions as an addition to studies in the laboratory.

# Endogenous opioid system as part of the pain system

The above described self-reported alterations in pain processing in individuals with NSSI suggest an involvement of endogenous opioids (endorphins, enkephalins, dynorphins, and endomorphins) as an additional possible proximal trait for NSSI engagement (Kaess et al., 2021). Endogenous opioids are primarily involved in the perception and regulation of social, emotional, and physical pain (Bresin & Gordon, 2013). The opioid  $\beta$ -endorphin is a  $\mu$ - and  $\delta$ -receptor antagonist and especially involved in the reduction and perception of pain.  $\beta$ -endorphin is released in central and peripheral regions of the body alike (Benarroch, 2012; Rachinger-Adam et al., 2011) and, therefore, theoretically especially suited for the assessment of tissue-damaging NSSI. Furthermore, the activity of its corresponding  $\mu$ - and  $\delta$ -receptors is linked to

pain reduction and relief (Benarroch, 2012). One example for  $\mu$ -receptor activity is a study with healthy individuals undergoing pain induction compared to a placebo condition. Increased  $\mu$ receptor activity in the anterior cingulate cortex was linked to lower levels of self-reported pain unpleasantness and higher activation of  $\mu$ -receptors in the amygdala was associated with lower perceived pain intensity (Zubieta et al., 2001). Regarding peripheral activity of  $\beta$ -endorphin, studies found that tissue damage initiates the release of peripheral  $\beta$ -endorphin in animals and humans (Bigliardi et al., 2003; O'Benar et al., 1987), further inspiring the idea that  $\beta$ -endorphin could be relevant for NSSI engagement. Based on these findings,  $\beta$ -endorphin has become the most investigated opioid in the context of NSSI.

Beyond the model of Kaess et al. (2021), opioid deficit theories like the *homeostasis model* (Sher & Stanley, 2008; Stanley et al., 2010) posit that individuals engage in NSSI to restore homeostasis due to low resting levels of  $\beta$ -endorphin. In line with this, lower plasma levels of  $\beta$ -endorphin were found in adolescents with NSSI during resting conditions compared to individuals without NSSI (van der Venne et al., 2021), and in rhesus-monkeys with selfdirected biting compared to those who did not show the behavior (Tiefenbacher et al., 2005). Furthermore, lower  $\beta$ -endorphin levels were found in the cerebral spinal fluid of individuals with cluster B personality disorder, a history of suicide attempts, and NSSI history, compared to a control group of individuals with the same characteristics but without NSSI history (Stanley et al., 2010). Additionally, Prossin et al. (2010) found in a study using positron emission tomography that individuals with BPD and a history of NSSI had significantly more  $\mu$ -opioid receptor availability than individuals without psychopathology. These findings were interpreted as indirect evidence for chronically low levels of  $\beta$ -endorphin.

Taken together, the biology of NSSI comprises multiple interacting systems in the brain as well as in peripheral areas of the human body. The interaction and function of those systems are not yet fully understood and innovative research approaches are needed to understand the onset and maintenance of NSSI. Even though all discussed biological systems interact, research

needs to focus on different parts of the mechanisms because it is impossible to assess all mechanisms in one study design. At the same time, separate studies on the biological mechanisms on NSSI may always be incomplete and can be interpreted only in the context of other studies. Nevertheless, understanding the biological mechanisms of NSSI would allow to develop specific psychopharmacological or neuro-modulatory treatments (Plener et al., 2018) for NSSI to reduce the harmful behavior, in addition to already well-established therapeutic interventions. Therefore, research in the area of the (neuro-) biological mechanism on NSSI is still a very important topic.

# 1.5 Research gaps and questions

# Research gaps

In this introduction, I have reviewed evidence of current studies on NSSI based on the Four-function Model (Nock, 2009; Nock & Prinstein, 2004) and the model of distal and proximal trait biology as well as biological states around NSSI (Kaess et al., 2021). In the field of AA, several studies already assessed intra- and interpersonal functions of NSSI as proposed by the Four-function Model, emphasizing behavioral and psychological mechanisms. Studies on biological mechanisms of NSSI are still sparse, especially regarding AA designs assessing biological processes surrounding NSSI in daily life. Studies assessing biological markers in daily life would be an important addition to those in the laboratory as they would allow to add new insights on biological states and proximal traits of NSSI as postulated by Kaess et al. (2021).

Looking at the results of AA studies on intra- and interpersonal functions of NSSI, results were overall ambiguous, with some studies finding evidence for intrapersonal negative/ positive reinforcement, whereas others did not. For the interpersonal function of NSSI, only a few studies assessed the relationship between IPEs and NSSI in daily life. Even though, results support the importance of IPEs in the context of NSSI more research in needed to clarify this.

Other conflicting AA findings in the context of NSSI were probably due to large methodological differences between the different studies. As mentioned above, key problems are the large differences in the total amount of NSSI acts analyzed in the studies (range = 22-143) as well as the fact that the different studies operated with widely different time-frames, ranging from 1.5 hrs. preceding and following NSSI to more than one day. In line with this, when interpreting the results of the AA findings, it is important to keep in mind that previous AA studies have only looked at the NSSI events or compared them to random time-points. Thus, with this data, it is impossible to conclude whether changes in affect/ tension surrounding NSSI are specific to NSSI moments (and not due to time effects) or whether comparable changes would also be observable during high-urge moments not followed by NSSI, as high-urges are related to an inverted U-shaped pattern in NA in previous work (Hepp, Carpenter, et al., 2021). To test this, a within group control condition with high-urge situations would help to identify whether changes in affect/ tension are unique for NSSI.

Additionally, less than half of the participants in the reviewed studies engaged in NSSI during the study periods, limiting the informative value of the study results. Participants in the majority of the reviewed samples were not selected because they had a *recent* history of NSSI or a NSSI diagnosis based on DSM-5 criteria. Rather, they were selected based on a diagnosis that has NSSI as a frequent co-occurring symptom, such as BPD or bulimia nervosa, or they were selected because they have a lifetime or past-year history of NSSI. Only three samples included participants who reported NSSI within the last two weeks. Consequently, another important improvement would be to include only individuals with recent and frequent NSSI to assess as many NSSI acts as possible to achieve more statistically robust findings.

Beyond these methodological issues, biological mechanisms are a central component for understanding the processes of engagement and maintenance of NSSI. Most of the studies examining biological mechanisms of NSSI were conducted in the laboratory (Kaess et al., 2021), where the stimuli and measurement methods were under maximal control. On the one

hand, this is a clear advantage as it is possible to assess biological mechanisms in a controlled setting and it is possible to rule out a large set of confounders (e.g., contamination of probes, environmental influences). On the other hand, NSSI-like stimulation in the laboratory is likely very different from self-inflicted NSSI (i.e., self-decided method, severity, frequency, and trigger situations) in a real-life context. Thus, it would be helpful to assess biological markers in the context of daily life to extend the results examined in the laboratory.

Considering the biological mechanisms of NSSI, different complex systems work together, and research often remains inconclusive in assessing those mechanisms. Nevertheless, in trying to shed a little more light on the mechanisms underlying NSSI, it seems worthwhile to focus on pain processing systems. The perception and regulation of pain are assumed to be central components of NSSI, as altered pain processes would explain parts of the question why individuals engage in NSSI and maintain the harmful behavior (Hooley & Franklin, 2018). This idea is also supported by different experimental studies which found that individuals with a history of NSSI report altered pain experience on pain induction tasks in comparison to individuals without NSSI history (Ammerman et al., 2018).

Based on the above-described research gaps, I conducted an AA study, which aims to improve previous work and further investigates the processes surrounding NSSI in daily life. The subsequent chapters II, III, and IV include three publications based on this AA study, focusing on biological mechanisms, the affect regulation function, and interpersonal problems in the context of NSSI. First, I introduce the design of the AA study briefly and then I derive the research questions for my dissertation project.

# Study design

The study design entailed five semi-randomized prompts per day, assessing affect, tension, IPEs, dissociation, urges and NSSI (yes/no), over a 15-day study period (for detailed description of AA prompts see appendix chapter II and chapter II Figure 1). The first day of the study was a "baseline day", assessing eight saliva samples every two hours to picture a possible

circadian trajectory of  $\beta$ -endorphin across the day. On the following days, participants answered on random prompts and were encouraged to self-initiate the app whenever they engaged in NSSI. After NSSI engagement, I tracked the trajectories of affect, tension, dissociation,  $\beta$ endorphin, and pain, using high-frequency sampling (every ten minutes over the first thirty minutes following NSSI). Parallelized with this, the app also sampled in moments with highurge for NSSI but without subsequent NSSI (also referred to as control condition).

#### Research questions

The *first research question* of the study asked in which way salivary  $\beta$ -endorphin is associated with the engagement in NSSI (chapter II). As summarized above, when looking at biological parameters, the perception and processing of pain seems to be one key mechanism in the development and maintenance of NSSI. Here, research has focused on  $\beta$ -endorphin as a potentially important biological marker, as it is involved in the processing and perception of pain (Bresin & Gordon, 2013) and reduced baseline levels of β-endorphin were found in individuals with NSSI history (Stanley et al., 2010). Following the assumption that individuals could engage in NSSI to initiate the release of β-endorphin (Bresin & Gordon, 2013; Stanley & Siever, 2010), I derived the research question if and how levels of  $\beta$ -endorphin change surrounding NSSI events and whether those changes are associated with NSSI in daily life. I hypothesized that peripheral  $\beta$ -endorphin should be lowered before NSSI engagement compared to post NSSI. Post NSSI engagement levels of  $\beta$ -endorphin should be higher than levels of  $\beta$ -endorphin in high-urge situations without subsequent NSSI. Furthermore, I expected an association between levels of  $\beta$ -endorphin and pain ratings, with higher levels of  $\beta$ -endorphin predicting lower levels of pain. Lastly, I hypothesized that NSSI severity is positively associated with levels of  $\beta$ -endorphin, as tissue damage leads to release of  $\beta$ -endorphin (Bigliardi et al., 2003).

The *second research question* of the study was to test the affect regulation function of NSSI (chapter III). Based on current models on NSSI (Chapman et al., 2006; Hooley &

Franklin, 2018; Nock & Prinstein, 2004) and the findings that the reduction of NA and tension through NSSI is indicated as primary motive by individuals with NSSI (Taylor et al., 2018), I hypothesized that NA and tension are increased prior to and decrease following NSSI. Additionally, the decrease in tension and NA should be steeper after an NSSI event than compared to a control condition with high-urge for NSSI.

Setting up this study, I tried to overcome some of the methodological shortcomings mentioned above. First, I only included individuals with frequent NSSI (min. one event per week > 3 month) to increase the probability that participants engage in NSSI during the study period. Second, I added moments of high-urge for NSSI without subsequent NSSI engagement as consequent control condition to test whether changes in NA and tension can uniquely be attributed to NSSI. Third, I included a high-frequency sampling scheme, prompting participants every ten minutes in the thirty minutes following NSSI and high-urges to adequately track short term changes in affect and tension following NSSI and high urges.

The *third research question* was to further investigate the interpersonal function of NSSI in daily life (chapter IV), as the role of IPEs were clearly underrepresented in the discussion of NSSI (Hepp et al., 2020). Therefore, negative and positive IPEs were assessed during random prompts and NSSI events. Additionally, I asked participants about the level of distress caused by IPEs and whether the IPE was a reaction to the last NSSI event. Testing interpersonal negative reinforcement I asked if NSSI is used to reduce IPEs in the future, as it is postulated that negative IPEs occur prior to NSSI and decrease afterwards (Nock & Prinstein, 2004). In detail, I hypothesized that negative IPEs at  $t_1$  (prompt preceding NSSI) increase the probability of NSSI engagement ( $t_0$ ). Furthermore, NSSI engagement ( $t_0$ ) should predict lower numbers of IPEs at  $t_1$  (prompt following NSSI). To test interpersonal positive reinforcement, I hypothesized that NSSI engagements are followed by a greater number of positive IPEs ( $t_1$ ).

# Study I: Salivary beta-endorphin in non-suicidal self-injury: an ambulatory assessment study

# **CHAPTER II**

An adapted version of this chapter has been published as 'Störkel, L. M., Karabatsiakis, A., Hepp, J., Kolassa, I. T., Schmahl, C., & Niedtfeld, I. (2021). Salivary beta-endorphin in nonsuicidal self-injury: an ambulatory assessment study. *Neuropsychopharmacology*, *46*(7), 1357-1363. doi.org/10.1038/s41386-020-00914-2'

# 2.1 Abstract

Non-suicidal self-injury (NSSI) is a prevalent and impairing behavior, affecting individuals with and without additional psychopathology. To shed further light on biological processes that precede and result from NSSI acts, we built on previous cross-sectional evidence suggesting that the endogenous opioid system, and especially  $\beta$ -endorphin, is involved in the psychopathology of NSSI. This is the first study assessing salivary  $\beta$ -endorphin in daily life in the context of NSSI acts. Fifty-one female adults with repetitive NSSI participated over a period of 15 days in an ambulatory assessment study. Salivary  $\beta$ -endorphin was assessed before and after engagement in NSSI, during high urge for NSSI, and on a non-NSSI day. Furthermore, NSSI specific variables such as pain ratings, as well as method, severity, and function of NSSI were assessed. We found that  $\beta$ -endorphin levels immediately before a NSSI act were significantly lower than directly after NSSI. However, there was no difference between  $\beta$ endorphin during high urge for NSSI and post NSSI measures. We found a positive association between severity of the self-inflicted injury and  $\beta$ -endorphin levels, but no significant association between  $\beta$ -endorphin levels and subjectively experienced pain. The results of the present study indicate that it is possible to assess salivary  $\beta$ -endorphin in daily life in the context of NSSI. Furthermore, our results provide a first indication that NSSI acts could be associated with a momentary increase of  $\beta$ -endorphin, and this might reinforce NSSI engagement. More research is needed to replicate and extend our findings on peripheral  $\beta$ -endorphin in daily life.

# **2.2 Introduction**

Non-suicidal self-injury (NSSI) is defined as the intentional and deliberate damage of one's own body tissue without suicidal intent (APA, 2013). It is considered as a transdiagnostic symptom, but is particularly prevalent in affective disorders and borderline personality disorder (BPD) (Kranzler et al., 2018; Turner et al., 2015). Due to its high prevalence and marked negative outcomes, including increased risk of suicide or accidental death (Ribeiro et al., 2016) and high associated health care costs (Sinclair et al., 2011), NSSI has been included as a new research diagnosis in the Diagnostic and Statistical Manual of Mental Disorders (APA, 2013). The pathogenesis of NSSI was repeatedly linked to prolonged experiences of psychosocial stress (Guerry & Prinstein, 2009; Hankin et al., 2015), body-objectification (Nelson & Muehlenkamp, 2012), or rejection or victimization by peers (Brunner et al., 2014), potentially moderated by genetic predispositions (Hankin et al., 2015).

In studies using self-report measures, those with NSSI indicated a reduction in negative feelings and aversive tension as their primary motive (Taylor et al., 2018). Therefore, theoretical models emphasize the role of negative reinforcement (e.g. escape from unwanted emotions) in the psychopathology of NSSI (Chapman et al., 2006; Nock, 2009). Empirically, studies using ambulatory assessment (AA) demonstrated a reduction in negative affect and aversive tension following NSSI (Kranzler et al., 2018; Turner, Yiu, et al., 2016). Studies on (neuro-) biological underpinnings used NSSI proxies in the laboratory and found that individuals with NSSI, as compared to healthy controls (HC), showed decreased subjective arousal (Russ et al., 1992) and a decreased heart rate in response to painful stimulation (Reitz et al., 2012; Weinberg & Klonsky, 2012). Likewise, decreased amygdala activation through pain was observed in samples of BPD individuals with NSSI (as reviewed by Ammerman et

# CHAPTER II: BETA-ENDORPHIN IN DAILY LIFE

al., 2018). Finally, involvement of the endogenous opioid system (EOS) has repeatedly been discussed with regard to the development and maintenance of NSSI (Bresin & Gordon, 2013), mainly due to its role in the perception and regulation of social, emotional, and physical pain (Bresin & Gordon, 2013). Peripherally released (conjugated)  $\beta$ -endorphin can pass the blood brain barrier and influences the concentration of  $\beta$ -endorphin in the cerebrospinal fluid, whereas influence of peripherally released  $\beta$ -endorphin on concentrations in the central nervous system is limited (Banks & Kastin, 1990; Dai et al., 2005). Furthermore, hormones in the central nervous system are able to initiate  $\beta$ -endorphin release in the periphery (Martins et al., 1997). Finally, locally released  $\beta$ -endorphin (e.g. skin) modulates the perception of pain in the concerned area in addition to central mechanisms (Bigliardi et al., 2003). Taken together, it seems that peripheral as well as central systems are involved in the perception and regulation of pain (Bresin & Gordon, 2013).

In previous studies linking the EOS and NSSI,  $\beta$ -endorphin was the most investigated opioid for several reasons. First, tissue damage leads to secretion of peripheral  $\beta$ -endorphin in animals and humans (Bigliardi et al., 2003; O'Benar et al., 1987). Second, lower peripheral levels of  $\beta$ -endorphin were found in humans with a history of NSSI during resting conditions (van der Venne et al., 2021), and in rhesus-monkeys with a history of self-directed biting (Tiefenbacher et al., 2005). Third, there is also evidence for altered central  $\beta$ -endorphin and corresponding changes in  $\mu$ -opioid receptor activity. One study assessed cerebrospinal fluid in individuals with personality disorders and found that those with a history of NSSI showed lower  $\beta$ -endorphin levels than those without (Stanley et al., 2010). In line with this, a study using positron emission tomography demonstrated that individuals with BPD and a history of NSSI had significantly more  $\mu$ -opioid receptor availability than HCs. The authors interpreted this as indirect evidence for chronically low levels of  $\beta$ -endorphin in the concerned brain regions (Prossin et al., 2010). Fourth, low levels of  $\beta$ -endorphin were theoretically linked to dysphoria,

inner emptiness and "the need to feel pain", which are well known symptoms reported by selfinjuring individuals (Stanley et al., 2010).

Taken together,  $\beta$ -endorphin appears to be involved in the regulation of different forms of pain, and reduced  $\beta$ -endorphin levels were found in individuals with NSSI. Therefore, homeostasis model proposed by Stanley and Colleagues (Sher & Stanley, 2008; Stanley et al., 2010) proposes that NSSI acts may be a strategy to initiate the release of  $\beta$ -endorphin (Bandelow et al., 2010; Bresin & Gordon, 2013; Sher & Stanley, 2009; Stanley et al., 2010). However, previous studies on  $\beta$ -endorphin in NSSI were conducted in a laboratory context where individuals did not actually engage in NSSI. Thus, although previous work demonstrated that individuals with NSSI history differ from those without with regard to baseline levels of  $\beta$ endorphin, further evidence for the assumption that NSSI is used to initiate the immediate release of  $\beta$ -endorphin is warranted, and can be tested by micro-longitudinal assessment before and after NSSI acts.

# The present study

We used AA (Trull & Ebner-Priemer, 2013) to investigate the effect of NSSI on peripheral  $\beta$ -endorphin in daily life, using a smartphone-based application. Thereby, we focus on the question if NSSI could be used to initiate a release of  $\beta$ -endorphin by directly assessing the effect of real-life NSSI on the EOS, using a within subjects design. We chose to assess  $\beta$ endorphin in saliva, because participants are able to provide and store samples without interfering with daily activities.

In line with the theoretical assumption that individuals engage in NSSI to initiate a release of  $\beta$ -endorphin (Bresin & Gordon, 2013; Stanley & Siever, 2010), we hypothesized that (H1) peripheral  $\beta$ -endorphin levels are elevated immediately after engagement in NSSI, as compared to a saliva sample taken directly before NSSI (H1a), and as compared to a control condition during high NSSI urge but without engagement in NSSI (H1b). Given the reported association between  $\beta$ -endorphin and experience of physical pain (Bresin & Gordon, 2013;

Zubieta et al., 2001), we further hypothesized that (H2) higher levels of  $\beta$ -endorphin are associated with lower levels of experienced pain during NSSI. Based on findings that tissue damage leads to release of  $\beta$ -endorphin (Bigliardi et al., 2003), we hypothesized that (H3) the severity of the injury is positively associated with  $\beta$ -endorphin levels.

# 2.3 Materials and Methods

#### **Participants**

Participants were 51 women (aged 18 - 45, M = 23.92, SD = 6.72), recruited via flyers at local in- and outpatient clinics, by contacting patients on the waitlist of the Central Institute for Mental Health (CIMH) Mannheim, and via Facebook groups on NSSI related topics. We recruited only women to reduce heterogeneity with regard to biological parameters. All participants met criteria for NSSI-disorder according to the Diagnostic and Statistical Manual of Mental Disorders (APA, 2013). Additionally, inclusion criteria were repeated engagement in tissue damaging NSSI for the last three months, with at least one NSSI incident per week. Exclusion criteria were current substance dependency, developmental disorders, schizophrenia, current pregnancy, medication influencing the EOS (e.g. Naltrexone or other opioid analgesics), as well as exclusion criteria directly related to the assessment of salivary  $\beta$ -endorphin (e.g. frequent gum bleeding, see appendix for details).

All participants provided written informed consent before participation and after they received a full description of the study protocol, which was approved by the ethics committee of the Medical Faculty Mannheim, Heidelberg University (2014-601N-MA). After participation, participants received 100 $\in$  for compensation, and an additional bonus of 50 $\in$  if they answered more than 80% of AA prompts.

## Procedure

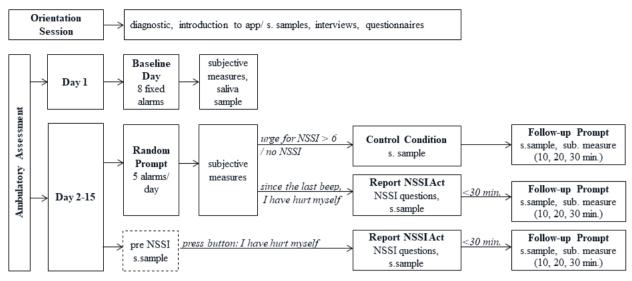
Participants were invited to an on-site orientation session or an online orientation session (via the secured platform *Patientus*, jameda GmBH, Munich, Germany), which

comprised clinical interviews (see measures), self-report questionnaires<sup>3</sup>, an introduction to handling the saliva samples, and an introduction to the smartphone-app (*movisensXS*, *Version* 0.7.4682, *movisens GmbH*, *Karlsruhe*, *Germany*) on the study smartphone. All participants were diagnosed by trained Master's level psychologists.

The 15-day study period started with a baseline day in order to measure peripheral  $\beta$ endorphin trajectory across a day without NSSI. On the baseline day, participants answered eight prompts (every two hours) and provided a saliva sample at each time-point. If participants engaged in NSSI (n=8), the baseline day was repeated if possible, or saliva samples following the NSSI act were removed from the analyses. The following 14 days included five semirandomized prompts per day (self-reports without saliva sample; interval between prompts min. 2hrs) within participants' normal waking hours. Additionally, participants were asked to selfinitiate a prompt as soon as possible following every NSSI act. Afterwards, participants were asked to provide a saliva sample and answered NSSI-related questions (see measures). After reporting a NSSI act, participants answered three follow-up prompts (after 10, 20, and 30 min), also including a saliva sample for each time point (see Figure 1). Additionally, we asked participants to provide a saliva sample shortly before they engaged in NSSI, if possible. However, saliva samples before NSSI were not implemented in our smartphone-app design to keep participant burden low. Finally, if participants reported a high urge for NSSI (> 6 on a 0 -10 scale) during a random prompt, but did not vet engage in NSSI, they were asked to provide a saliva sample for a control condition. In the next thirty minutes, participants answered three follow-up prompts, parallelized with the NSSI follow-up prompts. To keep participant burden as low as possible, this control condition occurred only as frequently as NSSI acts occurred. Besides NSSI acts, urges, pain, and salivary  $\beta$ -endorphin levels, we also assessed momentary affect, dissociation, and interpersonal stressors<sup>4</sup>.

<sup>&</sup>lt;sup>3</sup> Not part of this article, but a list of the questionnaires is included in the supplemental material

<sup>&</sup>lt;sup>4</sup> Results of the latter aspects are not subject of this paper.



*Figure 1*. Study design: Baseline day and random prompts assessed affect, interpersonal events, dissociation, tension, urge for NSSI, NSSI (yes/no), and control questions for  $\beta$ -endorphin. NSSI reports include NSSI specific questions about pain, method, motive, and severity. Control conditions followed a random prompt assessment and included a saliva sample. Follow-up prompts tracked the trajectory of affect, dissociation, tension, and pain, also including saliva samples. For a detailed description of assessments, see the measures section and appendix.

## Measures

Sociodemographic data. We assessed age, body mass index, years of school education, current employment status, and current medication (Table 1). The majority of our sample (n = 30; 58.82%) reported intake of permanent psychiatric medication, with antidepressants (n = 30) and atypical antipsychotics (n = 14) as the most common ones<sup>5</sup>. We also asked participants about their daily physical activity, sports, and possible gum bleeding, which are known confounders in the analysis of saliva samples (Tiwari, 2011).

*Clinical Interviews*. To assess current and past psychopathology, the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders for Axis 1 (Wittchen et al., 1997) was administered. We also administered the BPD section of the International Personality Disorder Examination (Loranger et al., 1998). On average, participants had 2.24 (SD = 1.45) comorbid diagnoses (Table 1). We used the self-injurious thoughts and behavior interview (Fischer et al., 2014) to assess NSSI diagnosis, frequency, and methods.

<sup>&</sup>lt;sup>5</sup> Including medication as a control variable did not change the results of our models.

# Table 1

Demographic and clinical characteristics.

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*a* Questionnaire data of The Self-injurious thoughts and behavior interview: German b Diagnosis according to SKID-I and IPDE

#### Ambulatory Assessment Measures

*Non-suicidal self-injury*. Following each NSSI act, participants reported how much time passed by since they self-harmed (in minutes), the method used (e.g. cutting), motives for NSSI (e.g. "reduce tension"), and the effectiveness of NSSI ("yes", "no", "I don't know"). They were also asked to self-rate the severity of the wound as "mild" (superficial cuts, bruise, scratching), "moderate" (not only skin, but also underlying tissue is damaged, strongly bleeding cuts, 2<sup>nd</sup>/3<sup>rd</sup> degree burns), or "severe" (cuts to fat tissue, damaged sinews, bone fractures, inner bleeding). They reported on current pain intensity, pleasantness/unpleasantness of current pain, and pain during NSSI (each on an eleven point Likert scale, ranging from "no pain" (0) to "worst imaginable pain" (10) or "pleasant" (0) to "unpleasant" (10)). A detailed overview of all AA items and answer options is presented in the appendix chapter I.

Urges for NSSI. This was assessed via the single item "during the last 15 minutes the urge to hurt myself was" on a visual analog scale from "no urge at all" (0) to "I can hardly contain myself" (10).

Control Questions. To minimize confounds with regard to  $\beta$ -endorphin, we asked participants at the end of each prompt, including a saliva sample, if they had used drugs/alcohol, had sex, or did sports within the 1.5 hours before sampling. If one of these options was answered with "yes", the respective saliva sample was excluded from analyses (n = 52).

*Saliva samples*. Participants were instructed to put the synthetic swab of the saliva sample (salivettes<sup>®</sup>, code blue, Sarstedt, Germany) into their mouth without using their hands, and chew the swap slightly for 30 seconds. Next, they were asked to translocate the swab directly back into the collection tube and freeze the sample immediately in their own freezer (at least  $-18^{\circ}$ C/  $-0.4^{\circ}$ F). After completion of the study, frozen tubes were collected from participants' homes and transported to the CIMH Mannheim using dry ice. Saliva samples were

stored at the *BioPsy* Biobank of the Department of Genetic Epidemiology in Psychiatry at the CIMH Mannheim (Witt et al., 2016) at -80°C (-112°F) for up to twenty-two months<sup>6</sup>.

#### Data Analysis

*Biological data.* We analyzed salivary  $\beta$ -endorphin using 15 ELISA kits (Cat.No.S-1134; Peninsula Laboratories International, San Carlos, USA) with the same LOT number. All samples were thawed for 2.5 hours at 4°C (39.2°F) in a refrigerator prior to centrifugation at 3,000 x g for 10 minutes. Saliva aliquots were analyzed using ELISA following protocol III of the manufacturer's manual (Peptide Enzyme Immunoassay (EIA) Protocols; Peninsula Laboratories International, San Carlos, USA; see supplementary material). ELISA plates were measured using a TECAN M400 ELISA plate reader, connected to a PC running the operating software MAGELAN (Tecan International, Germany). As the expected range of  $\beta$ -endorphin levels in saliva were not clearly defined in the literature, we decided to extend the range of the standard curve by adding two additional concentrations at the higher end (except for the first plate analyzed). The new standard curve now covered a concentration between 0.08 and 100 (ng/ml). For the calculation of the standard curve and the slope function, we used the calculation sheet provided by the manufacturer of the kit.

Statistical analysis. For the analysis of  $\beta$ -endorphin (ng/ml), we used log-transformed values to reduce skewness of the data. To account for the nested data structure in AA, we employed multi-level models (MLMs). We modeled random intercepts per participant and random slopes for central predictors (but not covariates) and performed all analyses in R, using the *lmer* and *glmer* functions from the package lme4 (Bates et al., 2014; Kuznetsova et al., 2017).

<sup>&</sup>lt;sup>6</sup> Including storage time (in months) as a control variable did not change the results of our models.

## 2.4 Results

Participants completed a total of 4,619 prompts, which is an average of 90.57 prompts (*SD* = 19.65) per participant, resulting in a high compliance rate of 92.04%. One participant lost the study smartphone (providing 60 data points), and two participants quit participation prematurely because they accepted an elective residential treatment unrelated to the present study (32 and 21 data points, respectively). All available data points were used for subsequent analyses.

All participants cumulatively provided 1,162 saliva samples (M = 23.24, SD = 11.14) (see Table 2 for descriptive data on  $\beta$ -endorphin). One participant did not return the saliva samples. We removed six saliva samples because they could not be assigned to app data due to wrong code input by participants. Three participants accidently completed two baseline days, so we removed the second baseline day from analysis (n = 18). Eight participants reported NSSI engagement on baseline day, so we removed saliva samples following the NSSI event (n = 24). Furthermore, 49 saliva samples were excluded because the  $\beta$ -endorphin concentrations were above the maximum of the standard curve of the ELISA (n = 5), or because participants reported sports activities (n = 43) or sexual activity (n = 1) 1.5 h before providing the saliva sample.

Participants reported 155 NSSI acts, which equates to an average of 3.04 NSSI acts per person (range 0 - 15), and completed a total of 391 NSSI follow-up prompts. Participants reported NSSI acts after 1 - 40 minutes (M = 6.83, SD = 5.75). For our analyses, we excluded NSSI acts that were reported later than thirty minutes post NSSI (n = 11) due to the enzymatic degradation of  $\beta$ -endorphin in saliva under room temperature (Mcknight et al., 1983). For the control condition, participants answered 109 prompts with 261 follow-up prompts. Furthermore, participants were able to provide saliva samples before NSSI acts in 18 cases, on average 8.89 minutes (SD = 3.49) before they engaged in NSSI. After the above-mentioned exclusions, 1,054 saliva samples were included in our final analysis.

# Table 2

Characteristics of NSSI acts.

Variable	п	%	Mean	SD	Range
Method					
Cutting	107				
Wound manipulation	28				
Scratching	19				
Burning/ ice burning	9				
Head banging/ punching self	4				
Other	2				
More than one method	14	8.28			
Motive					
reduce tension/ overwhelming emotions	99				
Self-hatred/ self-contempt	59				
To feel something (other than nothing)	31				
Help/ attention of others	8				
Other reason	20				
I don't know why I self-harmed	9				
More than one motive	71	45.81			
Severity of NSSI <sub>a</sub>					
Mild	47	31.76			
Moderate	88	59.46			
Severe	13	8.78			
Mean painfulness for severity of the					
wound <sub>b</sub>			1.8	2.08	
Mild			2.55	1.76	
Moderate			4.36	2.5	
Severe					
β-endorphin (ng/ml) <sub>c</sub>					
Pre NSSI	18		11.65	10.82	
Post NSSI	476		13.94	11.19	
Control condition	236		12.6	12.29	
Baseline day	333		14.33	15.47	
Variability within person			9.45	7.74	1.09 - 45.86
Variability between person			14.07	14.26	0.11 - 161.55

a severity categories: **mild**: superficial cuts, bruise, scratching, **moderate**: not only skin, but also the underlying tissue is damaged, strong bleeding cuts, 2/3 grade burning, **severe**: cuttings until fat tissue, damaged sinews, bone fractures, inner bleeding

b painfulness was rated on a elven-point Likert scale from 0 (no pain) to 10 (worst imaginable pain)

 $_{c}$  raw mean values of  $\beta$ -endorphin in ng/ml

#### Descriptive statistics for NSSI data

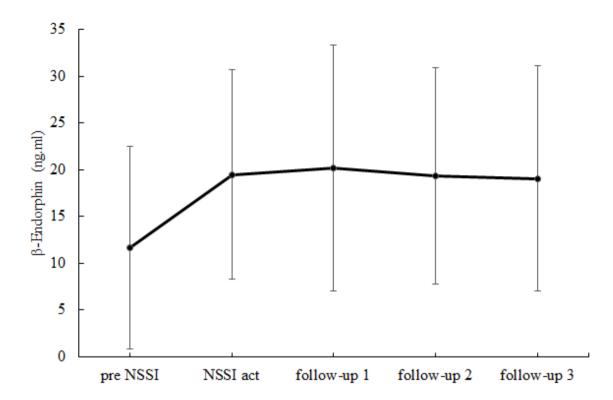
Cutting was the most frequent NSSI method (n = 107), and the most endorsed reason for NSSI was "to reduce aversive tension/ overwhelming emotions" (n = 99). Participants rated 148 NSSI acts with regard to severity (see Table 2). In most cases, they rated NSSI severity as "moderate" (59.46%). Over all three categories of wound severity, participants indicated rather mild pain (M = 2.26; SD = 2.08). More specifically, in 71.32% of NSSI acts, participants reported that they felt no or very mild pain.

