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Pain, stress, and stigma: an investigation of if and how social support makes a difference

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List of included Publications

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Further Publications

I. Siegel, M., Randall, A. K., Lannutti, R. J., … **van Stein, K. R.**, … & Zemp, M. (2022). Intimate Pride: A Tri-Nation Study on Associations between Positive Minority Identity Aspects and Relationship Quality in People with Diverse Sexual Orientations From German-Speaking Countries. *International Journal of Applied Positive Psychology*, 1-29. doi: 10.1007/s41042-022-00070-6

II. Hoy, M., **van Stein, K. R.**, Strauß, & Brenk-Franz, K. (2021). The Influence of Types of Stimulation and Attitudes to Clitoral Self-stimulation on Female Sexual and Orgasm Satisfaction: a Cross-sectional Study. *Sex Res Soc Policy*, 1-12. doi: 10.1007/s13178-021-00618-2

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IV. **van Stein, K. R.**, Strauß, B., & Brenk-Franz, K. (2019). Ovulatory Shifts in Sexual Desire But Not Mate Preferences: An LH-Test-Confirmed, Longitudinal Study. *Evolutionary Psychology,* 17(2). doi: 10.1177/1474704919848116

Summary

Social support is uniformly assumed to be beneficial for our general health. For the largest part, studies from the last decades report that social support is positively related to mental as well as physical health outcomes. However, due to differing definitions of social support and methods to assess it, there are mixed findings and caution is warranted when interpreting or generalizing them. This work aims to investigate the role of social support on different levels in order to understand how it is related to health outcomes.

In the first chapter, the concept of social support and how it is assumed to unfold its beneficial impact is outlined. The second chapter sets out the minority stress model: A model that aims to explain the relation between minority stressors, resilience factors, and health outcomes. It assumes that additionally to general stressors which everybody experiences, marginalized groups experience additional stressors specific to their minority status. These additional stressors are assumed to put an extra strain on marginalized individuals and thus, it is highly relevant to wellbeing. The third chapter comprises Paper #1, an original study which investigated the relation between internalized stigma, social resilience factors and mental health. It found social resilience factors (social support and community connectedness) to be negatively associated with mental health problems, but they did not significantly moderate the relationship of internalized stigma with mental health symptoms. Chapter four begins with explaining the disease endometriosis and its specific characteristics. Then, nociception, pain, and pain chronification processes are elaborated. Paper #2 provides an overview of the literature with a focus on the psychological burden of endometriosis. It emphasizes, among other aspects, the central role of social interaction, integration, and isolation in burden due to endometriosis. Derived from this, Paper #3 examines how social support is related to the experience of pain in endometriosis and chronic pelvic pain in every-day life. In this pre-registered psychophysiological ecological momentary assessment, social support on a between-person level was negatively related to pain levels. Further findings are reported and discussed. Chapter five summarizes the main findings and discusses, why broad-scale social support is often found to be positively associated with health outcomes, while on the momentary level findings are mixed. In conclusion, this dissertation combines novel findings from gender minorities and pain patients and relates them to established models of social support and health. These connections offer valuable insights for developing mental health prevention measures and interventions.

Chapter 1: Social Support

Social support and integration are universally recognized as fundamental human needs, essential for well-being (Baumeister & Leary, 1995; Bowlby, 1977). The significance of social support and the anticipation thereof extends across various aspects of health, including reducing the risk for physical (Holt-Lunstad, 2018) and mental illness (Fasihi Harandi et al., 2017), as well as mortality (Holt-Lunstad et al., 2010; Krause, 1997). In contrast, research findings connect loneliness with worse health outcomes (J. Wang et al., 2018). This work aims to explore the link between social support and mental as well as physical health.

What is Social Support?

Cobb (1976) defined social support as "information leading the subject to believe that he is cared for and loved, esteemed, and a member of a network of mutual obligations" (p. 300). It can comprise different aspects of assistance, of which the three most commonly evaluated are emotional, informational, and instrumental support (House & Kahn, 1985; Thoits, 2011). Emotional support is characterized by affection, understanding and care. Informational support encompasses the provision of advice information, e.g. to help with decision-making. Instrumental support provides assistance with tangible everyday tasks (e.g. help with chores, financial support).

Who provides Social Support?

Thoits (2011) describes that social support in this given sense can be performed by primary or secondary groups. Primary groups are defined as informal, intimate, enduring relationships, e.g. family members, relatives, friends, romantic partners. They are people who are subjectively valued as influential in one's life. Secondary groups are defined as less personal but more formal or guided by regulations or hierarchical positions. In contrast to the enduring character of primary groups, in secondary groups people can join and exit this group less predictably. Examples are work colleagues and members of a sport club or religious group. Previous research has demonstrated that the source of social support is highly relevant. For example, in a study with an adolescent LGBT sample, family support was the most important source of social support in order to positively influence mental health (McConnell et al., 2015). In the present dissertation, only social support by primary group members and only the receiving side of social support will be considered.

How and why is Social Support healthy?

There are two suggested pathways through which social support can unfold its effect (Cohen & Wills, 1985). They are not conflicting, but rather complement each other and are both supported by a recent review (Che et al., 2018):

According to the main effect model (Cohen & Wills, 1985), social support has a direct, overall beneficial effect on well-being. It assumes that being embedded in a cohesive social network is by itself a key mechanism for health. The feeling of being part of a social group and being important to others nurture the self-esteem and beliefs of self-efficacy, which in turn are central for mental health (Berkman et al., 2000; Cohen & Wills, 1985; Thoits, 2011).

From the perspective of the buffering model (Cohen & Wills, 1985), social support is understood as a stress buffer. For example, in a study by Szkody et al. (2021), perceived social support buffered the connection between worry about COVID-19 and psychological health in participants in self-isolation. Also, this model is in line with the transactional model of stress and coping (Lazarus & Folkman, 1984): Both models describe social support to impact on the stress appraisal process, suggesting that

individuals with higher levels of perceived social support are more optimistic to overcome future stressors and thus perceive stressors as less threatening.

Oxytocin and Social Support

One of the central neurobiological mediators of social support is oxytocin. This neuropeptide is essential for social functions such as social recognition (De Dreu & Kret, 2016; Domes et al., 2007), empathy (Burkett et al., 2016), trust, and attachment (Baumgartner et al., 2008; De Dreu & Kret, 2016). Also, it was found to dampen physiological and behavioral responses to stress by modulating the hypothalamic–pituitary–adrenal (HPA) axis (further information on the HPA axis can be found in Chapter 4) (DeVries et al., 2003; Eisenberger & Cole, 2012; Legros, 2001; Neumann et al., 2000; Stachowiak et al., 1995; Uvnäs-Moberg, 1998), and cardiovascular reactivity (Grewen & Light, 2011; Light et al., 2005). For instance, oxytocin was found to modulate the stress-inducing signaling and expression of corticotropin-releasing hormone (CRH) (Dabrowska et al., 2011; Winter & Jurek, 2019) and to inhibit the secretion of noradrenaline via activation of alpha-2-adrenoceptors (Díaz-Cabiale et al., 2000; Uvnäs-Moberg et al., 2014), consequently reducing stress reactivity and stress levels. Furthermore, anxiolytic properties were demonstrated in studies that found the increase of oxytocin to reduce the release of adrenocorticotropic hormone (ACTH) (Legros, 2001; Neumann et al., 2000) and to decrease the amygdala's response to fear-related stimuli (Domes et al., 2007; Eckstein et al., 2015; Huber et al., 2005; Kirsch et al., 2005; Petrovic et al., 2008).

Importantly, oxytocin not only acts independently but also interacts with social support: The effectiveness of social support moderating stress responses is suggested to be modulated by oxytocin (DeVries et al., 2003; Sue Carter, 1998). In line with this, a placebo-controlled study has demonstrated that when being alone during a laboratory stress test, oxytocin administration alone had no significant effect on cortisol levels. However, the combination of oxytocin administration and the presence of a friend resulted in reduced anxiety levels and lower cortisol concentrations (Heinrichs et al., 2003). The same effect was found in a randomized placebo-controlled fMRI study: At the neural level, oxytocin significantly amplified the positive effects of partner support after receiving unpleasant electric stimuli (Kreuder et al., 2019). Taken together, oxytocin is understood as the neurobiological basis of how social support and interaction are linked to physical and mental health (DeVries et al., 2003; Light et al., 2005; Sue Carter, 1998; Uvnäs-Moberg, 1998).

A more thorough overview of the neurobiological processes (also including HPA axis, sympathetic nervous system, and serotonin) and the relation of social behaviors and mental health can be found elsewhere (Ditzen & Heinrichs, 2014; Ozbay et al., 2008; Walker & McGlone, 2013).

Social Support in Marginalized Groups

In general, social support and therefor being part of a social network is most likely health-beneficial for all humans. But especially for marginalized individuals, the social network can play a crucial role. They frequently encounter discrimination, prejudice, and systemic inequalities, which can lead to increased psychological distress and physical health disparities. Thus, strong social ties are even more important for this population. For instance, in a sample of chronic pain patients, perceived social support protected against the harmful effects of pain invalidation (Coady et al., 2023). And in a sample of trans* individuals, social support acted as a buffer between internalized stigma and life satisfaction (Ott et al., 2017). Unfortunately, this mechanism also seems to apply in the opposite direction: In LGBTQ* adolescents, a lack of social support and integration is linked to lower levels of

mental health (Brecht et al., 2021; McDonald, 2018). And in endometriosis patients, perceived lack of understanding from the social environment is linked to higher disease burden (Schick et al., 2022).

To understand how marginalization, social support and mental health are associated, the following section will focus on gender minorities and the transgender minority stress model.

Chapter 2: The Transgender Minority Stress Model

Definition: Gender Minorities

The term gender minorities includes trans*, inter* and non-binary people.

Trans* refers to individuals whose sex assigned at birth does not match their gender identity or does not match it completely. The asterisk is a placeholder for the different endings transgender, transident and transsexual. People whose gender identity matches the gender assigned to them at birth are referred to as cisgender. Non-binary refers to individuals whose gender identity is not exclusively female or exclusively male. The terms trans* and non-binary can be self-designations by themselves or used as umbrella terms for all gender identities that do not conform entirely with the cisgender or binary norm, respectively.

Inter* is “an umbrella term for unique variations in reproductive or sex anatomy” (interACT, 2021). The term inter* includes the terms intersex, intergender and intersexual. In contrast to the terms trans* and non-binary that solely refer to gender identity, inter* refers to anatomical variations. Thus, inter* individuals can be trans* or cisgender (depending on the sex assigned at birth), as well as male, female or on the non-binary spectrum. Individuals who are not inter* are referred to as endosex.

Individuals belonging to gender minorities are often affected by exclusion, pathologization and discrimination (European Union Agency for Fundamental Rights, 2014; Factor & Rothblum, 2007; Frohn et al., 2020; Klöppel, 2016; Pöge et al., 2020) and have higher prevalence rates of mental health problems (Kasprowski et al., 2021; Kessler et al., 2005; Schützmann et al., 2009).

What is Minority Stress?

Woda (2016) distinguishes three meanings of the term stress: Firstly, the need to adapt to external or internal events, triggered by real or perceived, pleasant (e.g. sports) or unpleasant (e.g. exam) stressors; secondly, the adaptive behavioral or mental responses that strive to cope with those stressors (e.g. increased attention or increased motor activity); and thirdly, the physiological responses that elicit metabolic adaptations.

The concept of minority stress refers to the first meaning. It assumes that individuals who belong to minority groups are confronted with additional stressors due to societal marginalization (Meyer, 2003). Although all people experience stressors, e.g. losing one’s job, minority stress originates in prior experiences of prejudice and stigmatization (Frost et al., 2023). Depending on the social context and previous learning history, the same stressor can be general (e.g. all employees lose their jobs) or a minority stressor (e.g. motivated by prejudice against sexual and/or gender minorities) (Frost et al., 2023). However, in other cases, such as micro-aggressions, minority stressors do not have equivalents for non-minorities. Minority stress is recognized as a form of chronic stress since it is caused by relatively stable social and cultural mechanisms (Meyer, 2003). Chronic stress is associated with negative mental and physical health (Johansson et al., 2008; Pryce et al., 2011; Ursin & Eriksen, 2010).

The original Minority Stress Model

The minority stress model by Meyer (1995, 2003) aims to understand the additional stressors that minority groups experience due to their marginalized status in society, and how these stressors are related to health outcomes. Minority stressors can be caused by both external sources, such as discrimination and prejudice, and internal processes, such as internalized stigma and identity concealment. They collectively form the excessive burden that puts individuals from minorities at a higher risk of negative health outcomes. Additionally, the model posits that resilience factors such as coping strategies or social support can buffer the adverse health effects of stressors. A simplified overview of the model is depicted in Figure 1.

Originally, the model refers to sexual minorities (lesbian, gay, and bisexual individuals) and describes how sexual orientation specific stressors, e.g. experiences of microaggressions, are associated with reduced mental health. Also, Meyer (Meyer, 1995) describes that long before homosexual individuals become aware of their own homosexuality, they internalize society's homonegative attitudes and later turn them against themselves. This internalized stigma, known specifically as internalized homonegativity, is strongly associated with mental health outcomes like depressive and anxiety symptoms (Newcomb & Mustanski, 2010).

The minority stress model has been successfully used for interventions in public policy as well as counseling approaches (for an overview, see Frost et al., 2023).

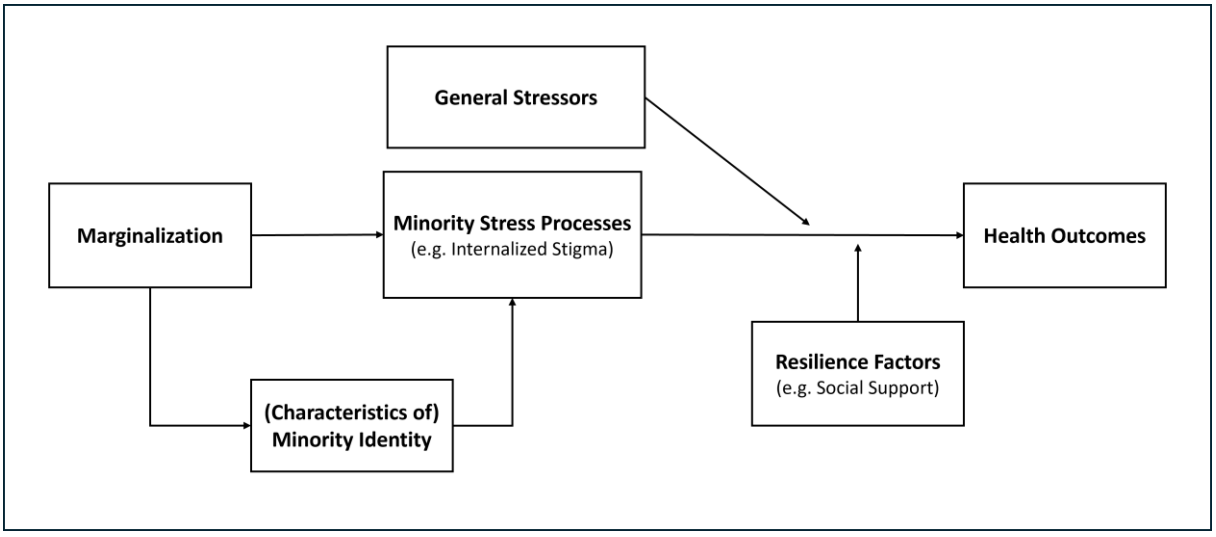

Figure 1. Simplified Overview of the Minority Stress Model, adapted from Meyer (2003)

The Transgender Minority Stress Model

Hendricks and Testa (2012) adapted the minority stress model for gender minorities. They added stressors specifically relevant for trans* and non-binary people, e.g. the stressor of gender non-affirmation. Also, the concept internalized homonegativity was replaced by internalized transnegativity and the resilience factors pride and community connectedness were introduced.

Internalized Transnegativity

Internalized transnegativity (also internalized transphobia or internalized trans-hostility) is a form of internalized stigma and is defined as the outcome of a process of internalizing negative societal attitudes and prejudices that are related to gender identity (Rood et al., 2017). Thus, internalized transnegativity does not originate in trans* individuals, but is a product of the nearer and farther social environment, society and policies through which trans* individuals are stigmatized. Internalized stigma is associated with decreased mental health (Tebbe & Moradi, 2016), and decreased insistence in seeking mental health care or other support services (Corrigan, 2004). Specific finding on the relation between internalized transphobia and mental health are rare, but conclusive: Internalized transnegativity is positively associated with depressive symptoms (Inderbinen et al., 2021).

Social Resilience Factors in the Minority Stress Model

The minority stress model argues that social support and community connectedness are resilience factors that can buffer the effects of stressors on mental health. So far, research on gender minorities has found associations between each of these constructs and mental health: Lower levels of reported community connectedness are associated with higher levels of depressive (Fredriksen-Goldsen et al., 2014; Jäggi et al., 2018; Testa et al., 2015) and social anxiety symptoms (Testa et al., 2015). The same was found for a combined measure of pride and community connectedness (Brennan et al., 2017). In a large sample from survey data, Testa (2014) found that prior contact with other transgender individuals was associated with lower fearfulness, lower suicidality, and greater comfort.

Likewise, social support was found to be negatively related to depressive (Budge et al., 2013; Fredriksen-Goldsen et al., 2014; Tebbe & Moradi, 2016) and anxiety symptoms (Budge et al., 2013) in gender minorties. Also, it was also found to be negatively related to internalized transnegativity (Tebbe & Moradi, 2016; Testa et al., 2015).

Chapter 3: Internalized Stigma, Social Resilience Factors, and Mental Health

The following paper will investigate the relation between internalized stigma, social resilience factors and mental health along the lines of the minority stress model. The aim of the study is to clarify, if and how social resilience factors contribute to mental health in marginalized groups.