## Baseline day trajectory

To assess the trajectory of  $\beta$ -endorphin across the day, we predicted  $\beta$ -endorphin levels in two MLMs with the participants' wake-time in (a) hours and (a) the time of day as predictors, modelling random slopes for these predictors. Results showed that  $\beta$ -endorphin levels did not vary systematically across participants' wake-times (*Est.* = -0.02, *SE* = 0.02, *p* = .456,  $\beta$  = -0.03, CI[-0.12, 0.05]), nor across time of day (*Est.* = -0.01, *SE* = 0.01, *p* = .473,  $\beta$  = -0.03, CI[-0.12, 0.05]). Therefore, these variables were not included as covariates in the following models.

## Momentary $\beta$ -endorphin

To test hypothesis H1a that  $\beta$ -endorphin in saliva is elevated directly after NSSI acts, as compared to samples collected directly before NSSI, we conducted an MLM, including only participants who provided a saliva sample prior to NSSI (pre NSSI samples: n = 18, post NSSI samples: n = 37, follow-up samples: n = 104). We predicted  $\beta$ -endorphin levels with a pre-post NSSI dummy variable (pre = 0, post = 1). Results indicated that  $\beta$ -endorphin levels were significantly higher in the post versus the pre NSSI conditions (*Est.* = 0.62, *SE* = 0.2, p = .032,  $\beta = 0.21$ , CI[0.07,0,34]) (see Figure 2). Further specifying the effect size, Cohens *d* (Cohen, 1977) with regard to a paired t-test was large (t = 3.67, p = .001, d = .82), and a Bayes factor (Rouder et al., 2009) of 21.49 also indicated strong evidence for a difference between pre and post NSSI samples.



*Figure 2.* Trajectory of salivary  $\beta$ -endorphin (ng/ml) from pre-NSSI to post-NSSI for the subsample, only including participants who provided a pre-NSSI saliva sample (n = 18). Pre NSSI samples were provided on average 8.89 minutes before the NSSI act. Time intervals between the report of the NSSI act and the follow-up prompts are 10 minutes each. Standard deviations are represented in the figure by the error bars attached to the line.

Next, we computed an MLM to compare saliva samples collected after NSSI to the control condition (H1b). Here, we predicted  $\beta$ -endorphin levels with a dummy variable coding post NSSI samples as 0 and control condition samples as 1 (see Figure 3). Results showed no significant differences between these conditions (*Est.* = -0.03, *SE* = 0.11, *p* = .766,  $\beta$  = -0.01, CI[-0.1, 0.07]), indicating that during high urge for NSSI,  $\beta$ -endorphin was not significantly lower than directly after NSSI. In an additional exploratory analysis, we also found no difference between post NSSI samples and  $\beta$ -endorphin levels on baseline day (i.e. non-NSSI day) (*Est.* = -0.01, *SE* = 0.08, *p* = .938,  $\beta$  = 0.0024, CI[-0.07, 0.06]).

To test hypothesis 2, we predicted subjective pain following NSSI with  $\beta$ -endorphin levels, while modeling a random slope for the  $\beta$ -endorphin predictor. Contrary to our hypothesis, higher salivary  $\beta$ -endorphin did not entail lower levels of experienced pain in the 30 minutes following NSSI (*Est.* = 0.4, *SE* = 0.31, *p* = .199,  $\beta$  = 0.1, CI[-0.05, 0.24]). However,

even though participants rated more severe wounds as significantly more painful (*Est.* = 1.14, SE = 0.48, p = .03,  $\beta = 0.33$ , CI[0.06, 0.6]), they reported rather mild pain overall, leading to low variance in pain ratings.

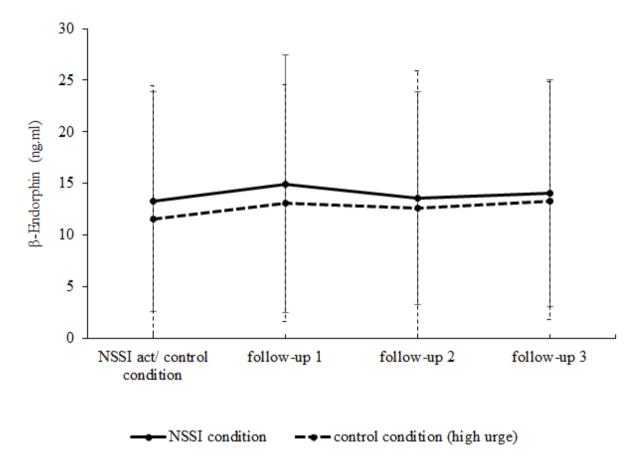


Figure 3. Trajectories of salivary  $\beta$ -endorphin (ng/ml) for the NSSI and the control condition. Time intervals between the first prompt and the follow-up prompts are 10 minutes each. Standard deviations are represented in the figure by the error bars attached to each line.

Finally, to test the association between injury severity and  $\beta$ -endorphin levels (hypothesis 3), we predicted  $\beta$ -endorphin levels with severity (-1 = mild, 0 = moderate, 1 = severe), again modeling a random slope for severity. We found a positive association between injury severity and levels of  $\beta$ -endorphin (*Est.* = 0.39, *SE* = 0.15, *p* = .009,  $\beta$  = 0.2, CI[0.05, 0.35]), indicating that more severe injuries were associated with greater  $\beta$ -endorphin release.

## **2.5 Discussion**

The present study evaluated potential effects of NSSI on the EOS in daily life. As hypothesized, we found that NSSI had a significant and large effect on  $\beta$ -endorphin levels in individuals with chronic NSSI. More specifically, we found that immediately before NSSI,  $\beta$ -endorphin levels were significantly lower as compared to post NSSI samples. This finding supports theoretical assumptions of the homeostasis model of NSSI (Sher & Stanley, 2009; Stanley et al., 2010), specifically that individuals use NSSI to return to their intraindividual norm-physiological  $\beta$ -endorphin range (Bandelow et al., 2010; Bresin & Gordon, 2013; Stanley et al., 2010). Furthermore, our study extends seminal previous work (Stanley et al., 2010), by assessing momentary activity of EOS in individuals with NSSI.

Contrary to our hypothesis, we did not find a significant difference in  $\beta$ -endorphin levels between post NSSI samples and a control condition with a high urge for NSSI. This is not in line with the assumption that low levels of  $\beta$ -endorphin are accompanied by high urges for NSSI (Stanley et al., 2010). However, our finding may be attributable to the relatively small number of saliva samples that were collected during very high levels of urge (n = 32). Furthermore, control conditions only occurred when urge was between 7 and 10 on an eleven-point Likertscale, resulting in restricted variance in the urge variable (M = 7.59, SD = 0.82). Due to limited sample size and restricted variance, we were not able to test the relationship between  $\beta$ endorphin and NSSI urge, based on our current sample. Future research could systematically assess the relationship between urge and  $\beta$ -endorphin to asses if low  $\beta$ -endorphin levels are uniquely associated with NSSI urges. However, we also did not detect significant differences when comparing post NSSI samples with a non-NSSI baseline day in an exploratory analysis. Taken together, we found no indication for higher-than-usual levels of  $\beta$ -endorphin directly after NSSI. Therefore, we conclude that one reason for the engagement in NSSI could be the release of  $\beta$ -endorphin to restore homeostasis, which is in line with previous theoretical assumptions (Bandelow et al., 2010; Bresin & Gordon, 2013; Stanley et al., 2010).

With regard to the relationship between tissue damage and changes in  $\beta$ -endorphin levels, we found a positive association between severity of the self-inflicted injury and levels of momentary  $\beta$ -endorphin, which is in line with previous research (Bigliardi et al., 2003; O'Benar et al., 1987). To the best of our knowledge, no study previously assessed the correlation between  $\beta$ -endorphin in saliva and in other peripheral bio-fluids (e.g. blood, urine, cerebrospinal fluid). Therefore, our raw values cannot be quantitatively compared to studies assessing  $\beta$ -endorphin in other peripheral bio-fluids.

We did not observe a significant association between salivary  $\beta$ -endorphin concentration and subjective pain ratings. Individuals in our sample frequently reported either analgesia or mild pain during NSSI. Even though more severe wounds were rated as significantly more painful and were associated with higher levels of  $\beta$ -endorphin, participants rated all three categories of severity with low to moderate painfulness. On the one hand, restricted variance in the pain variable may have caused these non-significant findings. On the other hand, the subjective experience of pain may be modulated by top-down cognitive processes (Benedetti et al., 1999; Price, 2000), in addition to  $\beta$ -endorphin response in the periphery. Thus, future studies should assess central mechanisms of pain regulation, and combine this with measures of  $\beta$ endorphin. Nevertheless, our findings on the effect of injury severity indirectly support previous assumptions of analgesic effects of  $\beta$ -endorphin (Bresin & Gordon, 2013; Chapman et al., 2006; Zubieta et al., 2001), and extend these findings to daily life. Notably, reduced pain sensitivity is related to repetitive engagement in NSSI (Koenig et al., 2016), possibly due to the absence of negative consequences of the harmful behavior.

In line with findings from a study assessing salivary  $\beta$ -endorphin in the morning and evening (Pikula et al., 1992), we did not find a circadian trajectory of  $\beta$ -endorphin in our sample. This simplifies the interpretation of our data at the momentary level.

#### Limitations

This study was the first with a micro-longitudinal AA design that allowed assessing the immediate effects of NSSI acts. It demonstrated that a non-invasive assessment of  $\beta$ -endorphin via saliva samples is possible in daily life and provides a methodological basis for future testing of the EOS theory in daily life. However, our study design has some limitations that should be improved in following research. Frist, although the current sample comprised 155 NSSI episodes with saliva samples post NSSI, which is comparable to previous studies in daily life (Kranzler et al., 2018), our main result is based on 18 saliva samples that were provided immediately before a NSSI act. Although  $\beta$ -endorphin increase from pre to post NSSI was a large effect, statistical power is limited by the small number of saliva samples. Since our study shows that participants were able to provide pre NSSI samples, future studies should systematically include pre-NSSI saliva samples, as well as pre-NSSI self-ratings (e.g. urge, affect), to enhance the understanding of the impact of NSSI on the EOS.

Second, participants self-administered the saliva samples. While we assessed several potential confounders and removed respective prompts from the analyses, saliva samples may still have been influenced by a range of other internal or external factors (e.g. food, freezer temperature, tobacco, stress). This could have reduced the reliability of the  $\beta$ -endorphin assessment and introduced large standard errors in the models. Evidently, this was a direct result of sampling in daily life and is a limitation that has to be weighed against the strengths of sampling real-life data. Finally, we only focused on intrapersonal changes of  $\beta$ -endorphin. Future research is needed to replicate and extend our findings, especially by including a control group without NSSI history to test between-person differences of  $\beta$ -endorphin in daily life.

## Conclusions

The present study was the first to demonstrate that a non-invasive assessment of  $\beta$ endorphin levels in daily life is possible and feasible via saliva samples. Our findings indicate that momentary changes in  $\beta$ -endorphin are potentially involved in the psychopathology of

#### CHAPTER II: BETA-ENDORPHIN IN DAILY LIFE

NSSI. First, levels of salivary  $\beta$ -endorphin were reduced immediately before NSSI, as compared to post NSSI samples, suggesting a return to normal  $\beta$ -endorphin levels by means of NSSI. Second, more severe tissue damage was associated with higher levels of  $\beta$ -endorphin. Further research is needed to replicate and extend our findings, especially with regard to reduced  $\beta$ -endorphin shortly before NSSI.

# Study II: Does self-harm have the desired effect? Comparing non-suicidal self-injury to high-urge moments in an ambulatory assessment design

# **CHAPTER III**

An adapted version of this chapter has been published as 'Störkel, L. M., Niedtfeld, I., Schmahl, C., & Hepp, J. (2023). Does self-harm have the desired effect? Comparing non-suicidal selfinjury to high-urge moments in an ambulatory assessment design. *Behaviour research and therapy*, *162*, 104273, doi.org/10.1016/j.brat.2023.104273'

## **3.1 Abstract**

All theoretical models of non-suicidal self-injury (NSSI) posit that regulation of negative affect (NA) is a central motive for NSSI, and cross-sectional work supports this. However, previous ambulatory assessment (AA) studies that examined NSSI found mixed results. We investigated the affect regulation function of NSSI in 51 women with DSM-5 NSSI disorder in a 15-day AA study with five random daily prompts and self-initiated NSSI prompts. We extend previous work by i) comparing NSSI moments to moments of a high-urge for NSSI, ii) adding high-frequency sampling following NSSI and high-urge moments, and iii) including tension as a dependent variable. We hypothesized that NA and tension would show a steeper decrease following NSSI than following high-urge moments, if NSSI was effective in reducing NA and tension. Results showed that the significant linear NA decline following NSSI was not steeper than that following high-urge moments. For aversive tension, we found that NSSI was associated with a significant linear decrease in tension, whereas resisting an urge was not. Highurge moments were better described by an inverted U-shaped pattern, likewise leading to decreased NA and tension following the reported urge. In exploratory analyses, we provide visualized clustering of the NA and tension trajectories surrounding NSSI using k-means and relate these to participants' self-rated effectiveness of the NSSI events. Findings indicate that resisting an urge may also be effective in managing NA and tension and underline the utility of interventions such as urge-surfing.

## **3.2 Introduction**

Individuals with and without psychopathology engage in non-suicidal self-injury (NSSI), resulting in a prevalence for NSSI of approximately 5% in the general adult population (Swannell et al., 2014). The behavior is defined as the intended and direct destruction of one's bodily tissue without suicidal intent and not for reasons that are culturally sanctioned (APA, 2013). In the long term, NSSI is associated with adverse outcomes, such as social exclusion due to visible scars (Bachtelle & Pepper, 2015), future suicidal ideation, and suicide attempts (Plener et al., 2015; Victor & Klonsky, 2014). Furthermore, severe NSSI was shown to be a predictor for aggravated future psychopathology (Hom et al., 2018). Beyond consequences for the individual, NSSI also has societal consequences, including high health care costs due to hospitalization after the injury (Dyvesether et al., 2022; Mitchell et al., 2018; Tsiachristas et al., 2020). To prevent engagement in NSSI and improve interventions that reduce the harmful behavior, the field has focused on the question of why individuals self-harm.

There are numerous theoretical models that aim to explain why individuals engage in NSSI. A common component across almost all of these models is the assumption that individuals engage in NSSI to reduce unwanted internal states, particularly negative affect (NA). For instance, the *experiential avoidance model* (Chapman et al., 2006) suggests that individuals engage in self-harm to avoid aversive experiences, including NA. The *emotional cascade model* (Selby et al., 2013) extends this by proposing that individuals engage in NSSI to distract from cascades of NA and cognitive rumination. The *four-function model of NSSI* (Nock, 2009; Nock & Prinstein, 2004) focuses on the immediate motivational reasons for engaging in NSSI, detailing an intrapersonal and an interpersonal function that take effect via positive or negative reinforcement. The intrapersonal negative reinforcement function

#### CHAPTER III: NEGATIVE AFFECT AND AVERSIVE TENSION IN DAILY LIFE

comprises that NSSI is used to reduce aversive intrapersonal states, such as NA or tension. Recently, the *benefits and barriers model of NSSI* (Hooley & Franklin, 2018) extended the other models by focusing on the question why self-harm feels beneficial for some individuals, whereas the costs of NSSI prevent others from engaging in the behavior. The model proposes that distal (e.g., abuse) and proximal (e.g., negative self-association) risk factors lower the barriers for NSSI engagement. Once an individual engages in NSSI, reinforcing benefits – including affect regulation – increase the probability for repetitive engagement.

Cross-sectional studies using self-report measures found substantial evidence for an affect regulation function of NSSI, as participants most commonly endorsed downregulation of NA and aversive tension as their primary motive for NSSI in self-reports (Klonsky, 2007; Taylor et al., 2018). This was also indirectly supported by laboratory and neuroimaging studies, which found that physical pain has an affect regulation function in individuals with NSSI (Ammerman et al., 2018; Kaess et al., 2021). In addition to these cross-sectional designs, several studies have employed ambulatory assessment (AA) to investigate NSSI in daily life. Ambulatory assessment is used as an umbrella term to describe real-time computerized or digital assessment (e.g. via smartphone) of personal characteristics in daily life (e.g. psychological variables, physiological data, see Trull & Ebner-Priemer, 2013). Participants typically report on the construct of interest several times per day via smartphone-app or other interactive devices (self-initiated or via random or fixed alarms). AA is particularly suited to assess the within-person dynamics of NSSI, as NSSI itself and its precursors and outcomes (including NA and tension) fluctuate across the day. Furthermore, AA designs, wherein participants report their inner states on a daily basis, help reduce memory biases and allow assessment of the immediate dynamics of NSSI (Trull & Ebner-Priemer, 2020).

Previous AA studies on the intrapersonal negative reinforcement function of NSSI mainly focused on assessing the level of NA surrounding NSSI events, whereas tension was rarely covered (for a recent review of these studies, see Hepp et al., 2020). In a recent meta-

analysis, Kuehn et al. (2022) re-analyzed 14 AA datasets and tested the effects of NSSI on NA. Ten of the included studies found significant changes in NA surrounding NSSI. Combining datasets, the authors found a small effect for increased NA prior to NSSI, and a medium to large effect for a decrease of NA following NSSI.

However, when interpreting the results of the individual studies that were included in the meta-analysis (and others that were not), it is important to note that studies measured NA at vastly different time-scales surrounding NSSI. Looking at relatively short time-frames prior to NSSI events (1-4 hours preceding NSSI), some studies were able to demonstrate a lagged effect, meaning that NA was elevated proximal to the NSSI event (Hughes et al., 2019; Koenig et al., 2020; Kranzler et al., 2018; Muehlenkamp et al., 2009). Houben et al. (2017) also found a lagged effect of NA (2-3 hours prior to NSSI), as well as a concurrent effect of NA, such that NA was elevated at the time of an NSSI report. Regarding the trajectory of NA after NSSI, Kranzler et al. (2018) found a decrease of NA in a three hour window following NSSI events. In contrast, Muehlenkamp et al. (2009) found no changes in NA within four hours after the NSSI event, whereas two studies found an increase of NA in a period of 1-1.5 hours succeeding NSSI (Houben et al., 2017; Koenig et al., 2020). Other studies modeled the whole trajectory of NA surrounding NSSI, using large time-frames of more than ten hours, and sometimes even across more than one day (Andrewes et al., 2016; Armey et al., 2011; Snir et al., 2015). Three out of four of these studies concluded that NA follows a curvilinear trajectory approximating an inverted U-shaped curve, with NA peaking shortly after the NSSI event (Andrewes et al., 2016; Armey et al., 2011). In contrast, Snir et al. (2015) found no effects for mean NA patterns on three consecutive time-points preceding and following NSSI.

Additionally, two studies compared affect patterns surrounding NSSI events to control events without NSSI, in a within or between group design (Armey et al., 2011; Snir et al., 2015). Comparing individuals who engage in NSSI with those who did not, Armey et al. (2011) found that NA is significantly higher in NSSI-associated situations compared to random time-points

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of individuals who do not engage in NSSI. Snir et al. (2015) likewise compared affect patterns surrounding NSSI events to randomly selected time-points without NSSI in a sample of individuals with NSSI. They found significantly increased dissociation and rejection/isolation patterns for NSSI moments, but not for random time-points and no changes for general NA.

Looking at the results described above, it is important to keep in mind that NSSI moments alone, as well as the comparison of NSSI moments with random time-points, are difficult to interpret. From previous studies, it remains unclear whether changes in NA surrounding NSSI are specific to NSSI moments, or whether changes in NA are also prevalent in comparable situations with a high level of urge for NSSI. Thus, it is impossible to conclude whether effects on NA are a specific outcome of NSSI, or whether NA would also decrease – in time – following a sustained NSSI urge.

Beyond NA, theories of NSSI often suggest that the behavior is associated with aversive inner tension (Chapman et al., 2006; Linehan, 1993; Nock & Prinstein, 2004). Inner tension refers to a state of aversive inner arousal that is not described by a concrete emotion (Daly et al., 1983; Russell, 1980). Especially in the context of borderline personality disorder (BPD), where NSSI is one of the most prominent symptoms, tension is often described as a trigger for NSSI (Linehan, 1993). Therefore, the construct of aversive tension was mainly studied in samples of individuals with BPD. Cross-sectional self-report and in daily life studies found that individuals with BPD experience more inner tension than individuals without BPD (Stiglmayr et al., 2005; Stiglmayr et al., 2001). In recent years, research on NSSI has become more independent from research on BPD, because NSSI is also prevalent in individuals without BPD (Bentley et al., 2015; Nock et al., 2006). However, individuals who engage in NSSI may have similar difficulties with labeling their exact affective states (Bresin, 2014; Ebner-Priemer et al., 2008), and are likely better able to indicate more unspecific states such as aversive tension. Previous work has shown that the higher such states of aversive inner tension are, the more likely individuals with NSSI are to attempt to reduce aversive tension through NSSI (Stiglmayr

et al., 2005). To the best of our knowledge, no daily life study has previously addressed the association between NSSI events and aversive tension. Therefore, in addition to NA, we assess the association between aversive tension and NSSI in daily life.

In conclusion, two central questions remain unanswered by previous studies. The *first* is whether the trajectories of NA and tension differ between NSSI episodes and episodes with a high-urge for NSSI that was resisted. In contrast to comparing NSSI time-points and random time-points, this would be a stricter test of whether changes in NA and tension surrounding NSSI are specific to NSSI engagement (and not due to time effects). To evince that NSSI is more effective than resisting an NSSI urge, the decrease in NA/ tension following NSSI should be steeper than following a resisted NSSI urge. The *second* open question refers to the temporal dynamics of changes in NA and tension prior to and following NSSI. Previous studies have operated with widely different time-scales, ranging from a few hours (Koenig et al., 2020; Kranzler et al., 2018; Muehlenkamp et al., 2009), to more than one day (Andrewes et al., 2016; Armey et al., 2011; Snir et al., 2015). However, for NSSI to be negatively reinforcing, a decrease in NA or tension has to occur relatively immediately following the event to be temporally contingent. Therefore, it would be important to include high-frequency sampling of NA and tension directly after NSSI to assess the immediate impact of NSSI on psychological variables.

#### The present study

The aim of the present study was to test the affect regulation function (negative intrapersonal reinforcement) of NSSI (Chapman et al., 2006; Hooley & Franklin, 2018; Nock & Prinstein, 2004) in daily life, using an AA design. Given the fact that the reduction of NA and tension through NSSI is indicated as primary motive by individuals who engage in NSSI (Taylor et al., 2018), and is suggested by a range of theories on NSSI (Chapman et al., 2006; Hooley & Franklin, 2018; Nock, 2009), we focus on the question whether the trajectories of NA and tension follow a linear or curvilinear trend surrounding NSSI events. To monitor

#### CHAPTER III: NEGATIVE AFFECT AND AVERSIVE TENSION IN DAILY LIFE

changes in tension and NA directly following NSSI events, we include a high-frequency sampling period in the 30 minutes after an NSSI event, sampling at 10, 20, and 30 minutes following NSSI engagement. Furthermore, we include a control condition of prompts in situations with high NSSI urge, as it has been shown that moments with high NSSI urge are also accompanied by increased NA (Hepp et al., 2020). This should be an adequate control condition in order to test whether changes in NA and tension are specific to NSSI, or rather attributable to time effects. Resisting the urge to self-injure is challenging for the individual and regulation of NA or tension, if successful, should take longer in high-urge chains than when engaging in NSSI. Thus, NSSI events should be succeeded by rapid changes in NA and tension forming a time-contingent, reinforcing mechanism that makes future engagement in NSSI more likely.

Based on theoretical models on an affect regulation function of NSSI and intrapersonal negative reinforcement (Chapman et al., 2006; Hooley & Franklin, 2018; Nock & Prinstein, 2004), we hypothesized that NA and aversive tension are increased prior to and decrease following NSSI events (H1). Extending previous work, we hypothesized that the decrease in NA and tension is steeper after an NSSI event than after high-urge moments (H2). Based on previous empirical work, which observed both linear and quadratic patterns of NA surrounding NSSI (e.g. Andrewes et al., 2016; Kranzler et al., 2018; Snir et al., 2015), we decided to model linear as well as quadratic trends of NA and tension surrounding NSSI. In exploratory analyses, we provide a detailed descriptive analysis of the temporal dynamics of NA and tension in close proximity to NSSI events by visualization of trajectories by k-means clustering.

## **3.3 Materials and Methods**

## **Participants**

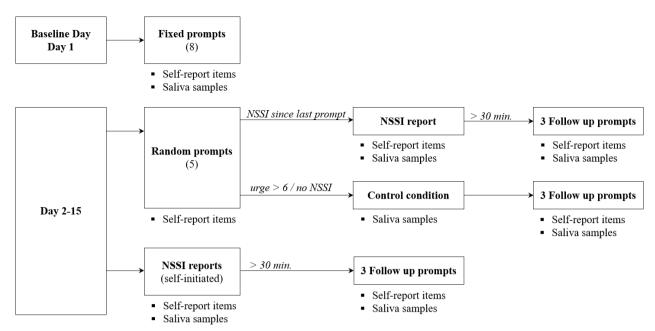
This sample has been reported in two previous publications, one of which focused on the release of  $\beta$ -endorphin following NSSI (Störkel et al., 2021), and the other on the interpersonal function of NSSI (Hepp, Störkel, et al., 2021). The project description at https://osf.io/ugmky/ provides further details. Data on NA and tension items were not reported in either of the previous publications. We recruited 51 cis-gender women (aged 18-45, M =23.92, SD = 6.72) between April 2017 and November 2018, via flyers at local in- and outpatient clinics, our institution patient waitlist, and Facebook groups on NSSI-related topics. Only women were recruited, due to the biological parameters assessed in the parent study (for more details see Störkel et al., 2021). Additional inclusion criteria were a diagnosis of NSSI disorder according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5, APA, 2013), and repeated engagement in tissue damaging NSSI for the last three months ( $\geq 1$ NSSI event/ week). Exclusion criteria were current substance dependency, developmental disorders, schizophrenia, as well as exclusion criteria directly related to the assessment of salivary  $\beta$ -endorphin<sup>7</sup>. Before participation and after they received a full description of the study protocol, all participants provided written informed consent. The study was approved by the ethics committee of the Medical Faculty Mannheim, Heidelberg University (2014-601N-MA). Participants received 100€ for compensation, with an additional bonus of 50€ for more than 80% compliance.

## Procedure

Participants completed self-report questionnaires<sup>8</sup> and an in-person or online orientation session (via the secured platform *Patientus*, jameda GmBH, Munich, Germany), which included clinical interviews (see measures) and an introduction to the smartphone-app (*movisensXS*, *Version 0.7.4682*, movisens GmbH, Karlsruhe, Germany) that was run on a study smartphone. A clinically trained Master's level psychologist diagnosed all participants.

<sup>&</sup>lt;sup>7</sup> We applied additional exclusion criteria related to the collection of saliva samples (see Störkel et al., 2021) and see supplemental material on osf <u>https://osf.io/t38sx</u>.

<sup>&</sup>lt;sup>8</sup> These are not reported herein, but a list of all assessed questionnaires is included in the supplemental material on osf <u>https://osf.io/t38sx</u>.



*Figure 4*. Study design: **Baseline day** and **random prompts** assessed affect, interpersonal events, dissociation, tension, urge for NSSI, NSSI (yes/no), and control questions for  $\beta$ -endorphin. **NSSI reports** included affect, interpersonal events, dissociation, tension and NSSI specific questions about pain, method, motive, and severity. **High-urge moments** (control conditions) followed a random prompt assessment and included a saliva sample. **Follow-up prompts** tracked the trajectory of affect, dissociation, tension, and pain, also including saliva samples. For a detailed description of assessments, see the measures section and appendix.

Participants completed a 15-day AA period. Figure 4 shows the different prompt types that were included in the study design (for biological parameters, see Störkel et al., 2021). Within participants' normal waking hours, they responded to five semi-randomized prompts per day (interval between prompts min. 2hrs). In case of an NSSI event, participants were asked to self-initiate a prompt as soon as possible, and respond to NSSI specific questions (see measures). After reporting an NSSI event, participants answered three follow-up prompts (after 10, 20, and 30 mins). Finally, participants responded to control condition prompts (also referred to as high-urge moments) if they reported a high NSSI urge (> 6 on a scale from 0 - 10) during a random prompt, but did not engage in NSSI afterwards. For this high-urge control condition, they also answered three follow-up prompts (after 10, 20, and 30 mins), parallelized with the NSSI follow-up prompts. To keep participant burden as low as possible, the control condition prompts were determined to occur a maximum of once more often than NSSI events occurred (per person). In addition to NSSI events, NSSI urges, momentary affect, and tension, we also

assessed pain,  $\beta$ -endorphin via saliva samples, dissociative symptoms, and interpersonal stressors (see also Hepp, Störkel, et al., 2021; Störkel et al., 2021).

#### Measures

For a detailed list of all measures, please see appendix and the supplemental materials at https://osf.io/t38sx/. Psychopathology was assessed using the *Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders fourth edition* (SCID-1; Wittchen et al., 1997), because the DSM-5 interview was not yet available in German at the time of data collection. Additionally, we administered the BPD section of the *International Personality Disorder Examination* (IPDE; Loranger et al., 1998). Participants had on average 2.24 (SD = 1.45) diagnoses (for a more detailed description, see Störkel et al., 2021), with the most common ones being depression (n = 33), BPD (n = 32), and post-traumatic stress disorder (n = 25). The proposed NSSI disorder diagnosis for DSM-5, NSSI frequency, and NSSI methods were assessed using the *Self-injurious Thoughts and Behavior Interview: German* (SITBI-G; Fischer et al., 2014).

*Non-suicidal self-injury*. Each NSSI report included the following questions: How much time had passed since the injury (in minutes), the method used (e.g., cutting), motives for NSSI (e.g. "reduce aversive tension/ overwhelming emotions"), and the effectiveness of NSSI ("Did the NSSI event have the desired effect?" with answering options "yes", "no", "I don't know"). Participants were also asked to rate the severity of the wound as "mild" (superficial cuts, bruises, scratching), "moderate" (not only skin, but also underlying tissue is damaged, strongly bleeding cuts, 2<sup>nd</sup>/3<sup>rd</sup> degree burns), or "severe" (cuts to fat tissue, damaged sinews, bone fractures, inner bleeding). Additionally, current pain intensity, pleasantness/unpleasantness of current pain, and pain during NSSI (each on an eleven point Likert scale, ranging from "no pain" (0) to "worst imaginable pain" (10) or "pleasant" (0) to "unpleasant" (10)) was reported.

*Urges for NSSI*. Urges for NSSI were assessed during random prompts using the single item "*during the last 15 minutes the urge to hurt myself was*" on a visual analog scale from "no urge at all" (0) to "I can hardly contain the urge" (10).

Affect. Momentary affect ("At the moment, I feel....") was assessed during random and self-initiated prompts with items taken from the *Positive and Negative Affect Scale* (PANAS-X, Röcke & Grühn, 2003). To reduce participant burden, we selected two items for each PANAS-X scale based on pilot work to identify the items with the highest factor loadings for their scales (see <a href="https://osf.io/t38sx/">https://osf.io/t38sx/</a>). We selected the following items for NA: *disgusted with self, loathing, downhearted, afraid, alone, hostile, nervous,* and *blameworthy*. Each item was rated on a Likert-scale ranging from 1 "very slightly/not at all" to 5 "extremely".

*Tension.* Current tension ("At the moment, I feel....") was assessed during random and self-initiated prompts by the *relaxed-tense* Item (bipolar visual scale: ---, --, -, 0, +,++, +++) of the *Multidimensional Mood Questionnaire* (MDBF; Wilhelm & Schoebi, 2007).

#### Data analysis

We analyzed the data using multi-level models (MLM), to account for the nested data structure (prompts nested within persons). We modelled random intercepts per participant, and random slopes for momentary-level predictors. We performed all analyses in R (R-Core-Team, 2021), using the *lmer* and *glmer* functions from the package *lme4* (Bates et al., 2014; Kuznetsova et al., 2017). Effect sizes were calculated using the package *effectsize* (Ben-Shachar et al., 2020). All models included the covariate weekend, as affect tends to be more positive during weekends as compared to weekdays (Stone et al., 2012). To compare changes in NA and tension surrounding NSSI events with moments of high NSSI urge, six consecutive time-points (also referred to as "NSSI chain" and "high-urge chain") were included within a maximum 7h time-frame surrounding the NSSI event or high-urge moment (3.5h before and after). Time was centered on the report of the NSSI event (t<sub>0</sub>) or high-urge moment (i.e. t<sub>0</sub>; urge > 6, resp.). Additionally, we selected one time-point prior to the NSSI or high-urge moment (t<sub>1</sub>), the three

follow up prompts ( $t_{0.1}$ ,  $t_{0.2}$ ,  $t_{0.3}$ ) in the thirty minutes following NSSI or high-urge moment, and the next random prompt ( $t_1$ ) after the NSSI or high-urge moment. All models include a linear and a quadratic time predictor and interactions of NSSI/ high-urge moments with the temporal predictors.

Additionally, we conducted exploratory analyses to further characterize the temporal dynamics of aversive tension and NA after NSSI events. To this end, we used k-means clustering (MacQueen, 1967) from the packages *stats* and *factoextra*. Following the elbow method to determine the best number of clusters (Cui, 2020), we decided to choose a five-cluster solution for NA and a seven-cluster solution for tension, clustered with a maximum of 100 iterations. For NSSI trajectories with missing data, we computed the differences to all cluster centroids and assigned the trajectories to the cluster with the smallest centroid difference. As a last step, we evaluated the clusters with regard to their effectiveness as rated by participants. Each NSSI report included the question whether the event had the desired effect ("yes", "no", "don't know"). Looking at these effectiveness ratings, we aimed to assess whether the clusters of NA and tension differed not only with regard to intensity and shape, but also with regard to the subjective effectiveness of the self-harm event.

## **3.4 Results**

## Descriptive results

Participants completed 4,619 observations (current analysis 1,220 data points) resulting in a high compliance rate of 92.04%. On average, participants reported 3.04 NSSI events per person (SD = 2.45; range = 0 - 15), accumulating to 155 NSSI events in total (with n = 390follow-up prompts). Additionally, participants completed 109 high-urge moments (with n = 270follow-up prompts). The most frequently endorsed method for NSSI was *cutting* (n = 107) and the most commonly endorsed motive was to "*reduce tension/overwhelming emotions*" (n = 99; note that in 45.81% of events participants choose more than one motive). With regard to

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severity, participants rated the majority of their wounds as *moderate* (59.46%), meaning that not only skin, but also underlying tissue was damaged, including strongly bleeding cuts and  $2^{nd}/3^{rd}$  degree burns. Overall, participants reported that the NSSI event had the desired effect in only 51.31% of cases (for more descriptive results see Störkel et al., 2021). At the individual level, n = 14 individuals describing every NSSI event as helpful, n = 8 participants rated the majority of their NSSI episodes as effective, n = 5 rated half of their episodes as effective and the other half as ineffective, n = 10 participants rated the majority of their NSSI episodes as ineffective, and n = 10 rated every NSSI episode as ineffective.

Table 3 presents descriptive data (within and between person M, *SD* and range) for the dependent variables NA and tension. We found that average levels of NA across all prompt types (random prompts, NSSI moments, follow-ups and high-urge moments and their follow-ups) lay within the same PANAS-X category ("a little"). Additionally, 88.33% of NSSI events and 85.29% of high-urge moments were preceded by low levels of NA, that is, a PANAS-X-NA mean score no higher than "a little". Furthermore, NA did not change at all in 31.92% of NSSI chains and 31.40% of high-urge chains - irrespective of the overall level of NA.

For tension, we observed average ratings for randomly prompted moments and post NSSI moments in the same category ("neutral"), whereas high-urge moments were, on average, rated as being accompanied with higher tension ("little tense"). Additionally, we found that 59.02% of NSSI events and 72.06% of high-urge moments were preceded by low tension (values smaller than four on the tension scale ranging from 0 "calm" to 6 "tense"). Furthermore, in contrast to NA findings, tension levels did not change in only 9.23% of NSSI chains, and 11.11% of high-urge chains (independent of the overall tension level). During the study period, we also assessed positive affect (PA), using six PA items of the PANAS-X. For the interested reader, we present descriptive findings and MLMs using PA with a short interpretation in the appendix for chapter III.

#### Confirmatory analyses

To test whether NA and tension were increased prior to NSSI and decrease following NSSI (H1), and whether this decrease is steeper in NSSI than in high-urge chains (H2), we conducted a MLM. Predictors were the linear and quadratic time predictor, chain type (NSSI chain vs. high-urge chain), and their interaction terms. The dependent NA variable was the momentary mean value of the PANAS-X scales. We modeled random intercepts per participant and random slopes for the linear and quadratic time predictors.

We found that NA was higher at high-urge moments than directly after NSSI (Est. = 0.15, SE = 0.04, p < .000). For the linear trend, we observed that NA significantly decreased from t<sub>1</sub> to t<sub>1</sub> in the NSSI chain (Est. = -0.12, SE = 0.04, p = .008), but not in the high-urge chain (Est. = -0.04, SE = 0.05, p = .412). However, the interaction term between chain type and the linear time predictor indicated that the difference between the conditions was not statistically significant (Est. = 0.08, SE = 0.06, p = .209). For the quadratic trend, we found that NA did not follow a quadratic pattern surrounding NSSI events (Est. = -0.11, SE = 0.06, p = .062) but it did follow a quadratic pattern (inverted U-shaped) surrounding high-urge moments (Est. = -0.35, SE = 0.07, p < .000). This difference in the quadratic trajectories (NSSI vs. high-urge chains) was statistically significant (Est. = -0.24, SE = 0.08, p = .002). Taken together, we found support for H1 (linear decrease of NA after NSSI). H2, in contrast, was not supported, as there was no stronger decrease in NA following NSSI compared to high-urge moments.

For tension, we found higher values at the moment of high NSSI urge (t<sub>0</sub> high-urge chains) than directly after NSSI (t<sub>0</sub> NSSI chains; Est. = 0.84, SE = 0.09, p < .000). Looking at the trajectories of tension, we found a significant linear decrease from t<sub>-1</sub> to t<sub>1</sub> in the NSSI chain (Est. = -0.32, SE = 0.09, p < .000). This decrease was not significant in the high-urge chain (Est. = -0.03, SE = 0.10, p = .729).

# Table 3

Mean values of negative affect and	tension per prompt type	(within and between person values)
J 0 JJ		

		Negative affe	ect <sup>a</sup>		Tension <sup>b</sup>					
Prompt type	Between pers. M (SD)	range	Within pers. M (SD)	range	Between pers. M (SD)	range	Within pers. M (SD)	range		
Random (t-1)	2.28 (0.78)	1.00-5.00	2.29 (0.75)	1.12-4.50	3.86 (1.31)	0.00-6.00	3.82 (1.04)	0.00-6.00		
Random (t <sub>1</sub> )	2.23 (0.77)	1.00-4.12	2.30 (0.73)	1.00-4.00	3.59 (1.37)	0.00-6.00	3.69 (1.11)	1.00-6.00		
NSSI	2.53 (0.93)	1.00-5.00	2.64 (0.90)	1.25-4.94	3.69 (1.52)	0.00-6.00	3.70 (1.36)	0.00-6.00		
<ol> <li>Follow-up</li> <li>Follow-up</li> </ol>	2.27 (0.87)	1.00-5.00	2.42 (0.89)	1.00-5.00	3.42 (1.32)	0.00-6.00	3.55 (0.98)	1.00-6.00		
3. Follow-up	2.18 (0.87)	1.00-5.00	2.31 (0.90)	1.00-5.00	3.34 (1.28)	1.00-6.00	3.45 (0.97)	1.00-6.00		
	2.09 (0.79)	1.00-4.50	2.18 (0.77)	1.00-3.88	3.14 (1.28)	0.00-6.00	3.18 (1.00)	1.00-5.50		
High-urge	2.73 (0.78)	1.25-5.00	2.77 (0.74)	1.25-4.75	4.45 (1.35)	0.00-6.00	4.64 (1.03)	2.33-6.00		
<ol> <li>Follow-up</li> <li>Follow-up</li> </ol>	2.53 (0.71)	1.00-4.38	2.54 (0.71)	1.00-4.38	4.32 (1.23)	0.00-6.00	4.38 (1.07)	0.00-6.00		
<ol> <li>Follow-up</li> <li>Follow-up</li> </ol>	2.43 (0.75)	1.00-4.50	2.46 (0.76)	1.00-4.50	4.21 (1.18)	0.00-6.00	4.32 (0.90)	2.00-6.00		
	2.40 (0.74)	1.00-4.38	2.44 (0.67)	1.00-4.19	4.07 (1.28)	0.00-6.00	4.23 (1.14)	1.00-6.00		

<sup>a</sup> PANAS-X-scale: 1 = very slightly/ not at all, 2 = a little, 3 = moderately, 4 = quite a bit, 5 = extremely <sup>b</sup> MDBF-scale: 0 = relaxed, 6 = tense

The interaction between the linear time variable and chain type indicated that this difference was statistically significant (Est. = 0.29, SE = 0.14, p = .034). In contrast, the quadratic trend was significant only for high-urge chains (Est. = -0.64, SE = 0.15, p < .000) but not for NSSI chains (Est. = 0.10, SE = 0.14, p = .467). This means that tension followed a quadratic trend surrounding high-urge moments, increasing before these moments and decreasing after them, while the same was not true for NSSI moments. The significant quadratic time × chain type interaction indicated that the difference in quadratic tension trajectory was significant between the two chain types (Est. = -0.74, SE = 0.17, p < .000). Thus, on the one hand, H1 was supported because tension increased prior to and decrease was steeper after NSSI than after high-urge moments (H2 supported). On the other hand, we also found a significant inverted U-shaped pattern surrounding high-urge moments, also resulting in significantly decreased values of tension after the reported urge.<sup>9</sup>

#### Exploratory analyses: K-means clustering

Thorough inspection of raw data plots indicated that the trajectories of NA and tension were highly heterogeneous. Therefore, we decided to use a k-means clustering approach to detect possible patterns of temporal dynamics in the trajectories of NA and tension surrounding NSSI. Results of an elbow analysis indicated a four or five cluster solution for NA. We decided to choose the five cluster solution because it explained a higher proportion of variance in the trajectories (61.4%), and every cluster included a substantial number of trajectories. For tension, the elbow analysis indicated two possible solutions, one with four and one with seven clusters, both explaining approximately 70% of the variance in the data. We decided to report the seven cluster solution, because we wanted to provide a differentiated and clinically meaningful

<sup>&</sup>lt;sup>9</sup> Following previous work, we also investigated the predictive value of concurrent and lagged affect and tension, the respective analyses are presented in the appendix for chapter III.

description of the trajectories. The cluster solutions for NA and tension are depicted in Figure 5 and Figure 6. For both NA and tension, 130 out of 155 NSSI events could be assigned to a cluster. The remaining events had more than two missing time-points in the NA/ tension trajectory surrounding NSSI and were therefore excluded from the analysis. Table 4 reports the number of trajectories assigned to each cluster.

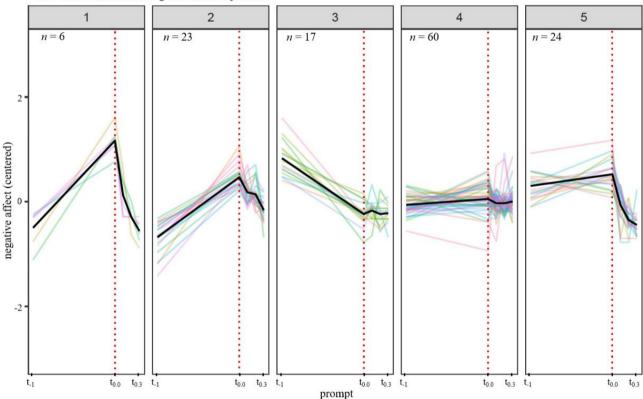
# Table 4

	NSSI	events	Desired effect						
			yes			no		don't know	
	n	%	п	%	n	%	n	%	
negative affect									
C1 "inverted U-shaped"	6	4.62	4	83.33	1	16.67	0	00.00	
C2 "small increase"	23	17.69	13	56.52	7	30.43	3	13.05	
C3 "small relief"	17	13.08	11	64.70	3	17.65	3	17.65	
C4 "unspecific line"	60	46.15	30	50.00	12	20.00	18	30.00	
C5 "follow-ups bring relief"	24	18.46	9	37.50	8	33.33	7	29.17	
tension									
C1 "short-lived relief"	15	11.55	8	53.33	4	26.67	3	20.00	
C2 "inverted U-shaped"	14	10.76	8	57.14	4	28.57	2	14.29	
C3 "relief"	21	16.16	13	61.90	4	19.05	4	19.05	
C4 "unspecific line"	34	26.15	17	50.00	7	20.59	10	29.41	
C5 "follow-ups bring relief"	33	25.39	16	48.49	8	24.24	9	27.27	
C6 "increase"	9	6.92	5	55.56	2	22.22	2	22.22	
C7 "steep decrease"	4	3.07	1	25.00	2	50.00	1	25.00	

## Descriptive data for the cluster solutions for negative affect and tension

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After clustering the NA and tension trajectories surrounding NSSI, we compared the different clusters on participants' ratings whether their NSSI engagement had the desired effect. This data is also reported in Table 4. First, we report the cluster solution for NA trajectories surrounding NSSI. Cluster one ("inverted U-shaped"), cluster two ("small increase"), and cluster three ("small relief") were rated as having had the desired effect in the majority of NSSI events. Clusters one and two were characterized by an initial increase in NA that peaked shortly after the NSSI event (when participants entered the data into the app at t<sub>0</sub>) and was followed by a subsequent decrease in NA.

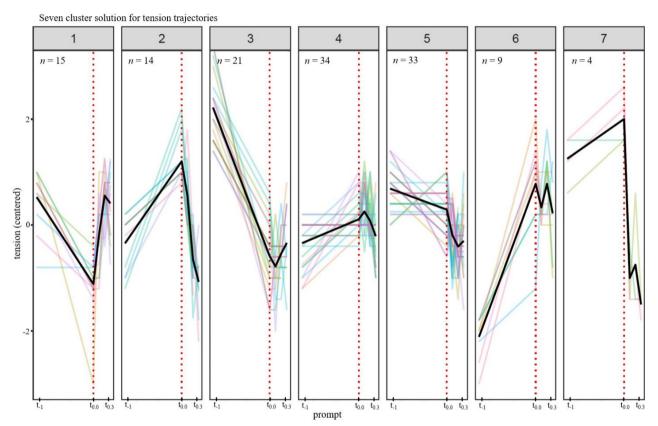


Five cluster solution for negative affect trajectories

*Figure 5.* Five cluster solution for NA trajectories surrounding NSSI events. Red dotted line marks NSSI event at  $t_0$ ,  $t_{0.1}$  -  $t_{0.3}$  were each ten minutes apart,  $t_{-1}$  was in a max. time window of 3.5h. The black lines in each cluster shows the mean trajectory of NA for each cluster.

In cluster two, NA remained elevated after the NSSI report, compared to NA levels preceding NSSI. Cluster three shows a decrease from  $t_{-1}$  to  $t_0$ , followed by almost no further changes in NA during the follow-ups. Participants rated 50% of NSSI events assigned to cluster four ("unspecific line") as ineffective. Importantly, cluster four included approximately half of

all assigned trajectories (n = 60 out of 130 trajectories) and shows almost no changes in NA surrounding NSSI. Cluster five ("follow-ups bring relief") was rated as being ineffective in the majority of the cases and is characterized by nearly no changes in NA between t<sub>-1</sub> and t<sub>0</sub> and a relatively steep decline of NA after the NSSI event. Clusters four and five have in common that they did not show changes in affect prior to NSSI, so we speculate that NA may not have been the main reason for NSSI engagement, such that the decrease in NA following the NSSI event is more a side effect and therefore didn't impact the effectiveness rating.



*Figure 6.* Seven cluster solution for tension trajectories surrounding NSSI events. Red dotted line marks NSSI event at  $t_0$ ,  $t_{0.1}$  -  $t_{0.3}$  were each ten minutes apart,  $t_{-1}$  was in a max. time window of 3.5h. The black lines in each cluster shows the mean trajectory of tension for each cluster.

For tension, we extracted seven clusters. In contrast to NA, where approximately half of all trajectories fell within one cluster ("unspecific line"), trajectories for tension were more evenly assigned to the different clusters (see Table 4). NSSI events in clusters one ("short-lived relief"), two ("inverted U-shaped"), three ("relief"), and six ("increase") were rated as having had the desired effect in the majority of cases. These first three clusters were characterized by

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a relatively steep decrease of aversive tension at some point in the trajectory. Cluster one shows a decrease in tension from  $t_{-1}$  to  $t_0$  with an increase directly after NSSI, meaning that the relief of tension was only experienced during or right after NSSI. Trajectories in cluster three showed a steep decrease from  $t_{-1}$  to  $t_{0.1}$  and a slight increase of tension afterwards. Cluster two showed an increase in tension prior to NSSI and a decrease in tension located within the thirty minutes following NSSI. Cluster six showed an overall increase of tension from  $t_{-1}$  to  $t_0$ , without noteworthy changes in tension after the NSSI event. At the first sight, it seems unusual that this cluster was rated as being effective, but we speculate that participants successfully stopped a further increase of tension by means of NSSI.

Cluster four ("unspecific line") was rated as being effective approximately half the time. On average, there were almost no changes in tension prior to NSSI, followed by a small relief of tension after NSSI. Clusters five ("follow-ups bring relief") and seven ("steep decrease") were more often rated as being ineffective than having had the desired effect. Cluster five is characterized by an overall slight decrease from tension from  $t_{-1}$  to  $t_0$  and a steeper decrease following NSSI, but compared to the other clusters, changes in tension were marginal. Cluster seven encompassed only four NSSI events, and shows that participants started at a high level of tension and experience further increase of tension directly following NSSI, with a consecutive and steep decline of tension afterwards.

## **3.5 Discussion**

The aim of the current study was to test the affect regulation function (also referred to intrapersonal negative reinforcement) of NSSI as postulated by theoretical models of NSSI (Chapman et al., 2006; Hooley & Franklin, 2018; Nock, 2009; Selby et al., 2012). We extended previous studies that used AA designs by (i) including inner tension as a dependent variable, (ii) adding a high-frequency sampling scheme, and (iii) including a control condition with high-urge moments to provide a stricter test for the affect regulation function of NSSI. In detail, we

tested whether short-term changes in NA and tension differ following NSSI events compared to high-urge moments. In line with the affect regulation function of NSSI, we hypothesized that NA and tension would show a steeper decrease following NSSI than following a high-urge (that was not acted upon). We modeled both linear and quadratic trajectories of NA and tension.

## Negative Affect

For NA, we found a significant linear decrease following NSSI, which is in line with the theoretically postulated affect regulation function of NSSI (Chapman et al., 2006; Hooley & Franklin, 2018; Nock & Prinstein, 2004; Selby et al., 2012) and with previous AA studies that demonstrated decreased NA following NSSI engagement (e.g. Andrewes et al., 2016; Armey et al., 2011; Kranzler et al., 2018; Kuehn et al., 2022). However, the slope of the NA decrease following NSSI did not differ significantly from that in the high-urge condition. In other words, like NSSI, resisting an NSSI urge also resulted in decreased levels of NA in the same time window.

For the quadratic trend, we found the opposite pattern: NA surrounding NSSI events did not follow a quadratic pattern, but NA surrounding high-urge moments *did* approximate a quadratic pattern (inverted U-shaped). The quadratic trajectory of NA surrounding urges is in line with previous work by Hepp, Carpenter, et al. (2021), who found inverted U-shaped trajectories of NA surrounding NSSI urges, albeit for the much longer time-frame of a whole day. Similarly, Snir et al. (2015) found an inverted U-shaped pattern, such that NA increased in the hours before an urge, continued to rise after the urge, and then faded gradually. In the present sample, the difference in the quadratic trajectories between the NSSI and high-urge condition was statistically significant. This indicates that NA increased in the hours preceding a strong urge to self-harm and decreased following reporting of that urge, whereas the same was not true for NA surrounding NSSI events. For NSSI events, the highest level of NA was endorsed during the prompt preceding the NSSI report, and NA then tended to decrease linearly.

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The difference in trajectories may partly be attributable to the fact that we were unable to assess NA at the exact moment of NSSI. For the NSSI chain,  $t_0$  was the time-point directly after NSSI, when participants reported the NSSI event on the app, which was on average 6.83 (*SD* = 5.75) minutes after they had completed self-harming. Therefore, we likely missed the peak of NA in the NSSI chain (directly *during* NSSI, when participants were unable to make reports on the app) more often than in the high-urge chain. At the same time, descriptive analyses showed that more than 85% of the NSSI events and high-urge moments were preceded by low levels of NA (PANAS-X-NA mean < 2), and NA did not change at all throughout around 30% of NSSI or high-urge chains. Therefore, even in the high-urge chains, we rarely saw substantial NA peaks at t<sub>-1</sub>. Despite this, the significant quadratic pattern in the urge chain suggests that NA decreased following high-urges for NSSI. This again underlines that resisting an urge also resulted in NA reduction.

Additionally, exploratory analyses of the temporal dynamics of NA surrounding NSSI through clustering showed that approximately half of all NA trajectories (n = 60 of 130) fell within the cluster "unspecific line" that showed almost no changes in NA surrounding NSSI. These descriptive findings are in line with findings from the MLMs showing only a small decrease in NA following NSSI. The model estimate indicated a reduction in mean NA by only 0.12 points on the PANAS-X for every one-unit change of the time variable. For instance, the model would predict an NA decrease of 0.12 points from the random prompt preceding NSSI to the NSSI report which was made directly after participants self-harmed. Notably, a 0.12 is only a small fraction of a single level of the PANAS-X (e.g., improving NA from the level of "a little" to " not at all" would require a full 1 point change). Thus, while MLM results supported NA reduction following NSSI, the descriptive data calls for caution in interpreting these results. Neither was NA substantially elevated at t<sub>-1</sub> nor was the decrease from t<sub>-1</sub> to t<sub>1</sub> large. Additionally, NSSI was not followed by a stronger decrease in NA than high-urge moments were. Taken together and considering the substantial caveat that our sampling may have missed

the peak of NA that directly preceded NSSI, the present data provides only weak support for NA regulation through NSSI (e.g. Chapman et al., 2006; Nock, 2009; Nock & Prinstein, 2004). At the same time, participants in the present sample frequently endorsed having the *aim* to regulate NA through NSSI (*"reduce tension or overwhelming emotions"* was endorsed as the primary motive in 99 out of 155 NSSI events), which underlines that this motive remains a central one, even though we did not see strong NA reduction in effect here.

#### Tension

Even though NA and tension were moderately correlated in the present sample (mean within-person correlation r = .523), results for tension differed from those for NA. Importantly, participants' endorsement of tension was generally higher and more variable than that for NA. This could suggest that it is easier for individuals with NSSI to indicate current tension than rate specific types of NA - a pattern that has also been shown for individuals with BPD (Bresin, 2014; Ebner-Priemer et al., 2008), but may also be due to differences in the way NA and tension were measured in the current study (see limitations). We observed a linear tension decrease from pre to post NSSI. This was not the case for high-urge moments, which were better explained by a quadratic pattern. Importantly, the linear trajectories differed significantly between NSSI and high-urge chains (which was not the case for NA), which suggests that NSSI was associated with a significant linear tension reduction, whereas resisting an NSSI urge was not. This is in line with participants self-reported motive "to reduce tension" in the present sample and adds the first AA evidence to cross-sectional work that reported tension reduction as a central function of NSSI (Klonsky, 2007; Taylor et al., 2018), though tension reduction is also subsumed under negative intrapersonal reinforcement more generally in the four function model (Nock, 2009; Nock & Prinstein, 2004). As with NA, an important caveat to consider is that the reduction in tension that the model estimated tended to be small (0.32 points on the

tension scale that ranges from 0-6). In contrast to the descriptive findings for NA, tension levels were elevated at  $t_{-1}$  in around 50% of NSSI chains.

Mirroring the findings for NA, we further observed that tension followed a quadratic trajectory surrounding moments of high NSSI urge, but not NSSI events. As discussed for NA, this may be attributable to the fact that we missed the exact moment of NSSI engagement and a potential initial reduction in tension due to our sampling scheme. Unfortunately, these differences in temporal dynamics (quadratic vs. linear) made it difficult to directly compare the two trajectories. Nonetheless, the results regarding tension clearly indicated increased levels of tension preceding NSSI and a pronounced reduction in tension following NSSI in the majority of events. Results from our exploratory k-means clustering further supported this. Slightly more than half of all tension trajectories (n = 68 out of 130) were rated as being *effective* by participants. The clusters that were rated as most effective were all associated with substantial changes in tension surrounding NSSI. The only exception was cluster seven, which was more frequently rated as being ineffective than being effective, but also showed a steep decrease in tension. However, this cluster included only four trajectories, therefore its informative value is restricted.

In conclusion, we observed a reduction in tension and NA following real-life NSSI events that is in line with the affect regulation function and intrapersonal negative reinforcement of NSSI but was very small in size and in the case of NA *not* different from the decrease following high-urge moments (Chapman et al., 2006; Hooley & Franklin, 2018; Nock, 2009; Nock & Prinstein, 2004; Selby et al., 2012). A clinical implication could be to increase and improve psychoeducation on the temporal dynamics of NA and tension for those affected by NSSI. Therapists could validate that it may be more challenging to resist an urge for self-harm, because the individual has to manage higher levels of NA or aversive tension, and at the same time underline that in the long run, resisting an urge is likely associated with an effective reduction in tension and NA. This underlines the importance of teaching patients effective ways

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to manage and resist urges to self-harm. In recent years, several approaches from treating substance use disorder have proven effective for the management of NSSI urges, including, for instance, "urge surfing"<sup>10</sup> (Marlett & Gordon, 1985) and a stronger integration of these into NSSI treatment could benefit patients. Additionally, the present results underline the clinical utility of the tension construct for monitoring NSSI. In contrast to NA reports, which relied on specific NA items that may have been challenging for participants to rate, participants reported substantial tension surrounding NSSI acts and urges. Thus, tracking aversive tension with tools such as those incorporated in dialectical behavior therapy (Linehan, 2014) could be helpful for monitoring the precursors and consequences of NSSI. In addition, findings from the k-means clustering suggested that trajectories of NA and tension surrounding NSSI can be differentiated by shape and effectiveness. Future studies should further investigate which trait and state variables (e.g. post-traumatic stress or severity of the injury) are associated with specific trajectory types. Especially state-level predictors could help patients in identifying which situations lead to especially reinforcing NSSI and therefore maintain the behavior.

#### Limitations

While the present study tried to overcome several of the limitations of earlier AA work on NSSI and NA, it is not without its own limitations. First, generalizability of the results is limited to young, primarily white, cis-gender women with frequent NSSI, since we excluded other sexes and genders to reduce sample heterogeneity due to the assessment of biological markers in the parent study (Störkel et al., 2021). However, this means that we are not able to extend findings on the affect regulation function of NSSI to individuals of other sexes, genders or races, which are equally or even more affected by NSSI than cis-gender women

<sup>&</sup>lt;sup>10</sup> In dialectical behavior therapy, urge surfing refers to a therapeutic technique were patients are instructed to imagine their urge (high tension/ NA) as a wave, which is increasing and decreasing with time. Instead of fighting against the wave, patients are instructed to imagine to "surf" on the wave, with the aim to resist the urge by knowing that it will decrease after time, once the wave "breaks".

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(Gholamrezaei et al., 2017; Jackman et al., 2018; Swannell et al., 2014). Furthermore, individuals of other sexes and/or races may face different levels of intensity of both NA and tension due to moderating variables such as discrimination or other life circumstances (Conron et al., 2010; Frost et al., 2015; Jones & Neblett, 2017; Madubata et al., 2022), which could also lead to substantially different findings than the ones reported herein.

Second, like all other studies examining NSSI in daily life until now, we were not able to assess affect ratings directly before or during NSSI. Therefore, we likely missed the peak in NA and tension for NSSI events. This was partially due to our AA design, which did not include a prompt type that encouraged participants to provide data directly before or while self-harming, and in large parts due to feasibility reasons. Of course, it would be extremely difficult and disrupting to ask to participants to respond to the study app while self-harming. Beyond this, asking participants to provide reports directly before they self-harm comes with a number of ethical concerns that, to date, remain unaddressed (e.g., necessity to provide real-time intervention). Nonetheless, future studies should explore ethical ways to allow participants to self-report the intention to self-harm directly before engaging in NSSI.

Third, the dependent variables NA and tension were assessed using different scale-types due to the questionnaire setup. NA was assessed via eight PANAS-X items that are on an unipolar scale. This means that low ratings indicate the absence of a specific affect item, with no possibility to directly report neutral mood, or map a change from NA into PA. To account for this, we reported separate models for PA in the online supplement (and appendix chapter III), following the idea that NA and PA loaded on different factors and should be considered as different dimensions (Rush & Hofer, 2014; Watson & Clark, 1994). For tension, we used the MDBF tension item, which is on a bipolar scale from 0 "calm" to 6 "tense", with neutral mood at the scale's midpoint. This difference in scaling could partially explain the differences between the results for NA and tension.

In addition to the different scales, NA and tension assessment also differed in that we used - a mean score of eight NA items as an indicator of NA, whereas tension was measured with one item. The aggregation of different NA items into a mean score could have obscured important signal of individual affect items being elevated while the mean values for NA were generally low (see descriptive results). To further investigate whether this was the case, we plotted endorsement of all individual NA items at each time-point (from  $t_1$  to  $t_1$ ) in both the NSSI and high-urge chains and provide these plots in the online supplement (and appendix chapter III, Figure C1 and igure C2). They illustrate that some items (especially hostile, blameworthy, and loathing) were very rarely rated above even a 1, independent of the timepoint. The figures also illustrate that all items were generally rated as low in both the NSSI and high-urge chains and that item distributions were generally very similar at the different timepoints. That is, an item that was largely rated as 1 at  $t_{-1}$  (such as loathing) was also rated in the same way at the following time-points. Items with more even endorsement of the different PANAS-X levels such as "alone" also showed this pattern at all time-points. Thus, descriptively, these figures do not suggest that there typically were specific negative affects that stood out substantially. Nonetheless, it would be interesting to follow up on the idea of specific types of NA peaking at different time-points in future work. However, this does not come without its own problems. When following the highest specific NA over time, one would likely miss important secondary emotions at later time-points. For instance, an individual may experience elevated "hostility" before an NSSI event that is reduced after self-harm took place. At the same time, "shame" and "guilt" may increase following the NSSI event, rendering it unclear whether effective emotion regulation took place or not. Alternatively, one could select the highest rated NA value at each time-point and follow its trajectory, but there will likely often be more than one elevated specific NA that precedes NSSI or, in fact, none. For instance, both "afraid" and "alone" may be rated as a 3 whereas everything else is rated as 1 or 2. Or all specific NA items may be rated as 2. In this case, it would be difficult to decide which affect trajectory to follow.

A fourth limitation is that we used high-urge moments without subsequent NSSI as a within group control condition but did not assess or compare context variables in high-urge and NSSI situations, such as lack of privacy, inability to get to preferred instruments, use of skills or other context variables, which could provide information why individuals resisted the urge to self-harm, or engaged in self-harm. Future studies should assess context variables that may differ between NSSI moments and moments with high-urge for NSSI.

Fifth, our results cannot speak to the role of intermittent reinforcement, which is underrepresented in the discussion on NSSI, but likely central in the maintenance of NSSI (Swerdlow et al., 2020). Intermittent reinforcement is characterized by reinforcement that does not follow every single behavior and is generally unpredictable for the concerned individual (Wagner, 1961). For NSSI this could mean that, even if NSSI is not in every case reinforcing, the expectation of the individual that the behavior could be effective sometimes is enough to maintain the behavior. Furthermore, frequently paired stimuli and behaviors (e.g. psychological distress as stimulus and NSSI as behavioral answer) can become a habit which is reinforcing by itself – independently of the expected reinforcing consequences (Swerdlow et al., 2020). This could also be the case in our sample, as individuals in the current study were all affected by chronic NSSI (engagement of years in NSSI M = 9.65, SD = 6.48). Unfortunately, the current data were not suitable to assess learning patterns of individuals over time. Nevertheless, the role of intermittent reinforcement in the development and maintenance of NSSI should be addressed in future studies.

Sixth, our study design had a relatively high participant burden. Individuals had to complete five random prompts per day and additional reports for high-urge and NSSI moments and follow-ups (during all of which they also provided saliva samples, see Störkel et al., 2021). This may have caused systematical missings for high-urge moments and NSSI reports. We cannot rule out that some individuals underreported NSSI urges in order to avoid the high-urge questions, or did not report NSSI events to avoid high frequent sampling following the report of an NSSI event.