Paper #1: Internalized Transnegativity, Resilience Factors, and Mental Health in a Sample of Gender Minorities From Germany and Switzerland

Due to societal marginalization and discrimination, trans*, inter*, and nonbinary individuals often suffer from poorer mental health than the general population (Kasprowski et al., 2021; Schützmann et al., 2009; Valentine & Shipherd, 2018). The minority stress model (Meyer, 2003) tries to explain how experiences of discrimination relate to the health of stigmatized groups. Minority stress is understood as a chronic social stress that encompasses specific additional burden for individuals of minority groups. To describe the relation between minority stress and health, the model links minority stress processes with factors like experiences of group-specific discrimination and resilience factors. Hendricks and Testa (2012) adapted the model to gender minorities utilizing the concept of

internalized transnegativity which describes the discomfort with one's own trans* identity due to the internalization of socially normative gender expectations (Bockting et al., 2020).

Research on the link between mental health and internalized transnegativity in gender minorities suggests that they are positively related (Inderbinen et al., 2021). Studies on the link between mental health and resilience factors (e.g. social support and community connectedness) in gender minorities suggest that there is a negative relationship (Brennan et al., 2017). The minority stress model proposes that resilience factors act as moderators on the relationship between minority stress and mental health (Meyer, 2003). While this assumption was found for sexual minorities (Doty et al., 2010), findings for gender minorities are mixed (Jäggi et al., 2018; Ott et al., 2017). Thus, it is necessary to further examine the role of resilience factors in the context of internalized transnegativity and mental health.

The aim of this pre-registered study was to assess the association between self-stigmatization (internalized transphobia) and mental health (depressive and anxiety symptoms) and to additionally investigate resilience factors (social support and community connectedness) as moderators. Data originate from a comprehensive, international, cross-sectional online survey on the well-being and relationship experiences of people in the LGBT+ community. The final sample consists of N = 243 adult German and Swiss trans*, inter*, and nonbinary individuals. Multiple linear regression and moderation analyses were computed to assess the proposed associations.

Internalized transnegativity was found to be positively related to depressive and anxiety symptoms; and it was found to be negatively associated with the resilience factors social support and LGBT+ community connectedness. However, there was no statistical evidence for a moderation of the association between internalized transnegativity and mental health by any of the resilience factors.

This study aligns with international findings regarding the association between self-stigmatization and mental health. The results suggest that not only experiences of discrimination per se, but also how these experiences are reflected in one's self-image (internalization of stigma) are important for understanding the burden of gender minorities. Concerning the negative associations of internalized transnegativity and resilience factors, two interpretations are possible: a) members of a minority can benefit from the community as a safe space and from other members to receive support with experienced marginalization and discrimination; b) individuals with high internalized stigma will less likely seek contact with the respective community or experience connectedness to that community.

The findings do not support the moderating role attributed to resilience factors by the minority stress model (Meyer, 2003). Neither social support nor community connectedness were found to weaken the association between internalized stigma and mental health. One possible reason is that the items used were not specific enough, as in their research on sexual minorities, Doty et al. (2010) found a significant moderation by sexuality-specific social support, but not general social support. This would also fit the notion by Cohen and Wills (1985) that the buffering effect of support does only work if the type of support is relevant in context of the specific stressor. Further research is needed to assess the mental health situation of gender minorities and to clarify the role of resilience factors in the minority stress model.

Chapter 4: Endometriosis and Chronic Pelvic Pain

Taken together, Paper #1 demonstrates that social support is associated with variables crucial for mental health. And although the presented findings do not support a buffering effect of social

support, other findings do. Chapter 4 will shed light on the impact of social support a) in another sample, and b) on a micro-level.

It will start with an introduction to the clinical symptom complex of endometriosis and to pain mechanisms and then present two studies. The first is a review that highlights why we decided to recruit a sample of endometriosis patients to investigate the influence of social support. The second is an ecological momentary assessment that investigates how single social support acts are associated with pain experience on a moment-to-moment level.

What is endometriosis?

Endometriosis affects an estimated 10% of the menstruating population. It is defined as the growth of endometrial-like tissues outside of the uterus (Eskenazi & Warner, 1997). Although it can be asymptomatic, its core symptoms are chronic pelvic pain (CPP), dysmenorrhea, dyspareunia, dysuria, dyschezia, and infertility (Mechsner, 2016). It is classified as benign, although the tissue implants can spread and damage affected organs (Mechsner, 2016). About 50% of the affected have a persistent need for therapy (Kuohung et al., 2002) and recurrence rates of 50-80% are a major problem (Schweppe, 2002). There are several theories concerning the origin of the disease, which complement each other, but none of them has yet been able to explain the pathogenesis in its entirety (for a summary see Mechsner, 2016). A comprehensive summary of the biochemical processes that contribute to the development, maintenance, and progression of the disease was written by Mechnser (2016). Endometriosis is understood as a gynecological disease, but it can affect the entire body and the psyche. Since there is no clear link between pain symptoms and localization of tissue implants or endometriosis stage (Carey et al., 2014; Triolo et al., 2013; Vercellini et al., 1996, 2007).

Diagnosis and diagnostic latency

To diagnose endometriosis, a laparoscopic examination was recommended by several large gynecological associations. Current guidelines set forth by the German Association of the Scientific Medical Societies (AWMF) emphasize that laparoscopic examinations are not mandatory for diagnosis; rather, a thorough patient history and sonography are recommended (AWMF, 2020).

An important issue in this context is the diagnostic latency. On average, it takes 8-11 years from the onset of symptoms for individuals to receive a correct diagnosis (Nnoaham et al., 2011). This delay stems, in part, from the taboo surrounding menstruation and gynecological health on one hand, and the normalization of pelvic pain in women on the other (Culley et al., 2013). Consequently, affected individuals often fail to take their own pain seriously, and may not seek medical care when in doubt. Furthermore, healthcare providers may also trivialize symptoms and may be constrained by time/financial pressures, leading to inadequate patient assessments and misdiagnoses (Culley et al., 2013). The prolonged diagnostic delay increases the risk of pain becoming chronic, transforming what initially might have been a manageable issue into a significantly more challenging one to address.

In 2022, a new diagnostic test based on salivary microRNA (Bendifallah et al., 2022) was introduced. On the one hand this is an important progress in facilitating diagnosis. On the other hand, the tests are currently still too expensive to be used in standard care, and they do not address the issue that medical staff must take patients seriously and draw appropriate conclusions from reported symptoms.

It is still to be assessed, if the mentioned new diagnosis recommendations, the new diagnostic saliva test, and the elevated public interest of the last years has a positive influence on the diagnostic delay and thus treatment begin.

Nociception, Pain, and Pain Chronification

"The problem is that although nociception is usually the cause of pain, it is neither necessary nor sufficient and is very often not linearly related to the resulting pain."

(Tracey, 2010, p. 1277)

Nociception

Nociception is the transmission of noxious stimuli from (peripheral) parts of the body to the brain. This sensory perception is automatically associated with an emotional dimension. This overall experience, comprising a sensory and a psychological component, is referred to as pain. The *International Association for the Study of Pain* (IASP) defines pain as an "unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage." (Raja et al., 2020). This definition captures the essence: It is not solely about actual or potential tissue damage, but also about experiences that are similar to those associated with such damage. Therefore, psychological mechanisms play a significant role in the perception of pain.

Pain Experience, Context, and Learning

Not only the peripheral pain stimulus itself, but also contextual factors and individual learning history are decisive for individual pain experience. For example, in a laboratory study using laser stimuli on participants' skin, the same stimulus intensity was rated significantly more painful when the procedure was announced to be potentially harmful in comparison to entirely safe (Wiech et al., 2010). This difference did also manifest on the neural level. A meta-analysis by Jackson et al. (2014) found that painful stimuli being appraised as threatening was associated with increases in pain intensity, impairment, and affective distress in chronic pain patients. Complementary to this, research shows that positive coping and reappraisal strategies successfully decrease pain levels and raise mental health variables (Ashar et al., 2022; Donatti et al., 2017; González-Echevarría et al., 2019). Also, the social context is important: A comprehensive review found dyadic coping strategies to be associated with higher relationship satisfaction and higher levels of physical and mental health (Weitkamp et al., 2021).

Chronification and Sensitization

When pain persists or recurs for longer than 3 months, it is categorized as chronic pain (World Health Organization (WHO), 2021). In the following section, chronification processes will be shortly explained. When a noxious stimulus occurs repeatedly (as it is often the case in endometriosis), changes can occur a) locally in the peripheral body parts, b) in the HPA axis, c) in the central nervous transmission chain, and d) in the neural network that is mainly responsible for pain processing.

a) Peripheral Sensitization

Peripheral Sensitization describes the process of sensory neurons becoming more easily excitable after exposure to noxious stimuli at the site of tissue damage or inflammation (for an overview see (Maddern et al., 2020). Inherently, this is a mechanism to protect already harmed tissues. But when inflammation continues, the respective nerve fibers can become chronically hypersensitive. Endometriotic lesions are known to be highly innervated by sensory nerve fibers, accompanied by different immune cells such as macrophages and mast cells (Morotti et al., 2014). The interaction between nerve fibers and immune cells through the release of pro-nociceptive and pro-inflammatory mediators such as estradiol might be an important contribution to peripheral sensitization (Godin et

al., 2021), stimulating further angiogenesis and neurogenesis (Liang et al., 2018). Peripheral sensitization results in lower pain thresholds, which may lead to hyperalgesia and allodynia.

b) Dysregulation of the HPA Axis

A relation between chronic pain conditions and a dysregulation of the HPA axis has been shown in several studies with chronic stress increasing the experienced level of pain and chronic pain being a physiological stressor (Kogler et al., 2015). This has been described for low back pain (Griep et al., 1998), chronic whiplash-associated disorder (Gaab et al., 2005) and endometriosis (van Aken et al., 2018) as well as for CPP (Heim et al., 1998) resulting from other conditions.
Dysregulation of the HPA axis is caused by chronic stress: Glucocorticoid and mineralocorticoid receptor sensitivity decreases and less cortisol is released, an adaptive process, which has been termed hypocortisolism. Hypocortisolism has been reported in patients with chronic stress as well as in patients with CPP (Heim et al., 1998), respectively with endometriosis (Petrelluzzi et al., 2012). The low levels of cortisol cause an increased synthesis of pro-inflammatory agents. These pro-inflammatory agents are drawn to damaged tissue and increase the sensitivity in these areas (Maddern et al., 2020) as described under a). Thus, the pain threshold can be lowered by the prolonged experience of stress. Higher inflammation in endometriosis does not only increase sensitivity, but also directly promotes further growth of endometriotic lesions. Macrophages are involved in the production of pro-inflammatory cytokines (Gibson et al., 2021), which are suggested to stimulate endometriotic stromal cells (Izumi et al., 2018). In endometriosis, stress and pain mutually influence each other while cause-effect relations remain unclear.

c) Central Sensitization

Central sensitization is a process triggered by sustained input from afferent sensory fibers, which themselves have undergone the process of peripheral sensitization (Woolf & Salter, 2000). Dependent on many factors, this can lead to an uncoupling: Through learning mechanisms, central sensitization becomes independent of peripheral sensitization (Woolf & Salter, 2000). This results in neurons of the central nociceptive system being more easily excitable and highly sensitive to sensory inputs. Thus, pain experience can intensify, and pain can even be perceived after the initiating pathophysiology is resolved (for an overview, see (Maddern et al., 2020)). It is suggested that central sensitization processes are often contributing to chronic pain without clear somatic causation (Nijs et al., 2011). These central sensitization processes have already been found in different conditions with CPP: When presented with acute pain stimuli, patients with endometriosis and dysmenorrhea report higher sensitivity and higher pain intensity than healthy controls (Bajaj et al., 2003; Iacovides et al., 2013). It is assumed that *central sensitization* is one of the key mechanisms that contribute emergence of endometriosis related pain (Stratton & Berkley, 2011).

d) The Pain Matrix

Pain chronification cannot only be measured in levels of hormones and pro-inflammatory agents but can also be observed on the neural level. The term *pain matrix* comprises brain areas that are involved in acute and chronic pain processing. Some of these areas also are part of the HPA axis. For example, the hippocampus, being a part of the pain matrix, was found to play a considerable role in cortisol secretion and HPA axis activity (Frodl & O'Keane, 2013; Jacobson & Sapolsky, 1991; Zhu et al., 2014).

However, researchers have found changes in neural pain processing, depending on whether pain is acute or chronic. In acute pain, the pain matrix is activated by a noxious stimulus in order to facilitate a fast reaction. But when acute pain transforms into chronic pain, neural processes in areas of pain processing change, e.g., in the insula (As-Sanie et al., 2016), anterior cingulate cortex (ACC) and hippocampus (Yu et al., 2021). For example, on the structural level, a study found changes in the anterolateral hippocampus after successful psychotherapy treatment of endo-related pain (Beissner

et al., 2018). On the functional level, As-Sanie et al. (As-Sanie et al., 2016) found higher connectivity between anterior insula and medial prefrontal cortex (mPFC) in endometriosis with CPP vs. asymptomatic endometriosis patients. Additionally, this higher connectivity was positively associated with anxiety and depression symptoms and pain intensity ratings. Yu et al. (2021) found women with endometriosis in comparison with a healthy control group to have a higher functional connectivity between ACC and hippocampus, two regions that are both part of the pain matrix. Li et al. (2018) found endometriosis to modulate gene expression in insula, amygdala, and hippocampus of mice. Interestingly, Hashmi et al. (2013) found in a longitudinal study that during chronification of pain, brain representation shifts from pain- to emotion-related networks. It was suggested that the combination of learning-related areas (e.g., hippocampus) and emotion-related areas (e.g., nucleus accumbens) form a basis for aversive learning (Mutso et al., 2014) - which in turn enables detrimental fear and avoidance mechanisms.

Implications

The described sensitization processes can cause considerable distress in patients. This can be explained by the pain itself, but also by the frustration that medical interventions are not necessarily effective. For example, endometriosis lesions can be surgically removed locally - which is an effective intervention at the onset of symptoms (He et al., 2010), but the changes in the biochemical transmission chain and neural processes cannot be surgically removed. Only long-term therapeutic approaches can help here (Mechsner, 2021). It is therefore important to take pain seriously from the outset and to include multimodal treatment options at an early stage. The situation is aggravated by the fact that patients are often confronted with trivialization and disbelief by social environment (putting strain on social ties) and medical staff (Culley et al., 2013). This can result in self-doubt, again adding to the distress. The following paper was written to systematize the evidence on this psychosocial burden in endometriosis patients.

Paper #2: Understanding Psychological Symptoms of Endometriosis from a Research Domain Criteria Perspective

Endometriosis has far-reaching consequences for those affected, because it can impact all aspects of life and thus often results in an overall reduced quality of life (QoL) (Culley et al., 2013) and elevated levels of psychological burden (Netzl et al., 2022; Triolo et al., 2013). Compared to the general public, endometriosis patients have high prevalences of mental health symptoms and diagnoses (Chen et al., 2016; Ferreira et al., 2016; G. Jones et al., 2004; Pope et al., 2015; Soliman et al., 2016). Due to the combination of physical and mental symptoms, endometriosis has a distinct negative impact on social life (Ferreira et al., 2016). The Research Domain Criteria (RDoC) framework was used to highlight the transdiagnostic processes involved in progression and maintenance of psychosocial burden in endometriosis.

Results demonstrate that endometriosis has far-reaching psychosocial consequences. Endocrinological dysregulation is interlocked with pain chronification processes and psychological symptoms. Self-perpetuating mechanisms of disease progression develop, which interact with each other and partly lead to symptoms that persist even after removal of the endometrial tissue.

Apart from psychological symptoms and mechanisms - such as chronic stress, loss of control, depressive mood, and catastrophizing - endometriosis and related pain can especially reduce societal participation. Unforeseeable pain, bleeding, fatigue and digestive malfunctions can interfere with work, social activities, and hobbies (Armour et al., 2019; Butt & Chesla, 2007; Gao et al., 2006; Lewinsohn & Graf, 1973; Mastrangelo & Turnbull, 2022; Moradi et al., 2014; Ramin-Wright et al., 2018). As a result, patients may withdraw from social encounters and activities, and miss out from

educational/career opportunities. Overall, this can lead to a complex cycle of lowered well-being, more social isolation, less positive reinforcement, and feelings of loneliness (Mastrangelo & Turnbull, 2022; Mellado et al., 2016; Nnoaham et al., 2011). Also, endometriosis and related pain have a deep impact on romantic relationship dynamics and family life (Butt & Chesla, 2007; Denny & Mann, 2007; Facchin et al., 2018; Fritzer et al., 2013; Moradi et al., 2014; Netzl et al., 2022; Pereira et al., 2021; Pluchino et al., 2016; Rossi et al., 2022; Schick et al., 2022; Van Niekerk et al., 2022a; Vercellini et al., 2012).

However, patients report social support to be a helpful resource in romantic and other personal relationships to cope with endometriosis (Mastrangelo & Turnbull, 2022). And in couples living with other chronic illnesses, dyadic coping is associated with better physical health, well-being, and overall relationship satisfaction (Weitkamp et al., 2021).

The paper discusses promising pain treatment approaches that can be helpful in addition to standard medical care (Aerts et al., 2018; Donatti et al., 2022; Evans et al., 2019, 2021; Gonçalves et al., 2017; Hållstam et al., 2018; Hansen et al., 2017; Moreira et al., 2022; Van Niekerk et al., 2022b; Williams et al., 2020), and the need to have more research focusing on these treatments and their long-term effects. Additionally, it highlights the need for long-term studies to uncover cause-effect relationships, and for studies that focus on how endometriosis influences romantic relationships and the family system. Concluding, the review emphasizes the need for multifaceted treatments, research funding, and more societal attention and education to improve quality of life for patients.

Transition

For several decades now, there has been research on social support by romantic partners or spouses. Results were mixed, depending highly on the sample, analysis level and support style. With the findings from paper #1 and #2 in mind, we aimed to investigate the association between endometriosis-related pelvic pain and social support on the micro-level. Additionally, stress, cortisol, and oxytocin were related to pain levels.