## Conclusion

In the present sample, we saw increased levels of NA and tension in the hours preceding real-life NSSI and a linear decrease in NA and tension following NSSI. However, we found that resisting an urge for NSSI was also associated with a reduction in NA and tension, albeit following an inverted U-shaped trajectory instead of a linear one. This suggests that resisting an urge may also be effective in managing NA and tension, although those affected by NSSI would probably have to endure an increase in NA and/ or tension before the reduction occurs. Thus, patients require substantial support in dealing with high levels of aversive tension and NA in order to be able to resist the impulse to engage in NSSI. At the same time, individual temporal trajectories of NA and tension could be explored in psychotherapy, in order to derive individually tailored intervention strategies. Beyond this, a symptom diary or diary card could be used to assess whether an NSSI act had the desired effect, in order to critically discuss that NSSI is not always actually effective in reducing NA or tension (based on our results, it is effective only half of the time). Taken together, the present findings highlight the importance of psychoeducation for individuals with NSSI in order to develop helpful interventions to resist urges to self-harm and to reliably monitor patient expectancies and outcomes of NSSI.

# Study III: A test of the interpersonal function of non-suicidal self-injury in daily life

# **CHAPTER IV**

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# 4.1 Abstract

Theoretical models of non-suicidal self-injury (NSSI) posit that individuals use NSSI to influence others, but this remains largely untested. We used ambulatory assessment to test the interpersonal function of NSSI in the daily lives of 51 women with DSM-5 NSSI disorder. Participants reported NSSI events, urges, motives, and positive/negative interpersonal events (IPEs) for 14 days, providing five semi-random daily assessments and event-related NSSI reports. We analyzed 3,498 data-points, including 155 NSSI events, using multilevel models. We observed a positive concurrent association between the number of negative IPEs and NSSI engagement. Additionally, perceived distress of negative IPEs was positively associated with concurrent NSSI events and urges, and predicted later events. We saw no reduction in negative or increase in positive IPEs following NSSI. In a trait-level interview, participants endorsed interpersonal motives only minimally, but indicated that others often trigger NSSI. In daily life, participants rarely endorsed the motive 'get help/attention'. The results suggest that negative IPEs trigger NSSI, but that individuals in this sample rarely used NSSI for interpersonal motives and did not experience interpersonal reinforcement of NSSI. We discuss limitations of and possible solutions for under-reporting of interpersonal motives and benefits of studying interpersonal triggers (rather than outcomes) in future studies.

# **4.2 Introduction**

Non-suicidal self-injury (NSSI) refers to the intentional, self-inflicted damage of body tissue without suicidal intent and is a prevalent, trans-diagnostic phenomenon that is recognized as a nosological entity in the DSM-5 (APA, 2013). NSSI can take many forms, for instance cutting or burning the skin or hitting oneself. NSSI afflicts approximately 5.5% of the adult population and prevalence peaks in adolescence with rates as high as 17.2% during this developmental period (e.g., Swannell et al., 2014). Beyond the mental health burden itself, NSSI is predictive of future suicide attempts (Victor & Klonsky, 2014) and creates substantial health care and economic costs related to productivity loss, increased morbidity, and mortality (e.g., Kinchin et al., 2017).

Given marked negative outcomes associated with NSSI, the field has produced several theoretical models aiming to explain why people self-injure. Most models posit an affect regulation function of NSSI, including the *Experiential Avoidance Model* (Chapman et al., 2006), the *Four-Function Model* (Nock & Prinstein, 2004), and the *Benefits and Barriers Model* (Hooley & Franklin, 2018). NSSI for the purpose of negative affect regulation has been researched in depth and is the most common self-reported motive for NSSI (Edmondson et al., 2016). Laboratory studies support this picture (Ammerman et al., 2018), as does an emerging body of daily-life evidence (see Hepp et al., 2020 for a review).

Interpersonal functions of NSSI are less researched. The Four-Function Model (Nock & Prinstein, 2004) suggests two interpersonal functions: Interpersonal positive reinforcement, which comprises NSSI aiming to elicit positive behavior from others, and interpersonal negative reinforcement, which includes NSSI aiming to reduce unwanted behavior from others or unwanted interactions, for instance ending a conflict. Similarly, the *Benefits and Barriers Model* (Hooley & Franklin, 2018) suggests that some NSSI is used to generate peer group affiliation and to communicate distress or strength to others. In a systematic review of 152

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studies, Edmondson et al. (2016) found that 87% of studies using self-report questionnaires found evidence for interpersonal functions, for instance seeking help from others. Adding to this, a recent meta-analysis of 46 studies found that NSSI with the goal of communicating distress or increasing support from others was endorsed by 32–56% of individuals, though most participants endorsed more than one function (Taylor et al., 2018).

Beyond cross-sectional self-report studies, few studies have assessed interpersonal functions of NSSI. Laboratory evidence appears to be lacking altogether, and the daily-life evidence on interpersonal functions of NSSI is sparse, as summarized in a recent review (Hepp et al., 2020). Only four of the 35 reviewed studies assessed interpersonal motives for NSSI in the moment (i.e. asking participants why they self-harmed right after it happened), and found endorsement of interpersonal functions in less than 15% of events. Beyond these, only three studies have explicitly tested the interpersonal function of NSSI in daily life. Two studies suggest that the probability of experiencing negative interpersonal events (IPEs) is increased prior to NSSI or on days with NSSI (Snir et al., 2015; Turner, Cobb, et al., 2016), but only one of these demonstrated a decrease following NSSI, suggesting negative reinforcement (Snir et al., 2015). Turner, Cobb, et al. (2016) further assessed the association between NSSI and social support and found that support increased on days following NSSI that was revealed to another person, suggesting positive reinforcement. Lastly, a study assessing NSSI in adolescents found no evidence of positive interpersonal reinforcement, but decreased feelings of attachment to the mother after NSSI (Koenig et al., 2020).

In sum, evidence for interpersonal functions of NSSI is sparse despite being included in leading theoretical models (Hooley & Franklin, 2018; Nock & Prinstein, 2004). Cross-sectional studies suggest that participants endorse interpersonal motives retrospectively, but daily-life studies have shown that participants rarely report interpersonal motives when asked directly after engaging in NSSI. Moreover, daily-life evidence on negative interpersonal reinforcement is limited to only two studies (Snir et al., 2015; Turner, Cobb, et al., 2016), as are examinations

of positive interpersonal reinforcement (Koenig et al., 2020; Turner, Cobb, et al., 2016). The present study sought to fill this gap and provide a test of both self-reported and inferred interpersonal functions of NSSI in daily life.

## The present study

The aim of the present study was to test the interpersonal function of NSSI as posited by the Four-Function Model (Nock & Prinstein, 2004) using ambulatory assessment (AA). Interpersonal negative reinforcement of NSSI suggests that negative IPEs occur prior to NSSI and decrease after NSSI, contributing to an increased likelihood of using NSSI to reduce negative IPEs in the future. Based on this, we derived the following hypotheses. *Hypothesis 1*: Negative IPEs at  $t_1$  predict a greater probability of engaging in NSSI at  $t_0$ . *Hypothesis 2*: NSSI at  $t_0$  predicts a lower number of negative IPEs at  $t_1$ . Additionally, interpersonal positive reinforcement suggests that the probability of experiencing positive IPEs, such as support or comfort from others, increases after NSSI. Therefore, we hypothesized that NSSI at  $t_0$  predicts a greater number of positive IPEs at  $t_1$  (*Hypothesis 3*).

# 4.3 Material and Methods

### **Participants**

We recruited participants via flyers at local clinics, our institution patient waitlist, and Facebook groups on NSSI-related topics. Only women were recruited to reduce heterogeneity, as the parent study assessed biological markers (see Störkel et al., 2021). Data were collected between April 2017 and November 2018. The total sample included 51 women (*M* age = 23.92 years, SD = 6.72, range = 18-45) who met criteria for DSM-5 NSSI-disorder, reporting repeated ( $\geq 1$  / week) NSSI acts that damaged body tissue for the past three months or more. Exclusion criteria were substance dependence in the past 6 months, lifetime developmental disorders or schizophrenia, current pregnancy, and current injuries unrelated to NSSI.<sup>11</sup>

<sup>&</sup>lt;sup>11</sup> We applied additional exclusion criteria related to the collection of saliva samples (see Störkel et al., 2021).

Participants reported frequent past-month NSSI (M = 10.36 events, SD = 6.44, range = 3-32) and past-year NSSI (M = 124.41 events, SD = 104.08, range = 5.5-624) on the Self-Injurious Thoughts and Behavior Interview (SITBI-G, Fischer et al., 2014). To assess further psychopathology, we used the Structured Clinical Interview for DSM-IV (SCID-I, First et al., 1995) and the BPD section of the International Personality Disorder Examination (IPDE, Loranger et al., 1997). All participants met criteria for at least one mental disorder, the most common being major depression (n = 33, 64.71%) and borderline personality disorder (n = 32, 62.75%). The majority of participants (n = 30, 58.82%) reported long-term use of psychiatric medication, most commonly antidepressants (n = 30, 58.82%) and atypical antipsychotics (n = 14, 27.45%). See Table D1 in the appendix for additional demographic and clinical characteristics.

#### Procedure

Following a description of the study protocol, participants provided written informed consent for the study, which was approved by the ethics committee of the Medical Faculty Mannheim, Heidelberg University (2014-601N-MA). Participants then completed an in-person or online (via the secure platform *Patientus*, jameda GmBH, Munich, Germany) orientation session, including clinical interviews and an introduction to the smartphone application (movisensXS, Version 0.7.4682, movisens GmbH, Karlsruhe, Germany), which was provided on study smartphones. Study smartphones were mailed to participants who completed the orientation session online. Additionally, we sent an email with video instructions on how to use the smartphone app to these participants, so they could refer back to the video after completing the online orientation session. Participants who received the instructions online did not report any problems with the app, which suggests that using an online orientation session and using instructional videos may be a feasible avenue in AA NSSI research. Following this, participants completed a 15-day AA assessment period (including a baseline day and 14 days of regular AA protocol). Figure 7 illustrates the different types of prompts that were included (also see Störkel

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et al., 2021). Participants completed five semi-random prompts per day (scheduled at least two hours apart during participants' normal waking hours), and were asked to self-initiate additional reports as soon as possible following NSSI. We included self-initiated prompts for NSSI events (and follow-up prompts for these) as we were interested in the psychological processes that unfold right after NSSI. If NSSI events were only assessed during random prompts, the time lag between the actual NSSI event and the reporting of that event during the next random prompt would be substantial (on average 2 hours in our sampling scheme). Therefore, including self-initiated prompts allowed for a much higher temporal resolution. In addition to the selfinitiated prompts, we included five semi-random prompts per day to capture psychological processes during the whole day on both NSSI and non-NSSI days. The combined sampling scheme has the benefit of capturing NSSI events as close in time as possible (self-initiated prompts) and ensures that no NSSI events get lost if participants forget to self-initiate a report, as they would be prompted to report them during the next random prompt. Participants took on average 87.75 seconds (SD = 57.61) to complete a random prompt. The design included no "skip-out" options, that is, participants always saw the total number of items and there were no item filters. IPEs were only assessed during random prompts and self-initiated NSSI reports outside the baseline day. For further detail on all prompt types and variables, see the online supplement. Following participation, participants received 100€ for compensation, with an additional bonus of  $50 \in$  for > 80% compliance. As an additional incentive, participants had the option to receive a personalized plot with their study data after completing the study, which many of them indicated to us was a motivating factor for high adherence to the study protocol.

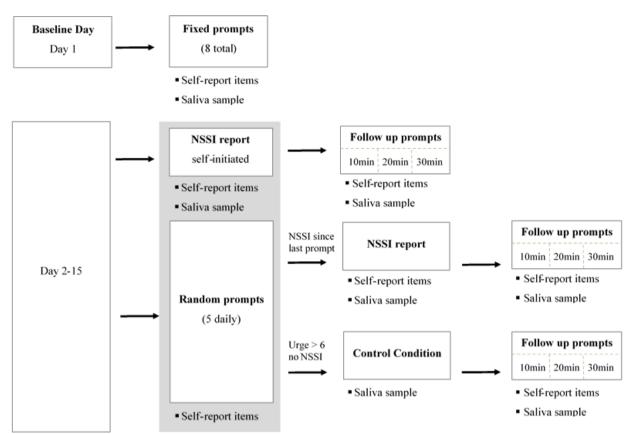


Figure 7. Overview of all prompt types included in the parent study. Prompts where interpersonal events were assessed are shaded in grey, only these were used for the current analyses. For further detail, see Störkel et al. (2020) and supplement

## Material

*NSSI Interview:* During the orientation session, a trained Master's level psychologist administered the SITBI-G (Fischer et al., 2014), a semi-structured interview that assesses motives of and triggers for NSSI on a scale from 0 ("low/little") to 4 ("very much/severe"). NSSI frequency, severity, and methods were also assessed via the SITBI-G. Scores for SITBI-G motives and triggers are presented in Table 5.

*NSSI events*. Participants were instructed to self-initiate an AA assessment whenever they self-injured, by clicking a button on the smartphone app that said "I have hurt myself." Additionally, participants were asked during all random reports: "Since the last prompt I have answered, I have hurt myself" (1 = yes, 0 = no).

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*NSSI urges.* Urge was assessed with the single item "*During the last 15 minutes, the urge to hurt myself was*" on a visual analog scale from 0 ("no urge at all") to 10 ("I can hardly contain the urge").

*NSSI motives*. Whenever participants reported NSSI, motives were assessed. Participants selected all that apply from the following: "I wanted to reduce aversive tension or overwhelming emotions," "I wanted to express my self-hatred/self-contempt," "I wanted to feel something (other than nothing)," "I wanted help/attention of others," "I had another reason," and "I don't know why I self-harmed."<sup>12</sup> Endorsement frequencies are presented in Table 5.

*Interpersonal events*. Participants reported significant positive and negative IPEs during random prompts ("Since the last beep, someone... ") and during self-initiated NSSI prompts ("Before I self-harmed, someone..."). We presented participants with five positive and five negative items that we piloted previously (for further detail, see online supplement). Individual items are presented in Table 6. Participants were instructed to select all items that applied. If any event was endorsed, participants were asked whether "What the person did was a reaction to my last NSSI" ("yes"/"no"/"don't know") and "What the person did distressed me" (0 = "not at all" to 5 = "very deeply").

## Data analysis

Data were analyzed using multi-level models (MLMs), treating prompts as nested within persons. We modelled random intercepts per person and random slopes for momentary-level predictors. Analyses were conducted in R using the package *lme4*. We used the function *lmer* for linear MLMs, *glmer* with a logit link function for logistic MLMs, and *glmer* with a log link for count outcomes. Significance tests were conducted using the package *lme7test*. All models adjusted for the person mean of the predictor variable (i.e. mean number of negative

<sup>&</sup>lt;sup>12</sup> Participants responded to additional questions following endorsement of NSSI (method, severity, painfulness, pleasantness of pain, momentary affect, dissociative symptoms), but these items were not included in the analyses for present study (see Störkel et al., 2021 and the online supplement for further details).

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IPEs for each individual, mean distress reported by each individual) to disaggregate withinfrom between-person effects. All models further included a covariate for the time since wake (in hours), as NSSI was more likely to occur toward the end of the individual day. Momentary predictors were centered on the person mean, and person-level predictors were centered on the grand mean. Lagged analyses did not include lags across days (e.g., the last prompt of day 2 was not treated as a lagged prompt for the first prompt of day 3).

## Table 5

	M/n	SD/%
SITBI-G NSSI triggers		
mental state at the time	3.40	0.76
problems with family	2.81	1.16
problems with work/school	2.76	1.15
problems with peers	1.99	1.33
problems with relationships	1.95	1.57
problems with friends	1.72	1.31
SITBI-G NSSI motives		
as a way to get rid of bad feelings	3.37	1.02 1.29 1.22
because you were feeling numb and empty	2.80	
to get out of doing something or to get away from others	1.36	
to communicate with someone else or to get attention	0.91	1.20
Momentary NSSI motives <sup>a</sup>		
To reduce aversive tension or overwhelming emotions	99	63.9%
Self-hatred/ self-contempt	59	38.1%
To feel something (other than nothing)	31	20.0%
To get help/ attention from others	8	5.2%

## Triggers and motives for NSSI at the trait and momentary levels.

*Note.* SITBI-G triggers and motives asses on a scale from 0 "low/little" to 4 "very much/severe". Momentary motives were assessed dichotomously (present/absent) whenever NSSI was reported.

<sup>a</sup> In 45.8 % of NSSI events participants chose more than one motive.

## 4.4 Results

### Descriptive results

Random prompt compliance was high (92.04%) and resulted in a total of 3,498 observations included in the present analysis. On average, participants reported 3.04 NSSI events per person (SD = 2.45; range 0-15), totaling 155 events. Endorsement rates for trait-level motives and triggers assessed using the SITBI-G (Fischer et al., 2014) are presented in Table 5. Problems with family were the second most endorsed trigger for NSSI and problems with all remaining interaction partners (peers, friends, partners) were endorsed to a moderate degree with average endorsement ranging around 2 (0 = "low/little", 4 = "very much/severe"). The two interpersonal motives for NSSI ("to get out of doing something or to get away from others", "to communicate with someone or get attention") were endorsed at very low levels. In addition to these trait measures, we assessed NSSI motives at the momentary level. Of note, the interpersonal motive, "to get help/attention from others," was only endorsed for eight NSSI events (5.16%).

Negative IPEs were endorsed on 15.3% of all random prompts and positive IPEs were endorsed on 38.3%. Of prompts where NSSI was reported, participants endorsed negative IPEs on 34.3% and positive IPEs on 19.7%. Table 6 presents endorsement rates for the specific types of negative and positive IPEs during NSSI and random prompts and a comparison of their frequency based on chi-square tests. Importantly, almost all negative IPEs were significantly more likely to be endorsed during NSSI prompts than random prompts, and all positive IPEs were significantly more likely to be endorsed during random prompts than NSSI prompts.

When negative or positive IPEs occurred, participants rarely reported that what their interaction partner did was a reaction to their most recent NSSI. Participants indicated this for only 1.11% of negative events and 1.81% of positive events. Additionally, participants reported how distressing the IPEs were. On average, participants rated the distress level of negative IPEs

during random prompts significantly lower (M = 3.09, SD = 1.42) than for events directly preceding NSSI (M = 3.77, SD = 1.16, t(47.44) = 3.47, p = .001).

## Table 6

Frequency of endorsement of interpersonal events by prompt type and Chi-square tests comparing frequencies between prompt types.

	NSSI prompts (Before I self- harmed, s/o)		Random prompts (Since the last prompt, s/o)		
	n	% of prompts	n	% of prompts	Chi-square test
Negative Events		prompto		prompto	
criticized me	13	9.49	236	7.02	$\chi^2(1) = 1.71$
rejected/excluded me	19	13.87	186	5.53	$\chi^2(1) = 18.81^{***}$
ignored my needs or	24	17.52	216	6.43	$\chi^2(1) = 28.52^{***}$
feelings					
behaved angry/	14	10.22	141	4.20	$\chi^2(1) = 12.85^{***}$
aggressive towards me					
let me down/	23	16.79	221	6.58	$\chi^2(1) = 23.97^{***}$
disappointed me					
none of the above	90	65.69	2847	84.71	$\chi^2(1) = 22.28^{***}$
Positive Events					
supported/ helped me	3	2.19	401	11.93	$\chi^2(1) = 11.28^{***}$
showed me affection	10	7.30	664	19.76	$\chi^2(1) = 11.62^{***}$
respected my needs or	6	4.38	454	13.51	$\chi^2(1) = 8.60^{**}$
feelings					
gave me their attention	18	13.14	892	26.54	$\chi^2(1) = 10.37^{**}$
or time					
was interested in me,	12	8.76	685	20.38	$\chi^2(1) = 9.67^{**}$
understood me					
none of the above	110	80.29	2073	61.68	$\chi^2(1) = 28.91^{***}$

*Note*. Participants reported 155 NSSI events in total, but only 129 events were reported during self-initiated NSSI reports; the other 26 events were captured during random prompts. Interpersonal events that participants indicated for the item "before I self-harmed ..." were only assessed during self-initiated NSSI reports. Therefore, the *n* for NSSI prompts for this descriptive data is 129 and the *n* for random prompts is 3343. \*p < .05, \*\*p < .01, \*\*\*p < .001.

### Hypothesis 1

To test whether negative IPEs are positively associated with the probability of subsequent engagement in NSSI, we conducted two generalized MLMs using a logit link function with momentary NSSI (yes/no) as the binary outcome variable. The first model included the concurrent and lagged *sum* of negative IPEs and covariates. We included the concurrent prompts because the self-initiated NSSI prompts asked individuals about negative IPEs occurring 'right before' any reported NSSI. Therefore, temporal precedence was present for NSSI prompts such that any reported negative interpersonal event preceded NSSI. The second model included the concurrent and lagged *distress* caused by negative IPEs as predictors.

Results indicated that a higher number of negative IPEs in the current moment (at t<sub>0</sub>) predicted a higher probability of reporting NSSI at that prompt (OR = 1.54, 95% CI = [1.24, 1.91], p <.001). In contrast, a higher number of negative IPEs at t<sub>1</sub> did not significantly predict NSSI at t<sub>0</sub> (OR = 1.11, 95% CI = [0.77, 1.60], p = .565)<sup>13</sup>. Results from model 2 showed that higher distress from negative events at t<sub>0</sub> and at t<sub>1</sub> positively predicted NSSI at t<sub>0</sub> (distress at t<sub>0</sub>: OR = 1.37, 95% CI = [1.20, 1.58], p <.001; distress t<sub>1</sub>: OR = 1.21; 95% CI = [1.01, 1.45], p = .040). For detailed results including effects for all covariates, see Tables D2-D3 as presented in the appendix chapter IV. Results are illustrated in Figure 8.

## Hypothesis 2

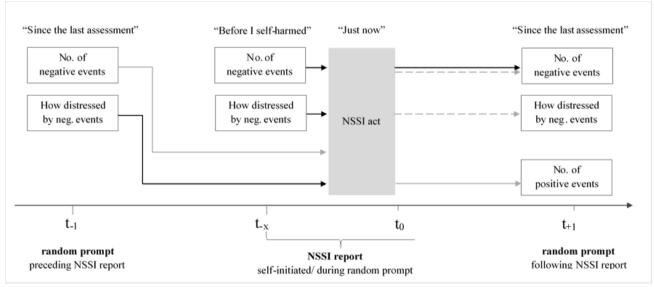
To test the hypothesis that NSSI would be negatively associated with the number of subsequent negative IPEs, we conducted two MLMs. The first, a generalized MLM using a log link function, included the *number* of negative IPEs reported since the last prompt as the outcome variable from a Poisson distribution. The second model was a linear MLM with the *distress* of negative IPEs reported since the last prompt as the outcome. Predictors in both

<sup>&</sup>lt;sup>13</sup> Using a dichotomous variable that codes whether any negative IPE occurred (coded 1) or none occurred (coded 0) produced the same results as the sum score.

models included NSSI at t<sub>1</sub>. Results indicated that NSSI was not significantly associated with either the number of negative IPEs reported in the subsequent moment (*Incidence Rate Ratio* [*IRR*] = 0.73, 95% *CI* = [0.25, 2.09], p = .555) nor their distress following negative IPEs ( $\beta = 0.01, 95\%$  *CI* = [-0.02, 0.05], p = .488)<sup>14</sup>. See Tables D4-D5 presented in the appendix and Figure 8.

## Hypothesis 3

To test the hypothesis that NSSI would be positively associated with the number of subsequent positive IPEs, we conducted a generalized MLM. The model mirrored that for hypothesis 2 but with positive IPEs as the outcome. Results indicated that NSSI at  $t_0$  was not significantly associated with the number of positive IPEs at  $t_1$  (*IRR* = 0.91, 95% *CI* = [0.58, 1.43], *p* = .679). See Table D6 and Figure 8.



*Figure 8.* Illustration of findings. Solid black arrows indicate significant positive associations. Solid grey arrows indicate hypothesized, but non-significant positive associations. Dotted grey arrows indicate hypothesized but non-significant negative associations.

## Exploratory analyses

*NSSI urges:* Previous studies suggest that negative IPEs are not only associated with NSSI acts but also with urges for NSSI and that most acts are preceded by urges (Hepp et al., 2020). Negative IPEs may thus precede urges that do not necessarily lead to acts of self-harm.

<sup>&</sup>lt;sup>14</sup> Again, using a dichotomous indicator of whether any negative IPE occurred produced the same results.

In an exploratory linear MLM, we tested whether the *sum* of negative IPEs predicts concurrent or subsequent NSSI urges. As for NSSI acts, the sum of negative IPEs were positively associated with concurrent urges ( $\beta = 0.26$ , 95% CI = [0.19, 0.33], p < .001) but not subsequent urges ( $\beta = 0.03$ , 95% CI = [-0.01, 0.08], p = .125; see Table D7 in the appendix). In a second MLM, we tested whether distress caused by negative IPEs predicted concurrent or subsequent NSSI urges. The degree of distress resulting from negative events was positively associated with concurrent urges ( $\beta = 0.23$  95% CI = [0.19, 0.27], p < .001) but not subsequent urges ( $\beta = 0.02$ , 95% CI = [-0.02, 0.05], p = .436; Table D8 in the appendix).

Day level analyses: Consistent with Turner et al. (2016), we conducted additional analyses to determine whether associations between NSSI and IPEs might be better captured at the day level of analysis (see appendix for details and results in Tables D9 - D10). We conducted two linear MLMs using the average number of negative/positive IPEs reported in a day as the outcome. The predictors of interest were whether NSSI was reported during the concurrent or lagged day (coded 0 or 1). NSSI on any given day was positively associated with the average number of negative IPEs reported on the same day ( $\beta = 0.08, 95\%$  CI = [0.02, 0.13], p = .005), but not the next day ( $\beta = 0.00, 95\%$  CI = [-0.06, 0.05], p = .904). We observed no significant association between positive IPEs and NSSI on the same day ( $\beta = -0.06, 95\%$  CI = [-0.11, 0.00], p = .062) or the next day ( $\beta = 0.03, 95\%$  CI = [-0.03, 0.09], p = .263).

## **4.5 Discussion**

We tested the interpersonal function of NSSI as proposed in the Four-Function Model (Nock & Prinstein, 2004) in the daily lives of 51 women with NSSI disorder over a period of two weeks. Using the SITBI-G (Fischer et al., 2014), we assessed participants' trait-level motives and triggers for NSSI. Participants showed only weak endorsement of interpersonal negative reinforcement motives at the trait level ("to get out of doing something/away from others") and rarely endorsed positive interpersonal reinforcement motives ("to get attention") at both the trait and momentary levels.

In contrast to the weak endorsement of interpersonal motives, participants strongly endorsed interpersonal triggers for NSSI (especially family members) in the SITBI-G and reported a significantly higher number of interpersonal problems as having occurred 'right before' NSSI (see Figure 8) than during other assessments. Compared to previous studies, we included a substantially broader set of IPEs and observed that participants most often endorsed 'someone ignored my needs or feelings' and 'someone let me down or disappointed me' as preceding NSSI.

Using a logistic MLM, we found that the number of negative IPEs that occurred directly before NSSI was positively associated with the probability of engaging in NSSI at that timepoint. Going further back in time and considering the last random assessment preceding NSSI did not reveal a significant association. The same pattern emerged in an exploratory analysis for NSSI urges. These results differ somewhat from findings by Snir et al. (2015), who sampled at a similar frequency (also including five semi-random daily prompts), and found elevated rejection in the prompts preceding NSSI events. However, their sample included individuals with BPD and avoidant personality disorder, both of which are characterized by increased reactivity to rejection. This could explain why Snir and colleagues (2015) observed a significant association between rejection and NSSI across a longer timeframe in their study, while we only observed this association with events that occurred immediately prior to NSSI. However, when considering the perceived *distress* caused by negative events rather than just the number of events that occurred, we observed significant associations with concurrent and later NSSI acts. In other words, negative IPEs that occurred around two hours earlier did not predict NSSI engagement, but negative IPEs that were perceived as highly distressing did. The same was observed for NSSI urges. It is possible that increased distress caused by negative IPEs also underlies the increased prevalence of negative IPEs preceding NSSI that was demonstrated by Snir et al. (2015), but additional studies are needed to clarify the types and intensities of interpersonal events that precede NSSI and further specify the time window for this association.

Next, we tested whether interpersonal problems decreased following NSSI, as this would facilitate interpersonal negative reinforcement. We found no significant association between NSSI at t<sub>0</sub> and the number of or the perceived distress caused by negative IPEs at t<sub>1</sub>. This contrasts findings by Snir et al. (2015), who observed a decrease in rejection following NSSI, and is inconsistent with the idea of NSSI eliciting interpersonal negative reinforcement (Nock & Prinstein, 2004). Likewise, we found no association between NSSI and a subsequent increase in positive events, as would be implied by interpersonal positive reinforcement. This was consistent with another source of data from our study: whenever participants reported IPEs, we asked whether they saw the other person's behavior as a reaction to their last NSSI. Participants rarely endorsed this (only 1.81% of positive events). It somewhat contrasts findings by König et al. (2020) who found decreased feelings of attachment to participants' mothers following NSSI in an adolescent sample. However, the present study is not directly comparable because i) the samples are different, ii) König et al. used a higher frequency sampling approach with hourly prompts, and iii) feeling attached is conceptually different from the positive behaviors by others we assessed.

Because a previous study found that positive IPEs did not increase immediately following NSSI, but only the next day (Turner, Cobb, et al., 2016), we conducted exploratory day-level analyses. Turner and colleagues (2016) found a positive association between the level of conflict in a day and the likelihood for NSSI that day, and we replicated this finding. They also found that conflict did not decrease on days following NSSI (including NSSI revealed to others), which we also replicated. Contrasting findings by Turner et al. (2016), we did not see an increase in positive IPEs on days following NSSI, whereas they observed increased support following NSSI days.

#### Limitations and future directions

First, the generalizability of results is limited to younger women with DSM-5 NSSI disorder, as we excluded men and restricted the age range (18-45 years) to reduce sample heterogeneity in light of the biological component of the parent study (Störkel et al., 2021). This reflects a problem of the field of AA NSSI research at large (see Hepp et al., 2020) – a selective focus on studying younger white women, resulting in a clear need for the assessment of more diverse samples.

A second limitation is the possibility of under-reporting of interpersonal motives because of social desirability. The way interpersonal motives are phrased in the SITBI-G and the momentary motive 'to get help/attention' could have suggested to participants that their NSSI was a manipulative means of getting attention from others. This is one of the central stigmas surrounding NSSI, and a fear of propagating it could have resulted in under-reporting of interpersonal motives. We relied on the SITBI-G as an established measure to assess NSSI motives, but suggest that future studies include additional, less stigmatizing items to assess interpersonal motives (e.g., 'to cope with interpersonal stress'). Moreover, the fact that we only assessed interpersonal motives. For instance, participants may have engaged in NSSI for interpersonal reasons other than seeking help/attention but were unable to reflect this on the AA surveys. Additionally, as detailed in Table 6, for the majority of NSSI events (65.69%), participants reported that none of the negative IPEs we assessed preceded the event. Participants may have experienced other negative IPEs which we did not assess, or may have experienced other triggers for NSSI of an intrapersonal nature.

A third limitation is that we did not assess whether NSSI was revealed to another person. Turner et al. (2016) found that interpersonal reinforcement of NSSI only occurred for events that were revealed to another person and, conceptually, someone else being aware that NSSI took place is a prerequisite for interpersonal reinforcement. We intended to implicitly assess

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whether NSSI was revealed to another person by asking participants whether another person reacted to it. However, responding "no" to the question we used ("Was the interpersonal event a reaction to the last NSSI?") could mean several different things. It could indicate that (a) the interaction partner did not know about the participant's NSSI act (it was not revealed to them), or (b) the interaction partner did know about the NSSI act, but did not react to it, or (c) that the interaction partner's reaction was not attributed to NSSI by the participant. Consequently, an additional direct assessment of NSSI revelation in combination with a question asking participants whether they perceived an interaction partner's behavior as a reaction to their latest NSSI would be ideal in future studies.

Fourth, the way that we aimed to establish temporal precedence of IPEs prior to NSSI may have introduced limitations. Whenever participants reported NSSI during NSSI prompts, we asked them to report whether any IPEs happened 'right before' the NSSI event. This suggests temporal precedence of IPEs prior to NSSI. However, it is possible that negative events occurred much earlier in the day and triggered NSSI despite not occurring 'right before' the NSSI event. For instance, an individual may feel rejected by their partner in the morning, resulting in sustained negative affect or self-loathing throughout the day that ultimately culminates in NSSI. In this instance, they might indicate affect regulation or self-loathing as the motive for NSSI and no IPEs occurring 'right before' NSSI, despite the initial trigger being rejection. Moreover, despite asking participants to report IPEs that occurred 'right before' NSSI engagement, these IPEs were still assessed at the same occasion as the NSSI event. Therefore, the time lag was only established based on the way the item was phrased, rather than being incorporated in the study design. It is therefore possible that these reports are biased, given that participants were asked to complete these reports directly following NSSI while they may have still experienced substantial distress.

A final limitation that affects the present study and previous work on interpersonal NSSI is the question of specificity of interpersonal events. By only assessing interpersonal stressors,

it remains unclear whether the specific interpersonal nature of the stressor was predictive of NSSI or whether other types of stressors (e.g., a job demand or financial trouble) would produce similar results. Therefore, future studies should consider comparing interpersonal stressors to other types to stressors with regard to predicting NSSI.