Paper #3: How Partner Support, Stress, and Hormones influence momentary Pain Experience in Chronic Pelvic Pain

The experience of pain is not only determined by physiological, but also psychosocial factors. While the relation between psychological burden and pain experience is quite clear, the role of social support is more complex: Contrary to the common belief that social support uniformly benefits individuals facing chronic pain challenges, previous research reveals a more differentiated picture: Although studies in diverse chronic pain conditions (yet not endometriosis or CPP) found distracting social support to be pain alleviating (Ginting et al., 2011; Thieme et al., 2005), they found solicitous support to be related to higher pain levels (McCracken, 2005; Nees et al., 2022; Thieme et al., 2005).

Experimental studies have found stress to be related to higher pain levels (Crettaz et al., 2013; Thieme et al., 2005), but there is little data on real life situations. Research on the endocrinological stress response suggests that chronic pain patients have a heightened cortisol response (Fischer et al., 2016; Jones et al., 1997; Mcbeth et al., 2005). The relation between pain and oxytocin appears to be more complex: There are differing findings, depending on whether the sample consist of chronic pain patients or healthy participants and whether oxytocin is administered, or endogenous levels are measured (Boll et al., 2018; Y. L. Wang et al., 2013; Zunhammer et al., 2015).

This preregistered study aimed to investigate how different social support styles, stress, cortisol level, and oxytocin level relate to pain on a moment-to-moment level. Participants used an Ecological Momentary Assessment (EMA) app to assess their individual wellbeing and pain levels throughout their everyday lives for seven consecutive days. If present, interactions with their romantic partner were also assessed. Questionnaires relevant for the presented research question were displayed 5 times per day, and in parallel, participants collected saliva samples to link the psychosocial data to endocrinological markers. Salivary cortisol was assessed at each of the five time points, oxytocin levels only once per day. Participants were assessed during a time when pain variability was expected to be highest: during the late premenstrual and early follicular phase of their menstrual cycle. Data was analyzed using multilevel models. Measurements within days were treated as nested in days which were treated as nested in persons. All models included the following control variables: age, contraceptive pill intake, cycle day, analgesic intake, and time within days.

The final sample consisted of N = 66 individuals with CPP of which N = 35 were in a relationship and thus eligible for the social support analyses. Both distracting and solicitous support were related to higher pain ratings on a between-person, but not within-person level. Reported stress was found to be related to higher pain ratings on a within- and between-person level. Neither cortisol nor oxytocin levels were significantly related to reported pain.

Our findings concerning distracting social support fit in a line of research indicating that distraction from pain contrasts with pain acceptance, a state that is associated with higher wellbeing (McCracken & Eccleston, 2005). The observations on solicitous support suggest a longterm couple dynamic, which is in line with previous research (Nees et al., 2022): A partner with a solicitous support style might unintentionally activate operant learning mechanisms where pain is reinforced through attention and care, potentially serving as a cue to process pain stimuli differently in the long run.

Reported stress and pain levels were found to be positively related and thus matched the hypotheses. However, salivary cortisol and pain levels were not significantly related. This finding contradicts our hypothesis and parts of previous research. However, there is evidence that self-reported stress and cortisol levels often do not correlate (Campbell & Ehlert, 2012). Additionally, this discrepancy may be amplified by the menstrual cycle (Albert et al., 2015; Montero-López et al., 2018). No significant relationship was found between oxytocin and pain levels. Further research is needed to determine whether spontaneous pain and endogenous oxytocin are unrelated or if more detailed studies on diurnal variations in oxytocin are required.

The findings on social support indicate long-term couple dynamics and a need for new dyadic coping strategies. Also, stress appears to play an important role in pain experience and should become an integral part of pain management therapies.

Chapter 5: Discussion

Summary of Findings: Paper #1

From Paper #1 we learned that community connectedness and social support at the macro level are both negatively associated with internalized stigma, which in turn is positively associated with mental health. No moderating role between internalized stigma and mental health was found for either community connectedness or social support. However, this may also have been due to the unspecific wording of the social items.

Summary of Findings: Paper #2

From Paper #2 we learn that endometriosis is a systemic disease that can affect all areas of life. It often has a negative impact on social participation, romantic relationships, family life, and education/career. However, endometriosis patients report that social support is an important resource in coping with their disease. Treatment approaches and the need for further research are discussed.

Summary of Findings: Paper #3

From Paper #3 we learn that on the microlevel, social support does not necessarily have a positive influence on pain perception. We found an association between pain levels and increased support behavior: Individuals who expressed more pain also received more social support. There was no difference between the investigated social support styles. Also, stress was found to be associated with pain perception, with higher stress levels being linked to higher pain levels. No association with pain was found with either oxytocin or cortisol.

Social Support: Better or worse Health Outcomes?

At first sight, the results of Paper #1 and #3 seem to contradict each other. Hence, in the following I will elaborate on what these findings mean, how they fit in the big picture and what this implies for future research and intervention strategies.

Firstly, in the gender minority sample, many subjects were not in a relationship, so only social support items concerning family and friends were analyzed; whereas in the CPP sample, we exclusively asked for support actions by a romantic partner. Literature suggests that the nature of the relation between the recipient and the provider plays a crucial role in how the social support affects them. For instance, internalized transnegativity was found to be associated with social support provided by friends and partners, but not by family members (Tebbe & Moradi, 2016). Also, in this case we assume, that this could play a role.

Secondly, while in the CPP study social support items asked for very specific actions that happened in direct temporal proximity and the used analyses enabled us to investigate moment-to-moment level associations between social support and pain ratings; in the gender minority study more general types of social support were investigated, more aiming at the perceived availability of social support and less at the specific support actions. Also, since Paper #1 was a cross-sectional study, hindsight bias should be considered when interpreting the data. This again makes it more probable that given responses correspond to an overall feeling of being supported rather than the effects of specific support actions.

Taken together, it becomes obvious that it is important to consider the exact details when comparing these two studies. Depending on the definition or the level of analysis or, the broad construct of social support can be linked to beneficial or detrimental health outcomes.

This is in line with previous research finding that the theoretical availability of support is positively associated with health variables (Broadwell & Light, 1999; Kroll & Lampert, 2011; Kroll & Lampert, 2007; López-Martínez et al., 2008; Smith et al., 2004; Szkody et al., 2021; Wilson et al., 2020), but that actually performed support actions yield mixed findings. For instance, Ginting et al. (2011) found acts of support to buffer detrimental effects of pain on quality of live. However, in an experimental study by Hurter (2014), participants reported higher pain levels when they perceived high levels of empathy from their partner.

Also, support style seems to be an important factor: Research found either no or negative associations of solicitous and punishing styles with health variables (Flor et al., 1987; McCracken, 2005; Nees et al., 2022; Thieme et al., 2005), while findings for a distracting support style are mostly positive (Ginting et al., 2011; Thieme et al., 2005), although Paper #3 as well as other studies found no or negative associations. In the following sub-sections, I will discuss further factors that could be of importance.

Costs of Social Support

Studies summarized by Rafaeli and Gleason (Rafaeli & Gleason, 2009) show that the following factors can contribute to social support being associated with detrimental health outcomes: Social Support can 1) discourage self-initiated actions and promote dependence on others; 2) promote feelings of inadequacy and lacking self-efficacy, competence or agency; 3) promote feelings of indebtedness and inequity; 4) shift unwanted attention to the stressor.

For instance, anticipated social support has been found to be associated with beneficial health outcomes – but this was mediated by feelings of self-efficacy (Bandura, 2004; Cheung & Sun, 2000). So, if individuals report low levels of self-efficacy, e.g. due to a chronic disease, social support may not unfold its positive effects or even emphasize the feeling of a lack of self-efficacy or competence. In a study by Allen (1991), participants had a higher physiological activity and poorer performance when in presence of a friend vs. being alone when performing a stressful task. This was interpreted as a feeling of being observed and evaluated and a resulting elimination of potential positive support effects.

Furthermore, the circumstances under which social support is performed should be considered (Rafaeli & Gleason, 2009): Is there a dependence or hierarchy between recipient and provider? Is there a match between the stressor/need and the support action? How satisfied was the recipient with the support act?

An additional factor which supposedly plays a crucial role in disease progression, is secondary gain: the fact that expressing symptoms is repeatedly reinforced by social support resulting in individuals experiencing symptoms more frequently and thus enhancing emotional distress (Taylor, 2011). A hint for this showed in Paper #3 and also, Nees et al. (2022) found a relation between dyadic coping and brain networks associated with chronic pain.

Avoiding the Costs

Most of the aforementioned factors can be avoided by the concept of invisible support, meaning that support actions can be performed under the radar of the recipient, enabling them to benefit from the positive effects while avoiding emotional costs (Rafaeli & Gleason, 2009). For instance, in a study by Bolger and Amarel (2007) receiving social support was associated with lower levels of distress when the recipient was unaware of the support act, i.e. only the provider reported the support act.

Another approach are the supportive equity hypothesis and the matching hypothesis. The equity theory (Adams, 1963) posits that individuals have a sense for fairness in social exchange relationships. Applied at the problem at hand, the theory implies that individuals who constantly receive social support without being able to reciprocate it, can develop feelings of dissatisfaction. Consistent with this, research has shown that without reciprocation, receiving support is related to increases in negative mood and that providing support eliminates the detrimental effects of constant support reception and additionally increases positive mood and relationship intimacy (Gleason et al., 2003, 2008). In a daily diary study of couples in which one had multiple sclerosis, supportive equity was related to increased self-esteem in both, patients and partners (Kleiboer et al., 2006). Thus,

supportive equity, i.e. the balanced receiving and providing of social support, can be beneficial for both individual mood and dyadic outcomes.

The matching hypothesis posits that support actions must match the specific needs of the recipient (Thoits, 1995). Rafaeli (2009) points out that support can only be effective if particular forms of support interact with characteristics of the stressful situation and buffer the effects of specific stressors to which they are matched. For instance, the perceived amount of needed social support, the adequacy of given support, or the timing of given support. If the match is given, recipients are more satisfied with support and negative effects are less likely to be evoked. Also, the hypothesis states that e.g. emotional support is more helpful when it comes from significant others (partner, close family/friends) whereas it is often unwanted by other acquaintances. Thus, in order to avoid the costs of social support, it is important to teach couples to recognize which specific need is present and which kind of support could be helpful (Rafaeli & Gleason, 2009).

Broader Implications

Broader implications of current research involve the use of app-based interventions for managing endometriosis, warranting careful evaluation. On the one hand, app-based disease management holds potential to restore feelings of self-efficacy and to become a tool for patient empowerment. Also, they represent a significant opportunity, especially as everyday interventions or as training programs aimed at improving dyadic interactions as suggested in Paper #3. On the other hand, there is a significant concern that in underfunded healthcare systems, apps may not merely supplement but substitute standard treatment due to time constraints and long appointment wait times. This issue extends beyond endometriosis to other medical conditions, highlighting the conflict between thorough patient consultations and financial limitations (see “Diagnosis and diagnostic latency” in Chapter 4). While apps and telemedicine can be an effective addition to treatment, there is a legitimate concern that they may become standard practice, potentially limiting access to comprehensive healthcare for many (most probably poorer or otherwise marginalized) individuals over time. The concept of social support is critical here: Do patients perceive their social network, including healthcare providers, as supportive and capable of addressing their needs? An app's ability to convey this crucial sense of social support availability remains questionable. Particularly for endometriosis patients who have faced disbelief, trivialization, and long diagnostic delays, the app can entail risks if not implemented carefully.

Strengths and Limitations

The presented work allows for deeper insights of social and stress processes in marginalized groups on two different levels of observation. Paper #1 is one of the few studies in German speaking countries that give insights into gender minority population and has a considerable sample size. It gives insights into minority stress processes associated with internalized transnegativity which is still a young field of research. Paper #2 gives an overview on psychosocial processes that are associated with endometriosis and related pain. The research domain criteria approach allows for a more comprehensive understanding of psychological burden in endometriosis and related pain – apart from classic diagnosis categories. Paper #3 is the first study connecting EMA, endocrinology and social factors in CPP patients. It has a comparably large sample size and used multilevel models to analyze behavior, hormone levels, and wellbeing on a moment-to-moment level.

However, there are some limitations that should be acknowledged: Firstly, the two empirical studies focused on different concepts of social support: Paper #1 assessed anticipated support on the macro level, possibly including a hindsight bias, whereas Paper #3 assessed actually performed acts of support on the micro level. This methodological difference makes it more challenging to compare the

findings. Secondly, both empirical studies investigated marginalized groups, but those groups – although there can be overlaps – have heterogenous challenges in their lives due to the characteristics, because of which they were included in the respective studies. Thus, the comparability of both groups and the generalizability of findings from one group to the other must not be given. Thirdly, due to the small number of participants in a relationship in Paper #1 and the associated low power, only social support from family and friends could be evaluated here. In this work, I compared this with social support from romantic partners from Paper #3. The comparability is therefore limited by this difference in support providers. Fourthly, in Paper #3 we investigated performed acts of social support, but not the broader social reality of participants. Support satisfaction and the larger social structure should be assessed when analyzing and interpreting the data to thoroughly understand how the variables are associated (thoroughly discussed by Bernardes (2017).

Outlook

Future research should take into account that the term social support is very broad and unspecific. There is a need for distinction between the anticipation / perceived availability of support and actually performed support acts. While the first is rather a proxy for social embeddedness and positively linked to health outcomes, for the latter it is more complicated. The broader social structure, situational factors, match of action and situational need as well as the relationship between provider and recipient play a role in how the support act has an impact. Furthermore, there is a need for the support provider's perspective and how both perspectives differ/overlap. Also, to investigate long-term impact of certain support styles and support actions on wellbeing, more long-term studies are needed.

To investigate minority stress processes on the micro-level, future studies should conduct EMA studies in e.g. gender minority samples and directly assess how stressors, acts of support by a partner, and mental health are associated on a moment-to-moment level. Also, it could be assessed which social support styles are (not) beneficial in minority stress contexts. Importantly, the specificity of support to stressor and situation should be considered. Also, minority stress in the context of a romantic relationship and how it affects the dyad should be further considered.

Future research could also test, if the minority stress model is applicable to psychological burden caused by endometriosis. Recently, other research groups have used the model to other marginalized groups, such as autistic individuals (Botha & Frost, 2018) and individuals with disabilities or chronic illness (Gowling et al., 2024; Lund, 2021). Although endometriosis and its consequences can often be hidden from the outside world, its consequences can be perceived by partners, friends, family members and work colleagues, and stigmatization is an often-reported topic (for an overview, see Sims et al., 2021). Resulting minority stress processes could be investigated by future studies.

In this dissertation, the focus is on the recipient side of social support acts. However, the provided support as reported by partners is of significance for understanding social support processes and outcomes.

Lastly, I find it important to address that while the scientific and medical knowledge of social support effects on stigmatization and pain is crucial for treatment and prevention measures, raising awareness on a societal level is also essential. Preventing stigmatization, marginalization, and chronification processes in the first place is the most important and powerful form of prevention. The social environment and medical staff need to listen to suffering individuals and their needs. We as a society need policies and educational programs in order to effectively address these issues.

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Appendix I: Paper #1

van Stein, K. R., Kleinn, N., Randall, A. K., Lannutti, R. J., Gandhi, Y., Martos, T., Meuwly, N., Rosta-Filep, O., Siegel, M., Ditzen, B. & Fischer, M. S. (2023). Internalisierte Transnegativität, Resilienzfaktoren und psychische Gesundheit in einer Stichprobe geschlechtlicher Minderheiten in Deutschland und der Schweiz. *Zeitschrift für Klinische Psychologie und Psychotherapie*. doi.org/10.1026/1616-3443/a000730

KvS's contributions according to the contributor roles taxonomy (CRediT) author statement (Allen et al., 2019):

conceptualization, methodology, formal analysis, writing - review and editing, visualization, project co-administration

Originalarbeit

Internalisierte Transnegativität, Resilienzfaktoren und psychische Gesundheit in einer Stichprobe geschlechtlicher Minderheiten in Deutschland und der Schweiz

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Zusammenfassung: *Theoretischer Hintergrund:* Trans*, inter* und nichtbinäre Personen erfahren Diskriminierung und weisen im Vergleich zur Gesamtpopulation eine höhere Prävalenz von affektiven und Angststörungen auf. *Fragestellung:* Diese präregistrierte Studie überprüft basierend auf dem Minderheiten-stressmodell den Zusammenhang zwischen Selbststigmatisierung (internalisierte Transnegativität) und psychischer Gesundheit und untersucht Resilienzfaktoren als Moderatoren. *Methode:* In einer Stichprobe deutscher und Schweizer trans*, inter* und nichtbinärer Personen (*N* = 243) wurden multiple lineare Regressions- und Moderationsanalysen berechnet, um Zusammenhänge zwischen internalisierter Transnegativität und Angst- und depressiver Symptomatik sowie Resilienzfaktoren zu prüfen. *Ergebnisse:* Die Ergebnisse zeigen positive Zusammenhänge zwischen internalisierter Transnegativität und Angst- und depressiver Symptomatik. Die Resilienzfaktoren soziale Unterstützung und Verbundenheit mit der LGBT+ Community sind negativ mit internalisierter Transnegativität assoziiert. Keiner der Resilienzfaktoren moderierte die Zusammenhänge zwischen internalisierter Transnegativität und psychischer Gesundheit. *Schlussfolgerungen:* Die Studie bestätigt internationale Befunden zum Zusammenhang zwischen internalisierter Transnegativität und psychischer Gesundheit. Mehr Forschung ist nötig, um die Rolle der Resilienzfaktoren im Minderheitenstressmodell zu klären.