#### Conclusion

In sum, results implicate negative IPEs as a trigger for NSSI and suggest that assessing the level of distress caused by IPEs is an important extension to assessing their incidence. Only negative IPEs with high levels of associated distress, but not mere incidence of negative events, predicted subsequent NSSI. At the same time, we found no evidence for positive or negative interpersonal reinforcement following NSSI, which questions the role of these processes in the maintenance of NSSI. Overall, we found only limited evidence for interpersonal functions of NSSI, as individuals rarely endorsed these as self-reported motives. However, conclusions on motives are likely limited by the restricted assessment of interpersonal motives and possible under-reporting due to social desirability. Future studies may benefit from assessing IPEs as *triggers* of NSSI and a careful assessment of interpersonal motives using non-stigmatizing items. A careful assessment of the quality of IPEs, for instance how distressing they are, with whom they occur, or even cognitive aspects such as whether they violate prior beliefs (e.g., betrayal by a trusted person) may help further elucidate which IPEs are the most potent triggers of distress and NSSI, to ultimately inform prevention and treatment approaches.

We note that the empirical evidence on interpersonal functions of NSSI is still limited, as this is only the fourth study to directly test it. Therefore, any clinical implications must be considered preliminary. Yet, so far, studies have found little evidence for interpersonal reinforcement following NSSI, suggesting that the behavior is unlikely to be substantially maintained by outside attention from others. Therefore, rather than focusing on the role of parental, spousal, or peer behavior in response to NSSI, clinicians may better help their patients

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by helping them identify interpersonal triggers of NSSI and how the distress resulting from negative interpersonal events can be regulated so that NSSI does not occur.

## **Thesis Discussion**

# **CHAPTER V**

This thesis comprises three publications, all of which aimed to shed more light on the antecedents and consequences of NSSI in daily life on a psychological as well as a biological level by assessing  $\beta$ -endorphin, affect and tension (together as affect regulation function of NSSI), and IPEs (interpersonal function of NSSI) in the context of NSSI. All three constructs touch different aspects of NSSI on different dimensions, showing that the engagement in NSSI is affected by multiple factors. The assessment of  $\beta$ -endorphin is representative for biological processes, which reflect unconscious mechanisms that influence the individual affected by NSSI, whereas the affect regulation function of NSSI is a mechanism, which describes more or less conscious inner psychological states, also affecting self-injurious behavior. In addition to this, the interpersonal function of NSSI shows how social interactions are able to influence the probability of NSSI engagement. In parts, these constructs are theoretically related. For example, in the context of NSSI β-endorphin is one important marker of the EOS, involved in the perception of emotional and physical pain (Bresin & Gordon, 2013), and therefore theoretically associated with NA and tension but more research is needed to clarify this (Bandelow et al., 2010; Bresin & Gordon, 2013). Furthermore, in previous work, negative IPEs were associated with increased NA and tension in individuals with BPD (who are at especially high risk for being affected with NSSI; Hepp et al., 2018; Stiglmayr et al., 2005) and NA was associated with a higher probability to engage in negative IPEs (Chaudhury et al., 2017; Hepp et al., 2018). Thus, to provide a more inclusive picture of NSSI in daily life, I decided to assess these three constructs representing different facets of antecedents and consequences of NSSI.

Using an AA design, I investigated 51 cis-gender woman with chronic NSSI over a study-period of 15 days. I decided to use an intensive longitudinal design, as AA is especially suited to assess within-person dynamics such as biomarkers or affect and tension, which

fluctuate across the day. Additionally, AA designs help to overcome memory biases, which typically occur when participants are asked to aggregate variables such as inner states across more than a couple of hours (Solhan et al., 2009).

First, I focused on salivary  $\beta$ -endorphin released surrounding NSSI and high-urge moments. In line with my first hypothesis and theoretically assumptions (e.g., Stanley & Siever, 2010), salivary  $\beta$ -endorphin increased significantly from pre to post NSSI, which indicates that one reason why individuals engage in NSSI may be that they try to return to a normphysiological level of  $\beta$ -endorphin through NSSI engagement. However, this finding must be seen as highly preliminary, as only 18 pre NSSI samples were collected during the study period. Furthermore, results demonstrated that the self-rated severity of the injury showed a significant positive association with levels of  $\beta$ -endorphin. This finding supported the a priori assumption that it is possible to detect  $\beta$ -endorphin in human saliva, and that those changes are associated with NSSI variables. Contrary to my hypothesis, results did not show a significant difference in  $\beta$ -endorphin levels between moments of high-urge and moments directly following NSSI events, which suggests that high-urge moments were not necessarily accompanied by low levels of  $\beta$ -endorphin. Additionally, there was no association between pain ratings and levels of  $\beta$ endorphin, which indicates that pain ratings could be partly moderated by cognitive processes.

Second, I investigated the role of the affect regulation function in the context of NSSI, as postulated by almost all theoretical models on NSSI (Chapman et al., 2006; Hooley & Franklin, 2018; Nock & Prinstein, 2004)<sup>15</sup>. NA and tension were assessed as two components of the affect regulation function and I compared moments of high-urge to NSSI moments to differentiate whether changes in NA and tension can be attributed to NSSI. The linear trajectory of NA did not differ between moments of high-urge and NSSI, whereas for tension, results show a stronger linear decrease following NSSI moments than following high-urge moments.

<sup>&</sup>lt;sup>15</sup> The role of positive affect is presented and briefly discussed in the appendix of chapter III

Nevertheless, high-urge moments for both, tension and NA, followed an inverted U-shaped pattern that indicates a significant decrease of NA and tension in the same time-window as NSSI. The difference in shape between the two conditions (NSSI vs. high-urge) may be partly attributable to the fact that data of NA/ tension were missing in the moment of NSSI engagement, because participants reported on their NA/ tension after completing self-harm (on average M = 6.83, SD = 5.75 min. after NSSI engagement). Therefore, their self-reports on NA and tension could be biased through the already experienced relief after self-harm, preventing the inverted U-shaped pattern I found for high-urge moments.

In the third publication, I focused on the interpersonal function of NSSI by assessing positive and negative IPEs and their association with NSSI in daily life. Additionally, participants were asked whether the IPE caused distress and if, in case of a recent NSSI act, the IPE was a reaction to their last self-harm episode. Results show that concurrent negative IPEs, but not earlier ones, were associated with NSSI. When including the amount of distress caused by the IPEs, highly distressing negative IPEs at  $t_0$  and  $t_1$  were associated with NSSI. When testing negative interpersonal reinforcement, results indicated that NSSI was not significantly associated with either the number of IPEs or the caused distress of the IPEs. In other words, there was no reduction in negative IPEs following NSSI events. In line with this, but contrary to my hypothesis, there was no association between NSSI and the number of positive IPEs in the subsequent prompts.

In the following sub-sections, I will integrate the findings from these three AA publications into the existing literature on NSSI. I aim to highlight where the findings are in line with previous work and where the results add new insights to the understanding of NSSI. Furthermore, I discuss limitations of the current publications and derive research implications to inform future work and present ideas for clinical practice.

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## 5.1 Summary and Integration of Study Findings

Previous studies on the association between the EOS system and pain and/or NSSI mainly focused on central processes in the brain and found evidence for reduced pain sensitivity after  $\mu$ -receptor stimulation (Zubieta et al., 2001), chronically reduced levels of  $\beta$ -endorphin (Stanley et al., 2010b), and higher  $\mu$ -opioid receptor availability in the brain (Prossin et al., 2010). Only one study assessed peripheral  $\beta$ -endorphin in individuals with NSSI (van der Venne et al., 2021), examining blood plasma during rest. This study found reduced levels of  $\beta$ -endorphin in individuals with NSSI compared to individuals without NSSI. None of these studies assessed release or changes in the EOS or in  $\beta$ -endorphin before, during or after NSSI or during NSSI-like stimulation. Therefore, my study was the first extending these findings to daily life and assessing intraindividual changes in  $\beta$ -endorphin rather than group differences. My preliminary findings supported the theoretical assumption that individuals engage in NSSI to restore a norm-physiological level of  $\beta$ -endorphin through NSSI (Bandelow et al., 2010; Bresin & Gordon, 2013) and added new insights on biological states (changes of  $\beta$ -endorphin across an episode of NSSI) as postulated by the model of distal and proximal trait biology as well as biological states around NSSI (Kaess et al., 2021).

Contrary to my hypothesis, I did not find a significant difference between high-urge moments and post-NSSI samples, which is not in line with previous theoretical assumptions that high-urges for NSSI should be accompanied by low levels of  $\beta$ -endorphin, raising the need to engage in NSSI (Stanley & Siever, 2010). One explanation for the non-significant finding could be that participants provided only n = 32 saliva samples during very high levels of urge for NSSI (13.56% of the saliva samples in the control condition), probably indicating that moderate stages of urge for NSSI do not sufficiently stimulate neurobiological processes which trigger the release of  $\beta$ -endorphin. However, there were also no significant differences between  $\beta$ -endorphin levels on the baseline day (non-NSSI day) and post NSSI samples, which underlines that there is no evidence for higher than usual levels of  $\beta$ -endorphin after NSSI in

my preliminary data. This is in line with assumptions of Bandelow and colleagues (2010) who stated that individuals engage in NSSI to restore homeostasis after experiencing low levels of  $\beta$ -endorphin.

Furthermore, I did not find a significant association between self-rated pain and levels of  $\beta$ -endorphin, even though more severe injuries were rated as significantly more painful. In contrast to this, the self-rated severity of the injury was significant and positively associated with levels of  $\beta$ -endorphin, which means that more severe injuries lead to higher release of peripheral  $\beta$ -endorphin. Interestingly, participants reported overall mild pain or even analgesia over all categories of injury severity (mild, moderate, severe). This is in line with the findings of two meta-analyses showing that individuals with BPD and NSSI and individuals with a history of NSSI showed reduced pain sensitivity during laboratory pain-induction tasks (Fales et al., 2021; Koenig et al., 2016). However, pain ratings in my sample should theoretically be linked to levels of salivary  $\beta$ -endorphin since the severity of the injury indicated a release of an appropriate proportion of  $\beta$ -endorphin. According to previous work, cognitive coping strategies and the self-efficacy to withstand pain are important for the perception and downregulation of pain, beyond biological mechanisms in the opioid system (Bandura et al., 1987; Fernandez & Turk, 1989). Therefore, I speculate that I did not find an association between self-rated pain and levels of  $\beta$ -endorphin due to expectations or appraisal of participants about the self-inflicted pain. The intensity of the self-inflicted pain might be experienced as low (even though the injury is moderate or severe) if the individual appraised the pain as pleasant or used other cognitive strategies to deal with the painful stimulus. A positive evaluation of pain (e.g., "I deserve the pain", "pain is a pleasant distractor"), would furthermore lower the barriers for future NSSI engagement (Hooley & Franklin, 2018), due to the absence of negative consequences.

Shifting away from biological mechanisms of NSSI, I complemented the picture of NSSI by assessing affect, tension, and IPEs (chapters III and IV) in daily life. My study was the first comparing NSSI moments to moments with high-urge for NSSI, which allowed me to

test whether changes in tension and NA were specific for NSSI engagement. The results on NA contrast some findings of previous work that included only NSSI moments or compared NSSI moments to random time-points, as they all reported a reduction in NA following NSSI (Andrewes et al., 2017; Armey et al., 2011; Houben et al., 2017; Hughes et al., 2019; Kranzler et al., 2018; Snir et al., 2015). Even though results demonstrated a significant decrease in NA from the prompt preceding NSSI to the next random prompt following NSSI, the decrease was very small. The reduction in mean NA was only 0.12 points on the PANAS-X between one prompt and the next following prompt, whereas a change on the PANAS-X from the category "a little" to "not at all" would require a full 1-point change. Additionally, the decline in NA surrounding NSSI was not different from that during high-urge moments. Furthermore, in the cluster analysis approximately half of all NA trajectories were in the cluster "unspecific line", showing almost no changes in NA following NSSI (see chapter III, Figure 5). In line with this, self-rated NA was low over all assessed time-points and more than 85% of the NSSI events were preceded by low levels of NA (mean PANAS-X < 2). Thus, these NA findings are more in line with those of Muehlenkamp et al. (2009) and Snir et al. (2015), who both observed no significant changes in NA following NSSI. Taken together, even though the reduction of NA through NSSI is frequently endorsed by participants presented in literature (e.g., Taylor et al., 2018) as well as in the current AA work, it seems that NSSI often fails to have that effect. This is also supported by my descriptive finding that NSSI is rated as having had the desired effect only in half of the cases.

In contrast to my findings on NA, the significant findings with regard to tension are more in line with previous work on the affect regulation function of NSSI, which posits that tension reduction is a central function of NSSI (Klonsky, 2007; Taylor et al., 2018). This is also more generally summarized together with NA in the Four-function model as negative interpersonal reinforcement (Nock, 2009; Nock & Prinstein, 2004). However, as with NA, it is important to keep in mind that for tension, too, the model estimates tended to be small (0.32

points change on the MDBF scale between prompts). Nevertheless, significant findings of the MLMs were additionally supported by the descriptive findings of my cluster analysis, which showed that slightly more than half of all tension trajectories were rated as having had the desired effect and that the clusters that were rated as being effective were associated with a pronounced decrease in tension.

Additionally, the descriptive analysis on NA and tension showed that NSSI engagement does not always lead to the same shape in the trajectories, for instance, a downregulation of NA/ tension as postulated by theoretical models on NSSI (Chapman et al., 2006; Hooley & Franklin, 2018; Nock, 2009; Selby et al., 2013). I demonstrated that my sample comprised different patterns of NA/ tension trajectories, suggesting that probably different trigger situations lead to different trajectories surrounding NSSI. Furthermore, one can speculate that there could be interpersonal differences, leading to different NA/ tension trajectories. These findings give a first hint that it could be worthwhile to focus on inter- and intrapersonal differences in NA/ tension trajectories surrounding NSSI engagement. This could be done by, for instance, the assessment of more diverse context variables of NSSI or the assessment of detailed motives for NSSI (e.g., "did you try to stop further increase of NA/ tension") instead of global ones (e.g., "emotion regulation").

Lastly, I tested the interpersonal function of NSSI as postulated in the Four-function model (Nock, 2009; Nock & Prinstein, 2004). Findings showed that, in my sample, IPEs were rarely endorsed as motives for NSSI on a trait level *and* during daily life. In contrast to this, IPEs were strongly endorsed by participants as triggers for NSSI (especially interactions with family members) on a trait level and a significantly higher number of distressing IPEs preceded NSSI events (as compared to non-NSSI time-points). This finding suggests that distressing IPEs could be relevant triggers for engagement in NSSI. It is highly plausible that negative IPEs (as triggers) contribute to NSSI by increasing aversive inner states such as NA and tension (current motive for NSSI) which lead to an engagement in NSSI (e.g., Hepp et al., 2018). This

assumption is supported by recent findings of a study that compares the reaction to social stressors in individuals with a history of NSSI to those without a history of NSSI on a daily basis (Berghoff et al., 2022). Results indicated that individuals affected by NSSI showed higher NA in response to social stress than individuals without NSSI, underlining the important association between interpersonal stress and high negative internal states in individuals with NSSI. Additionally, I found that the amount of distress caused by an IPE was significantly associated with later NSSI engagement, whereas the pure number of IPEs preceding NSSI was not. The number of negative IPEs was associated only with concurrent NSSI. These findings are supported by recent findings of a DD study by Haliczer (2022), who also found that higher than usual distress raised by social stressors (e.g., conflict) was associated with same day NSSI urges and behavior and by Turner et al. (2016) who found a positive association between the level of daily conflict and NSSI engagement on that day.

Regarding interpersonal reinforcement, I did not find support for either interpersonal positive or negative reinforcement, as NSSI was not associated with a subsequent reduction in negative IPEs or a higher number of positive IPEs (same day or subsequent day). Therefore, I did not find evidence for a direct involvement of interpersonal reinforcement in the maintenance of NSSI as indicated by the Four-function model (Nock, 2009; Nock & Prinstein, 2004). This is contrasted by findings from other studies, assessing the interpersonal function of NSSI in daily life. Snir et al. (2015) found a reduction of events where participants felt rejected after NSSI engagement, and Turner et al. (2016) found that positive IPEs increased on the days following NSSI, if the act was revealed to another person. However, in the study by Snir et al. (2015) individuals with BPD and avoidant personality disorder were assessed. Both personality disorder diagnoses are characterized by being very sensitive to rejection, which might not apply to the current sample. The findings by Turner et al. (2016) were limited by the fact that the analysis was based on only n = 10 individuals because most of the participants in their sample did not reveal the NSSI act to another person. This is in line with other findings of my study:

whenever participants reported an IPE, I asked whether they think that the behavior of the person was a reaction to their last self-harm. This was endorsed only in 1.81% of the positive IPEs, which implies that, in the majority of the cases, NSSI was not revealed to another person, which would be the requirement for positive reinforcement of NSSI through IPEs.

# **5.2 Limitations**

One central aim of the current work was to overcome some of the methodological problems of previous studies and pioneer the assessment of salivary  $\beta$ -endorphin in daily life. Nevertheless, this work also has its own limitations, which need to be addressed when discussing the results and further implications. As all three publications are based on one AA study, the limitations regarding all publications were outlined first.

When discussing the results and drawing implications for future research and therapy, it is important to keep in mind that the results are based on self-reports of 51 young (M age = 23.92, SD = 6.72, range 18-45), cis-gender women, primarily without migration background or affiliation to a minority regarding ethnicity or race. This restricted diversity of the sample was not intended. All eligible participants who contacted us for participation were included. However, since individuals of racial or ethnic minorities are equally or even more effected by NSSI than individuals without minority affiliation (Gholamrezaei et al., 2017), it would be important to assess a balanced sample. Furthermore, individuals of ethnic/ racial minorities could be affected by other or even more triggers for NSSI, probably leading to different facets of affect, than individuals without minority affiliation because they face different situations due to discrimination and racism in daily life (Jones & Neblett, 2017; Madubata et al., 2022).

In addition, while trying to reduce the heterogeneity of the sample as much as possible for the assessment of  $\beta$ -endorphin in daily life, we decided to exclude other sexes, genders and cis-gender women older than 45 to minimize factors like hormonal changes during menopause, hormonal differences between biological sexes or hormonal differences due to gender

transitions. This selectivity of the sample leads to restricted generalizability of the results that excludes, for instance, adolescents, elderly individuals and other sexes or genders. We know that NSSI is a behavior which is most prevalent in adolescence and early adulthood (Plener et al., 2015; Swannell et al., 2014), with a significant ratio of individuals stopping NSSI around the age of 18+. Nevertheless, lifetime prevalence of NSSI in adulthood is still around 6% (Swannell et al., 2014), which is comparable to other psychopathology in adulthood (Kessler, 2010). Therefore, it could be important to especially focus on individuals who maintain the behavior over the lifespan. Furthermore, older individuals, like individuals of other races, could also be affected by other problems than younger adults (e.g., more severe physical illness, loneliness; Parks & Feldman, 2006) leading to different trigger situations for NSSI.

Subsequently, we could also not speak for sexes and genders other than cis-gender women such as cis-men, transgender or non-binary individuals. Especially transgender individuals are at high risk for NSSI engagement with a lifetime prevalence of 45.65% (Liu et al., 2019). This high rate is probably due to moderating variables such as stigmatization, social exclusion and other life stressors which are potentiated for gender minorities (Jackman et al., 2018; Swannell et al., 2014), which could also have led to different results in this study.

Second, all participants were selected based on NSSI which leads to injuries, such as cuts or burns, to ensure the release of  $\beta$ -endorphin. Therefore, 91.12% of the reported NSSI episodes caused wounds and the results can only be interpreted for those forms of NSSI and not for other forms of self-harming behaviors such as head-banging or punching oneself. Other forms of NSSI may be accompanied by other levels of released biomarkers, urge or affect/tension patterns. It is also unclear in which way individuals who choose, for instance, cutting or burning may differ from those who choose other forms of NSSI. There is some evidence that men in general tend to choose other methods such as hitting one-self or wall/object punching (Kimbrel et al., 2018; Sornberger et al., 2012) rather than cutting or

burning, but probably individuals differ also across sex and genders due to other personality facets or psychopathology.

Third, like all other AA studies in the field until now (see Hepp et al., 2020 for an overview), the data for the moments directly before and during NSSI engagement are missing. Even though participants reported their NSSI engagement on average 6.83 minutes (SD = 5.75) afterwards, we probably missed the peak of affect and tension as well as changes in  $\beta$ endorphin. Furthermore, the self-reports could be biased by additional effects such as the effectiveness of the NSSI event. A clear advantage of the study design is that we included highfrequency sampling directly following NSSI and high-urge moments, to track changes in NSSI relevant variables. On the other side, a clear shortcoming is that we do not have the same for the prompts preceding NSSI or high-urge moments. The pre-NSSI prompts had a betweenprompt interval from one minute to 3.5 hours, which is a relatively large time interval, probably leading to systematic differences in pre-levels of affect and tension. For high-urge moments, these intervals were more evenly distributed because high-urge was reported during random prompts and participants did not have the possibility to self-initiate a high-urge report. Future studies should adapt their research design such that participants have the chance to self-report the intention to self-harm, right before NSSI engagement (for more detail on this issue, see "research implications" section).

Additionally, it is important to note that we cumulatively assessed 155 NSSI events across 51 participants. This number is comparable to other studies in the field (Kranzler et al., 2018) and more than most previous studies captured (e.g., Andrewes et al., 2016; Andrewes et al., 2017; Houben et al., 2017; Koenig et al., 2020). Furthermore, we observed that 85% (n =40) of our sample self-harmed more than once (M = 3.04) during the study period of two weeks, which indicates frequent NSSI engagement. To understand NSSI in more detail, it would be helpful to extend our descriptive cluster analysis to detect, for instance, individual patterns of NSSI engagement (e.g., specific affect/tension patterns) by clustering data per individual. Unfortunately, this analysis was not possible with our data because a lot more events per person would be required.

Fourth, as discussed in chapters III and IV, the assessment of our dependent variables (affect and IPEs) could also be improved. We assessed affect using the mean value of eight NA items and six PA items, preselected in an online survey. Following the results of the online study, we used the two items that had the highest load on each PANAS-X scale after a factor analysis. Tension was assessed via the single item "calm-tense" of the MDBF on a visual analog scale from zero to six. First, using different scales (bi-dimensional vs. unidimensional) for two different facets of the affect regulation function of NSSI make results difficult to compare and complicates the interpretation of our findings. Furthermore, in aggregating the single items to a mean value, we included the risk of floor effects for the affect ratings of the PANAS-X. While individuals were able to report downregulation from a high amount of tension to total relaxation on the MDBF item, the same was not possible for the PANAS-X items. Additionally, participants could rate only the absence of PA or NA but did not have the chance to actively report a neutral mood, which was also possible on the bi-dimensional scale of the MDBF. Nevertheless, we saw that the distribution of NA and PA items were restricted over all conditions, meaning that individuals generally rated NA and PA as low.

Regarding IPEs, we concluded that, first, the assessment of only one motive ("I wanted help/attention of others") for the interpersonal function of NSSI was to narrow. Individuals could also have engaged in NSSI for other interpersonal reasons than seeking help or attention. Second, the way the motives were formulated on state as well as on trait levels increased the chance of under-reporting due to social desirability, as participants could have had the feeling that their NSSI engagement could be interpreted as manipulative if they report this motive. Thus, it is possible that participants rather chose the options "I had another reason" or "I don't know why I self-harmed" than choosing the interpretsonal motive, because they did not want to be judged. Using another, more neutral formulation could have increased the interpersonal

motive endorsement. Additionally, we did not assess whether the NSSI event was revealed to another person or if another person found out about the NSSI event, which is necessary to assess interpersonal reinforcement. If no other person knew about the NSSI event, no one could react to the self-harm (which was another question in our design). Therefore, we do not know whether there is really no evidence for interpersonal reinforcement even though it would have been possible, or whether individuals in our sample did not regulate their interpersonal relationships through NSSI engagement as they did not reveal it to anyone.

Lastly, as far as we know, ours was the first study to assess salivary  $\beta$ -endorphin in daily life in the context of NSSI. Our results show that it is possible to assess biological markers for NSSI in daily life, even though we cannot rule out different kinds of confounders. We instructed participants to immediately put the saliva sample in the freezer after they provided them, and only included participants with access to a freezer with at least -18°C/-0.4°F. Nevertheless, we were not able to verify if saliva samples were stored correctly, so we did not know if a degradation process under room temperature had already started (Mcknight et al., 1983). Furthermore, even if we asked participants to stop eating or drinking in the thirty minutes preceding saliva delivery, samples could be contaminated especially by foods containing high amounts of sugar or caffeine immediately before sample collection by lowering saliva PH and increasing bacterial growth (Klein et al., 2010; Schwartz et al., 1998). Taken together, even though an AA design is especially suited for the assessment of NSSI because it allows to capture the behavior in the naturalistic environment, replication for our biological findings is needed in a larger AA sample as well as under controlled laboratory conditions with NSSI-like stimulation. As a final comment, we only assessed one biomarker of the EOS, which of course is inconclusive. To fully understand the different systems relevant for NSSI engagement, the assessment of much more different biomarkers from all parts of the body would be important.

# **5.3 Research Implications**

Several implications can be derived from the three presented publications to improve further work on NSSI in the field of daily life assessment. Implications, which are relevant for all three publications, are discussed first.

First, an important improvement would be to assess a more diverse sample, including all sexes, ethnicities, and genders to draw a more realistic picture of NSSI in daily life. As discussed in the limitation section, our sample was primarily comprised of young women without migration background or affiliation to ethnic minorities. Future work should focus on a balanced sampling to represent society in all facets, for instance, through more inclusive advertisement by addressing especially people of color and/or diverse ethnicities on flyers or online advertisement. Furthermore, recruitment could focus on online groups or communities especially for individuals of ethnic or gender minorities. Regarding dependent variables, a more diverse sample would necessitate larger samples for including, for example, gender or ethnicities as covariates to assess different activation patterns due to mediating variables such as discrimination. Regarding biological markers, sex and age could be relevant covariates to rule out possible confounds due to different hormonal concentrations, which could influence release and concentration of biomarkers.

An additional major improvement would be to find an ethical way to ask participants whether they have the intention to self-harm in the next minutes. This could overcome the problem that the data directly before the engagement in NSSI are missing. Using this design, it would be possible to assess the moments directly before NSSI, capturing more relevant tension, affect, or distress patterns or biological markers, than using the random prompt preceding NSSI engagement. For example, participants could have the possibility to self-initiate the app if they experience high-urge for NSSI. After some minutes, the app could ask participants whether they engaged in NSSI or, if not, how high the current urge is. Additionally, participants should have the opportunity to self-initiate the app whenever they engage in NSSI. To reduce the

possibility that participants feel that they "have" to engage in NSSI after self-initiating the app and reporting a high-urge, it would be important to also ask study-relevant questions, if participants did not engage in NSSI after reporting a high-urge. This procedure would ensure that both outcomes, NSSI engagement and resisting an urge, are perceived to be equally important and avoid the impression that resisting an urge could harm the cause of the study. In this case, it could be helpful to ask which skills participants used to resist the urge or which context variables helped to prevent them from NSSI engagement (e.g., being around other people). This could also be included in a therapeutic (app-) approach.

In the next step, it is important to increase the amount of data of NSSI events. In our study, assessing individuals with chronic and severe NSSI helped to increase the number of NSSI events over the course of the study. Another option to include individuals with a range of NSSI severity *and* capture a high amount of NSSI events would be to extend the study period. Here, it is important to carefully weigh the costs and benefits of a more intensive study design. To reduce participant burden, one option is fewer random prompts across the day. Furthermore, one could think about a design where some days include frequent random prompts to capture fluctuations of affect, tension and biological markers across the day, whereas other days are free of random prompts and participants just have to initiate the app, if they experience the urge to self-harm. Using this more dynamic design, participants could be motivated to keep engaged in the study even with a longer time-frame for data collection. This procedure would additionally be more suitable to fit in a working day and relatively high-functioning individuals are not excluded from participation.

Another way to adapt and improve the AA design is the use of mobile sensing. The term mobile sensing is an umbrella term, which is used to describe the assessment of environmental data (e.g., geographical data, physiological data) via smart devices (e.g., smartphones, smartwatches; Lane et al., 2010). In analyzing those data, individual patterns of, for instance, stress, sleep, activity, and frequently visited places can be tracked in a non-invasive way and

enrich the assessment of behavioral data. In our research area on NSSI in daily life, one could additionally think about a design where participants are prompted only if they experience physiological markers associated with stress (e.g., elevated respiratory frequency, pulse or blood pressure; Henry, 1986; Suess et al., 1980). First, this would allow to capture NSSIrelevant triggers such as negative IPEs, bothering memories or states of high psychological distress which lower the barriers for NSSI engagement (Hepp et al., 2020). Second, even in longer study periods, where participants might forget to self-report NSSI events or high-urges in an event-based design, this would be an evidence-based reminder for participants to selfreport high-urge situations and probably NSSI events. In conclusion, using mobile sensing (e.g., physiological markers) as a prompting basis could be an effective way to increase the number of NSSI events per participant, even if the base rate of NSSI per participant is low, as it would allow to increase the study duration without a significant increase in participant burden.

Regarding dependent variables, we saw that the NA and PA items did not differentiate between moments of high-urge and NSSI events and were generally rated as low. The eight NA and six PA were rated on a Likert-scale and participants had to think about every item separately, which demands the involvement of cognitive processes. For tension, participants could swipe on a visual analog scale between "relaxed" and "tense", which is a measurement method that is probably better suited to cover the first impulse. For the tension ratings, we also found substantially more variance and differentiation between moments of high-urge and NSSI. Thus, transferring the insights of our data analysis to future studies, one could think about assessing NA and PA in a more universal way, using formulations such as "how good/ bad do you feel at the moment" on a visual analog scale ranging from "neutral" to "very bad/good", rather than using a variety of different emotional facets. This suggestion is also supported by findings on individuals with low emotion differentiation skills and NSSI, who showed higher rates of NSSI engagement compared to healthy controls or individuals with NSSI and high skills of emotion differentiation (Bresin, 2014; Zaki et al., 2013). Another option could be to

assess specific affect facets relevant for each participant. For this approach it would be necessary to analyze relevant affect patterns for each participant prior to participation, using for example the "chain/ or behavior analysis" as used in the Dialectical Behavioral Therapy (Rizvi & Ritschel, 2014). This design would allow to follow affect individually, monitoring whether affect is stable across intra-individual episodes of NSSI or varies in association with context variables such as IPEs, bothering memories or other triggers.

When looking at the interpersonal function of NSSI, it would be helpful to choose more neutral formulations such as "coping with interpersonal stressors" or "problems with other people" to prevent that participants feel judged as "manipulative" for choosing the interpersonal motive. Furthermore, future studies should present a set of interpersonal motives rather than one single item. In addition to in-person IPEs in daily life, it seems important to assess also interpersonal experiences online such as instant messaging (e.g. Instagram, WhatsApp) or online commentaries (e.g. commentaries on uploaded stories on Tick tock or Instagram), as it was shown that online interaction influences affective states of especially young people and, therefore, probably affects NSSI (You et al., 2013).

Focusing on biological markers, it is possible to describe NSSI as an attempt to reduce psychological or emotional pain (Kim et al., 2022). Previous research has already shown that comparable areas in the brain and identical biological markers were responsible for both psychological and physical pain (see Bresin & Gordon, 2013 for an overview). Therefore, we focused on peripheral  $\beta$ -endorphin in the current work and found first promising but very preliminary results. Clearly, more research is needed to support and extend our findings in the laboratory under controlled conditions as well as in daily life. Furthermore, other biomarkers of the pain systems certainly warrant further investigation. One important system is the endocannabinoid system (ECS) which is involved in emotion regulation, pain perception, and reward processing (Kim et al., 2022). All of those functions are also relevant for the discussion around NSSI. Studies assessing the ECS in NSSI populations are lacking, but there is first

evidence that reduced ECS functionality leads to suicidal ideation and self-harm in humans (Nguyen et al., 2019). Additionally, there are two studies showing that individuals with BPD (in whom one major symptom is NSSI) tend to have reduced baseline levels of anandamide (a component in the ECS) in their cerebrospinal fluid (Koethe et al., 2014) and hair (Wingenfeld et al., 2018). First, one could test the EOS and ECS with NSSI-like stimulation (e.g., with a blade) in the laboratory, where blood and/or saliva would be available to assess the release of EOS and ECS biomarkers before and after NSSI-like stimulation. In a second step, those systems should be tested in daily life, using saliva samples to capture changes in release of EOS and ECS. Furthermore, it could be important to add non-NSSI pain to the study design to assess whether physical non-NSSI pain leads to comparable release of EOS and ECS markers.

# **5.4 Clinical Implications**

Beyond the limitations and the directions for future research that have been discussed in the preceding sections, our findings also add new insights that could be implemented in clinical work in the field of psychotherapy.