Schlüsselwörter: Internalisierte Transnegativität, psychische Gesundheit, Minderheitenstress, Resilienz

Internalized Transnegativity, Resilience Factors, and Mental Health in a Sample of Gender Minorities From Germany and Switzerland

Abstract: *Background:* Trans*, inter*, and nonbinary individuals experience discrimination and exhibit a higher prevalence of affective and anxiety disorders than the general population. *Objective:* Based on the minority stress model, this preregistered study examines the association between self-stigmatization (internalized transphobia) and mental health and investigates resilience factors as moderators. *Methods:* In a sample of German and Swiss trans*, inter*, and nonbinary individuals (*N* = 243), we computed multiple linear regression and moderation analyses to examine the relationships between internalized transphobia, depressive and anxiety symptoms, and resilience factors. *Results:* The results show associations between internalized transphobia and depressive and anxiety symptoms. The resilience factors social support and LGBT+ community connectedness are negatively associated with internalized transphobia. None of the resilience factors moderated the relationships between internalized transphobia and mental health. *Conclusions:* This study aligns with international

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findings regarding the association between self-stigmatization and mental health. Further research is needed to clarify the role of resilience factors in the minority stress model.

Keywords: internalized transnegativity, mental health, minority stress, resilience

Trans*, inter* und nichtbinäre Personen[1] weichen von der heteronormativen Zweigeschlechternorm[2] ab und werden in vielen gesellschaftlichen Bereichen durch Ausgrenzung und Diskriminierung sanktioniert (z. B. Franzen & Sauer, 2010). Diskriminierungserfahrungen im Alltag stellen eine Belastung dar, die sich in einer schlechteren psychischen Gesundheit äußern kann. In einem umfangreichen systematischen Review zeigte sich, dass US-amerikanische trans* Personen erhöhte Prävalenzen an psychischen Belastungen, wie Depressionen und Angststörungen, aufweisen (Valentine & Shipherd, 2018). Eine Untersuchung in Deutschland zeigte eine stark erhöhte Prävalenz von Depressionsdiagnosen bei trans* Personen im Vergleich zu cis-hetero Personen (Kasprowski et al., 2021). Über die psychische Situation von inter* Personen in Deutschland ist bisher kaum etwas bekannt, spärlich vorhandene Daten weisen aber ebenfalls auf deutlich erhöhte psychische Belastungen hin (Schützmann et al., 2009).

Wie Diskriminierungserfahrungen mit der Gesundheit von stigmatisierten Gruppen zusammenhängen, versucht das Minderheitenstressmodell (Meyer, 2003) zu erklären. Meyer (2003) beschreibt Minderheitenstress als eine Form des chronischen sozialen Stresses, der spezifische und zusätzliche Belastungen für Personen mit einem Minderheitenstatus umfasst. Im Modell, das sich ursprünglich auf sexuelle Minderheiten, also lesbische, schwule und bisexuelle Personen bezogen hat, werden Minderheitenstressprozesse mit Faktoren wie Aspekten der Minderheitsidentität (z. B. Diskriminierungserfahrungen) und Resilienzfaktoren assoziiert, um die Beziehungen zwischen Minderheitenstress und Gesundheit zu beschreiben. Ein zentrales Konstrukt in der für geschlechtliche Minderheiten adaptierten Version (Hendricks & Testa, 2012) ist die internalisierte Transnegativität[3] (ITN), die Bockting et al. (2020) als das Unbehagen mit der eigenen trans* Identität aufgrund der Verinnerlichung gesellschaftlicher normativer Geschlechtererwartungen definieren. Bisherige Studien lassen keine Aussagen darüber zu, wie verbreitet ITN in der Gesamtpopulation der geschlechtlichen Minderheiten im deutschsprachigen Raum ist, da die meisten Studien mit Gelegenheitsstichproben arbeiten, die zum Teil aus klinischen oder Beratungskontexten stammen, in denen eine stärker ausgeprägte ITN zu erwarten ist (z. B. Brennan et al., 2017).

Bisherige Befunde zu Zusammenhängen zwischen ITN und der psychischen Gesundheit geschlechtlicher Minderheiten beschränken sich auf wenige Studien, die Inderbinen et al. (2021) in einem systematischen Review zusammenfassen: ITN zeigt einen positiven Zusammenhang mit Angst- und depressiver Symptomatik. Weiterhin gibt es Studien zum Zusammenhang zwischen psychischer Gesundheit und Resilienzfaktoren in geschlechtlichen Minderheiten: Soziale Unterstützung und Verbundenheit mit der Community (engl. Community Connectedness) stehen als Resilienzfaktoren des Minderheitenstressmodells bei geschlechtlichen Minderheiten mit geringeren Angst- sowie depressiven Symptomen in Verbindung (z. B. Brennan et al., 2017).

Das Minderheitenstressmodell schreibt den Resilienzfaktoren eine moderierende Wirkung auf die Beziehung zwischen Minderheitenstress und psychischer Gesundheit zu (Meyer, 2003). Während Untersuchungen diese Annahme des Modells bei sexuellen Minderheiten stützen können (Doty et al., 2010), ist die Befundlage für geschlechtliche

[1] Mit dem Begriff trans* bezeichnen sich Personen, deren Geschlecht nicht (ausschließlich) mit dem bei der Geburt zugeschriebenen Geschlecht übereinstimmt. Das Gegenstück hierzu heißt cis. Intergeschlechtlichkeit ist ein Sammelbegriff für spezifische Variationen der reproduktiven oder geschlechtlichen Anatomie. Dieser Begriff ist eine medizinische Kategorie zur (Fremd-)Einteilung von Menschen. Einige Personen, die mit diesen körperlichen Variationen leben, bezeichnen sich als inter*. Das Gegenstück heißt endogeschlechtlich. In dieser Studie wurde inter* ausschließlich als Geschlechtsidentität erhoben. Mit dem Begriff nichtbinär bezeichnen sich Personen, deren Geschlecht nicht (ausschließlich) binär (männlich oder weiblich) ist. Nichtbinarität kann eine Geschlechtsidentität an sich sein oder als Spektrum / Sammelkategorie verstanden werden.

[2] Der Begriff heteronormative Zweigeschlechternorm bezeichnet die weit verbreitete Weltanschauung, es gäbe nur zwei Geschlechter, die Gegensätze darstellen und sich zwangsläufig sexuell aufeinander beziehen. Damit einher gehen bestimmte soziale Rollenerwartungen.

[3] Der Begriff Transnegativität schließt alle trans* und nichtbinären Personen ein, jedoch nicht explizit inter* Personen. Die Autor_innen benutzen diesen Begriff in dieser Studie trotzdem für alle drei Gruppen: Erstens, weil ein Großteil der inter* Teilnehmer_innen sich nicht ausschließlich als inter* identifizierte, sondern auch als z. B. trans*. Zweitens, weil es im Kern bei internalisierter Transnegativität darum geht, dass Personen aufgrund ihrer vermeintlichen Nichtpassung in die von der heteronormativen Zweigeschlechternorm geprägten Gesellschaft Diskriminierung und Ausschluss erfahren. Hiervon können inter* Personen ebenso betroffen sein, weswegen das Konstrukt auch für diese Population von Relevanz ist und auch bei nicht idealer Passung des Begriffs diese Ausweitung einem Ausschluss von inter* Personen aus dieser Studie vorgezogen wurde.

Minderheiten bisher uneindeutig (Jäggi et al., 2018; Ott et al., 2017). Die Beziehung zwischen ITN und sozialer Unterstützung bzw. Verbundenheit mit der LGBT+[4] Community stand bisher nicht im Fokus der Forschung. Dies ist jedoch notwendig, um die Rolle der Resilienzfaktoren für geschlechtliche Minderheiten zu klären.

Studienziele und Hypothesen

In dieser Arbeit sollen der Zusammenhang zwischen ITN, Resilienzfaktoren und psychischer Gesundheit in einer großen deutschen und Schweizer Stichprobe von geschlechtlichen Minderheiten beleuchtet werden. Zusätzlich soll in einer explorativen Analyse überprüft werden, ob der Zusammenhang von ITN mit Angst- bzw. depressiver Symptomatik weiter besteht, wenn für das jeweils andere Konstrukt psychischer Gesundheit kontrolliert wird.

Die folgenden Hypothesen wurden präregistriert[5]:

H1: ITN geht bei geschlechtlichen Minderheiten mit erhöhter Angst- und depressiver Symptomatik einher.

H2a: Soziale Unterstützung geht bei geschlechtlichen Minderheiten mit niedriger ITN einher.

H2b: Verbundenheit mit der LGBT+ Community geht bei geschlechtlichen Minderheiten mit niedriger ITN einher.

H3a: Soziale Unterstützung moderiert den Zusammenhang zwischen ITN einerseits und Angst- und depressiver Symptomatik andererseits. Der Zusammenhang ist bei größerer Unterstützung schwächer.

H3b: Verbundenheit mit der LGBT+ Community moderiert den Zusammenhang zwischen ITN einerseits und Angst- und depressiver Symptomatik andererseits. Der Zusammenhang ist bei größerer Verbundenheit schwächer.

Methode

Versuchsplan

Die Daten stammen aus einer umfangreichen, internationalen querschnittlichen Online-Erhebung[6] zu Wohlbefinden und Beziehungserfahrungen von Personen der LGBT+ Community. Die Erhebung in Deutschland und der Schweiz wurde vom 12.07.2021 bis 13.10.2021 auf der Onlineplattform SoSciSurvey durchgeführt. Die Rekrutierung fand über soziale Medien, NGOs, Mailverteiler und Flyer statt. Eingeschlossen wurden Personen, die zum mindestens 18 Jahre alt waren und sich als sexuelle und / oder geschlechtliche Minderheit identifizierten. Die Teilnahme war freiwillig, nach Abschluss des Fragebogens gab es die Möglichkeit an einer Verlosung von Büchergutscheinen teilzunehmen. Die jeweils zuständigen Ethikkommissionen haben die Studie genehmigt.

Stichprobenauswahl

Aus der Gesamtstichprobe (N = 1089) aus Deutschland und der Schweiz wurde eine Substichprobe geschlechtlicher Minderheiten entnommen (N = 328). Zu den geschlechtlichen Minderheiten wurden Personen gezählt, die sich mit mindestens einem der Begriffe trans*, nichtbinär, transmaskulin, transfeminin, agender, genderfluid und genderqueer identifizierten oder ein Identitätsgeschlecht angaben, das nicht ausschließlich männlich oder ausschließlich weiblich ist. In weiteren Schritten wurden Personen ausgeschlossen, die in den für diese Arbeit relevanten Maßen und Kontrollvariablen fehlende Werte aufwiesen (Alter: n = 17; finanzieller Stress: n = 1). Eine Person wurde bei der Umcodierung der Variable Geschlecht entfernt, da eine eindeutige Zuordnung zu den Kategorien nichtbinäres Spektrum, trans* weiblich und trans* männlich nicht möglich war.

Im Umgang mit fehlenden Werten in den Skalen der Studienvariablen wurden zwei Strategien angewendet. Zunächst wurden Personen mit mehr als 20 % unbeantworteten Items innerhalb einer Skala ausgeschlossen (n = 62). Anschließend wurde nach Empfehlungen von Parent (2012) nach der „Available Item Analysis"-Methode verfahren: Skalengesamtwerte wurden aus dem Mittel der vorhandenen Itemwerte berechnet. Vier weitere Personen wurden aufgrund von Ausreißerwerten (M +/- 3SD) in den für diese Studie relevanten Fragebogendaten ausgeschlossen (eine Person aufgrund sehr hoher Angstsymptome, drei Personen aufgrund sehr niedriger Werte auf der Skala Verbundenheit mit der LGBT+ Community). Die demographischen Eigenschaften der finalen Stichprobe (N = 243) sind in Tabelle 1 veranschaulicht.

[4] LGBT+ steht für lesbisch, schwul (gay), bisexuell, trans*. Es soll als Sammelbegriff unterschiedliche Identitäten und Erfahrungen jenseits der Cis- und Heteronorm zusammenfassen. Mit dem Plus-Symbol wird darauf hingewiesen, dass das Akronym aus Platz- und Lesbarkeitsgründen nicht alle dazugehörigen Identitätsbegriffe nennt. Die Autor_innen haben sich auf dieses Akronym geeinigt, weil es auch dem Wortlaut des Maßes für LGBT+ Community Connectedness entspricht.

[5] https://aspredicted.org/25pk9.pdf

[6] https://osf.io/tsj8v

Tabelle 1. Demographische Eigenschaften (*N* = 243)

		% (*n*)
Alter	18 – 65, *M* = 29.8, *SD* = 10.6	
Wohnland	Deutschland	77.37 (188)
	Schweiz	22.63 (55)
Beziehungsstatus	eine Beziehung	36.21 (88)
	mehr als eine Beziehung	9.05 (22)
	keine Beziehung	54.73 (133)
Geschlechtsidentität	nichtbinäres Spektrum	85.18 (207)
	trans* weiblich	8.64 (21)
	trans* männlich	6.17 (15)
Intergeschlechtlichkeit	ja	2.88 (7)
	nein	97.12 (236)
race	BPoC	3.70 (9)
	weiß	69.14 (168)
	Uneindeutig / keine Angabe	27.16 (66)
Finanzieller Stress	*M* = 2.01, *SD* = 0.94	

Anmerkungen: BPoC = Black and People of Color.

Maße

Demographische Variablen

Geschlecht, finanzielle Belastung und *race*[7] wurden zur statistischen Kontrolle demographischer Faktoren auf die folgende Weise erfasst und operationalisiert:

Geschlecht

Die Angaben zum Geschlecht der Personen erfolgten in zwei Schritten. Zunächst wurde das bei der Geburt zugewiesene Geschlecht dichotom erfragt. Im zweiten Schritt konnten Teilnehmende ihre derzeitige Geschlechtsidentität mittels einer Mehrfachauswahl angeben. Zur Auswahl standen die Begriffe weiblich, männlich, trans*, nichtbinär, transmaskulin, transfeminin, agender, genderfluid, genderqueer, inter* sowie ein Feld für eine offene Angabe. Um Geschlecht als Kontrollvariable in die Analysen aufzunehmen, wurden diese Angaben zu einer Variable mit drei Kategorien zusammengefasst[8]: nichtbinäres Spektrum, trans* weiblich und trans* männlich (Vorgehen siehe Anhang A; es gibt keine Überschneidungen dieser drei Kategorien). Zusätzlich wurde eine dichotome Variable mit 1 = inter* und 0 = endogeschlechtlich erstellt. Als inter* wurden die Personen erfasst, die auf die Frage nach der derzeitigen Geschlechtsidentität die Antwortoption „inter*“ ausgewählt hatten.

Finanzielle Belastung

Finanzielle Belastung wurde durch folgendes Item erhoben: „Wie schwierig ist es für Sie, Ihre monatlichen laufenden Kosten (z. B. Miete, Strom, Kredit) zu begleichen?“ (übersetzt aus Lantz et al., 2005). Die Antwortskala war 5-stufig (1 = überhaupt nicht schwierig, 5 = extrem schwierig).

Race

Die Variable *race* wurde als Selbstbezeichnung mittels Mehrfachauswahl mit den folgenden Antwortmöglichkeiten erhoben: Schwarze_r, Person of Color, Nichtweiße_r, Weiße_r, kein Begriff und die Möglichkeit, einen eigenen Begriff anzugeben. Die Aufnahme der Variable *race* sollte für Unterschiede im Minderheitenstress kontrollieren, die aufgrund von Mehrfachmarginalisierung für rassifizierte trans, inter* und nichtbinäre Personen entstehen können. Die Angaben wurden in eine dreistufige Variable zusammengefasst[9]: BPoC, *weiß* und uneindeutig / keine Angabe.

[7] In dieser Arbeit wird der Begriff race anstelle von Begriffen wie „Ethnizität“ oder „ethnischer Zugehörigkeit“ verwendet, da es sich bei den Antwortbegriffen nicht um Ethnien, sondern um Positionierungen im Machtverhältnis Rassismus handelt. Im Gegensatz zum deutschen Begriff „Rasse“ hat der englische Begriff einen sogenannten „racial turn“ durchlaufen und wird als soziales Konstrukt verstanden (Kelly, 2020). Der originale Wortlaut der *race* Items ist im Anhang A wiedergegeben.

[8] Den Autor_innen ist bewusst, dass eine Zusammenfassung in diese drei Kategorien der Vielfalt der Identitäten der Teilnehmenden nicht entsprechen kann. Dies wird ausschließlich aus methodischen Gründen für die statistische Analyse vorgenommen.

[9] Den Autor_innen ist bewusst, dass eine Zusammenfassung in diese Kategorien der Vielfalt der Identitäten der Teilnehmenden nicht entsprechen kann. Dies wird ausschließlich aus methodischen Gründen für die statistische Analyse vorgenommen.

Als BPoC (Black and People of Color) wurden alle Personen mit mindestens einer der Angaben „Schwarze_r", „Person of Color" und „Nichtweiße_r" erfasst, als *weiß* die Personen mit der Angabe „Weiße_r" oder einer Identifikation mit dem Begriff *weiß* über die offene Angabe. Personen mit der Angabe „Kein Begriff" oder einer uneindeutigen Antwort im offenen Angabefeld wurden zu „uneindeutig / keine Angabe" zusammengefasst.

Internalisierte Transnegativität (ITN)

ITN wurde mit der Internalized Transphobia Subskala des Gender Minority Stress and Resilience Measure gemessen (GMSR-IT, Testa et al., 2015). Die Skala wurde ins Deutsche übersetzt und erfragt Zustimmung zu allen 8 Items auf einer 5-stufigen Skala von 0 = „stimme überhaupt nicht zu" bis 4 = „stimme voll und ganz zu". Beispielitems sind „Aufgrund meiner Geschlechtsidentität / meines Geschlechterausdrucks fühle ich mich wie ein Freak" und „Wenn ich über meine Geschlechtsidentität / meinen Geschlechterausdruck nachdenke, fühle ich mich unglücklich". Die interne Konsistenz war in der aktuellen Studie α = .91.

Angst- und depressive Symptomatik

Für die Erfassung der Angst- und depressiven Symptomatik wurden die Depressions- und Angstskalen (DASS-D und DASS-A) aus einer deutschsprachigen Übersetzung der 21-Item-Kurzform der Depression, Anxiety, Stress Scale verwendet (DASS-21, Lovibond & Lovibond, 1995). Jede der Subskalen umfasst 7 Items und erfragt auf einer 4-stufigen Skala, inwieweit die Items in der letzten Woche auf die Teilnehmer_innen zutrafen, von 0 = „traf *gar nicht* auf mich zu" bis 3 = „traf *sehr stark* auf mich zu oder *die meiste Zeit*". Die interne Konsistenz lag in der aktuellen Studie bei einem α = .93 für die Depressionsskala und α = .85 für die Angstskala.

Soziale Unterstützung

Soziale Unterstützung wurde mit den Subskalen *Freund_innen* und *Familie* einer deutschsprachigen Übersetzung des Multidimensional Scale of Perceived Social Support (MSPSS, Zimet et al., 1988) gemessen. Beide Subskalen wurden als Maß zur sozialen Unterstützung zu einem MSPSS-FF Score zusammengerechnet. Sie bestehen jeweils aus vier Items mit 7-stufiger Skala (1 = „stimme überhaupt nicht zu", 7 = „stimme voll und ganz zu"). Beispielitems sind „Meine Familie bemüht sich sehr, mir zu helfen" und „Ich kann mit meinen Freund_innen über meine Probleme sprechen". In der aktuellen Studie lag die interne Konsistenz bei α = .94 für die Familien-Subskala und α = .93 für die Freund_innen-Subskala.

Verbundenheit mit der LGBT+ Community

Die Verbundenheit mit der Community wurde mit einem nach Frost und Meyer (2011) adaptierten Maß für LGBT+ Community Connectedness erfasst. Die Skala besteht aus 8 Items. Es wurde Zustimmung auf einer 4-stufigen Skala von 1 = „Starke Ablehnung" bis 4 = „Starke Zustimmung" erfragt. Ein Beispielitem ist „Sie fühlen sich mit der LGBT + Community verbunden". Die interne Konsistenz lag in der vorliegenden Studie bei α = .82.

Datenanalyse

Die Datenanalyse wurde mit SPSS 27 für Windows durchgeführt. Für Modelle mit der gleichen Outcomevariable (4 Modelle: DASS-D, 4 Modelle: DASS-A, 2 Modelle: GMSR-IT) wurde das Signifikanzniveau jeweils mit der Bonferronikorrektur angepasst und wird im jeweiligen Fall berichtet. Es wurden multiple lineare Regressionen und Moderationsanalysen berechnet. Für letztere wurde das SPSS Macro PROCESS (Hayes, 2018) verwendet. Die zero-oder und semipartialen Korrelationen für die Moderationsanalysen wurden mit R Version 4.3.1 für Windows berechnet. Die Voraussetzungen für die Regressions- und Moderationsanalysen wurden für alle Skalen geprüft (siehe Anhang B). In allen Modellen wurden Alter, finanzieller Stress, Geschlecht, Intergeschlechtlichkeit[10] und *race* als Kovariaten aufgenommen.

Ergebnisse

Deskriptive Ergebnisse

Deskriptive Statistiken aller kontinuierlichen Studienvariablen sind in Tabelle 2 aufgelistet. Der Cut-off-Empfehlung von Nilges und Essau (2015) für DASS-D und DASS-A folgend, hatten 27.98 % eine erhöhte Wahrscheinlichkeit für das Vorliegen einer depressiven Störung und 33.75 % eine erhöhte Wahrscheinlichkeit für das Vorliegen einer Angststörung.

[10] Aufgrund der starken Unterschiede in der Zellenbesetzung wurde eine Sensitivitätsanalyse durchgeführt. Ohne die Variable Intergeschlechtlichkeit änderten sich weder Richtung noch Signifikanz der Effekte. Daher wurde die Variable, der Präregistrierung entsprechend, in allen Modellen beibehalten.

Tabelle 2. Wertebereiche, Mittelwerte und Standardabweichungen der kontinuierlichen Variablen

Variable	Möglicher Bereich	*Tatsächlicher Bereich*	*M*	*SD*
GMSR-IT (internalisierte Transnegativität)	0 – 4	0 – 3.88	1.43	1.03
DASS-D (depressive Symptomatik)	0 – 3	0 – 3	1.04	0.83
DASS-A (Angstsymptomatik)	0 – 3	0 – 2.57	0.75	0.66
MSPSS-FF (soz. Unterstützung Freund_innen und Familie)	1 – 7	1.13 – 7	4.98	1.16
LGBT+ Community Connectedness	1 – 4	2 – 4	3.37	0.49

ITN und psychische Gesundheit

Die Ergebnisse der multiplen linearen Regressionsmodelle sind in Tabelle 3 zusammengefasst. Der GMSR-IT-Score hing unter Kontrolle relevanter Kovariaten mit dem DASS-D-Score positiv zusammen. Der Zusammenhang bestand weiter, wenn zusätzlich für DASS-A kontrolliert wurde. GMSR-IT hing ebenfalls positiv mit dem DASS-A zusammen. Der Zusammenhang verlor jedoch seine Signifikanz, nachdem DASS-D als zusätzliche Kovariate aufgenommen wurde.

Resilienzfaktoren und ITN

Soziale Unterstützung

Der Prädiktor MSPSS-FF sagte unter Kontrolle demografischer Variablen statistisch signifikant das Kriterium GMSR-IT voraus (B = -0.27, r = -.28, sr = -.29, $t(234)$ = -4.83, $p < .001$; Gesamtmodell: korrigiertes R^2 = .12, $F(8, 234)$ = 5.06, $p < .001$). Auch nach der Bonferronikorrektur ($\alpha = 0.025$) sind die Werte signifikant. Die Richtung des Effekts entsprach der Hypothese: Je höher die soziale Unterstützung, desto niedriger die ITN.

LGBT+ Community Connectedness

Der Prädiktor LGBT+ Community Connectedness sagte unter Kontrolle demografischer Variablen statistisch signifikant das Kriterium GMSR-IT voraus (B = -0.43, r = -.18, sr = -.20, $t(234)$ = -3.17, $p < .01$; Gesamtmodell: korrigiertes R^2 = .07, $F(8, 234)$ = 3.29, $p < .01$). Auch nach der Bonferronikorrektur ($\alpha = 0.025$) sind die Werte signifikant. Die Richtung des Effekts entsprach der Hypothese: Je größer die LGBT+ Community Connectedness, desto niedriger die ITN.

Resilienzfaktoren als Moderatoren

Alle vier Modelle waren signifikant und hatten eine Varianzaufklärung zwischen 22 und 33 % (siehe Anhang C). Der GMSR-IT-Score war in allen Modellen ein signifikanter Prädiktor und positiv mit DASS-D und DASS-A assoziiert. Der MSPSS-FF-Score zeigte einen signifikanten negativen Zusammenhang mit DASS-D, aber nicht mit DASS-A. LGBT+ Community Connectedness zeigte keine signifikanten Zusammenhänge mit DASS-D oder DASS-A. Keine der untersuchten Moderationen war signifikant.

Diskussion

In dieser Arbeit wurde an einer deutschen und Schweizer Stichprobe geschlechtlicher Minderheiten getestet, ob ITN mit höherer Angst- und depressiver Symptomatik zusammenhängt, ob aus dem Minderheitenstressmodell abgeleitete Resilienzfaktoren Zusammenhänge mit ITN zeigen und ob diese Resilienzfaktoren die Beziehung zwischen ITN und psychischer Gesundheit moderieren.

Die Ergebnisse zeigen, dass ITN bei geschlechtlichen Minderheiten mit erhöhter Angst- und depressiver Symptomatik einhergeht. Diese Arbeit fügt sich in eine Reihe von Studien, die Annahmen des Minderheitenstressmodells für geschlechtliche Minderheiten empirisch prüfen (Brennan et al. 2017; Jäggi et al. 2018; Testa et al., 2015). Auch wenn aufgrund des querschnittlichen Designs keine Kausalität nachgewiesen werden kann, untermauern diese Befunde jedoch die Annahme, dass ITN eine Rolle in den erhöhten Prävalenzen depressiver Störungen in dieser Population spielen könnte. Der Zusammenhang mit Angstsymptomen bestand jedoch unter Kontrolle der depressiven Symptomatik nicht weiter. Insgesamt liefern die Ergebnisse jedoch Hinweise, dass nicht nur Diskriminierungserfahrungen per se, sondern auch wie sich diese Erfahrungen im eigenen Selbstbild spiegeln (Verinnerlichung des Stigmas), wichtig sind für ein Verständnis psychischer Belastungen geschlechtlicher Minderheiten.

Die Resilienzfaktoren soziale Unterstützung durch Freund_innen und Familie sowie Verbundenheit mit der LGBT+ Community sind in der vorliegenden Studie mit ITN negativ assoziiert. Der Befund, dass größere Verbundenheit mit der LGBT+ Community mit niedrigeren Werten von ITN einhergeht, passt zu den von Jones et al. (1984) beschriebenen Coping-Funktionen der Minderhei-

Tabelle 3. Multiple lineare Regressionsmodelle mit Angst- und depressiver Symptomatik als abhängige Variablen (Kontrolle für die jeweils andere abhängige Variable im zweiten Schritt)

	B	*SE*	β	*t*	*r*	*sr*	*p*	
Modell 1 Abhängige Variable: DASS-D; Total R^2 = .472 (N = 243)								
Schritt 1 (R^2 = .258, p < .001)								*
(Konstante)	0.963	0.300		3.212			< .01	*
GMSR-IT	0.353	0.046	.435	7.603	.478	.421	< .001	*
Alter	-0.005	0.005	-.066	-1.126	-.177	-.062	.261	
Finanzieller Stress	0.169	0.050	.190	3.357	.265	.186	.001	*
Geschlecht_männlich[a]	-0.144	0.169	-.049	-0.856	-.025	-.047	.393	
Geschlecht_weiblich[a]	-0.064	0.196	-.019	-0.330	-.055	-.018	.742	
Intergeschlechtlichkeit	0.034	0.282	.007	0.121	-.023	.007	.904	
*race*_weiß[b]	0.054	0.247	.030	0.219	.087	-.012	.827	
*race*_uneindeutig/keineAngabe[b]	-0.219	0.258	-.117	-0.848	-.116	-.047	.397	
Schritt 2 (ΔR^2 = .214, p < .001)								*
(Konstante)	0.446	0.258		1.725			.086	
GMSR-IT	0.258	0.040	.318	6.396	.478	.299	< .001	*
Alter	0.004	0.004	.054	1.054	-.177	.049	.293	
Finanzieller Stress	0.062	0.044	.069	1.404	.265	.066	.162	
Geschlecht_männlich[a]	-0.125	0.142	-.042	-0.882	-.025	-.041	.379	
Geschlecht_weiblich[a]	-0.045	0.165	-.013	-0.273	-.055	-.013	.785	
Intergeschlechtlichkeit	0.077	0.238	.015	0.322	-.023	.015	.748	
*race*_white[b]	-0.101	0.208	-.056	-0.484	.087	-.023	.629	
*race*_uneindeutig/keineAngabe[b]	-0.228	0.218	-.122	-1.048	-.116	-.049	.296	
DASS-A	0.649	0.066	.515	9.774	.621	.457	< .001	*
Modell 2 Abhängige Variable: DASS-A; Total R^2 = .420 (N = 243)								
Schritt 1 (R^2 = .186, p < .001)								*
(Konstante)	0.797	0.277		3.200			< .01	*
GMSR-IT	0.146	0.040	.227	3.787	.306	.220	< .001	*
Alter	-0.014	0.003	-.232	-3.788	-.305	-.220	< .001	*
Finanzieller Stress	0.165	0.040	.235	3.956	.294	.229	< .001	*
Geschlecht_männlich[a]	-0.029	0.169	-.012	-0.207	.013	-.012	.837	
Geschlecht_weiblich[a]	-0.030	0.180	-.011	-0.185	-.060	-.011	.854	
Intergeschlechtlichkeit	-0.066	0.225	-.017	-0.280	-.041	-.016	.780	
*race*_weiß[b]	0.072	0.238	.051	0.353	.070	.020	.725	
*race*_uneindeutig/keineAngabe[b]	0.015	0.248	.010	0.068	-.078	.004	.946	
Schritt 2 (ΔR^2 = .234, p < .001)								*
(Konstante)	0.366	0.189		1.702			.090	
GMSR-IT	-0.012	0.040	-.019	-0.332	.306	-.016	.741	
Alter	-0.012	0.003	-.195	-3.759	-.305	-.184	< .001	*
Finanzieller Stress	0.090	0.035	.127	2.483	.294	.122	.014	*
Geschlecht_männlich[a]	0.036	0.133	.015	0.302	.013	0.15	.763	
Geschlecht_weiblich[a]	-0.001	0.122	< .001	-0.008	-.060	< .001	.993	
Intergeschlechtlichkeit	-0.081	0.162	-.020	-0.409	-.041	-.020	.683	
*race*_weiß[b]	0.097	0.147	.068	0.558	.070	.027	.578	

Tabelle 3. Multiple lineare Regressionsmodelle mit Angst- und depressiver Symptomatik als abhängige Variablen (Kontrolle für die jeweils andere abhängige Variable im zweiten Schritt) (Fortsetzung)

	B	*SE*	β	*t*	*r*	*sr*	*p*	
*race*_uneindeutig / keineAngabe[b]	0.113	0.156	.076	0.621	-.078	.030	.535	
DASS-D	0.448	0.054	.565	9.774	.621	.478	< .001	*

Anmerkungen: * signifikant nach Bonferroni-Korrektur ($p < .0125$); alle R^2 sind korrigiert; *r* = zero-order Korrelation; *sr* = semipartiale Korrelation; DASS-D: Depression, Anxiety, Stress Scale, Subskala Depression; DASS-A = Depression, Anxiety, Stress Scale, Subskala Angst; GMSR-IT: Gender Minority Stress and Resilience Measure, Subskala Internalisierte Transnegativität; [a] = Geschlecht wurde dummykodiert, die Referenzkategorie ist Geschlecht_nichtbinär; [b] = race wurde dummykodiert, die Referenzkategorie ist *race*_BPoC. Die Bootstrap-Konfidenzintervalle schlossen für alle signifikanten Prädiktoren den Wert Null nicht ein, so dass diese Ergebnisse robust waren.

tengruppenzugehörigkeit: Angehörige von Minderheiten profitieren vom Kontakt zu einer Community, da diese einen diskriminierungsfreien Raum und Unterstützung für erlebtes Stigma bieten können. Da diesem Ergebnis querschnittliche Daten zugrunde liegen, ist auch die andere Wirkrichtung denkbar: Internalisiertes Stigma hält Personen davon ab, Kontakt zu einer Community zu suchen und Verbundenheit zu erleben.

Die moderierende Rolle, die den Resilienzfaktoren vom Minderheitenstressmodell nach Meyer (2003) zugeschrieben wird, konnte nicht belegt werden: Weder soziale Unterstützung noch Verbundenheit mit der LGBT+ Community konnten den Zusammenhang zwischen ITN und psychischen Symptomen abschwächen. Es ist möglich, dass die eingesetzten Fragbögen für soziale Unterstützung und für Verbundenheit mit der Community zu unspezifisch waren. Zur Erläuterung kann ein Befund aus der Minderheitenstressforschung mit sexuellen Minderheiten herangezogen werden: Doty et al. (2010) fanden eine signifikante Moderation durch sexualitätsspezifische Unterstützung, nicht aber durch unspezifische soziale Unterstützung. Dieses Ergebnis lässt sich durch die Passung der Unterstützung auf den Stress erklären: Die Pufferwirkung von Unterstützung kann sich nur entfalten, wenn die Art der Unterstützung auf die spezifischen Stressoren eingeht (Cohen & Wills, 1985). Daraus folgt, dass Kontakt zur trans* Community für die spezifischen Probleme und Bedürfnisse von trans* Personen vorteilhafter sein sollte als der Kontakt zur breiteren LGBT+ Community, welcher in dieser Studie gemessen wurde. Doch auch die spezifischere trans* Community Connectedness (als Kombinationsmaß mit Stolz) hat bei Jäggi et al. (2018) keine signifikante Moderation zwischen Minderheitenstressoren und psychischer Gesundheit gezeigt. Jäggi et al. (2018) stellen infrage, ob Verbundenheit mit der Community als valider Resilienzfaktor angesehen werden kann und betonen die Notwendigkeit weiterer Forschung.

Es lässt sich festhalten, dass ITN ein gesundheitlich relevantes Thema für geschlechtliche Minderheiten ist. Klare Schlüsse über die Prävalenz von ITN, Angst- und depressiver Symptomatik können auf Basis der vorliegenden Daten nicht gezogen werden. Jedoch wird deutlich, dass in der psychotherapeutischen Arbeit mit trans*, inter* und nichtbinären Personen internalisiertes Stigma als Faktor berücksichtigt werden sollte.

Außerdem fehlt Forschung zu der Frage, welche Faktoren beim Prozess der Verinnerlichung von Stigma (also der Entstehung von ITN) eine Rolle spielen. Von besonderem Interesse sind die Fragen, ob und unter welchen Umständen ITN zur Distanzierung von der LGBT+ Community führt und ob der frühe Kontakt zur LGBT+ Community vor dem Verinnerlichen von transnegativem Stigma schützt. Solche Daten könnten unter anderem zur besseren Unterstützung von trans*, inter* und nichtbinären Menschen in Beratungskontexten beitragen.

Stärken und Limitationen

Diese präregistrierte Studie ist eine der ersten dieser Größenordnung im deutschsprachigen Raum zur psychischen Gesundheit geschlechtlicher Minderheiten. Sie liefert Ergebnisse, die auf Hypothesentestung mit robusten statistischen Verfahren basieren. Der große nichtbinäre Anteil der Stichprobe ist als Chance zu betrachten, Aussagen über eine Subgruppe der trans* Population zu treffen, die in vielen Studien zu trans* Identität ausgelassen oder nur am Rande betrachtet wurde. Dennoch sind einige Limitationen zu beachten.