Results on the effects of NSSI on the EOS system showed preliminary evidence for the hypothesis that one reason why individuals engage in NSSI may be that they try to reach norm-physiological levels of  $\beta$ -endorphin. If this hypothesis would be supported by more empirical research in the laboratory as well as in daily life, this finding could be the basis for developing new and more targeted psychopharmacological treatments to help individuals suffering from NSSI to stabilize  $\beta$ -endorphin levels in stressful situations. Until now, individuals with NSSI are often treated with psychotropic medication (e.g., selective serotonin reuptake inhibitors, atypical antipsychotics, serotonin–norepinephrine reuptake inhibitors) to reach a reduction of NSSI episodes, even though evidence for a beneficial outcome is still sparse, primary due to small sample sizes and a lack of randomized control trails (Eggart et al., 2022; Turner et al., 2014). Therefore, the current psychopharmacological treatment of NSSI for adolescents and

adults can only be an addition to established psychotherapeutic interventions and cannot be recommended per se (Guerdjikova et al., 2014; Plener et al., 2016). Thus, thinking about new forms of psychopharmacological treatments especially targeting the endogenous opioid system or  $\beta$ -endorphin could improve effectiveness of medication in reduction of NSSI episodes. This is supported by a small set of studies, showing an effect of medication addressing the dopaminergic, serotonergic, and endogenous opioid system (Turner et al., 2014), which is in line with the findings of our study.

Furthermore, our results showed a clear gap between self-rated pain and levels of  $\beta$ endorphin/severity ratings. We speculated that pain ratings were influenced by cognitive coping strategies and expectations about the physical pain. This assumed process could inform psychotherapeutic approaches to focus also on the functions of pain during NSSI. In addition to well-established therapeutic interventions that focus on the reduction of NSSI, it could be helpful to include a discussion about the functionality of pain. Such discussions could lead to new insights about the motivation for self-harm. Discovering which expectations or beliefs the patient has about pain during NSSI could also help the therapists and their patients to identify new skills in dealing with NSSI urges.

Second, our exploratory cluster analysis of affect and tension showed that their trajectories surrounding NSSI could look very different and vary with regard to experienced effectiveness. Even though we were not able to assess whether the trajectories differentiated between individuals or if individuals experience different trajectories depending on the trigger situation of NSSI, the insights of our cluster analysis could enrich psychotherapy. Following our results, it would be helpful to track individual trajectories of affect and tension surrounding NSSI in the therapeutic process, to understand individual patterns of NSSI in therapy. Thus, it would be possible to capture individual triggers leading to specific affect/tension patterns (e.g., high tension leads to strong relief after NSSI whereas the feeling of being alone leads to nearly no changes of affect after NSSI). In this context, it seems additionally important to ask

participants whether their NSSI had the desired effect. To reduce memory bias as much as possible, patients should report affect, tension, and effectiveness as soon as possible after NSSI (digitally or on their diary card) and if possible, at several time-points during the next hour. On the topic of effectiveness, we saw that NSSI was rated as being effective only in half of the cases. It seems to be worthwhile to evaluate the effectiveness of NSSI events per episode to see how often the behavior has the desired effect and how often the costs and consequences overshadow the effectiveness. In this context, therapists could enrich the discussion by talking about NSSI and the way in which learning patterns are built over time. Psychotherapists should educate their patients about learning patterns of positive and negative reinforcement as postulated by existing theories of NSSI (Chapman et al., 2006; Hooley & Franklin, 2018; Nock & Prinstein, 2004; Selby et al., 2013). Additionally, they could extend psychoeducation by information about intermittent reinforcement (Wagner, 1961) and the possibility that NSSI can become a habit that is reinforcing by itself, even if it is no longer effective as a strategy (Swerdlow et al., 2020). Discussing intermittent reinforcement in the context of NSSI is especially suited to shed more light on the development of NSSI as an automatic strategy in response to stressful triggers. When NSSI does not have to be positive or negative reinforcing for every single event, the expectation that it *could* have the desired effect this or next time is enough to maintain the behavior. Therefore, it could be helpful for patients to think and understand NSSI also in terms of intermittent reinforcement to gain more insight in subconscious processes which could be relevant for the development and maintenance of NSSI.

The findings on the affect regulation function show that resisting an urge may be an effective way in managing affect and tension, probably comparable to the effect of NSSI. This finding underlines the impact of therapeutic strategies such as urge surfing (Linehan, 2014; Marlett & Gordon, 1985), which encourages patients to resist the urge to self-harm, through imagining their urge for NSSI as a wave which increases and decreases with time. Our results show that it is beneficial to resist the urge for NSSI, because tension and affect both decline

within a relatively small time window and the difference to NSSI moments is small. For therapists and their patients, these findings indicate that it is especially important to find individual short-term interventions, like individual "skill-chains" as implemented in the DBT (Linehan, 2014). Such skill-chains could prevent patients from the engagement in NSSI through, for instance, emotion-regulation strategies, shifting attention to something else other than the urge to self-harm, or strong physiological sensations (e.g., non-injurious pain). Our findings on the decrease of NA and tension in high-urge situations suggest that it could also be worthwhile to extend those skill-chains to cover a longer time range, such that patients are busy with their skills for a minimum of thirty minutes to one hour. Those interventions could include distraction strategies such as leaving the house for thirty minutes or an hour or playing a videogame which takes a minimum time of thirty minutes. Before or afterwards, patients should follow their skill-chains to downregulate their urge to self-harm.

Lastly, we found limited evidence for interpersonal positive or negative reinforcement as postulated by the Four-function Model (Nock, 2009). In other words, we found no evidence in our sample that the engagement in NSSI has an impact on the experience of more positive (e.g., social support) or less negative (e.g., arguments) IPEs. However, we found that negative IPEs predict concurrent NSSI engagement and highly distressing IPEs at t.<sub>1</sub> predict NSSI engagement at t<sub>0</sub>. Taken together, in our study IPEs had a triggering function for NSSI rather than a reinforcing function that maintains the behavior. This indicates that therapists and their patients should focus on interpersonal stressors which are highly distressing and trigger subsequent NSSI rather than focusing on the "signaling function" (Nock, 2009) of NSSI. To prevent the escalation of negative IPEs, therapy should focus on the improvement of social interaction skills as well as on emotion-regulation skills to downregulate high distress after interpersonal stressors. Furthermore, it seems important to carefully assess which kind of negative IPEs cause high distress because negative IPEs alone (even a high number of IPEs) predict only current but not future NSSI engagement. Therefore, a detailed assessment of the

quality of IPE such as with whom highly distressing IPEs occur, which content those events have, and if they trigger specific emotions (e.g., violated expectations trigger the feeling of being alone or downhearted) could help patients to better understand those interpersonal triggers. Additionally, knowing which kind of negative IPE causes high distress and, therefore, makes NSSI engagement more likely, is probably important for patients to predict individual urge trajectories, which could render the urge more manageable because the individual already knows that the urge to self-harm could rise in the following hours and can plan appropriate interventions.

# **Thesis Summary**

Non-suicidal self-injury (NSSI) is intended to be harmful to oneself through tissue damage without the intention to die. Individuals suffering from NSSI are affected by many short and long-term negative consequences, for instance, severe wounds, scars, and a high risk for aggravated psychopathology. Theories on NSSI postulated that NSSI is mainly used to regulate aversive inner states such as negative affect (NA), but there seem to be also other relevant triggers for NSSI, for instance, interpersonal problems. These assumptions are supported by self-report and cross-sectional studies, whereas findings in daily life using ambulatory assessment (AA) were more ambiguous. Looking at biological mechanisms of NSSI, evidence is still sparse but current findings suggest that individuals engaging in NSSI differ from those without NSSI in various ways. Mainly, individuals engaging in NSSI show altered activation patterns with regard to the perception and regulation of affect and pain in the brain and in peripheral systems (e.g., pain system) compared to those without NSSI. As NSSI is defined to be a harmful behavior, pain processing seems to be a central biological component involved in the development and maintenance of NSSI. The endogenous opioid system (EOS) is especially involved in the perception and regulation of emotional and physical pain. In the context of NSSI,  $\beta$ -endorphin is one important marker of the EOS, as it is released during tissue damage in central and peripheral regions of the body alike. Therefore,  $\beta$ -endorphin seems to be especially suited for the assessment of NSSI in daily life.

Within this thesis, I presented three publications, all based on an AA study. The purpose of the study was to test the affect regulation and interpersonal function of NSSI as well as changes in  $\beta$ -endorphin surrounding NSSI in daily life. I assessed 51 cis-gender women, aged between 18 - 45 years, with DSM-V diagnosis of NSSI disorder and frequent NSSI engagement

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(min. one NSSI episode/ week > 3 month). Participants attended in the study over a 15-day study period, reporting on five semi-randomized prompts per day as well as on event-based prompts in case of NSSI. Furthermore, I sampled during high-urge for NSSI. To assess changes after NSSI or high-urge moments in the dependent variables more closely, I included a high-frequency sampling in the first thirty minutes (three follow-up prompts, each ten minutes apart) after NSSI or high-urge moments. Participants completed 4,619 prompts, resulting in a high compliance rate of 92.04% and engaged in 155 NSSI acts.

The first publication comprised the assessment of salivary  $\beta$ -endorphin in daily life. First, I assessed  $\beta$ -endorphin on eight time-points on a non-NSSI day (first day of study period), to represent the trajectory of  $\beta$ -endorphin across the day. Afterwards, participants completed two additional weeks of the AA study. Saliva samples were collected during high-urges for NSSI, before and after NSSI events, and on three follow-ups in the thirty minutes following NSSI or high-urge moments. In line with my hypothesis, results show that salivary  $\beta$ -endorphin significantly increases from pre to post NSSI, which supports theoretically assumptions on the involvement of the EOS in NSSI. Furthermore, I found a significant association between the severity of the injury and levels of  $\beta$ -endorphin. Contrary to my hypothesis, I did not observe a significant difference in  $\beta$ -endorphin levels in moments of high-urge vs. NSSI moments, which is not in line with theoretical assumptions, which postulate that moments of high-urge should be accompanied by especially low levels of  $\beta$ -endorphin. Interestingly, I also did not find a significant finding could be due to cognitive processes involved in pain management.

The second publication focused on the assessment of the affect regulation function of NSSI as postulated by almost all theories on NSSI. Those theories posit that NA and tension are increased prior to NSSI and decrease after the engagement in NSSI. I captured NA and tension as two facets of the affect regulation function at random prompts, during high-urge,

NSSI moments and follow-up prompts. To tease apart whether effects of NSSI on NA and tension are specific for NSSI engagement or rather due to time effects, I compared moments of NSSI to moments of high-urge without subsequent NSSI (using high-urge moments as a consequent within-group control condition).

For NA, I found that the decline in the NSSI condition was *not* steeper than in the highurge condition, indicating that NSSI engagement did not outperform the resistance of an urge for NSSI. Results on tension showed that NSSI was associated with a significant linear decrease in tension, whereas resisting an urge was not. Nevertheless, trajectories in the high-urge condition for both, NA and tension, were better described by an inverted U-shaped pattern, leading to a significant decrease in NA and tension. This indicates that resisting an urge is also followed by significant reduction in NA and tension in the same time-window as engaging in NSSI. The described findings show only limited evidence for the affect regulation function of NSSI in my sample, as I only found a significant effect for tension regulation. The findings on NA and tension were descriptively supported by my exploratory analyses. Here, I used k-means clustering to visualize NA and tension trajectories surrounding NSSI and relate these to participants' self-rated effectiveness of the NSSI events. Taken together, my results indicate that resisting an urge to self-harm may also be effective in managing NA and tension, highlighting the importance of well-established therapeutic interventions such as urge-surfing.

The third publication of this thesis concentrated on the evaluation of the interpersonal function of NSSI, which postulated that negative interpersonal events (IPEs) should increase prior to and decrease following NSSI, whereas the number of positive IPEs should increase after NSSI. To test these assumptions in daily life, I presented a set of five negative and positive IPEs on each random prompt. Additionally, I asked participants how distressing the IPE was for them and if the behavior of the other person was a reaction to their last self-harm episode. In case of NSSI, I asked whether participants experienced a positive or negative IPE before they engaged in NSSI and if yes, how distressing the event was for them.

# THESIS SUMMARY ENGLISH VERSION

I found a positive concurrent association between the number of negative IPEs and the engagement in NSSI. Furthermore, highly distressing negative IPEs were positively associated with concurrent NSSI events and urges *and* predicted later events. I observed no reduction in negative or increase in positive IPEs following NSSI, which suggests that there is no evidence for positive or negative interpersonal reinforcement through NSSI in this sample. Additionally, participants endorsed interpersonal motives for NSSI only rarely in a trait-level interview, but indicated that others, especially family members, often trigger NSSI. In line with this, participants infrequently endorsed the motive 'get help/attention' in daily life. These results suggest that negative IPEs (especially highly distressing ones) trigger NSSI, but participants rarely used NSSI for interpersonal motives.

Taken together, I found evidence that IPEs could be seen as triggers for NSSI rather than a mechanism, which is involved in maintaining NSSI through positive or negative reinforcement. For the clinical practice, one implication could be that clinicians and they patients should focus on identifying interpersonal triggers of NSSI and how the amount of distress from IPEs can be regulated to prevent NSSI engagement, rather than focusing on the role of other people's behavior in response to an NSSI event.

# Zusammenfassung der Dissertationsschrift

Nicht suizidale Selbstverletzung (NSSV) ist definiert als die intentionale Schädigung von eigenem Körpergewebe, ohne die Intention zu sterben. Menschen mit NSSV sind von vielen kurz- und langfristigen negativen Konsequenzen betroffen. Hierzu zählen schwere Wunden, Narben und verstärkte Psychopathologie. Theorien über NSSV postulieren, dass betroffene Personen NSSV vor allem nutzen, um aversive innere Zustände, wie zum Bespiel starken negativen Affekt (NA), zu regulieren. Zusätzlich scheinen jedoch auch noch weitere Faktoren wie interpersonelle Probleme auslösend für NSSV zu sein. Diese theoretischen Annahmen wurden durch Ergebnisse von Selbstberichts- und Querschnittsstudien unterstützt, während Ergebnisse aus dem ambulanten Assessment (AA) zu gemischten Ergebnissen kamen.

Die Datenlage bezüglich biologischer Mechanismen, die NSSV mitbegünstigen, ist zum aktuellen Zeitpunkt nur limitiert aussagekräftig, doch es scheint so, dass von NSSV betroffene Individuen sich in verschiedenen biologischen Prozessen von Individuen ohne NSSV unterscheiden. So scheinen bei Betroffenen, im Vergleich zu Menschen ohne NSSV, sowohl veränderte Aktivierungsmuster im Bereich der Wahrnehmung und Regulation von Emotionen und Schmerz in verantwortlichen Gehirnregionen als auch in peripheren Systemen (v.a. dem Schmerzsystem) vorzuliegen.

Da NSSV durch die intentionale Verletzung des eigenen Gewebes definiert wird, liegt eine Beteiligung des Schmerzsystems für die Entwicklung und Aufrechterhaltung von NSSV nahe. Das endogene Opioid System (EOS) ist vor allem in die Wahrnehmung und Regulation von körperlichem und emotionalem Schmerz involviert. Im Zusammenhang mit NSSV hat sich  $\beta$ -Endorphin als ein prominenter biologischer Marker des EOS herausgestellt, da  $\beta$ -Endorphin während der Verletzung von Körpergewebe in zentralen und peripheren Regionen des Körpers

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freigesetzt wird. Aus diesem Grund scheint  $\beta$ -Endorphin ein besonders geeigneter Marker zu sein, um NSSV im Hinblick auf biologische Prozesse zu untersuchen.

Diese Doktorarbeit beinhaltet drei Publikationen, welche alle auf einer AA Studie basieren. Das Ziel der Studie war es die Affektregulationsfunktion, die interpersonelle Funktion und Veränderungen von  $\beta$ -Endorphin vor und nach NSSV im Alltag zu untersuchen. Hierzu wurden 51 cis-gender Frauen zwischen 18 und 45 Jahren mit NSSV Diagnose (DSM-V) und häufiger NSSV untersucht (min. eine NSSV pro Woche > 3 Monate). Die Studienteilnahme erfolgte an 15 aufeinanderfolgenden Tagen. Die Probandinnen beantworteten fünf semirandomisierte Abfragen am Tag und zusätzlich ereignisbasierte Abfragen im Falle einer NSSV. Weiterhin erfolgten Abfragen während starkem Drang nach NSSV. Um Veränderungen in den abhängigen Variablen nach NSSV engmaschig zu erfassen, wurden drei Abfragen (Follow-up Abfragen) in 10 Minuten Abständen in den ersten 30 Minuten nach einer NSSV oder nach starkem NSSV-Drang inkludiert. Insgesamt vervollständigten die Teilnehmerinnen 4,619 App Abfragen (155 NSSV Episoden), was insgesamt zu einer hohen Compliance von 92,04% führte.

Die erste Publikation beinhaltete die Erhebung von Veränderungen in der Konzentration von  $\beta$ -Endorphin im Alltag. Um den möglichen Verlauf von  $\beta$ -Endorphin über den Tag abzubilden, wurden am ersten Tag zunächst acht Speichelproben erhoben. Die Teilnehmerinnen sollten sich and diesem Tag nach Möglichkeit nicht selbst verletzen. Anschließend folgten zwei weitere Wochen der Studienteilnahme. Speichelproben wurden während hohem NSSV-Drang, vor und nach NSSV und an den drei Follow-up Abfragen erhoben. Übereinstimmend mit den a priori Hypothesen konnte gezeigt werden, dass  $\beta$ -Endorphin im Speichel vor NSSV signifikant niedriger ist als nach NSSV. Dies unterstützt die theoretischen Annahmen, dass  $\beta$ -Endorphin eine Rolle bei NSSV spielt. Weiterhin zeigten die Ergebnisse eine signifikante Assoziation zwischen der Schwere der Verletzung und Konzentrationen von  $\beta$ -Endorphin im Speichel. Dies deutet darauf hin, dass schwerere Verletzungen zu einer höheren Freisetzung von  $\beta$ -Endorphin führen könnten. Im Gegensatz zu

meinen Hypothesen, konnte kein signifikanter Unterschied zwischen Konzentrationen von  $\beta$ -Endorphin in Momenten mit hohem NSSV-Drang und NSSV Episoden gefunden werden. Dies steht im Kontrast zu den von biologischen Modellen über NSSV gemachten Annahmen, dass Momente mit hohem NSSV-Drang in Zusammenhang mit besonders niedrigen Konzentrationen von  $\beta$ -Endorphin stehen sollten. Es konnte zudem auch keine signifikante Assoziation zwischen der Intensität des selbst berichteten Schmerzes und  $\beta$ -Endorphin Konzentrationen gefunden werden. Eine mögliche Interpretation wäre, dass diese nicht signifikante Assoziation in Teilen durch kognitive Prozesse erklärt werden kann, die zur Regulation von Schmerzreizen beitragen.

Die zweite Publikation fokussierte sich auf die Untersuchung der Affektregulationsfunktion von NSSV, die von beinahe allen Theorien über NSSV postuliert wird. Diese Theorien nehmen an, dass NA und Anspannung vor der NSSV ansteigen und danach abfallen. NA und Anspannung (als zwei Facetten der Affektregulationsfunktion) wurden während randomisierter Abfragen, hohem NSSV-Drang, nach einer angegebenen NSSV und während der Follow-up Abfragen gemessen. Um zu unterscheiden, ob die Effekte von NSSV auf NA und Anspannung spezifisch für NSSV oder eher Zeiteffekten zuzuschreiben sind, wurde NSSV in den Modellen mit hohem NSSV-Drang verglichen. Die NSSV-Drag Bedingung fungierte so als gruppeninterne Kontrollbedingung.

Für NA konnte gezeigt werden, dass der Abfall in der NSSV-Bedingung nicht stärker war als in der NSSV-Drang Bedingung. Dies legt nahe, dass die Regulationsfunktion von NSSV im Hinblick auf NA nicht effektiver ist, als dem Drang zu widerstehen NSSV durchzuführen. Im Gegensatz hierzu konnte für Anspannung gezeigt werden, dass sie nach NSSV signifikant stärker abnahm als in der NSSV-Drang Bedingung. Die NSSV-Drang Bedingungen für NA und Anspannung können jedoch besser durch eine umgekehrt U-förmige Kurve beschrieben werden als durch einen linearen Verlauf. Für sowohl Anspannung als auch für NA konnte gezeigt werden, dass die NSSV-Drang Bedingung ebenfalls zu einer signifikanten Reduktion von NA

und Anspannung im gleichen Zeitfenster wie NSSV führte. Somit zeigen die beschriebenen Ergebnisse insgesamt nur eingeschränkte Evidenz für die Affektregulationsfunktion im Alltag. Unterstützt werden diese Befunde durch meine deskriptiven, exploratorischen Analysen. Ich verwendete k-means Clustering, um die Verläufe von Anspannung und NA um NSSV Episoden herum zu visualisieren und verknüpfte die Ergebnisse mit der selbstberichteten Effektivität der NSSV Episode. Zusammenfassend kann gesagt werden, dass die hier dargestellten Ergebnisse zeigen, dass der Widerstand gegen einen NSSV-Drang ebenfalls effektiv in der Regulation von NA und Anspannung sein kann. Dies unterstreicht die Wichtigkeit von bereits gut erprobten therapeutischen Techniken wie "urge-surfing".

Die dritte Publikation dieser Doktorarbeit konzentriert sich auf die Evaluation der interpersonellen Funktion von NSSI. Es wird theoretisch angenommen, dass negative interpersonelle Ereignisse (IEs) vor einer NSSV gehäuft vorkommen und als Reaktion des Umfelds nach einer NSSV abnehmen, während die Anzahl der positiven IEs zunehmen sollte. Um diese Annahmen im Alltag zu testen, wurden fünf negative und fünf positive IEs bei jeder randomisierten Abfrage präsentiert. Zusätzlich wurde gefragt, wie belastend das IE für die Person war und ob die Reaktion des Gegenübers eine Reaktion auf die letzte NSSV der Teilnehmerin war. Im Falle einer NSSV wurde gefragt, ob ein IE vor der Selbstverletzung stattfand und wie belastend dieses Ereignis war.

Die Ergebnisse zeigten eine positive Assoziation zwischen der Anzahl der momentanen negativen IEs und NSSV. Die Hinzunahme der Frage, wie belastend das IE war, zeigte, dass hoch belastende IEs sowohl momentane als auch spätere IEs prädizierten. Im Hinblick auf positive oder negative Verstärkung von NSSV durch IEs konnte weder eine Reduktion von negativen IEs im Nachgang von NSSV noch ein Anstieg von positiven IEs nach NSSV gefunden werden. In Übereinstimmung mit diesen Ergebnissen wurde deutlich, dass Teilnehmerinnen in der aktuellen Studie in einem vorab geführten Interview interpersonelle Motive nur sehr selten als Grund für NSSV nannten, während negative IEs (vor allem mit

Familienmitgliedern) häufig als Auslöser für NSSV genannt wurden. Weiterhin wurde das Motiv "Hilfe/ Aufmerksamkeit bekommen" auch in der AA Studie nur sehr selten gewählt. Die Ergebnisse deuten darauf hin, dass negative IEs und vor allem belastende IEs Auslösefaktoren für NSSV sein können, auch wenn sie selten als tatsächliches Motiv für eine aktuelle NSSV Episode verwendet werden.

Zusammengefasst kann angenommen werden, dass IEs eher als auslösende Faktoren für NSSV gesehen werden können, aber nicht als verstärkende Mechanismen, welche für die Aufrechterhaltung des Verhaltens relevant sind. Für die klinische Praxis könnte eine Implikation sein, dass Therapeut:innen und ihre Patient:innen ihren Fokus auf interpersonelle Auslösesituationen legen sollten und darauf, wie die daraus entstandene Belastung reduziert werden kann. Die Reaktion des Umfelds auf die NSSV Episode scheint hingegen weniger relevant zu sein.

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# **Curriculum Vitae**

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	Was ist machbar, wenn nichts mehr hilft?"
04/2018	Fachverband Sucht, Zürich, Schweiz
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#### **Publications**

- Störkel, L. M., Niedtfeld, I., Schmahl, C., & Hepp, J. (2023). Does self-harm have the desired effect? Comparing non-suicidal self-injury to high-urge moments in an ambulatory assessment design. *Behaviour Research and Therapy*, 162, 104273. doi.org/10.1016/j.brat.2023.104273
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# Appendix Chapter I

## Table A 1

## Descriptive statistics, method and context for NSSI acts

Study	NSSI assessment	N (%) participants reporting acts	N total acts	M acts per participant	Method	ContextofNSSIand pain associated with NSSI
Ammerman et al. (2017)	NSSI (y n) since last call	N = 13 (26%)	1	/	77.8% banging head 60.3% poking/biting 39.6% cutting 22.2% burning 51.9% other	1
Andrewes et al. (2016) + Andrewes et al. (2017)	NSSI (y n) since last prompt	N = 24 (22%)	N = 52	M = 0.49  across all M = 2.17  across participants $w \ge 1 \text{ act}$	70% cutting 15% scratching 6% hitting object/self 2% biting 2% burning 2% strangling	29% on weekends 33.3%: 10- 2 pm 33.3%: 2- 6 pm 33.3%: 6- 10 pm
Anestis et al. (2012)	NSSI Sum of: Cutting (y n), burning (y n), hitting (y n), head banging (y n) <i>time frame n.r.</i>	/	/	NSSI Sum: <i>M</i> = 0.28, <i>SD</i> = 0.97	Percentages n.r.	/
Armey et al. (2011) + Armey et al. (2012)	NSSI (y n) since last prompt	N = 17 (47%)	N = 22		<ul><li>29.4% cutting</li><li>23.5% wound picking</li><li>23.5% scrape skin</li><li>11.8% beat/ hit self</li></ul>	Time spent planning: none at all, a few seconds, a few minutes, <1 hour, <1 day, $1 - 2$ days, > 2 days

Bresin et al.	NSSI (y n)		N = 9	M = 0.13 across	11.8% biting 0 % burning	94.1% reported less than 1 h other percentages n.r.
Bresin et al. (2013)	for that day		N = 9	M = 0.15 across participants $w \ge 1$ act	7	7
Czyz et al. (2019)	NSSI (y n) for that day	N = 15 (44%)	N = 70	M = 2.06  across all M = 4.7  across participants w $\geq 1$ act	/	38.6% afternoon (12 pm- 6 pm)         22.9% nighttime (12 am- 6 am)         20.0% evening (6 pm- 12 am)         18.6% morning (6 am- 12 pm)
Hochard et al. (2015) + Hochard et al. (2019)	for that day	For that day: N = 16 (22%) Since wake-up: N = 11 (15%)	For that day: N = 9 Since wake- up: N = 19	For that day: M = 0.13 across all M = 0.56 across participants $w \ge 1$ act Since wake-up: M = 0.26 across all M = 1.73 across participants $w \ge 1$ act	/	
Houben et al. (2017) + Vansteelant et al. (2017)	NSSI (y n) since last prompt	N = 30 (94%)	N = 88	$M = 2.75 \text{ across all}$ $M = 2.93 \text{ across}$ participants w $\geq 1$ act	/	/
Horowitz et al. (2017)	NSSI (y/n) for that day	N = 16 (42%)	N = 46		/	/
Kranzler et al. (2018) + Selby et al. (2019) + Hughes et al. (2019)	NSSI (y/n) since last prompt	N = 40 (85%)	N = 442 in 145 episodes M  number of acts per episode = 3.05 (SD = 3.65)	Counting episodes: M = 3.09 across all M = 3.63 across participants $w \ge 1$ act	40.7% cutting 32.4% punching 17.9% scratching 9.7% biting 9.0% burning	Pain assessed $0 - 10$ : pain before, during, after NSSI episode (retrospectively) M before = 1.94, $SD = 2.77M$ during = 4.51, $SD = 3.10M$ after = 3.37, $SD = 2.91Modal duration 1 - 30 mins$

Law et al. (2015)	"I hurt myself on purpose in the last 60  minutes" $(0-5)$	/	/	/	/	/	
Lear et al. (2019)	NSSI (y n) for that day	N = 20 (43%)	N = 48	M = 1.02  across all M = 2.40  across participants $w \ge 1 \text{ act}$	50.0% wound manip. 41.7% Cutting 27.1% scratching 18.8% pinching 12.5% pulling Hair 10.4% hitting self All other < 5%	Mean time of NSS Pain assessed 0-10 Pain during NSSI	-
Muehlenkamp et al. (2009)	any 1 or more of: Cutting (y n), Burning (y n), Hitting (y n), Head banging (y n) since last prompt	N = 19 (15%)	N = 55	M = 0.42  across all M = 2.90  across participants $w \ge 1 \text{ act}$	Individual frequencies for different methods not reported	/	
Nock et al. (2010) + Selby et al. (2014)	NSSI act (y n) since last prompt	N = 26 (87%)	N = 104	M = 3.47  across all M = 4.00  across participants $w \ge 1 \text{ act}$	/	Who with?           49.0% alone           16.3% peer           16.3% friend           9.6% mother           5.8% father           5.8% stranger           3.8% sibling           1.9% other	Doing what? 21.2% socializing 20.2% resting 19.2% homework 17.3% music 14.4% tv/games 15.4% recreation 13.5% eating 4.8% drugs 3.8% alcohol
Pearson et al. (2016)	NSSI (y n) of: Cutting (y n) Burning (y n) Hitting (y n) Head banging (y n) Scratching (y n) Since last prompt	N = 19 (14%)	/	/	Frequencies not reported	/	

Selby et al. (2013)	NSSI (y n) since last prompt	N = 7 (35%)	N = 25		52% picking skin 24% cutting 24% scratching 12% hitting self	Amount of time between urge and act: < 1min (68%), 1 - 5 min between (20%), 10 - 30 min (12%)
						Pain during NSSI assessed (y/n): Reported yes for 20 acts (80%)
Shingleton et al. (2013)	NSSI (y n) just now	N = 24 (80%)	N = 83	$M = 2.77 \text{ across all}$ $M = 3.46 \text{ across}$ participants w $\ge 1$ act	/	/
Snir et al. (2015)	NSSI (y n) since last prompt	N = 29 (29%)	N = 110	$M = 1.11 \text{ across all}$ $M = 3.79 \text{ across}$ participants w $\geq 1$ act	/	/
Turner et al. (2016ab, 2018) + Kleiman et al. (2018) + Miller et al. (2019)	NSSI act (y n) retrospective report in the evening for three different episodes of the day	N = 31 (52%)	N = 107	M = 1.78 across all M = 3.45 across participants $w \ge 1$ act	29.9% scratching 16.8% cutting 15.9% hitting 15.9% other 4.7% biting	1
Victor & Klonsky (2014)	No. of NSSI acts indicate y n for 12 NSSI methods drawn from ISAS for that day	/	/	/	frequencies for individual methods n.r.	/
Zaki et al. (2013) <i>lote</i> . N.r. = not report	NSSI act (y n) since last prompt			M = 1.0 acts in BPD group, SD = 2.1, range 0-8	/	/

*Note*. N.r. = not reported

#### Table A 2

Evidence on intrapersonal and interpersonal functions of non-suicidal self-injury.

Study	Affect and interpersonal items	Intrapersonal negative	Intrapersonal positive	Interpersonal function
Ammerman	PANAS NA (M)	Not supported:	/	/
et al. (2017)	Current	Daily NA was not associated with NSSI		
Andrewes	PANAS NA (M)	NA increased pre NSSI	PA decreased pre NSSI	/
et al. (2016)	PANAS PA (M)	NA decreased post NSSI	PA increased post NSSI	
N = 107	Current	(quadratic curve)	(quadratic curve)	
		Function 'affect regulation' self-endorsed 45%	Function 'sensation seeking'	
		events	self-endorsed in 5% of events	
		Function 'anti-dissociation' self-endorsed in 5% events		
Andrewes et	PANAS NA (M) incl. distressed item	NCE increased pre NSSI	/	/
al. (2017)	PANAS PA (M)	NCE decreased post NSSI		
N = 107		(quadratic curve)		
	'Negative complex emotions' (NCE):			
	Number of NA items rated $>2$	distress increased pre NSSI		
		distress decreased post NSSI		
	Current	(quadratic curve)		
Armey et al.	PANAS NA (M)	NA & guilt increased pre NSSI	Not supported:	/
(2011)	PANAS PA $(M)$	NA & guilt decreased post NSSI	PA did not show significant	
N = 36	PANAS-X guilt $(M)$	(quadratic curve)	pattern surrounding NSSI	
	PANAS-X hostility (M)	Exploratory:		
	Exploratory: Irritable, angry, loathing item	'Angry' increased pre NSSI		
		'Angry' decreased post NSSI		
	Current	(quadratic curve)		
Horowitz et	/	Function 'affect regulation' most commonly		Functions 'setting
al. (2017)		endorsed		interpersonal boundaries',
N = 38				'revenge', 'influencing
				others', 'establishing
				autonomy' all self-
				endorsed for 0% of events

Harber	NA M of one down and the	NIA image days NICCI	Not compared de	/
Houben et $(2017)$	NA $M$ of: angry, depressed, anxious, stragged	NA increased pre NSSI	Not supported:	/
al. (2017)	stressed	NA was high during NSSI	PA decreased post NSSI	
N = 30	PA $M$ of: happy, relaxed	Not supported: NA increased post NSSI		
TT 1 . 1	Scale 0 – 100; <i>current</i>		,	/
Hughes et al.	NA <i>M</i> of: sad, angry, frustrated,	NA increased pre NSSI	/	/
(2019)	overwhelmed	Overwhelmed increased pre NSSI		
N = 47	hurt/rejected, guilty, physically numb,	Anxious increased pre NSSI		
	empty/ numb, anxious/ afraid, lonely,			
	ashamed			
	Scale 0 – 10; <i>current</i>			
Kranzler et	NA M of: overwhelmed, sad, frustrated,	NA increased pre NSSI	Lag PA not associated w	/
al. (2018)	angry, hurt/ rejected, ashamed,	NA decreased post NSSI	NSSI	
N = 47	anxious/afraid, lonely, embarrassed,		PA increased post NSSI	
	empty/numb, guilty, physically numb	Exploratory:		
		Sad, angry, overwhelmed, lonely, frustrated, hurt,	Exploratory:	
	PA M of: content, relieved, proud, rush or	anxious items decreased post NSSI	happy, content, satisfied,	
	a high, excited, satisfied, happy		proud, relieved, calm items	
	calm/relaxed	Function 'to get rid of bad or negative feelings'	increased post NSSI	
	Scale 0–10; <i>current</i>	self- endorsed for 53.8% of events	Function second most	
			endorsed	
Law et al.	NA <i>M</i> of: Irritable, angry, ashamed, guilty	NA, angry, irritable high during NSSI Lagged NA	/	/
(2015)	Scale $0-5$ ; <i>last 60 minutes</i>	not associated w NSSI		
N = 255				
Lear et al.	PANAS-X guilt (M), hostility (M), sadness	Daily guilt was associated with increased	/	/
(2019)	(M), fear $(M)$	probability for daily NSSI		
	Created subsets of 4 items for each scale	Daily hostility, sadness, fear were not		
	For the past day			
Muehlen-	PANAS NA (M) subset	NA increased pre NSSI (linear trend)	PA decreased pre NSSI	/
kamp et al.	PANAS PA (M) subset	No change in NA following NSSI	PA increased post NSSI	
(2009)	Time frame not reported		(quadratic curve)	
N = 131				

#### Nock et al. Only reported as a context for urges, see Function endorsed in 64.7% of events self-endorsed in Interpersonal Function negative function self-endorsed in Specifically 'reducing/escaping': 24.5% of events (2010)urge table N = 30- anxiety (34.8%), sadness (24.2%), anger (19.7%) 14.7% of events - bad thought (28.8%), bad memory (13.6%)Interpersonal positive function self-endorsed in 3.9% of events Participants Selby et al. / self-reported engaging in NSSI to: (2014)N = 30Feel something (35% of events) Feel satisfaction (20% of events) Feel stimulation (16% of events) Shingleton Function endorsed in 4% of events / et al. (2013) 'get rid of anxiety/ bad thoughts' NA M: tense, disappointed, afraid, sad, Not supported: Function 'feeling generation' AB increased pre NSSI Snir et al. angry, irritated NA did not show a significant pattern surrounding endorsed on average in 47% AB decreased post NSSI (2015)Scale 0-4; time frame not reported of events in the BPD group N = 94NSSI (quadratic curve, and 18% in the APD group in APD group) M: Function 'emotion relief' endorsed on average in Avoidant behavior (AB) Cancelled/avoided social plans, avoided 52% of events in the BPD group and 27% in the RI increased pre NSSI conflict by keeping quiet, isolated self RI decreased post NSSI APD group Yes/ No scale; since last entry (quadratic curve, in APD and BPD group) Rejection/isolation (RI) M : lonely, isolated, abandoned, rejected, accepted 'interpersonal Function (re), my needs are being met (re) avoidance' endorsed on Scale 0–4; time frame not reported average in 6% of events in

#### APPENDIX CHAPTER I

average in 6% of events in the BPD group and 9% in the APD group

				Function 'interpersonal communication' endorsed on average in 12% of events in the BPD group and 17% in the APD group
Turner et al. (2016a) N = 60	MDMQ valence, calmness, energetic arousal Bipolar scale; > 0 negative valence and	Function 'to get rid of thoughts or feelings' endorsed in 67.3% of events	Function 'to feel something' endorsed in 14.3% of events	Conflict was increased on days with NSSI
11 - 00	high arousal			Conflict did not decrease on days post NSSI
	Conflict day <i>M</i> of 'Test of Negative Social Exchange' Scale 0– 17 (number of negative events)			Social support increased on days post NSSI that was revealed to others
	Day $M$ of 'Goldsmith Social Support Scale' Scale 1 (very unsupportive) - 7 (very supportive)			Function 'to escape people or task' endorsed in 16.3% of events, 'to
	All retrospective for morning, midday, evening			communicate' in 2% of events
Turner et al. (2016b) N = 25	Sad/worthless, overwhelmed, scared/anxious, angry at self, self-hatred, angry at other, rejected/hurt, numb/nothing <i>Retrospective for feelings right before</i> <i>NSSI</i>	Increased feelings of being rejected / hurt were reported pre NSSI	/	

Note. PANAS = Positive negative affect scale with a range of 1 (very slightly/ not at all) to 5 (extremely), NA = negative affect, PA = positive affect, BPD = Borderline Personality Disorder, APD = Avoidant Personality Disorder.

## Table A 3

# Demographics and design of all reviewed studies

Study	Sample	NSSI inclusion	Age	Gender	Race/ Ethnicity	Data collection	Study focus
Ammerman	51 BPD patients with	/	19-53	75%	33% Caucasian	AA	State vs. trait level
et al. (2017)	comorbid DD		<i>M</i> =28.8	female	51% African American	7 days	predictors of daily
					10% Asian	4 phone calls from	NSSI acts
					6% Other	interviewer	
Andrewes et	107 youth with BPD	/	15-25	83%	/	AA	Change in affect
al. (2016)			<i>M</i> =18.1	female		6 days	before and after NSSI
						6 random prompts	
Andrewes et	107 youth with BPD	/	15-25	83%	/	AA	Complex and
al. (2017)			<i>M</i> =18.1	female		6 days	conflicting emotions
[Andrewes						6 random prompts	before and after NSSI
et al. 2016]							acts and urges
Anestis et al.	127 females with	/	18-55	100%	96.9% Caucasian	AA	Interaction of
(2012)	bulimia nervosa		<i>M</i> =25.0	female	1.5% Native American	14 days	affective lability and
					0.8% Asian	6 random prompts	previous suicide
						1 1	attempts in predicting
							NSSI
Armey et al.	36 college students	Lifetime history	18-35	75%	"predominantly Caucasian"	AA	Changes in negative
(2011)	with NSSI history		<i>M</i> =18.7	female		7 days	affect preceding and
						6 random prompts	following NSSI acts
	[diagnoses n.r.]					+ event-based prompts	
	-					after NSSI	
Armey et al.	36 college students	Lifetime history	18-35	75%	"predominantly Caucasian"	AA	Negative affect,
(2012)	with NSSI history		<i>M</i> =18.7	female		7 days	trauma, life stress,
						6 random prompts	affect dysregulation
[Armey et al.	[diagnoses n.r.]					+ even-based prompts after	interact in predicting
2011]						NSSI	NSSI acts
Bresin et al.	67 college students	Min. 1 episode in the	<i>M</i> =19.6	57%	/	Daily diaries	Interaction between
(2013)	with NSSI history	past year		female		14 days	trait impulsivity and
							daily negative affect

	[diagnoses n.r.]						in predicting daily NSSI urges
Czyz et al. (2019)	34 adolescents post inpatient treatment for suicidality [diagnoses n.r.]	/	13-17 <i>M</i> =15.5	76% female	<ul><li>85.3% Caucasian</li><li>8.8% African American</li><li>8.8% Asian American</li><li>5.9% Hispanic</li><li>2.9% American Indian</li><li>2.9% Pacific Islander</li></ul>	<b>Daily diaries</b> 28 days	Daily suicidal ideation as a predictor of NSSI urges and acts, depending on coping strategies
Hochard et al. (2015)	72 college students with NSSI history [diagnoses n.r.]	/	18-32 <i>M</i> =21.0	89% female	/	AA 5 days 2 reports before and after sleep	Association between nightmare occurrence and NSSI acts/ urges in the morning
Hochard et al. (2019) [Hochard et al. (2015)]	72 college students with NSSI history [diagnoses n.r.]	/	18-32 <i>M</i> =21.0	89% female	/	AA 5 days 2 reports before and after sleep	Nightmare content is not associated with risk of NSSI acts/ urges in the morning
Horowitz et al. (2017)	38 community people with NSSI history [diagnoses n.r.]	Min. 5 lifetime NSSI acts + Min. 2 NSSI urges in the previous month	18-30 <i>M</i> =21.9	89% female	<ul> <li>57.9% European</li> <li>15.8% East Asian</li> <li>15.8% Mixed</li> <li>5.3% South Asian</li> <li>2.6% African</li> <li>2.6% South/Central Am.</li> </ul>	Daily diaries 21 days	Association between NSSI functions and interpersonal trauma
Houben et al. (2017) [sub-sample Vansteelant et al. 2017]	30 inpatients w. high BPD features and depression scores [diagnoses n.r.]	/	<i>M</i> =29.0	87% female	/	<b>AA</b> 8 days 10 random prompts	Changes in negative affect preceding and following NSSI acts
Hughes et al. (2019) [Kranzler et al. 2018]	47 youth with NSSI acts in past two weeks [25 MDD, 13 BPD]	Min. 2 NSSI acts the in past 2 weeks	15-21 <i>M</i> =19.1	68% female 2% trans- gender	<ul> <li>38% Caucasian</li> <li>19% Asian</li> <li>15% African American</li> <li>17% Hispanic/Latinx</li> <li>11% multi-racial</li> </ul>	AA 14 days 5 random prompts + event-based after NSSI urges & NSSI acts	Negativeaffect,repetitivenegativethinking as predictorsforNSSIbehavior/thoughts

Humber et al. (2013)	21 male inmates [11 met current mental disorder]	/	22-58 <i>M</i> =36	0 % female	<ul><li>76% White British</li><li>14% Asian/Black British</li><li>10% White Irish</li></ul>	<b>AA</b> 6 days 6 prompts (coupled w. routine activities)	In- and outward directed anger as predictors of NSSI urges
Kleiman et al. (2018) [sample 1 from Nock et al., 2009]	30 adolescents	NSSI acts in the past 2 weeks	12-19 <i>M</i> =17.3	88% female	<ul><li>86.7% Caucasian</li><li>6.7% Hispanic</li><li>6.7% Other</li></ul>	AA 14 days 2 prompts (noon, evening) + NSSI event-based	Daily stress and daily fatigue interacted to predicted daily suicidal ideation but not NSSI
[sample 2 from Turner et al., 2016a]	60 adults with NSSI history [33 anxiety dis. 14 mood dis. 16 BPD]	Min. 10 acts lifetime + Min.1 act in last year + Urges in past 2 weeks	18-35 <i>M</i> =23.3	85% female	<ul> <li>53% Caucasian</li> <li>18% East Asian</li> <li>8% Southeast Asian</li> <li>3% Native Canadian</li> <li>2% African Canadian</li> <li>2% Hispanic/Latinx</li> </ul>	<b>Daily diaries</b> 14 days Retrospective ratings for morning, afternoon, evening	
Kranzler et al. (2018)	47 youth with NSSI acts in past two weeks [25 MDD, 13 BPD]	Min. 2 NSSI acts the in past 2 weeks	15-21 <i>M</i> =19.1	68% female 2% transgender	38% Caucasian 19% African American 19% Asian American 17% Hispanic/Latinx 11% Multiracial	AA 14 days 5 random prompts + event-based after NSSI urges & NSSI acts	NA and PA change from pre to post NSSI and their impact on urge intensity
Law et al. (2015)	255 adults w BPD features [120 mood dis. 110 anxiety dis. 27 AUD/ SUD 77 BPD]	/	<i>M</i> =44	68% female	60% Caucasian 34.5% African American	AA 14 days 5 scheduled prompts a day	Predict momentary BPD symptoms with momentary negative affect
Lear et al. (2019)	47 undergraduate students w NSSI history [diagnoses n.r.]	NSSI in the past year	<i>M</i> =19.9	92% female	80.9% Caucasian	<b>Daily diaries</b> 14 days	Traitself-critic ismanddailyself-punishmentaspredictorsofNSSIactsandurges

Miller et al. (2019) [sub- sample from Turner et al. 2016a]	40 Adults with NSSI history [diagnoses n.r.]	Min. 10 lifetime episodes Min.1 act in the last year Thoughts/ urges in past 2 weeks	18-25 <i>M</i> =21.6	100% female	/		Daily diaries 14 days Retrospective ratings for morning, afternoon, evening	Daily stress as a predictor of NSSI thoughts and acts
Muehlen- kamp et al. (2009)	131 women with bulimia nervosa	)	<i>M</i> =25	100% female	96.9% Cauca		AA 21 days 6 random prompts + event-based after NSSI acts & ED behaviors + evening report	Changes in negative affect preceding and following NSSI acts
Nock et al. (2010)	<ul> <li>30 adolescents with NSSI urges in past 2 weeks</li> <li>[15 mood dis.</li> <li>16 anxiety dis.</li> <li>10 AUD/SUD]</li> </ul>	NSSI urges in the last 2 weeks	12-19 <i>M</i> =17.3	87% female	86.7% Cauca 6.7% Hispan 6.7% Other		AA 14 days 2 prompts (noon, evening) + event-based after NSSI urges & NSSI acts	Social context of NSSI urges, prediction of NSSI acts
Pearson et al. (2016)	133 women with bulimia nervosa	/	18-55 <i>M</i> =25.3	100% female	95.5% Cauca	asian	AA 14 days 6 random prompts 1 bedtime report + event-contingent (eating disorder behavior)	Association between personality pathology and NSSI or substance use in women with bulimia nervosa
Scala et al. (2018)	36 BPD patients 18 anxiety disorder patients	/	BPD: <i>M</i> =34.2 ANX: <i>M</i> =26.1	87% female	BPD: 92% White 8% Other	ANX: 72% White 17% Other	AA 21 days 6 random prompts	Negative affect and self-concept clarity as predictors of NSSI urges
Selby et al. (2013)	20 students with NSSIhistory27communityparticipants	Min. 4 dysregulated behaviors (incl. NSSI) in past 2 weeks	/	66 % female	64% Caucas 19% African 9% Hispanic 6% Asian Ar 2% Native A	American nerican	<b>AA</b> 14 days 5 random prompts	Negative affect and rumination (instability) as predictors of NSSI

	[14 MDD, 8 PTSD]						
Selby et al. (2014) [Nock et al., 2009]	<ul> <li>30 adolescents with NSSI urges in past 2 weeks</li> <li>[15 mood dis.</li> <li>16 anxiety dis.</li> <li>10 AUD/SUD]</li> </ul>	NSSI urges in the last 2 weeks	12-19 <i>M</i> =17.3	87% female	<ul><li>86.7% Caucasian</li><li>6.7% Hispanic</li><li>6.7% other</li></ul>	AA 14 days 2 prompts (noon, evening) + event-based after NSSI urges & NSSI acts	Automatic positive reinforcement as a motive for NSSI
Selby et al. (2019) [Kranzler et al., 2018]	47 youth [25 MDD, 13 BPD]	NSSI acts in the past 2 weeks	15-21 M=19.1	68% female 2% transgender	<ul> <li>38.3% Caucasian</li> <li>19.1% Asian</li> <li>17.0% Hispanic/Latinx</li> <li>14.9% African American</li> <li>10.6% multiracial</li> </ul>	AA 14 days 5 random prompts + event-based after NSSI urges & NSSI acts	Pain offset following NSSI
Shingleton et al. (2013)	30 adolescents with NSSI history [15 MDD; 8 GAD]	NSSI acts in the past 2 weeks	12-19 <i>M</i> =17.0	87% female	87% Caucasian (?) Table seems broken	AA 14 days only event-contingent (NSSI acts/ thoughts)	Relationship between NSSI and Binging/purging
Snir et al. (2015)	56 BPD 43 avoidant PD 53 healthy control	/	18 – 65 <i>M</i> =X	70% female	<ul><li>55.9% Caucasian</li><li>23.7% African American</li><li>10.5% Asian</li><li>10.5% Other</li></ul>	AA 21 days 5 random prompts	Affectiveandinterpersonalantecedentsandconsequences of NSSIin BPD, APD, and HC
Turner et al. (2016a)	<ul><li>60 Adults with NSSI history</li><li>[33 anxiety dis. 14 mood dis. 16 BPD]</li></ul>	Min. 10 lifetime episodes Min.1 act in the last year Thoughts/ urges in past 2 weeks	18 – 35 <i>M</i> =23.3	85% female	<ul> <li>53% Caucasian</li> <li>18% East Asian</li> <li>8% Southeast Asian</li> <li>3% Native Canadian</li> <li>2% African Canadian</li> <li>2% Hispanic/Latinx</li> </ul>	Daily diaries 14 days Retrospective ratings for morning, afternoon, evening	Interpersonal conflict and perceived social support during and following NSSI days
Turner et al. (2016b)	25 youth with NSSI acts & ED from 2016a sample	Min. 10 lifetime episodes Min.1 act in the last year	M=23.1	92% female	68% Caucasian 12% Asian 12% South Asian 8% other	Daily diaries 14 days Retrospective ratings for morning,	Socioemotional contexts and association between

[sub- sample from Turner		Thoughts/ urges in past 2 weeks				afternoon, evening	NSSI and disordered eating
et al. 2016a] Turner et al. (2018) [Turner et al. 2016a]	60 Adults with NSSI history [14 MDD; 33 anxiety dis. 24 PD]	Min. 10 lifetime episodes Min.1 act in the last year Thoughts/ urges in past 2 weeks	18 – 35 <i>M</i> =23.3	85% female	<ul> <li>53% Caucasian</li> <li>18% East Asian</li> <li>8% Southeast Asian</li> <li>3% Native Canadian</li> <li>2% African Canadian</li> <li>2% Hispanic/Latinx</li> </ul>	Daily diaries 14 days Retrospective ratings for morning, afternoon, evening	Characteristics of NSSI thoughts and urges and their associations with daily coping and later NSSI acts
Vansteelant et al. (2017)	32 BPD	<i>Ì</i>	<i>M</i> = 28	84% female	/	AA 8 days 10 random prompts	Within-person variance in affect valence and activation was associated with NSSI frequency
Victor & Klonsky (2014) Study 1	<ul> <li>36 without NSSI history</li> <li>18 recent NSSI history</li> <li>[21 mood dis., 13 anxiety dis. ]</li> </ul>	NSSI acts within past 6 months	19-43 <i>M</i> =X	71% female	<ul> <li>54.8% East Asian</li> <li>28.6% Caucasian</li> <li>5.6% South Asian</li> <li>5.6% Multiracial</li> <li>2.4% Hispanic</li> <li>1.2% Middle Eastern 1.2%</li> <li>African</li> </ul>	<b>Daily diaries</b> 14 days	Differences in daily positive and negative affect between individuals with and without NSSI history
Victor et al. (2018)	62 women with NSSI urge history [17 BPD]	NSSI acts or thoughts in the past month	18-24 <i>M</i> =22.0	100% female	69.4% African Am. 24.2% Caucasian 4.8% Multiracial 1.6% Hispanic	AA 21 days 6 random prompts +1 prompt after wake	Association between negative affect, rejection, criticism and subsequent NSSI and suicide urges
Zaki et al. (2013)	38 BPD w NSSI history	Lifetime history of NSSI	<i>M</i> =29.9	84% female	61% Caucasian 18% African American 18% Hispanic 8% Asian 5% Other PD = Borderline Personality Disord	AA 21 days 5 random prompts	Negative emotion differentiation predicts NSSI acts and urges in BPD

*Note*. Diagnoses n.r. = diagnoses not reported, AA = ambulatory assessment, DD = daily diary, BPD = Borderline Personality Disorder, MDD = major depressive disorder. Italicized compliance values were computed by the review authors.

Table A 4

Sample type, recruitment strategy, compliance rates and filters and compensation scheme of all reviewed samples

Study	Sample	Clinical recruitment	Community recruitment	Compliance	Compliance filter	Compensation
Ammerman et al. (2017)	51 BPD patients with comorbid DD		recruited from an urban Midwestern community	30% of calls (428 total)		/
Andrewes et al. (2016) Andrewes et al. (2017)	107 youth with BPD	through the triage systems of two government-funded youth mental health services		52% of prompts (1986 total)	Six participants were excluded due to technical failure in the AA safety alert system and/or failure to complete any of the AA questionnaires	\$40 compensation regardless of compliance
Anestis et al. (2012)	127 females with bulimia nervosa	through advertisements placed in local clinics	advertisements placed in the community and a university campus	/		\$200 compensation \$50 bonus for compliance > 85%
Armey et al. (2011) Armey et al. (2012)	36 college students with NSSI history [diagnoses n.r.]		undergraduates enrolled in general psychology	38% of random prompts (569 total)		credit toward their research requirement in general psychology or 'a small payment'
Bresin et al. (2013)	67 college students with NSSI history [diagnoses n.r.]		1612 college students screened with the DSM, included participants reported at least 1 NSSI event in the last year	79% of days (613 total)	Six participants were excluded from the initial sample because they did not complete ratings on any days	course credit for compensation bonus credit for > 11 days
Czyz et al. (2019)	34 adolescents post inpatient treatment for suicidality [diagnoses n.r.]	hospitalized due to last		68.9% of days (650 total)		<ul><li>\$222 maximum</li><li>compensation</li><li>\$4 per each completed</li><li>daily survey</li></ul>

		suicide attempt and/or last-week suicidal ideation				
Hochard et al. (2015) Hochard et al. (2019)	72 college students with NSSI history [diagnoses n.r.]		university students	91.1% of reports (320 total)	36 participants were excluded from the initial sample because they did not return any diary entry within the	course credit for compensation
	[ulugh03e3 h.i.]				specified times	
Horowitz et al. (2017)	38 community people with NSSI history [diagnoses n.r.]	through health and mental health clinics and mental health websites	through universities, social media, and university websites.	Nearly 70% of participants completed all days (X total)		/
Humber et al. (2013)	21 male inmates [11 met current mental disorder]	through adult male penitentiary for those at risk for self-harm and suicide		69% of prompts (534 total)		/
Kranzler et al. (2018) Selby et al. (2019) Hughes et al. (2019)	47 youth with NSSI acts in past two weeks [25 MDD, 13 BPD]	Through local treatment centers and flyers and print/online advertisements		40 participants completed > 80% of random prompts (3356 total)	/	\$150 compensation \$150 bonus for compliance >80%
Law et al. (2015)	255 adults w BPD features [120 mood dis. 110 anxiety dis. 27 AUD/ SUD 77 BPD]	through referrals from an outpatient psychiatry clinic	through postal mailings, community fliers, and snowball sampling	1	26 participants were excluded from the initial sample because they completed less than 20% prompts	\$170 maximum compensation (deduction scheme unclear)

#### Lear et al. (2019) 47 larger 81.8% of days participant \$25 or course through credit the 1 was undergraduate excluded from the initial campus community (n = (538 total)compensation if sample due to invalid compliance >85% students 31) w NSSI history through the psychology responses research pool (n = 17)[diagnoses n.r.] Muehlenkamp et al. through the community / 10 participants \$200 compensation 131 women were \$50 bonus for compliance (2009)with and local campuses exclude from the initial bulimia sample due to drop out > 85%nervosa or incomplete data Nock et al. (2010) 30 adolescents through contacting local 25 participants \$100 compensation or keep from the surrounding completed 100% Shingleton et al. with NSSI treatment centers community of device а (2013)of prompts if compliance > 80%northeastern University urges Selby et al. (2014) in past 2 weeks (1227 total) Kleiman et al. (2018) [15 mood dis. 16 anxiety dis. 10 AUD/SUD] Pearson et al. (2016) women through eating disorder via targeted advertising 133 1 throughout with bulimia and psychiatric clinics the community nervosa Scala et al. (2018) BPD from a large university-74% of prompts 36 / / affiliated community (5061 total) patients 18 anxietv mental health center disorder patients >80% of random / Selby et al. (2013) through through mass screening 20 students flyers in \$50 or course credit compensation with NSSI community of mental undergraduate prompts history psychology students and \$50 bonus for compliance health centers (X total) 27 community individuals from the > 80%participants community recruited [14 MDD, 8 through local and online PTSD] advertisements Zaki et al. (2013)<sup>a</sup> adult individuals from Snir: 70% of 8 participants (BPD 3, \$100 56 BPD through treatment maximum APD 1, HC 4) with less compensation Snir et al. (2015) 43 avoidant PD clinics, disorder specific the New York City area random prompts

	53 healthy control	support groups, and related research projects in area hospitals + ads	were recruited through newspaper ads, online forums, and flyers for a	(11172 total) Zaki: 72% of	entries (two standard deviations below the	\$1 per completed diary entry
		targeted at individuals with BPD or APD	study on personality and mood	random prompts (2873 total)	sample average) were excluded from the initial sample	
Turner et al. (2016a) Turner et al. (2016b) Turner et al. (2018) Kleiman et al. (2018) Miller et al. (2019)	60 Adults with NSSI history [33 anxiety dis. 14 mood dis. 16 BPD]	through flyers in mental health clinics	throughonlineadvertisementsoncommunity websites(e.g., craigslist.org)andflyersposted in storesandcommunityspacesnearuniversitycampuses	88% of days (735 total)		\$45 per week if compliance >70% \$60 per week if compliance 100%
Vansteelant et al. (2017) Houben et al. (2017)	32 BPD	through psychiatric hospitals, 23 p. at the Univ. Psychiatric Center KU Leuven, 9. at the Psychiatric Hospital in Duffel, Belgium		63% of prompts (1512 total)	2 participants were removed from the initial sample because they responded to less than 20% of the scheduled signals	no compensation to ensure voluntary participation
Victor et al. (2014)	36 w/o NSSI history 18w recent NSSI [21 mood dis.,13 anxiety dis.]		through advertising to students at a Canadian university and its surrounding community	77% of days (582 total)		coursecreditorcompensationorhonorarium(notfurtherspecified)
Victor et al. (2018)	62 women with NSSI urge history [17 BPD]		through the Pittsburgh Girls Study, a longitudinal community cohort study of women	75.2% of prompts (6853 total)	4 were excluded from the initial sample because they dropped out, completing less than 5 assessments	"a payment structure that incentivized completion of at least 85% of prompts"

*Note*. Diagnoses n.r. = diagnoses not reported, AA = ambulatory assessment, DD = daily diary, BPD = Borderline Personality Disorder, MDD = major depressive disorder. Italicized compliance values were computed by the review authors.

<sup>a</sup> Both studies used a sub-sample of an ambulatory assessment study on the association between rejection and rage in BPD (Berenson et al., 2011).

# **Appendix Chapter II**

# A. Sample

- 51 women (aged 18-45, M = 23.92, SD = 6.72)
- Inclusion criteria: aged between 18 45 years, NSSI according to DSM-5 (and ≥1 NSSI acts per week for the last three months), female.
- Exclusion criteria: Life-time diagnosis of schizophrenic disorders, mental retardation/developmental disorders, substance dependency within the last 6 months, current injuries not related to NSSI (e.g. slipped disc, operation etc.), BMI < 17.5 or > 34, pregnancy, current use of cannabis or other stimulating drugs, and medication with opiates, naltrexone, cortisone, opioid analgesics. Additional exclusion criteria related to the collection of saliva samples were frequent gum bleeding (e.g. gum bleeding while brush one's teeth), tooth or root canal treatment in the last 2 weeks, no access to a freezer (at least -18°C/-0.4°F).

### **B.** Orientation session:

#### **Clinical Interviews:**

*Structured Clinical Interview for DSM-IV (SCID-I)* (Wittchen et al., 1997). Borderline Personality Disorder section of the *International Personality Disorder Examination (IPDE)* (Loranger et al., 1998).

*Self-injurious thoughts and behavior interview: German* (SITBIG, Fischer et al., 2014). The SITBIG is a semi-structured interview assessing thoughts, affect, motives and interpersonal problems concerning suicidal tendencies and NSSI. Furthermore, it captures frequency, methods, and severity of NSSI.

### Self-report questionnaires:

*Screening Questionnaire for DSM-IV Axis II Diagnosis (SCID-II).* The SCID-II screening questionnaire (Spitzer et al., 1990) is a 117-item forced choice (yes/ no) self-report questionnaire, assessing indications of axis II personality disorders according to DSM-IV. The questionnaire addresses behavior, experiences, and beliefs over the last ten years, showing long lasting patterns of personality.

*Questionnaire for Assessment of the Severity of NSSI (QASN; Landau).* The QASN is a not yet validated German self-report questionnaire, assessing frequency, methods, body parts, severity, motives, and impulsivity of NSSI. Furthermore, it assesses urges for NSSI and captures if participants are willing to reduce NSSI.

*Assessment of pain during NSSI:* Participants were asked on a scale from *no pain (0)* to *highest imaginable pain (10)* if they: 1) Feel pain during NSSI in general, 2) Felt pain the last time they engaged in NSSI, 3) Felt pain the first time they engaged in NSSI, 4) Felt pain when they began damaging body tissue, 5) Felt pain in the minutes after engaging in NSSI.

Furthermore, we asked participants: "How long does it take, on average, until your feeling of pain returns to normal after engaging in NSSI?" The answer options were: a) "my feeling of pain is not different during NSSI", b) "ten minutes or less", c) "ten to thirty minutes", d) "thirty minutes to an hour", e) "one hour to one day", f) "more than one day".

We further asked participants: "Has the intensity of physical pain during NSSI changed since the first time you engaged in NSSI?" The answer options were: a) "Now, I feel muss less pain than during my first NSSI", b) "Now, I feel a little less pain than during my first NSSI", c) "I feel the same amount of pain during NSSI than during my first NSSI", d) "Now, I feel a little more pain than during my first NSSI, e) "Now, I feel much more pain than during my first NSSI".

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*Suicidal thoughts and behaviors:* We also added questions to assess suicidal thoughts and behaviors, asking participants if they: 1) had ever thought about suicide, 2) had ever made a suicide attempt, if yes 3) how many suicide attempts they had made and 4) when they had made the most recent suicide attempt.

*HEXACO Personality Inventory*. The German version of the HEXACO (Moshagen et al., 2014) is a 60-item self-report questionnaire, assessing the personality dimensions Honesty-Humility, Emotionality, Extraversion, Agreeableness, Conscientiousness, and Openness to Experience with a five-point Likert scale from *strongly disagree (1)* to *strongly agree (5)*.

*Borderline Symptom List (BSL-23).* The German adaption of the BSL-23 (Bohus et al., 2009) is a 23-item self-rating scale, based on the criteria of the DSM-IV (revised version), to assess core symptoms of the Borderline Personality Disorder. Individuals answer on a five-point scale from *not at all (0)* to *absolutely true (4)*.

*Dissociation Tension Scale (DSS).* The German version of the DSS (Stiglmayr et al., 2010) is a 21-item self-report questionnaire, assessing dissociative symptoms over the last seven days, using an 11-point Likert scale from no (0%) time of the day to *always* (100%) during the day. Another single item assesses frequency of aversive tension during the last seven days on the same scale.

*Childhood Trauma Questionnaire (CTQ)*. The German version of the CTQ (Wingenfeld et al., 2010) is a retrospective self-report questionnaire, screening for childhood maltreatment (sexual, physical, and emotional abuse as well as physical and emotional neglect), using a five-point Likert scale from *not at all (1)* to *very frequently (5)*.

*Social Network Index (SNI).* The German version of the SNI (Cohen et al., 1997) is a 12-item self-report questionnaire, assessing quality and quantity in twelve different types of social

interaction in daily life. It addresses the different social roles of the participants, as well as social loneliness and diversity and size of social networks.

*Potentially confounding Variables:* Menstruation cycle (days), smoking behavior (yes/ no and cigarettes per day), daily physical activity (sports) (in minutes).

### C. Ambulatory Assessment sampling scheme

Participants completed 15 days of Ambulatory Assessment (AA). First, they completed a baseline day with 8 prompts every two hours (self-report and saliva sample), and then participants completed 14 study days. During the 14 study days, sampling was as follows:

- 5 semi-random (> 2h apart) prompts (self-report data)
- self-initiated prompts after NSSI act, entailing self-reports and saliva sample, with three follow-up prompts (10, 20 and 30 minutes after report of NSSI act), assessing self-reports and saliva samples
- control condition with high urge for NSSI (>6 on visual analog scale 0 = no urge at all to 10 = I can hardly contain myself), entailing self-reports and saliva sample, with three follow-up prompts (10, 20 and 30 minutes after report of high NSSI urge), assessing self-reports and saliva samples

### **D.** Ambulatory Assessment Items

Random prompts (five pseudo-randomized prompts per day, >2h apart):

*Momentary affect:* We assessed mood and current emotions to capture momentary affect. Current mood ("At the moment, I feel....") was assessed by *Multidimensional Mood Questionnaire (MDMQ)* (Wilhelm & Schoebi, 2007), using the items tired-awake, contentdiscontent, agitated-calm, full of energy-without energy, unwell-well, relaxed-tense (bipolar scale: +++, ++, +, 0, -, --, ---). Thirteen items from the *Positive and negative Affect Scale* 

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(PANAS-X, Röcke & Grühn, 2003) were used to assess positive affect ("At the moment, I feel....") via the items daring, attentive, delighted, bold, happy, and concentrating (Likert-scale, 1-5). Negative affect was assessed with the items disgusted with self, loathing, downhearted, afraid, hostile, nervous, and blameworthy (Likert-scale, 1-5). Additionally to the PANAS-X-items, we included two items *dead inside* and *empty inside* to capture feelings of emptiness, which are discussed with regard to NSSI (Gratz, 2003; Rallis et al., 2012) and were also described as a symptom of borderline personality disorder (APA,2013). To reduce patient burden, two items of each scale of the PANAS-X (Röcke & Grühn, 2003) were selected for our study, based on factor analysis after evaluation in an online study (for more details on online study, see paragraph on interpersonal events).