Die Studie verwendete ein Querschnittsdesign an einer online gesammelten Gelegenheitsstichprobe. Durch die Verbreitung des Fragebogens über Webseiten, soziale Medien und Mailverteiler von queeren und LGBT+ Organisationen, Gruppen und Einzelpersonen, erreichte der Fragebogen vorrangig Personen, die bereits eine hohe Anbindung an die Community hatten. Die Stichprobe überschätzt vermutlich die Verbundenheit mit der Community der Gesamtpopulation geschlechtlicher Minderheiten in der Schweiz und in Deutschland.

Der Fragebogen erlaubte durch die Mehrfachauswahl und offene Angabe eine Identifikation mit vielen verschiedenen Geschlechtsbegriffen, wodurch eine heterogene

Stichprobe mit einer großen Vielfalt an unterschiedlichen Identitäten gewonnen wurde. Für die statistische Analyse wurden die Geschlechtsbegriffe in drei Kategorien zusammengefasst. Es ist davon auszugehen, dass Teilnehmer_innen in der großen Gruppe des nichtbinären Spektrums trotz der Gemeinsamkeit, dass ihre Geschlechtsidentität nicht (ausschließlich) weiblich oder männlich ist, sehr unterschiedliche Erfahrungen mit ihrem Geschlecht und aufgrund ihres Geschlechts machen. Außerdem sind trotz der Aggregierung einiger Angaben die Zellenbesetzungen innerhalb der Variablen Intergeschlechtlichkeit, race und Geschlechtsidentität sehr unterschiedlich verteilt. Dies sollte bei der Interpretation berücksichtigt werden.

Trotz dieser Limitationen geben die vorliegenden Daten wertvolle Hinweise darauf, welche Minderheitenstressbezogenen Faktoren eine Rolle spielen für die psychische Gesundheit von trans*, inter* und nichtbinären Personen.

Fazit

Die Ergebnisse zeigen einen negativen Zusammenhang zwischen ITN und psychischer Gesundheit und einen negativen Zusammenhang zwischen ITN und sozialer Unterstützung bzw. Verbundenheit mit der LGBT+ Community bei trans*, inter und nichtbinären Personen. Die Entwicklung und Evaluierung von Präventions- und Interventionsprogrammen sollte ein Fokus zukünftiger Forschung sein, um die psychische Gesundheitssituation geschlechtlicher Minderheiten zu verbessern. Langfristiges Ziel ist es, Diskriminierungen und gesellschaftliche Stigmata abzubauen, um ITN und den damit verbundenen Folgen vorzubeugen.

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Anhang A

Race Item

Hier finden Sie den Originalwortlaut der *race* Items. Zu statistischen Analyse wurden nur die Antworten auf das Item 2 verwendet.

1. Wie beschreiben Sie selbst Ihre nationale/ethnische/kulturelle Identität und Zugehörigkeiten? (offenes Antwortfeld)
2. Benutzen Sie außerdem auch einen oder mehreren der folgenden Begriffe zur Selbstbezeichnung? (Kreuzen Sie bitte alle an, die für Sie zutreffen).
   - Schwarze_r
   - Person of Color
   - Nichtweiße_r
   - Weiße_r
   - Einen anderen und zwar: ___
   - Keinen

Zuordnung zu Geschlechtskategorien

Teilnehmende konnten ihre derzeitige Geschlechtsidentität mittels einer Mehrfachauswahl angeben. Zur Auswahl standen die Begriffe weiblich, männlich, trans*, nichtbinär, transmaskulin, transfeminin, agender, genderfluid, genderqueer, inter* sowie ein Feld für eine offene Angabe. Um Geschlecht als Kontrollvariable in die Analysen aufzunehmen, wurden diese Angaben zu einer dreistufigen Variable zusammengefasst[11]: nichtbinäres Spektrum, trans* weiblich und trans* männlich.

[11] Den Autor_innen ist bewusst, dass eine Zusammenfassung in diese drei Kategorien der Vielfalt der Identitäten der Teilnehmenden nicht entsprechen kann. Dies wird ausschließlich aus methodischen Gründen für die statistische Analyse vorgenommen.

Dem nichtbinären Spektrum wurden alle Personen zugeordnet, die nichtbinär, agender, genderqueer oder genderfluid angegeben hatten, deren offene Angabe weder ausschließlich männlich noch ausschließlich weiblich war, deren Geschlechtsidentität nur inter*, nur trans*, nur transfeminin oder nur transmaskulin war, deren Geschlechtsidentität männlich und weiblich war, deren Geschlechtsidentität nur transmaskulin und trans*, nur transfeminin und trans* oder männlich und transfeminin bzw. weiblich und transmaskulin war. Als trans* weiblich galten Personen mit männlichem Zuweisungsgeschlecht und weiblicher Geschlechtsidentität (mit optionalen weiteren Angaben: transfeminin, trans* oder inter*). Als trans* männlich galten Personen mit weiblichem Zuweisungsgeschlecht und männlicher Geschlechtsidentität (mit optionalen weiteren Angaben: transmaskulin, trans* oder inter*).

Anhang B

Voraussetzungen für die Regressions- und Moderationsanalyse

Die Normalverteilung aller Studienvariablen wurde mit dem Shapiro-Wilk-Test überprüft. GMSR-IT, DASS-D, DASS-A, MSPSS-FF und LGBT+ Community Connectedness waren nicht normalverteilt, $p < .001$. Durch eine visuelle Beurteilung der Histogramme wurde die Möglichkeit von mehrgipfligen Kurven ausgeschlossen. Die leichten Abweichungen von der Normalverteilung wurden aufgrund der Stichprobengröße ($N = 243$) als unproblematisch eingestuft[12]. Die Skalenwerte für GMSR-IT (ITN), MSPSS-FF (soziale Unterstützung), LGBT+ Community Connectedness und DASS-A sowie DASS-D (Angst- und depressive Symptomatik) wurden zentriert. Die Variablen Geschlecht und *race* wurden für die Analysen dummykodiert, die Referenzkategorie ist immer Geschlecht_nonbinär bzw. *race*_BPoC.

Multiple lineare Regressionsmodelle

Die Normalverteilung der Residuen der multiplen linearen Regressionsmodelle wurde mit dem Shapiro-Wilk-Test überprüft. Die Normalverteilungsannahme war bei allen Modellen verletzt, $p < .05$. Eine visuelle Überprüfung der Histogramme der standardisierten Residuen zeigte keine starken Abweichungen von der Normalverteilungskurve.

Zur Überprüfung der Homoskedastizität der Residuen wurden Streudiagramme mit den unstandardisierten vorhergesagten Werten auf der einen Achse und den studentisierten Residuen auf der anderen Achse erstellt und visuell bewertet. Die Homoskedastizität der Residuen war bei vier von sechs multiplen linearen Regressionsmodellen gegeben. Für die beiden übrigen (beide Modelle mit DASS-A als abhängige Variable) wurde Bootstrapping mit 1000 Iterationen eingesetzt.

Moderationsanalysen

Für die Moderationsanalysen wurden für alle Modelle die Prädiktorvariable GMSR-IT und die Moderatorvariablen MSPSS-FF bzw. LGBT+ Community Connectedness auf Multikollinearität geprüft. In keinem Fall lag Multikollinearität vor (Variance Inflation Factor < 5). Es wurde pro Moderationsanalyse ein Bootstrapping mit 5000 Iterationen zusammen mit Heteroskedastizitäts-konsistenten Standardfehlern (HC3[13]; Davidson & MacKinnon, 1993) eingesetzt, um 95 %-Konfidenzintervalle (KI) zu berechnen.

[12] Lumley, T., Diehr, P., Emerson, S., & Chen, L. (2002). The Importance of the Normality Assumption in Large Public Health Data Sets. Annual Review of Public Health, 23(1), 151 – 169. https://doi.org/10.1146/annurev.publhealth.23.100901.140546

[13] Davidson, R. & MacKinnon, J. G. (1993). *Estimation and inference in econometrics.* Oxford Univ. Press.

Anhang C

Tabelle C1. Ergebnisse der Moderationsanalysen

	R^2	*B*	*SE*	*t*	*r*	*sr*	*p*	
Modell 1. Abhängige Variable: DASS-D	.329						< .001	*
(Konstante)		1.046	0.343	2.900			.004	
GMSR-IT		0.297	0.053	5.468	.478	.352	< .001	*
MSPSS-FF		-0.161	0.047	-3.607	-.321	-.223	< .001	*
GMSR-IT × MSPSS-FF		-0.037	0.037	-0.984	-.082	-.064	.326	
Alter		-0.010	0.005	-2.055	-.177	-.124	.041	
Finanzieller Stress		0.155	0.046	3.297	.265	.197	.001	*
Geschlecht_männlich[a]		-0.214	0.196	-1.069	-.025	-.082	.286	
Geschlecht_weiblich[a]		-0.084	0.227	-0.355	-.055	-.028	.723	
Intergeschlechtlichkeit		0.073	0.296	0.238	-.023	.017	.812	
*race*_weiß[b]		0.005	0.294	0.017	.087	.001	.986	
*race*_uneindeutig/keineAngabe[b]		-0.100	0.303	-0.314	-.116	-.011	.754	
Modell 2. Abhängige Variable: DASS-D	.285							*
(Konstante)		0.950	0.349	2.583			.010	
GMSR-IT		0.350	0.052	6.288	.478	.412	< .001	*
CommConn		-0.043	0.113	-0.353	-.077	-.026	.725	
GMSR-IT × CommConn		-0.063	0.110	-0.534	-.050	-.043	.594	
Alter		-0.005	0.005	-1.150	-.177	-.071	.251	
Finanzieller Stress		0.169	0.047	3.529	.265	.209	.001	*
Geschlecht_männlich[a]		-0.170	0.195	-0.852	-.025	-.062	.395	
Geschlecht_weiblich[a]		-0.067	0.217	-0.292	-.055	-.022	.771	
Intergeschlechtlichkeit		0.059	0.281	0.198	-.023	.013	.843	
*race*_weiß[b]		-0.038	0.307	-0.117	.087	-.004	.907	
*race*_uneindeutig/keineAngabe[b]		-0.197	0.316	-0.600	-.116	-.020	.549	
Modell 3. Abhängige Variable: DASS-A	.222							*
(Konstante)		0.864	0.284	2.906			.004	*
GMSR-IT		0.129	0.043	2.896	.306	.189	.004	*
MSPSS-FF		-0.053	0.032	-1.673	-.121	-.088	.096	
GMSR-IT × MSPSS-FF		0.023	0.028	0.797	.016	.045	.427	
Alter		-0.016	0.004	-4.353	-.305	-.235	< .001	*
Finanzieller Stress		0.158	0.041	3.740	.294	.233	< .001	*
Geschlecht_männlich[a]		-0.042	0.162	-0.250	.013	-.019	.803	
Geschlecht_weiblich[a]		-0.038	0.194	-0.188	-.060	-.015	.852	
Intergeschlechtlichkeit		-0.079	0.234	-0.326	-.041	-.022	.745	
*race*_weiß[b]		0.076	0.246	0.300	.070	.010	.765	
*race*_uneindeutig/keineAngabe[b]		0.030	0.257	0.113	-.078	.004	.910	
Modell 4. Abhängige Variable: DASS-A	.229							*
(Konstante)		0.750	0.287	2.446			.015	
GMSR-IT		0.163	0.041	3.763	.306	.249	< .001	*
CommConn		0.159	0.084	1.822	.100	.118	.070	
GMSR-IT × CommConn		-0.090	0.084	-1.022	-.078	-.075	.308	
Alter		-0.013	0.004	-3.490	-.305	-.201	.001	*
Finanzieller Stress		0.162	0.041	3.874	.294	.242	< .001	*
Geschlecht_männlich[a]		-0.020	0.170	-0.115	.013	-.009	.909	
Geschlecht_weiblich[a]		-0.062	0.186	-0.312	-.060	-.024	.756	
Intergeschlechtlichkeit		-0.074	0.250	-0.282	-.041	-.020	.779	

Tabelle C1. Ergebnisse der Moderationsanalysen (Fortsetzung)

	R²	*B*	*SE*	*t*	*r*	*sr*	*p*
*race*_weiß[b]		0.067	0.250	0.255	.070	.009	.799
*race*_uneindeutig/keineAngabe[b]		0.040	0.259	0.147	-.078	.005	.884

Anmerkungen: * signifikant nach Bonferroni-Korrektur (p < .0125); N = 243; *r* = zero-order Korrelation; *sr* = semipartiale Korrelation; DASS-D = Depression, Anxiety, Stress Scale, Subskala *Depression*; DASS-A = Depression, Anxiety, Stress Scale, Subskala *Angst*; GMSR-IT = Gender Minority Stress and Resilience Measure, Subskala *Internalisierte Transnegativität*; CommCon = LGBT+ Community Connectedness; MSPSS-FF = Multidimensional Scale of Perceived Social Support, Subskalen *Freund_innen* und *Familie;* [a] = Geschlecht wurde dummykodiert, die Referenzkategorie ist Geschlecht_nichtbinär; [b] = race wurde dummykodiert, die Referenzkategorie ist *race*_BPoC. Die Bootstrap-Konfidenzintervalle schlossen für alle signifikanten Prädiktoren den Wert Null nicht ein, so dass diese Ergebnisse robust waren.

Appendix II: Paper #2

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* shared first authorship

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conceptualization, literature search, writing - original draft, writing - review and editing, project co-administration

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Review

Understanding Psychological Symptoms of Endometriosis from a Research Domain Criteria Perspective

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Abstract: Endometriosis is currently the second most common gynecological disease and is associated with severe pain, vegetative impairment, and infertility. In association, there are considerable psychological symptoms that limit the quality of life of those affected. In this narrative review, the Research Domain Criteria (RDoC) framework was utilized to display the different transdiagnostic processes involved in disease progression and maintenance in regard to psychosocial functioning. Using the RDoC framework, it becomes clear that immune/endocrinological dysregulation is interlocked with (pelvic) pain chronification processes and psychological symptoms such as depressive mood, loss of control, higher vigilance toward the onset or worsening of symptoms, social isolation, and catastrophizing. This paper will discuss and identify promising treatment approaches, in addition to medical care, as well as further research implications. Endometriosis can come with substantial psychosomatic and social burden, requiring more research to understand the interdependence of different factors involved in its chronic development pathway. However, it is already clear that standard care should be extended with multifaceted treatments addressing pain, as well as the psychological and social burden, in order to halt the cycle of aggravation of symptoms and to improve quality of life for patients.

Keywords: endometriosis; infertility; pelvic pain; RDoC; stress-related diseases; women's health

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1. Introduction

Endometriosis is a chronic inflammatory disease that is defined by the growth of endometrial-like tissues outside of the uterus [1]. It is estimated to affect up to 10% of premenopausal individuals with ovaries and a uterus and, although classified as benign, the tissue implants can spread and damage affected organs [2]. The pathogenesis of endometriosis is not clear and studies report a delay from symptom onset to diagnosis of 10 years on average [3].

Endometriosis can be asymptomatic, but is predominantly associated with chronic pelvic pain (CPP), dysmenorrhea, dyspareunia, dysuria, dyschezia, and infertility [2]. Symptom presentation varies across the menstrual cycle and between patients; however, importantly, there is no clear link between pain symptoms and endometriosis stage or localization of tissue implants [4–6]. This, and the fact that there is a high prevalence of psychological symptoms in endometriosis patients [7,8], suggests that endometriosis is not exclusively a gynecological condition.

In addition to somatic symptoms, endometriosis patients frequently experience depressive mood and heightened anxiety [9], higher levels of perceived stress, as well as various kinds of pain [10], all of which influence their social life [11]. Infertility/subfertility and concerns about potential infertility may also lead to worry, depression, and feelings of

inadequacy [12]. Cross-sectional studies find higher risks for the diagnosis of depression, generalized anxiety disorder [13], and post-traumatic stress disorder [14] in patients with endometriosis. Previous reviews have illustrated that endometriosis reduces psychosocial wellbeing [15] and overall quality of life (QoL) in patients [16]. Nevertheless, the unclear pathogenesis of endometriosis includes the etiology of its psychological symptoms [17], which is yet to be fully understood.

The Research Domain Criteria (RDoC) are an evolving research structure considering the major domains of neuropsychosocial functioning instead of categorizing symptoms. Promoted by the US National Institute of Mental Health, the RDoC project provides a multidimensional approach to understanding mental health and illness with six key domains, each including several constructs. These constructs can be measured by different units of analysis, ranging from genes to self-reports. The RDoC were not primarily designed for clinical use, but as a research tool to integrate (neuro-)biological findings into the understanding of psychopathology [18]. This transdiagnostic approach, which focuses not only on symptomatic and behavioral aspects, but also includes underlying neurobiological mechanisms, seeks to inspire translational research for the better prevention and treatment of mental illness [19]. The RDoC take the interdependence of psychological symptoms and physiological circuits into account, making it a promising tool for investigating the complex somatopsychic connections in endometriosis.

The aim of this narrative review is to not only demonstrate the burden that patients with endometriosis carry, but to also detect transdiagnostic interrelations in the pathogenesis and perpetuation of psychological symptoms to further identify possible prevention and treatment approaches addressing these mechanisms. Therefore, the review of current evidence was structured by the two RDoC domains of Negative Valence Systems and Systems for Social Processes, since these seem to capture the psychopathology of endometriosis most accurately; the Negative Valence Systems are linked to symptoms of depression [20], anxiety [21], and post-traumatic stress [22], while Systems for Social Processes cover the social factors relevant to endometriosis such as social withdrawal, perceived injustice, and social support [23]. Both will shortly be illustrated at the beginning of each respective section.

With regard to levels of psychosocial functioning, the focus of this review is on units of analysis starting on the level of circuits, going up to physiology, behavior, and self-report. The units of analysis, genes, molecules, and cells, and their relevance regarding psychosocial functioning in endometriosis, were left out of this review and can be found elsewhere [24,25].

The primary literature search was conducted from date of inception (May 2021) until August 2022 via the platforms pubmed, PsycInfo, and PSYNDEX. The initial search term was "endometriosis psych*" and no temporal restriction was used. Subsequent literature searches included topics and authors that were discovered during the initial search.

2. Negative Valence Systems

The domain Negative Valence Systems includes adverse motivation and responses to adverse situations or contexts [26]. It is divided into the five subconstructs: Acute Threat, Potential Threat, Sustained Threat, Loss, and Frustrative Nonreward. Acute Threat and Frustrative Nonreward are being left out of this review since they are not considered to be relevant for a comprehensive understanding of the psychological symptoms of endometriosis.

2.1. Potential Threat

Potential Threat refers to an activation due to potential harm that is distant and uncertain or of low certainty [27]. The Generalized Unsafety Theory of Stress [28] postulates that the human stress response serves as a default mode, which can be deactivated through the perception of safety signals. The theory can explain prolonged stress responses in the absence of acute stressors.

Living with endometriosis always entails the possibility of disease progression, of the development of new symptoms, and of the worsening of persisting symptom manifestation [29]. Endometriosis patients live with potential low imminence threats, such as pain or flare-ups, and without remediate treatment, which could otherwise serve as a signal of safety. Therefore, endometriosis is often experienced as a highly uncontrollable disease [30]. Uncontrollable stress led to higher rates of endometriosis progression in rats [31]. The absence of safety signals might play a role as it could possibly lead to higher vigilance in regard to onset or worsening of symptoms. This, in turn, supports constant symptom monitoring as an additional factor for a dysregulated stress response. People with diagnosed endometriosis are also more likely to be diagnosed with post-traumatic stress disorder [14] compared to people without endometriosis. In particular, people who experienced physical or sexual abuse during childhood are more at risk of developing endometriosis later in life. Harris et al. [32] report a 79% higher risk of developing endometriosis for those who experienced both severe physical and sexual abuse during childhood. Childhood abuse and PTSD can leave victims with the concept of the world as an unsafe place in general [33], causing further suspicion of potential threat in many situations of everyday life. Reis et al. [30] conclude that childhood stress, e.g., negligence and abuse, should be considered a risk factor for the development of endometriosis, since these adverse events may cause persistent alterations in the neural and hormonal stress responses [34] relevant to pain severity and disease progression, such as a chronic inflammatory response and dysregulated hypothalamic–pituitary–adrenal axis (HPA axis).

2.2. Sustained Threat

The RDoC subconstruct of Sustained Threat describes prolonged exposure to negative experiences, either external or internal. Some patients are exposed to unpleasant states, such as chronic pain and light or heavy bleeding [35], on most days, not only during certain phases of their menstrual cycle. Chronic pain, among other symptoms, often equals chronic stress and contributes to the lasting dysregulation of the HPA axis in individuals with endometriosis [36]. This dysregulation often leads to higher levels of pro-inflammatory agents which lower the pain threshold [37] and, in turn, can cause higher subjective chronic stress [36]. Even the treatment and day-to-day management of the disease and of subfertility is possibly perceived as a sustained threat. Lazzeri et al. [38] found a link between treatment intensity and levels of perceived stress in endometriosis patients with a strong association between repeated surgery and higher self-reported measures of psychological stress. Research on other long-term effects of medical treatment on HRQoL is relatively scarce. Most studies on long-term mental health effects report an overall positive outcome of both pharmacological [39,40] and surgical treatment [41,42]. In their review, D'Alterio et al. [43] report that surgical and pharmacological treatments have comparable long-term effects on pain levels and QoL. However, the follow-up intervals in these studies were rather short (up to 18 months). This is critical, since pain recurrence after surgery can occur many months later [44,45], which might, in turn, lead to a lower QoL.

2.3. Loss

The Loss subconstruct of the negative valence systems refers to both the episodic and sustained unwanted disappearance of any object or situation that is not easy to replace. It includes loss of relationships, status, or behavioral control, and is associated with negative emotions as well as rumination and possible shifts in attention. The subjective experience of loss is the result of individual evaluation based on values and beliefs, leading to interindividual differences regarding the extent and intensity of perceived loss. Oftentimes, patients with endometriosis must deal with many kinds of loss from all areas of life: they are likely to lose predictability in everyday life [46], resulting in possible loss of income [10] as well as loss of social relationships, satisfying sex life (see Section 3), and hobbies due to the interference of symptoms with social and other activities [47].

Furthermore, some patients report experiencing loss of their identity as a woman because of possible struggles with fertility and not being able to meet society's expectation of womanhood [48]. The burden through infertility becomes even higher with experienced pregnancy loss [49]. In their qualitative study, Hållstam et al. [50] summarized living with endometriosis as a constant struggle for coherence with difficulties in establishing meaning and feeling understood. Patients described feelings of loneliness and guilt, sorrow over childlessness and existential grief [50].

Rush and Misajon [51] identified loss of control as a central topic relevant to patients with endometriosis. Young patients in particular reported feelings of frustration regarding educational/job opportunities and intimate relationships [51]. The loss domain is often associated with symptoms of depression [20] that are also quite common among patients with endometriosis; patients with endometriosis show symptoms of depression more often than healthy controls [52] and are more likely to be diagnosed with major depression or other forms of depression over their lifetime [13].

The experience and intensity of chronic pain is discussed as a moderating variable for depressive symptoms [53,54], although some of the behaviors listed as typical for the Loss domain, such as worrying and being biased toward negatively valenced information, might also influence the psychological burden of living with endometriosis. In their study, Van Aken et al. [25] found that pain catastrophizing independently influences health-related quality of life (HRQoL), even when pain intensity was included in their regression model. When looking at sexual stress, negative metacognitive beliefs seem to play an even larger role. In the cross-sectional study of Zarbo et al. [55], negative metacognitive beliefs predicted sexual distress in hierarchical logistic regression, while dyspareunia and chronic pain did not. Their findings provide support for the presumption that cognitive processes, such as rumination and metacognitive beliefs, have an additional, independent effect on psychological symptom severity. Donatti et al. [56] identified a solution-oriented focus on clear-cut problems instead of catastrophizing as a successful coping strategy associated with decreased symptoms of depression. The cognitive restructuring of unhelpful thoughts was identified as another helpful coping strategy by González-Echevarría et al. [57], as it was associated with higher HRQoL. Facchin et al. [58] highlight the need for actively restoring continuity in living with endometriosis to overcome a sense of disruption and loss. Hållstam et al. [50] stress the importance of professional support and acknowledgement throughout the process of grief, so that a sense of coherence and the experience of a purpose in life can be re-established.

3. Systems for Social Processes

The domain Systems for Social Processes subsumes all reactions to interpersonal events and interactions regarding different social contexts. It contains the four subconstructs: Affiliation and Attachment, Social Communication, Perception and Understanding of Self, and Perception and Understanding of Others. Affiliation and Attachment, as well as Perception and Understanding of Self, were included as relevant in the context of psychosocial functioning in those with endometriosis.

3.1. Affiliation and Attachment

The Affiliation and Attachment subconstruct describes the processes for friendly social approach and bonding. Affiliation, as social approach behavior and engagement in positive social interactions, can result in attachment, which is selective affiliation. Attention to social cues, as well as social learning and memory, are required to engage in affiliation and attachment.

The experience of social affiliation, closeness, and forming attachment are fundamental human needs and, oftentimes, preconditions to psychological well-being [59,60]. As endometriosis symptoms can interfere with work, social activities, and hobbies [47,61], patients have less time and fewer opportunities to take part in positive social interaction. They are, therefore, less able to experience positive reinforcement through positive social

interaction [62], which might contribute to the risk of developing depressive symptoms. The diagnosis of endometriosis comes with many barriers to societal participation; some patients describe the need for the spontaneous cancellation of plans due to symptoms such as pain, irregular bleeding [63], or fatigue [64], missing out on family events, and fear of letting other people down [65]. Further social withdrawal seems to be a consequence of not feeling understood by friends and family members [66], resulting in increased feelings of loneliness and isolation [65,67].

The extensive effects of endometriosis on patients' day-to-day life becomes even more apparent when considering its influence on intimate romantic relationships and family life. Other than not participating in as many social occasions to meet potential new partners, patients describe feelings of shame and fear with regard to dating [63], because they anticipate being a burden to potential new partners. They often find it particularly difficult to disclose how dyspareunia and vaginal bleeding affect their experience of penetrative sex and physical intimacy [63]. Some patients even prefer the silent endurance of pain during and after intercourse over engaging in a conversation with their partner [68].

In established romantic relationships, endometriosis can have a tremendous effect on relationship dynamics [46,69,70] and requires individually aligned coping strategies, as symptom severity in endometriosis, marital satisfaction, and sexual satisfaction are each associated with the other [71,72]. Many patients experience sexual distress, since they are nine times more likely to experience dyspareunia than healthy controls. Loss of satisfying sex life can occur due to pain [73], bleeding [63], and other kinds of impairments in sexual functioning [7]. In Fritzer et al.'s study [74], patients with endometriosis and dyspareunia reported less sexual intercourse, and disruption or avoidance of it (with 46% of participants stating that their partner's satisfaction was their main motivation for sexual interactions). Pluchino et al. [72] underline the role of other determinants of sexual health apart from dyspareunia. Cognitive coping strategies, such as catastrophizing and a partner's negative reaction to sexual pain, might aggravate distress. Hence, it is not surprising that Van Niekerk et al. [75] report an association between vulvar/clitoral pain and lower quality of life in their cross-sectional study. Many couples report feeling left alone by health practitioners regarding their sex life [46].

Reduced fertility or infertility is another severe burden for those trying to conceive [58], further adding to the strain on sexual health. In the sample of Fritzer et al. [74], 30% of participants named wanting to conceive as the main motivation for penetrative sex. In a qualitative study by Márki et al. [76], some patients even recall losing a previous partner due to sexual distress or having to undergo strenuous fertility treatment. Infertility, or the risk thereof, is also perceived as a threat to female identity by some patients [71]. Believing that childless women were of less value than mothers was associated with lower mental health and self-esteem for patients in Facchin et al. [77]. These effects could then, again, affect relationship dynamics negatively [71]. Additionally, patients with children oftentimes report the negative impact of endometriosis on domestic duties and childcare [78,79]. Their concerns include not being able to play with them [12] and their illness limiting family activities [50]. One participant in a qualitative study by Jones et al. [12] described worrying whether her daughter will receive adequate care for her own endometriosis symptoms.

On the oher hand, helpful social support in romantic and other personal relationships can play an important positive role in coping with endometriosis [65]. Márki et al. [76] highlight the need for adequate, reliable information enabling both patients and partners to engage in useful coping strategies. Dyadic coping in couples living with chronic illness is associated with better physical health, well-being, and overall relationship satisfaction [80]. In couples dealing with endometriosis, McKay et al. [81] also discovered a link between higher levels of perceived emotional intimacy and the relationship satisfaction of both partners. Overcoming the joint struggle of living with endometriosis could even serve as an opportunity for mutual growth, creating a stable, lasting relationship [46].

In the last decades, another means of social support for people with endometriosis in the form of online communities has emerged [75]. Most endometriosis patients are

open to finding information and sharing experiences online, with higher trust in official endometriosis sites [82]. Online communities for people with physical disabilities have been proven effective in offering social support and advice [83]. Thiel et al. [84] even suggest utilizing this interest in online platforms to provide more well-founded information to avoid nocebo-effects in treatment. Online platforms and communities seem to be a promising approach for additional support.

3.2. Perception and Understanding of Self

The subconstruct Perception and Understanding of Self includes the two subconstructs of agency and self-knowledge. It describes processes and representations for assessing one's own internal states and traits, and for supporting self-awareness, self-monitoring, and self-knowledge.

Many patients with endometriosis describe changes in or loss of agency, especially when in acute pain [85]. In their qualitative study, Bullo et al. [86] found some patients to share a perception of pain as the loss of agency to an externalized attacker. These findings are supported by a study in which endometriosis patients wrote narratives about their life with the disease, finding 68% of the sample to feel powerless, at least to some extent [87]. This feeling of missing agency was significantly positively correlated with depressive symptoms and neuroticism, while being negatively correlated with life satisfaction. Other patients even describe disconnection from their thoughts and losing their sense of self, largely due to the overwhelming intensity of pain and becoming paralyzed during its peaks [85], illustrating that severe pain can, in fact, reduce agency.

With regard to the evaluation of their own body, endometriosis patients show higher levels of body image concerns [88,89]. In Sayer-Jones et al.'s qualitative study [90], patients reported experiencing a sense of betrayal from their own body or compared their body to a prison. Another participant stated that postoperative scarring made her feel unattractive [90]. Geller et al. [91] found that body image and self-criticism moderated differences in depression and anxiety levels between patients. In turn, Van Niekerk et al. [35] discovered an association of body compassion with higher HRQoL. Falconer [92] criticizes the methodological issues of existing research on body image in endometriosis, pointing out the need for a standardized assessment of satisfaction with body image and body image concerns.

Concerning the appropriate perception of their competences, skills, beliefs, and desires, patients with endometriosis might be vulnerable to developing deficits in this area. In particular, if their self-confidence is impacted, they might suffer from it even more than healthy controls. Higher rates of self-criticism mediated differences in the symptoms of depression in the study of Geller et al. [91]. Marschall et al. [87] also found that some patients' illness narratives, which centered around negative self-change, were associated with more symptoms of depression in comparison to narratives centered around less negative self-change and communion. González-Echevarría et al. [57] report on self-criticism as a negative coping strategy associated with lower HRQoL.

In accordance with the cognitive model of depression, negative self-evaluation might constitute a risk factor for the development of depressive symptoms [93]. Cause–effect relations of negative self-evaluation and depressive symptoms remain unclear within the context of the psychological symptoms associated with endometriosis. Nevertheless, these findings highlight the need for mind–body interventions that target psychological symptoms and hopefully improve HRQoL.

4. Discussion

In our review, previous findings on psychosocial functioning in endometriosis were restructured, utilizing the RDoC framework. The domains Negative Valence Systems and Social Processes were explored, aiming to illustrate the transdiagnostic interrelations in symptom perpetuation.

It becomes apparent that endometriosis can have far-reaching psychological consequences. Endometriosis is stress-associated, with HPA dysregulation supporting chronic

inflammation and pain chronification. A high physical and mental load, combined with loss of resources, can result in higher levels of stress and vigilance toward the worsening of symptoms. People who experienced childhood abuse are more likely to develop endometriosis later in life due to their already dysregulated stress response. Fearful symptom monitoring, in turn, can cause a worsening of symptoms, lower self-esteem, rumination, and negative meta-cognitive beliefs affecting many areas of life; endometriosis can interfere with work, social activities, hobbies, and relationship/family life and family planning. Therefore, patients might withdraw from social encounters and activities, which can lead to a complex cycle of lowered well-being, more social isolation, less positive reinforcement, and feelings of loneliness and despair. Romantic and sexual relationships can be especially affected by endometriosis symptoms. Taken together, endometriosis is a disease that can affect all areas of life. It creates self-sustaining mechanisms of disease progression that interact with each other, partially leading to symptoms that persist even after the extensive removal of endometrial tissue.

These findings support the call of other authors (e.g., [94,95]) who demand that endometriosis be widely recognized as a systemic disease. An early diagnosis and an early start of not just medical therapy is vital in order to avoid the emergence of the described connections and, thus, to maintain well-being and quality of life.

4.1. Wider Implications for Treatment and Future Research

There is a need for additional multimodal therapy, focusing on broader stress and pain processes in endometriosis, to reverse the many pathogenetic mechanisms that play a role in the progression of psychological symptoms.

Psychotherapy for patients with endometriosis would have to acknowledge and validate all these challenges, while at the same time providing profound tools for mastering them and re-establishing a sense of coherence [50]. Pilot studies show a positive effect of different mind–body interventions [96–99], which matches study findings demonstrating that patients often wish for more holistic care [100]. In particular, studies including elements from cognitive behavioral therapy (CBT) could significantly improve quality of life in patients [101]. CBT has been proven as effective in the treatment of chronic pain [102], depression [103], and chronic stress [104], making it a promising candidate for improving HRQoL in endometriosis. CBT allows for the restructuring of automatic thoughts, as well as acceptance of events in the outer world and of internal experiences (e.g., uncomfortable thoughts and emotions) [105]. Patients could probably benefit from these strategies when dealing with symptoms such as rumination, high levels of perceived stress, and fear of movement. To the authors' knowledge, no RCT study has yet examined the effects of CBT interventions for patients with endometriosis, although some study protocols have been published [106,107]. Some potentially useful treatment elements could be psychoeducation, pacing daily activities and movement, navigating the workplace, relationship and sexual therapy, managing fertility treatment, and/or grieving infertility. The feeling of loss of agency and alienation from one's own body could be specifically tackled, e.g., with self-compassion-based interventions [108]. Research on psychosexual interventions in endometriosis patients is still scarce, but it is promising for pain symptoms and sexual functioning [95]. With regard to any kind of additional treatment, individualized therapy approaches are necessary based on the individual symptomatic profile. Every patient is affected by endometriosis in a possibly unique way, although the various symptoms stem from quite distinct somatic grounds.

There is still a knowledge gap regarding the etiology, pathogenesis, pain chronification, subfertility mechanisms, and cause–effect relationships in the context of endometriosis. The impact of endometriosis on not just romantic relationships, but on the family system and child development, is still to be explored in more detail. Furthermore, the psychological long-term effects of different kinds of treatment need to be further investigated. Research on mind–body interventions for patients with endometriosis has only emerged over the last two decades. In order to generate better screening tools, to potentially develop preventive

programs, and to improve any kind of treatment, we need more research, especially longitudinal cohort studies. Research on endometriosis could benefit from consistent use of validated outcome measures for not only pain, but HRQoL. Bourdel et al. [109] discuss the strengths and weaknesses of commonly used outcome measures and recommend the use of the SF-36 [110] and the EHP-30 [111]. The EHP-30 is an endometriosis-specific HRQoL questionnaire that was developed from interviews with patients [111]. The EHP-30 + 23 consists of a core questionnaire with five subscales and six modular components, covering different areas of life possibly relevant to patients (e.g., work life, infertility). It is sensitive to change [112] and relatively easy to administer [109].