*Dissociative symptoms:* We assessed dissociation via the Dissociation Tension Scale (DSS-4) (Stiglmayr et al., 2009). Participants answered four items ("At the moment I have the impression that....") on a 10 point Likert scale from 0 = "not present" to 9 = "very strong". 1) "My body does not belong to me" (depensionalization), 2) "I have problems hearing, e.g. I hear sounds from nearby as if they come from far away" (somatoform dissociation), 3) "Other people or things around me are unreal" (derealization), "My body or parts of it are insensitive to pain" (analgesia).

*Interpersonal events:* Participants indicated significant interpersonal events ("Since the last prompt, another person...") with positive and negative valence (checkboxes with multiples possible answers). For positive events, they could choose one of the following options: a) "supported/helped me", b) "showed me affection", c) "respected my needs or feelings", d) "gave me their attention or time", e) "was interested in me or took me seriously", f) "none of the above". If any event was endorsed, they additionally answered questions on the impact ("What the person did bothers me", 0 = "not at all" to 10 = "very deeply") and relation to NSSI ("What the person did was a reaction to my last NSSI", "yes", "no", "I don't know"). Similarly,

participants were asked to indicate negative interpersonal events (checkboxes with multiples answers possible) with the following options: a) "criticized me", b) rejected me/ excluded me", b) "ignored my needs or feelings", c) "behaved angry or aggressive towards me", d) "let me down/ disappointed me", e) "none of the above". If any event was endorsed, they additionally answered questions on the impact ("What the person did bothers me", 0 = "not at all" to 10 ="very deeply") and relation to NSSI ("What the person did was a reaction to my last NSSI", "yes", "no", "I don't know"). Items for positive and negative interpersonal events were chosen based on an online survey with 376 participants. Participants were aged between 18 - 65 (M =30.2, SD = 10.2), the majority of the sample was female (n = 283), and many fulfilled the clinical cut-off for borderline features (n = 119) in the German version of the *Personality* Assessment Inventory (Engel et al., 2012; Stein et al., 2007). During this pilot study, participants were asked to describe one positive and one negative interpersonal event they experienced with a significant other person during the last seven days. After that, they were asked to retrospectively rate their emotions for each of the two previously described interpersonal events with the 60 items of PANAS-X (Röcke & Grühn, 2003). In a next step, participants were asked to rate each event (positive and negative) on nine different categories. We used the five most commonly endorsed categories for positive and negative events in the current study.

NSSI: "Since the last beep I answered, I have hurt myself." ("yes"/"no").

*Urge for NSSI:* "During the last 15 minutes the urge to hurt myself was" (visual analog scale: 0 = "no urge at all", 10 = "I can hardly contain myself").

Optional items for random prompts, whenever participant indicated an NSSI event:

*Time since NSSI:* "Since I have hurt myself, XX minutes passed by" (sliding wheel, list of minutes).

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Saliva sample: Participants were instructed as follows. Screen one: "Please flush your mouth with water and make sure that you don't have food left over in your mouth. Please wait until your salivation is normal again. Please try not to smoke, eat, or drink in the next 30 minutes. Now, put the swab from the collection tube in your mouth without using your hands. Once you have the swab in your mouth, please report the number on the collection tube. Press the "continue" button to start the timer (30 seconds). Screen two: "For the next 30 seconds, please chew the swab slightly to stimulate your salivation. Keep the swab in your mouth until you have the impression that the swab is saturated with saliva. This is very important for our study!" Screen three: "Spit the swab back into the collection tube, without using your hands, and put the collection tube back in the larger tube. Please close the collection tube with the cap. Now, put the collection tube in your freezer as fast as possible. Thank you for your participation!"

*NSSI method:* "I have hurt myself through..." (checkboxes/multiple answers possible) cutting, wound manipulation, scratching, burning/ ice burning, head banging/ punching self, other.

*NSSI motives*: "I have hurt myself because I…" (checkboxes/ multiple answers possible) wanted to reduce aversive tension or overwhelming emotions, wanted to express my self-hatred/ self-contempt, wanted to feel something (other than nothing), wanted help/ attention of others, had another reason, don't know why I self-harmed.

*NSSI effectiveness*: "Did the NSSI act have the desired effect?" (forced choice: "yes", "no", "I don't know")

*NSSI severity*: "The severity of my wound is..." (forced choice): Mild/ superficial wound (superficial cuts, bruise, scratching), Moderate wound (not only skin, but also underlying tissue is damaged, strongly bleeding cuts,  $2^{nd}/3^{rd}$  degree burns), Severe wound (cuts to fat tissue, damaged sinews, bone fractures, inner bleeding).

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*Intensity/ painfulness during NSSI*: "During self-injury, the intensity of pain was..." (visual analog scale: 0 = "no pain"; 10 = "worst imaginable pain").

*Pleasantness of pain during NSSI*: "During self-injury, the pain was..." (visual analog scale: 0 = "pleasant"; 10 = "unpleasant")

Actual pleasantness of pain: "At the moment pain is..." (visual analog scale: 0 = "pleasant"; 10 = "unpleasant")

Actual intensity/painfulness: "At the moment, intensity of pain is..." (visual analog scale: 0 = "no pain"; 10 = "worst imaginable pain")

*Control questions*: To assess possible confounders of -endorphin, participants indicated "In the last 1, 5 hours I have..." (checkboxes/ multiple answers possible) done sport, consumed drugs, consumed alcohol, had sex, nothing of the above.

### NSSI report (self-initiated):

In case of an NSSI event, participants were asked to self-initiate the app as soon as possible. During the event-related prompts, the following information was assessed (for full list of items, see paragraph on random prompts above): Time since NSSI, saliva sample, NSSI method, NSSI motive, NSSI effectiveness, NSSI severity, intensity/ painfulness during NSSI, pleasantness of pain during NSSI, actual pleasantness of pain, actual intensity/ painfulness, momentary affect (MDBF, PANAS), dissociative symptoms (DSS-4), interpersonal events, control question. Each NSSI event triggered three follow up prompts (10, 20 and 30 minutes later), each entailing a saliva sample, actual pain intensity/ actual pain valence, momentary affect (MDBF, PANAS), and dissociative symptoms (DSS-4). For (for full list of Items, see paragraph on random prompts above).

### Control condition:

If participants reported an NSSI urge > 6 (0 = "no urge at all", 10 = "I can hardly contain myself") during a random prompt, but did not engage in NSSI, a control condition was triggered. To reduce patient burden, control conditions occurred only as frequently as NSSI acts. Control conditions comprised of a saliva sample and control questions (for full list of Items, see paragraph on random prompts above).

Each control condition triggered three follow up prompts (10, 20 and 30 minutes later), entailing a saliva sample, and assessment of momentary affect (MDBF, PANAS) and momentary dissociation (DSS-4). For full list of Items, see paragraph on random prompts above.

### E. Processing of Saliva Samples

We used Protocol III (Std. Ab1hr.Bt) for the analysis of salivary beta-endorphin in NSSI, as provided by the manufacturer of the ELISA kits (Cat.No. S-1134; Peninsula Laboratories International, San Carlos, USA).

### 1 - Into each well of the immunoplate add

50 µl standard or sample (in diluent)

25 µl antiserum (in EIA buffer)

Add 50 µl diluent and 25 µl EIA buffer to blank wells.

2 – Incubate at room temperature for 1 hour. Shorter pre-incubations may result in lower sensitivity.

3 – Rehydrate the Bt-tracer (in EIA buffer) and add 25  $\mu$ l / well.

### 4 – Incubate at room temperature for 2 hours.

5 – Wash immunoplate 5 times with 300  $\mu$ l/well of EIA buffer. Be very careful not to cross-contaminate between wells in the first wash/ dispensing cycle. In each wash cycle empty plate contents with a rapid flicking motion of the wrist, then gently blot dry the top of

the plate on paper towels. Dispense  $300 \ \mu$ l of EIA buffer into each well and gently shake for at least a few seconds. Thorough washing is essential.

**6** – **Add 100 µl/ well of streptavidin-HRP.** Trap or centrifuge the SA-HRP vial to collect all liquid contents on the bottom of the vial. Dilute 1/200 in EIA buffer (60 µl /12ml) and vortex. Add 100 µl to all wells, including the blanks.

7 – Incubate at room temperature for 1 hour.

8 – Wash immunoplate 5 times (see step 5).

9 – Add 100 µl/ well of TMB solution. Add to all wells, including the blanks.

10 – Incubate at room temperature (usually 30 - 60 minutes). You may read the

developing blue color at 650 nm and use the data for your calculations.

11 – Terminate reactions by adding 100 µl 2 N HCI per well.

12 - Read absorbance at 450 nm within ten minutes.

# F. Additional exploratory results

Table B 1

# Descriptives of individuals who provided pre NSSI samples vs. those who did not

	Individuals providing	Individuals <i>not</i> providing
	pre NSSI sample $(n = 8)$	pre NSSI sample $(n = 43)$
Variable	$M\left(SD ight)$	M (SD)
Age	30.00 (8.04)	22.79 (5.88)
Years of education	11.88 (0.99)	11.87 (1.52)
% psychotropic medication	62.5	62.79
Comorbid diagnoses <sub>a</sub>	2.50 (1.60)	2.19 (1.44)
Age at first engagement in NSSI	15.25 (3.59)	14.14 (3.59)
Years of engagement in NSSI	14.75 (5.34)	8.69 (6.27)
Number of NSSI acts last month	8.94 (3.99)	10.63 (6.81)
Pain intensity during NSSI <sub>b</sub>	4.12 (2.47)	4.49 (1.99)
Severity of NSSI <sub>c</sub> (last three	2.25 (0.46)	2.19 (0.50)
months)		
Correlation $\beta$ -endorphin and NSSI	r = -0.23	r = -0.01
urge		

a assessed with SCID-I interview

<sup>b</sup> painfulness was rated on a ten-point Likert scale from 1 (no pain) to 11 (worst imaginable pain)

c severity categories: 1 = mild: superficial cuts, bruise, scratching, 2 = moderate: not only skin, but also the underlying tissue is damaged, strong bleeding cuts, 2/3 grade burning, 3 = severe: cuttings until fat tissue, damaged sinews, bone fractures, inner bleeding

# **Appendix Chapter III**

### Analyses on the association between positive affect and NSSI in daily life

Beyond the effect of NSSI on negative affect, theoretical models also proposed an association between positive affect (PA) and NSSI (Hooley & Franklin, 2018; Nock, 2009; Nock & Prinstein, 2004). Studies based on self-report support these theoretical assumptions whereas findings in the laboratory context are more ambiguous (for an overview see Perini et al., 2021). On a daily basis, only a few studies assessed positive affect in the context of NSSI, leading to mixed results. Two daily life studies found a decrease of PA prior to NSSI events and an increase of PA following NSSI (Andrewes et al., 2016; Muehlenkamp et al., 2009). Kranzler et al. (2018) also observed an increase in PA following NSSI, but they did not find a decrease of PA prior to NSSI. Contrasting this, Armey et al. (2011) did not find a significant pattern of PA surrounding NSSI and Houben et al. (2017) found decreased PA following NSSI.

The current study also assessed PA using the *Positive and Negative Affect Scale* (PANAS-X, Röcke & Grühn, 2003) items *daring, attentive, delighted, bold, happy,* and *concentrating* (see main manuscript for more information). We hypothesized that PA is decreased prior to and increases following NSSI (H2a). This increase in PA should be larger following NSSI events as compared to high-urge moments (H2b).

To test this, we used a MLM, with random intercepts per participant. Unfortunately, we were not able to calculate random slopes for the linear and quadratic trends, because models became singular. This is probably due to restricted variance in the PA values, as all prompt types were rated in the answer category "very slightly/ not at all" (see descriptive Table X1). Predictors were the linear and quadratic time predictors and chain type (NSSI chain vs. high-

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urge chain) and their interactions. The dependent PA variable was the momentary mean value of the corresponding PANAS-X-scales (joviality, self-assurance, attentiveness).

There was no difference in PA directly after NSSI as compared to  $t_0$  of high-urge moments (Est. = 0.01, SE = 0.03, p = .685,  $\beta = 0.00$ , CI [-0.03, 0.05]). For the linear time predictor we did not find any significant in- or decrease of PA surrounding NSSI (Est. = -0.03, SE = 0.03, p = .301,  $\beta = -0.04$ , CI [-0.08, -0.01]). In contrast, high-urge moments were characterized by a linear decline from  $t_1$  to  $t_1$  (Est. = -0.07, SE = 0.03, p = .020,  $\beta = -0.04$ , CI [-0.08, -0.01]). However, a non-significant interaction term indicates that this difference was not statistically meaningful (Est. = -0.04, SE = 0.04, p = .275,  $\beta = -0.02$ , CI [-0.06, 0.02]). Regarding the temporal dynamics of PA surrounding NSSI we found that PA followed an U-shaped pattern from  $t_1$  to  $t_1$  (Est. = 0.11, SE = 0.03, p = .002,  $\beta = 0.07$ , CI [0.03, 0.11]), the same was true for PA surrounding high urge moments (Est. = 0.09, SE = 0.04, p = .029,  $\beta = 0.07$ , CI [0.03, 0.11]). Nevertheless, a non-significant interaction terms underlies that the quadratic patterns were not significantly different (Est. = -0.02, SE = 0.05, p = .680,  $\beta = 0.00$ , CI [-0.04, 0.03]). Taken together, in the current sample we were not able to find a significant association between NSSI engagement and the regulation of PA (rejecting H2a and H2b).

Ta	ble	С	1

ween person M(SD) 1.69 (0.62)	range	Within person M (SD)	Range
1.69 (0.62)	1.00-3.50		
· /	1 00-3 50		
	1.00-5.50	1.70 (0.58)	1.00-3.22
1.63 (0.58)	1.00-3.50	1.60 (0.51)	1.00-2.83
1.55 (0.54)	1.00-3.33	1.53 (0.49)	1.00-3.00
1.55 (0.55)	1.00-3.17	1.50 (0.44)	1.00-2.50
1.56 (0.59)	1.00-3.33	1.52 (0.55)	1.00-3.00
1.56 (0.57)	1.00-3.00	1.54 (0.54)	1.00-3.00
1.62 (0.60)	1.00-3.17	1.56 (0.52)	1.00-2.67
1.55 (0.54)	1.00-3.50	1.50 (0.55)	1.00-3.50
1.52 (0.54)	1.00-3.50	1.48 (0.50)	1.00-2.83
1.55 (0.57)	1.00-3.17	1.50 (0.58)	1.00-3.17
	$\begin{array}{c} 1.55 & (0.55) \\ 1.56 & (0.59) \\ 1.56 & (0.57) \\ 1.62 & (0.60) \\ 1.55 & (0.54) \\ 1.52 & (0.54) \end{array}$	1.55 (0.55)1.00-3.171.56 (0.59)1.00-3.331.56 (0.57)1.00-3.001.62 (0.60)1.00-3.171.55 (0.54)1.00-3.501.52 (0.54)1.00-3.50	1.55 (0.55)1.00-3.171.50 (0.44)1.56 (0.59)1.00-3.331.52 (0.55)1.56 (0.57)1.00-3.001.54 (0.54)1.62 (0.60)1.00-3.171.56 (0.52)1.55 (0.54)1.00-3.501.50 (0.55)1.52 (0.54)1.00-3.501.48 (0.50)

Mean values of positive affect per prompt type (within and between person values)

PANAS-X-scale: 1 = very slightly/ not at all, 2 = a little, 3 = moderately, 4 = quite a bit, 5 = extremely

### **Replication analyses**

Following previous work, we looked at the predictive value of concurrent and lagged affect and tension. For NA we found, that together in one model, only concurrent NA has a significant value for the likelihood of engaging in NSSI (lag: Est. = -0.30, SE = 0.18, p = .102,  $\beta = -0.24$ , CI [-0.53, 0.05], current: Est. = 0.92, SE = 0.17, p < .000,  $\beta = 0.75$ , CI[0.46, 1.03]). For PA we found the same picture, together in one model, only concurrent PA was predictive for the likelihood of engaging in NSSI (lag: Est. = 0.18, SE = 0.21, p = .392,  $\beta = 0.11$ , CI[-0.14, 0.36], current: Est. = -0.57, SE = 0.23, p = .013,  $\beta = -0.35$ , CI[-0.63, -0.07]).

For tension, the lagged effect was significantly predictive for the engagement in NSSI between t<sub>-1</sub> and t<sub>0</sub> whereas the concurrent was not (lag: Est. = 0.18, *SE* = 0.08, *p* = .034,  $\beta$  = 0.25, CI [0.02, 0.48], current: Est. = 0.04, *SE* = 0.08, *p* = .601,  $\beta$  = 0.06, CI [-0.17, 0.29]). This suggest that individuals experiencing high levels of inner tension at t<sub>-1</sub> are more at risk for engagement in NSSI at t<sub>0</sub>.

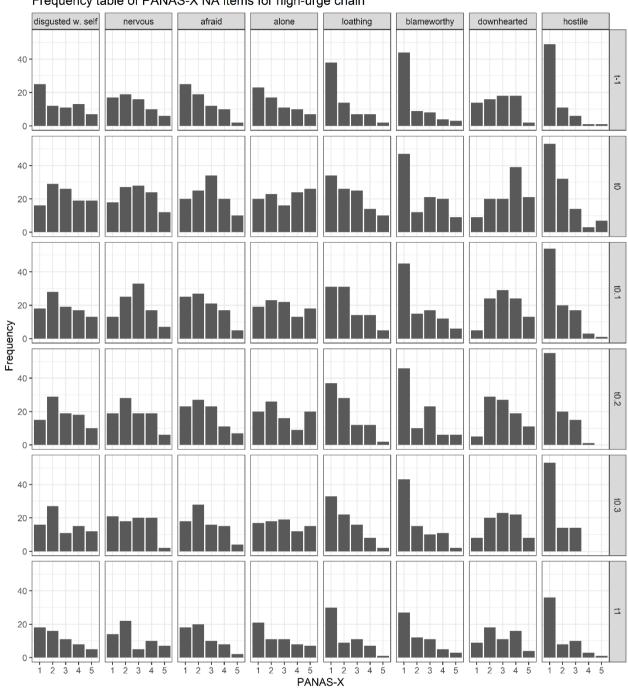
### APPENDIX: CHAPTER III



# Frequency table of PANAS-X NA items for NSSI chain

Figure C 1. Frequency ratings of PANAS-X negative affect items from t<sub>-1</sub> to t<sub>1</sub> in NSSI chains

### APPENDIX: CHAPTER III



# Frequency table of PANAS-X NA items for high-urge chain

*Figure C* 2. Frequency ratings of PANAS-X negative affect items from  $t_{-1}$  to  $t_1$  in high-urge chains

# Table C 2

# EMA protocol

<b>Reporting Criterion recommended</b> by Trull & Ebner-Priemer (2020)	Details from the present study
Justify sample size (e.g., using a multilevel power analysis)	We assessed 51 women with repetitive and frequent NSSI ( $\geq$ 1 NSSI event/ week for the last three month) to increase the probability of NSSI events. Sample size was determined by participant fees and foundation of the study (100- 150€ per person and costs for biological analysis). Post hoc multi-level power analysis indicates 91.70% CI [89.81, 93.34] power to find a medium effect for the random prompts. For the NSSI and high-urge moments, we estimated two NSSI events and two control conditions per participants. We hat 84.00% CI [81.58, 86.22] power to find a medium within group effect in the current sample.
Explain rationale for the sampling design (e.g., random, event-based, etc.)	We sampled at five semi-random time-points throughout the day, because we wanted to capture different levels of momentary affect, tension and urge to determine whether these variables were associated with NSSI. In case of high urge for NSSI (and already min. one NSSI event), we included an event based control condition (urge > 6 on a ten point Likert-scale) assessing affect and tension during high urge. Additionally, we included an event-based design whenever participants engaged in NSSI to assess effects of NSSI as soon as possible after the event. Control conditions and NSSI events were attended by three follow-up prompts, ten, twenty and thirty minutes after the event. This high-frequency sampling was included to capture short-term effects of NSSI and high urge on the dependent variables.
Explainrationaleforsamplingdensity(e.g., assessments per day) and scheduling(i.e., when the assessments are scheduled)	We sampled at five semi-random time-points within the waking hours of the participants and implemented a minimum spacing of 2h between the next random prompt/ a possible random prompt following a self-initiated prompt or a control condition. This way, we aimed to balance participant burden (i.e. not presenting too many prompts throughout the day) and robust assessment of fluctuating variables such as affect and tension.

<b>Provide technical details of sampling</b> (e.g., prompting and recording practices; procedures for event-based entries; ability to suspend/delay responses; branching details, triggering assessments, follow-ups or dense sampling of events/experiences)	Prompts were presented at five semi-random time-points via audible signal/ vibration and opening of the study app on screen. Participants had the opportunity to delay random prompts by 5, 10 or 20 minutes. NSSI prompts were self- initiated by participants via a button on the smartphone screen. For NSSI prompts, control condition and their follow-ups delay of the prompts were denied. As soon as the smartphone entered W-Lan, data were uploaded on a secured server.
Report full text of items, rating timeframes, response options/scaling	All self-report items with all answer options (random prompts, event-based prompts and follow-ups) were described in the supplemental material on osf ( <u>https://osf.io/t38sx</u> ).
Report psychometric properties of	The origin of the items and the selection processes
items in the current EMA-study	were described in the main text and on osf
(between and within person), as well as the origin of the items	(https://osf.io/t38sx).
Fully describe hardware and	The study phone was a Moto E, 2nd generation
software used	running the movisensXS app (Movisens GmbH, Karlsruhe, Germany, <i>Version 0.7.4682</i> ).
Define valid and missing data	A random prompt, event-based prompt or follow-
(for participants broadly, and specific to individual EMA reports); report descriptive analyses regarding valid data (e.g., mean per person, range, % participants above and below 80% threshold), systematic influences of compliance rates, justification for thresholds for compliance necessary	up counted as completed if participants had answered all self-report questions of the prompt. Participants completed 4,619 prompts (person $M$ = 90.57, person $SD$ = 19.66, person range = 21 - 138) over 740 person days, resulting in a compliance rate of 92.04%. Three participants were below the threshold of 80% compliance (range = 71.76% - 100%). Overall eight participants missed at least one complete day, one participant lost the study smartphone (providing 60 data points), and two participants quit participation earlier because they accepted an elective residential treatment unrelated to the study (32 and 21 data points, respectively).
Describe the procedures used to enhance compliance and participation (e.g., remuneration schedule, participant training)	Participants were trained to use the smartphone app during an orientation session in person or via an instruction video in case of an online orientation session. The experimenters were available by phone throughout the study period for any technical problems or questions regarding the study. Participants were paid a compensation of $100\varepsilon$ , and a bonus of $50\varepsilon$ if they completed more than 80% of prompts.
<b>Describe the final data set</b> number of reports (total; person average; group average), days in study and retention rates, and rates of delayed or suspended responding (if applicable)	Data of 51 woman were reported, including 1,220 data points in the current analysis (t-1, t0, t0.1, t0.2, t0.3 and t+1). The remaining random prompts were not included in the current analysis. Participants reported on average 3.04 NSSI events

<b>Preparation for data analyses</b> describe centering of predictor variables and at what level; report covariates	per person ( $SD = 2.45$ , range = 0 - 15, total = 155 events) and a total of 390 NSSI follow-up prompts (person $M = 8.30$ , $SD = 5.57$ , range = 0 - 28). Furthermore, participants provided in total 109 high-urge moments (person $M = 2.42$ , $SD = 1.29$ , range = 1 - 7) with 270 follow-up prompts (person M = 6.00, $SD = 3.30$ , range = 0 - 12). Centering and covariates are described in the main text and data analytic code is provided on https://osf.jo/uomky/
and at what level; report covariates included in the models	https://osf.io/uqmky/.
Data analysis Describe levels of analysis (momentary, day, person); explain how time is taken into account in analyses; specify and justify choices of random versus fixed effects in models; describe analytic modeling used as well as statistical software used	We described the data analysis in detail in the manuscript and all code in R is available a <u>https://osf.io/uqmky/</u> .

# Appendix Chapter IV

# Table D 1

Demographic and clinical characteristics

	Ν	%	Range	Mean	SD
Demographic variables					
Years of education			8-15	11.87	1.44
Employment status					
Employed	17	33.33			
Student or pupil	16	31.37			
Unemployed	14	27.45			
Disability pension	4	7.84			
Current DSM-IV diagnoses					
Mood disorders					
Major depression	33	64.71			
Dysthymia	4	7.84			
Anxiety disorders					
Social phobia	11	21.57			
Specific phobia	6	11.76			
Generalized anxiety disorder	2	3.92			
Panic disorder	6	11.76			
Agoraphobia without panic	2	3.92			
Posttraumatic stress disorder	25	49.02			
Obsessive compulsive disorder	6	11.76			
Substance abuse	2	3.92			
Somatic pain disorder	1	1.96			
Eating disorders					
Anorexia	6	11.76			
Bulimia	5	9.80			
Attention deficit disorder	1	1.96			
Borderline personality disorder	32	62.75			
Any mental disorder	51	100	1-5	2.24	1.45

### Pilot of interpersonal events items

Items for positive and negative interpersonal events were pre-tested in an online survey with 376 participants. Participants were between the ages of 18 - 65 (M = 30.2, SD = 10.2), the majority were women (n = 283), and many scored above the clinical cut-off for Borderline Personality Disorder features (n = 119) in the German version of the Borderline scale of the Personality Assessment Inventory (Engel et al., 2012; Stein et al., 2007). In this pre-test, we asked participants to describe one positive and one negative interpersonal event they experienced with a significant other person during the last seven days. Next, participants were asked to indicate whether each event (positive and negative) fit into nine different categories of events. For negative events, these were: someone 1) criticized me, 2) rejected/excluded me, 3) ignored my needs or feelings, 4) behaved angry/ aggressive towards me, 5) let me down/ disappointed me, 6) had a fight with me, 7) demanded too much of me, 8) ridiculed me, 9) abused me. For positive interpersonal events, the categories were: 1) supported/ helped me, 2) showed me affection, 3) respected my needs or feelings, 4) gave me their attention or time, 5) was interested in me, understood me, 6) stood up for me, 7) made me a compliment or praised me, 8) took time for me, 9) did something for me. We selected the five categories with the highest endorsement rates for each, positive and negative events. We did this, because we wanted to include interpersonal events that were relatively common and not so rare that there would only be a small chance of observing them during the study period.

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# **Detailed results for Hypothesis 1**

# Table D 2

Predicting engagement in non-suicidal self-injury with the number of current and lagged negative interpersonal events and covariates in a logistic multilevel model.

	Estimate	OR	95% CI	SE	р
Intercept	-3.89	0.02	[0.01; 0.03]	0.22	<.001
Concurrent negative events	0.43	1.54	[1.24; 1.91]	0.11	<.001
Lagged negative events	0.11	1.11	[0.77; 1.60]	0.19	.565
Person-average negative events	-0.25	0.78	[0.46; 1.33]	0.27	.359
Hour after wake	0.10	1.10	[1.05; 1.16]	0.03	<.001

*Note*. OR = odds ratio.

# Table D 3

Predicting engagement in non-suicidal self-injury with the level of distress caused by current and lagged negative interpersonal events and covariates in a logistic multilevel model.

	Estimate	OR	95% CI	SE	р
Intercept	-3.77	0.02	[0.02; 0.03]	0.21	<.001
Concurrent distress by negative events	0.32	1.37	[1.20; 1.58]	0.07	<.001
Lagged distress by negative events	0.19	1.21	[1.01; 1.45]	0.09	.040
Person-average negative events	-0.11	0.90	[0.60; 1.33]	0.20	.583
Hour after wake	0.09	1.10	[1.04; 1.15]	0.03	<.001

*Note*. OR = odds ratio.

# **Detailed results for Hypothesis 2**

# Table D 4

Predicting the number of negative interpersonal events following NSSI in a generalized multilevel model with a log link function (specifying a Poisson distribution for the outcome).

v	Estimate	IRR	95% CI	SE	p
Intercept	-1.94	0.14	[0.10; 0.21]	0.18	<.001
Lagged NSSI	-0.31	0.73	[0.25; 2.09]	0.54	.555
Person-average NSSI	-6.01	0.00	[0.00; 57.43]	5.13	.242
Hour after wake	0.02	1.02	[1.01; 1.04]	0.01	.008

*Note*. IRR = incidence rate ratio.

# Table D 5

	Estimate	β	95% CI	SE	р
Intercept	0.45			0.09	<.001
Lagged NSSI	0.10	0.01	[-0.02; 0.05]	0.14	.488
Person-average NSSI	-0.85	-0.02	[-0.16; 0.11]	2.57	.742
Hour after wake	0.01	0.04	[0.00; 0.07]	0.01	.025

Predicting the level of distress caused by negative interpersonal events following NSSI in a linear multilevel model.

*Note.* IRR = incidence rate ratio.

# Detailed results for Hypothesis 3

# Table D 6

Predicting the number of positive interpersonal events following NSSI in a generalized multilevel model with a log link function (specifying a Poisson distribution for the outcome).

	Estimate	IRR	95% CI	SE	р
Intercept	-0.63	0.53	[0.41; 0.70]	0.14	<.001
Lagged NSSI	-0.10	0.91	[0.58; 1.43]	0.23	.679
Person-average NSSI	-7.87	0.00	[0.00; 1.18]	4.10	.054
Hour after wake	0.03	1.03	[1.02; 1.04]	0.01	<.001

*Note*. IRR = incidence rate ratio.

# **Exploratory Analysis for NSSI Urges**

# Table D 7

# Predicting NSSI urge with the number of current and lagged negative interpersonal events and covariates in a linear mixed model.

	Estimate	β	95% CI	SE	р
Intercept	3.59			0.26	<.001
Concurrent negative events	0.86	0.26	[0.19, 0.33]	0.12	<.001
Lagged negative events	0.12	0.03	[-0.01, 0.08]	0.07	.125
Person-average negative events	0.28	0.05	[-0.13, 0.24]	0.48	.571
Hour after wake	0.03	0.05	[0.02, 0.08]	0.009	<.001

*Note.* Effect sizes ( $\beta$ ) represent standardized parameters and were computed using the R package sjstats.

### Table D 8

	Estimate	β	95% CI	SE	р
Intercept	3.59			0.26	<.001
Concurrent distress by events	0.53	0.23	[0.19; 0.27]	0.05	<.001
Lagged distress by events	0.04	0.02	[-0.02; 0.05]	0.05	.436
Person-average distress by negative events	0.27	0.06	[-0.10; 0.23]	0.36	.466
Hour after wake	0.03	0.05	[0.02; 0.08]	0.01	<.001

Predicting NSSI urge with the level of distress caused by current and lagged negative interpersonal events and covariates in a linear mixed model.

*Note.* Effect sizes ( $\beta$ ) represent standardized parameters and were computed using the R package sjstats.

### **Exploratory Day Level Analyses**

We conducted additional exploratory analyses to determine whether the expected associations between momentary NSSI and subsequent interpersonal events might be better captured at the day level of analysis. This procedure was consistent with Turner et al. (2016), who assessed whether NSSI predicted a change in positive and negative interpersonal events following NSSI days. We specified two linear MLMs using the average number of negative interpersonal events in a day as outcome in the first model (Table S6) and the same for positive interpersonal events (Table S7). The predictors of interest were whether NSSI was reported at any moment on the concurrent or lagged day. We also included the proportion of days across the study that each participant endorsed any NSSI as a person-level covariate. We specified random person intercepts. We originally also specified random slopes for the two day-level predictors, but in both models, we set those effects as fixed due to non-convergence

# Table D 9

· · · · · · · · · · · · · · · · · · ·	Estimate	β	95% CI	SE	р
Intercept	0.28			0.07	<.001
Same day NSSI	0.12	0.08	[0.02; 0.13]	0.04	.005
Past day NSSI	-0.01	0.00	[-0.06; 0.05]	0.04	.904
Person average NSSI	-1.49	-0.08	[-0.29; 0.13]	2.03	.466

Predicting the average number of negative interpersonal events in a day with whether NSSI was reported during the same day or previous day, in a linear multilevel model.

*Note.* Effect sizes ( $\beta$ ) represent standardized parameters and were computed using the R package sjstats.

# Table D 10

Predicting the average number of positive interpersonal events in a day with whether NSSI was reported during the same day or previous day, in a linear multilevel model.

	Estimate	β	95% CI	SE	р
Intercept	0.88			0.10	<.001
Same day NSSI	-0.14	-0.06	[-0.11; 0.00]	0.07	.062
Past day NSSI	0.08	0.03	[-0.03; 0.09]	0.07	.263
Person average NSSI	-4.14	-0.14	[-0.34; 0.05]	2.92	.162

*Note.* Effect sizes ( $\beta$ ) represent standardized parameters and were computed using the R package sjstats.