Hudson [113] points out that endometriosis has suffered from a lack of recognition and research funding for decades, even though its significant impact on patients is widely recognized already. Additionally, not all individuals affected by endometriosis receive the same attention in the medical care system. Gender, race, culture, and class play important roles in the quest for finding the right diagnosis and receiving adequate treatment [114,115]. The influence of these social intersections should be acknowledged by researchers and practitioners and carefully kept in mind when designing studies, analyzing data, and treating patients. Especially in endometriosis, gender is a crucial factor; the lack of recognition and funding might partially be an indirect result of academic research being shaped by male researchers not taking a so-called women's disease seriously [113]. At the same time, whenever endometriosis is reduced to a women's disease, affected individuals who do not identify as female (e.g., trans men or nonbinary individuals) are excluded. They may, on the one hand, experience gender dysphoria whenever confronted with their so-called female disease [116]. On the other hand, the process of transitioning and undergoing testosterone treatment and/or hysterectomy sometimes interferes with endometriosis symptoms and treatment [117]. More research on how to provide trans, intersex, and nonbinary individuals with safe and adequate health care free of discrimination is needed.

4.2. Limitations

Although we provide a detailed and comprehensive insight into the complex mechanisms creating psychosocial burden, our review is not systematic and does not offer the same accuracy as could have been reached with a meta-analytic approach. However, meta-analyses and systematic reviews on endometriosis often suffer from lack of methodological quality in original studies and call for studies with clear, replicable study designs and better reliability (e.g., [101,118]). Instead of conducting a systematic literature review, the linking of existing evidence on the psychosocial burden of endometriosis across diagnoses seemed to be of value. Therefore, the RDoC structure, with its transdiagnostic dimensional perspective, provided a helpful framework for this review. Its neurobiological foundations and the idea of mapping psychopathological phenomena with distinct (neuro)physiological circuits, molecules, and genes might be perceived as reductionistic [119] when used with the intent of forming conclusive models of every interrelation between units and domains of analysis. Conceptualizing psychiatric disorders as merely brain disorders in the sense of one-to-one correspondence is, indeed, not doing justice to the complexity and interpersonal heterogeneity of human experience [119]. However, it might be helpful to keep in mind that RDoC were primarily designed as a constantly evolving research tool to inspire constructive dialogue about integrating neurobiological findings into the understanding of mental illness [18]. They are meant to be an additional framework to the International Classification of Diseases (ICD) and Diagnostic and Statistical Manual of Mental Disorders (DSM) [120], not a superior framework to replace them. In the context of endometriosis, where relations between the different factors contributing to progression of the disease itself, and to the development of mental burden, remain unclear, they can provide a new perspective supporting the need for psychotherapeutic treatment. The perspective on endometriosis through the RDoC framework can be of additional value for future research.

5. Conclusions

In this review, we presented the psychosocial mechanisms within, and as a consequence of, endometriosis, a disease that can, using the RDoC, be defined as systemic rather than only gynecological. We were able to show the different facets of the condition and how it impacts wellbeing and health-related quality of life. It became clear that early diagnosis and adequate, multimodal treatment are vital. Specifically, mind–body interventions, such as psychotherapy to reduce stress and support healthy coping, are needed in addition to medical care. On a societal level, endometriosis needs to be taken more seriously, since it can put such a strain on a patient's quality of life. Better availability of knowledge will hopefully shorten the time between symptom onset and correct diagnosis and, thus, help to halt the chronification processes early on, as well as generate more public interest, leading to more research and treatment funding.

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Appendix III: Paper #3

van Stein, K. R., Stoffel, M., Marshall, A., Germeyer, A., Herpertz, S., Grinevich, V., Eckstein, M., & Ditzen, B. (in peer review). How Partner Support, Stress, and Hormones influence momentary Pain Experience in Chronic Pelvic Pain. Submitted to the European Journal of Pain.

KvS's contributions according to the contributor roles taxonomy (CRediT) author statement (Allen et al., 2019):

methodology, formal analysis, investigation, data curation, writing – original draft, writing - review and editing, visualization, project administration

EJP European Journal of Pain

How Partner Support, Stress, and Hormones influence momentary Pain Experience in Chronic Pelvic Pain

Article category	Original article
A running head	*Support and Stress in Chronic Pelvic Pain*
Name of Author(s)	van Stein, Katharina R.[1,2]; Stoffel, Martin[2]; Marshall, Anne[3]; Germeyer, Ariane[3]; Herpertz, Sabine[4]; Grinevich, Valery[5]; Eckstein, Monika[2]; Ditzen, Beate[1,2]
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Is this an observational study?	☐ No ☒ Yes

	→ Have you uploaded the STROBE checklist? ☒
Is this a systematic review?	☒ No ☐ Yes → Have you uploaded the PRISMA checklist? ☐ → Registered in PROSPERO? ☐ (*Please provide the number*)
Plagiarism Declaration	☒ We hereby declare that this paper is our own work, except where acknowledged, and has not been submitted elsewhere.
Is the reviewer list appropriate?	☒ Yes, we confirm that. To avoid conflicts of interest, please suggest reviewers from different countries and with different nationalities (only one reviewer from your country can be allowed). Please note that it is the authors' responsibility to suggest appropriate reviewers. The failure to do so signifies that your work will not draw broad attention from readers and is susceptible to rejection.
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Number of references	53
Reference/citation styles comply with the authors' guideline	☒ Yes, we confirm that.
Number of Figures	8 (+5 in supplement)
Number of Tables	7
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Any conflicts of interest?	The authors have no competing interests to report.
Significance statement	This study broadens the understanding of how social support styles influence pain experience in individuals with CPP and endometriosis. The results underscore the importance to re-evaluate social support mechanisms, as they may inadvertently exacerbate pain symptoms. These insights are crucial for developing more effective psychosocial interventions: In addition to standard therapy, incorporating stress reduction interventions and involving partners in treatment approaches should be considered. This strategy may improve the effectiveness of pain management in daily life for CPP patients.

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Abstract

Background

Chronic pelvic pain (CPP) is a debilitating condition frequently associated with gynecological disorders, such as endometriosis or adenomyosis. It imposes a significant burden on affected individuals, including personal distress and strains on romantic relationships. Existing research highlights the substantial influence of social support, stress, and hormonal factors on pain experience, but real-life data is scarce.

Methods

This ecological momentary assessment (EMA) study aimed to explore the association of stress, cortisol, oxytocin, and partners' social support styles in daily life with pain experiences among individuals with CPP (N = 66) across 7 days.

Results

The findings suggest that both, distracting and solicitous social support were positively related to higher pain levels on a between-person-level but showed no or slightly negative associations with pain on a within-person-level. Stress was found to be positively correlated with higher pain ratings both within and between individuals, while no significant associations were observed between salivary cortisol or oxytocin levels and pain perception.

Conclusion

These findings indicate that both distracting and solicitous social support are associated with higher pain ratings on a between-person level, a pattern which did not show within individuals. This suggests long term learning mechanisms within the dyad and highlights the complexity of social interactions in the context of chronic pain.

1. Introduction

Chronic pelvic pain (CPP) affects up to 27 % of individuals with ovaries and uterus (Ahangari, 2014) and can mean severe restrictions in quality of life (Netzl et al., 2022). Between 25 and 70 % of CPP have endometriosis (Mathias et al., 1996; Tirlapur et al., 2013), by itself a benign disease in which endometrial-like tissues grow outside the uterus (Eskenazi & Warner, 1997). In many cases however, current treatment methods cannot satisfactorily alleviate pain symptoms in endometriosis and other CPP conditions (Brandsborg et al., 2007, 2009). Thus, it is crucial to further elucidate pain processes and influential factors.

Contrary to the common belief that social support uniformly benefits chronic pain patients, previous research reveals a more complex picture (Thieme et al., 2005): Different styles of social support may evoke different outcomes. Studies in diverse chronic pain conditions (yet not CPP) found solicitous support to be related to higher pain (Nees et al., 2022), and distracting support to be pain alleviating (Ginting et al., 2011).

In healthy samples and chronic pain patients, studies found that stress renders individuals more susceptible to pain stimuli (Crettaz et al., 2013). However, results from these experimental conditions cannot be generalized to real life experiences. Real life data from the few existing ecological assessment studies suggest that stress significantly predicts momentary pain levels (Fischer et al., 2016).

Cortisol, a main outcome parameter of the hypothalamic pituitary adrenal (HPA) axis, is frequently utilized as a biological marker for experienced stress. However, in chronic pain patients, the HPA axis is often dysregulated, a phenomenon that can impact cortisol reactivity (Woda et al., 2016): Chronic pain patients have been found to have a heightened cortisol response (Fischer et al., 2016).

The relation between oxytocin and pain seems to be more complex. Exogeneous oxytocin administration seems to be linked to reduced pain sensitivity in healthy samples (Goodin et al., 2015) and in chronic pain patients (Wang et al., 2013). Interestingly, intranasally administered oxytocin seems to reduce perceived heat pain, but not spontaneous pain in chronic lower back pain patients (Boll et al., 2020). The few existing studies focusing on endogenous oxytocin levels and pain experience have resulted in mixed findings (Boll et al., 2018).

Taken together, a conclusive assessment of the roles of different social support styles, stress, and endogenous cortisol and oxytocin levels on pain experience in CPP is still missing. Therefore, the following hypotheses were preregistered[1]:

H1: Higher distracting social support is associated with lower pain levels on the between- and within-person level.

H2: Higher soliciting social support is associated with higher pain levels on the between-person level but lower pain levels on the within-person level.

H3: Higher subjective stress levels are associated with higher pain levels on the between- and within-person level.

H4: Higher endogenous cortisol levels are associated with higher pain levels on the between- and within-person level.

[1] [anonymized for peer-review]

H5: Higher endogenous oxytocin levels are associated with lower pain levels on the between- and within-person level.

2. Methods

The data presented here are derived from a preregistered, overarching project that examined the influence of social support and stress on pain experiences in individuals with CPP (Principal Investigator: [anonymized for peer-review]). Data collection occurred between December 2020 and June 2023. The overarching project received approval from the ethics committee of [anonymized for peer-review]. All participants gave written informed consent and received a reimbursement of 120 Euros.

2.1. Recruitment

An initial sample size of N = 60 was pre-registered. Due to the unpredictable nature of the recruitment process (e.g. cycle fluctuations and participant availability), at a certain point, it was decided to complete the process for all participants already engaged, without recruiting additional participants, resulting in the final sample size of N = 66. All participants identified as female and mean age was 29.4 (SD = 6.09), ranging from 18-43 years. Individuals were recruited via the Endometriosis Consultation of the [anonymized for peer-review] and via social media posts combined with a pain screening (Chronic Pain Grade by Klasen et al., 2004). The main inclusion criterion was chronic or recurrent pelvic pain as reported in the Endometriosis Consultation or having a Chronic Pain Grade of 2 or higher. Also, participants were required to be able to roughly estimate their next menstrual onset. Exclusion criteria were: being younger than 18 or older than 45 years, current psychotic disorders, current psychopharmacological treatment, psychoactive medication, preceding alcohol abuse or substance abuse, current hormonal fertility treatment, any kinds of cancer, acute infections, chronic pain disorders apart from CPP, taking the pill in long-term cycle. Endometriosis-status was confirmed by laparoscopic surgery by the Endometriosis Consultation or by diagnosis letters from other medical institutions. All participants were required to live in a 2-hour radius around [anonymized for peer-review] to ensure the saliva samples remained frozen during the transfer from participants' homes to the lab. The recruitment process is outlined in the flowchart (Figure 1).

2.2. Procedure

Participants were pre-screened and informed about the study via phone and received all study documents, a study phone and saliva collection kits via mail. They filled in a baseline online questionnaire via the platform SoSciSurvey.de before starting the ecological momentary assessment (EMA). Participants were assessed for 7 consecutive days, starting 3 days before estimated start of next menstrual bleeding. Thus, data collection was planned to take place during late luteal and early follicular phase, to cover a high variability in pain intensity.

Participants were provided with a study phone running the EMA app movisens XS. At 5 times per day, they received prompts to report on social interactions, subjective stress and pain ratings and to collect saliva samples. Except for the awakening and pre-sleep questionnaire, all questionnaires were presented following a time-based schedule. However, prompts were allowed to be postponed to later or to be responded to before the actual measuring time, resulting in a high response rate. Questionnaires were assigned to a measurement time as long as they were not responded to more than 15 minutes before or after the scheduled

measurement time. There were more prompts and additional hormones assessed, which are however not relevant for the aims of this study. For the detailed schedule, see electronic supplement S1.

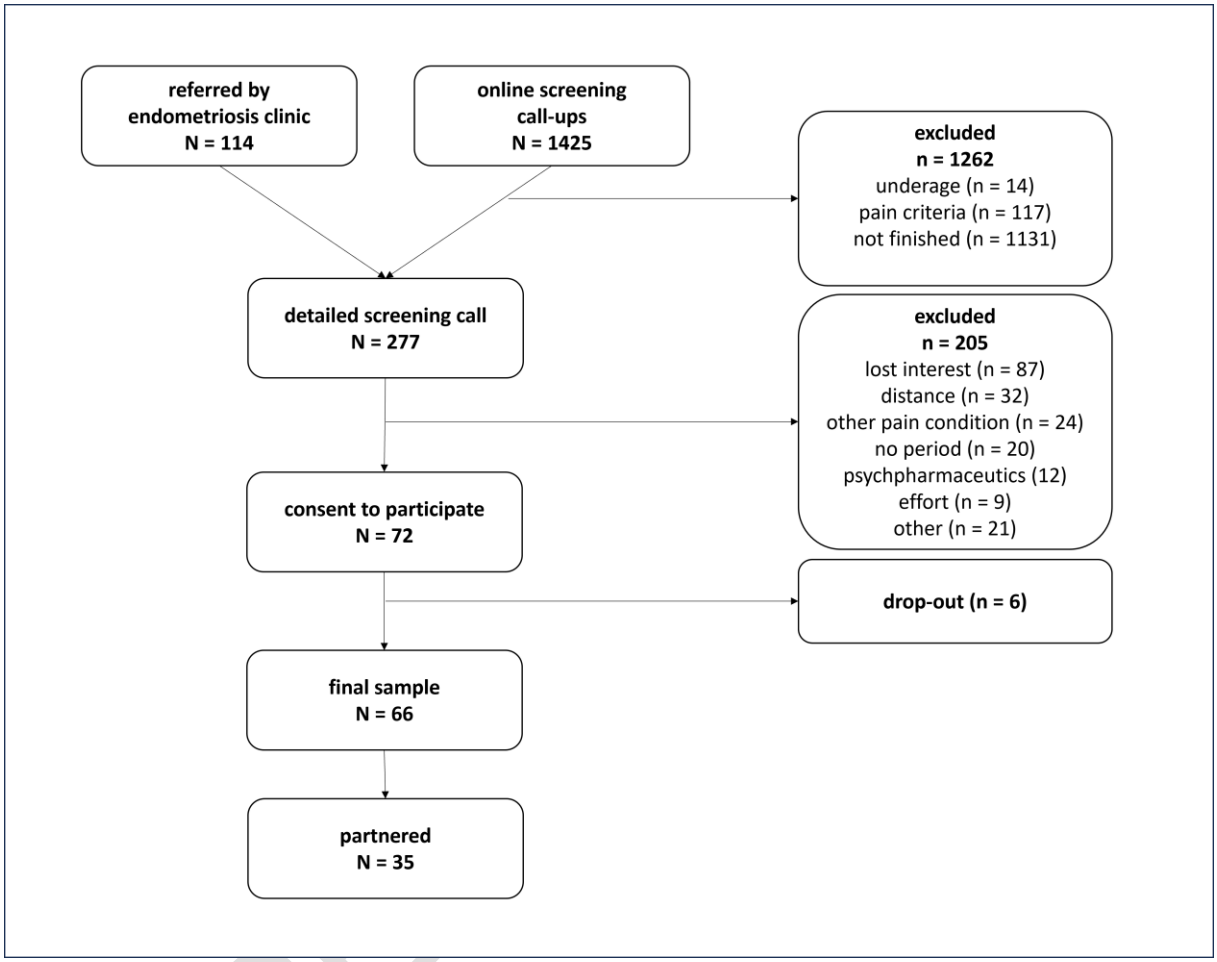

Fig. 1. Flowchart of the recruitment process. Participants were recruited between December 2020 and June 2023, via the endometriosis clinic and social media. In total, 72 individuals met the criteria, of whom 66 participants finished the assessment. Out of these, 35 participants were partnered and thus relevant for the social support hypotheses.

2.3. Materials

2.3.1. Questionnaires

Sociodemographic and basic medical information was assessed with the baseline questionnaire. The EMA questionnaire always started with a directive to collect a saliva sample and accompanying quality control questions. Subsequently, various items regarding the psychosocial situation followed. The processing time averaged around 5 minutes. For this study, the following items were relevant:

Pain was assessed with a single item (“Estimate the extent of your current pain (right now)!”) on a 7-point-Likert scale ranging from 0 (no pain) to 6 (the most extreme pain I have ever experienced).

Stress was assessed with a single item (“How nervous and stressed do you feel at the moment?”) on a 7-point-Likert scale ranging from 1 (not at all) to 7 (very much).

Information on analgetic use was taken from a general question on medication use since the last prompt.

In the pre-sleep questionnaire, participants were asked if their menstrual bleeding started on this day with a single item.

Social support was assessed in a subsample of participants who were in a relationship and who spent a significant amount of time with their partner. Here, part II of the German version of the Multidimensional Pain Inventory (MPI; Kerns et al., 1985)) assessing social support styles was used. Participants were asked, how their partners reacted to their pain and eleven different partner reactions were suggested. Only reactions coded as solicitous (e.g., ‘gives me a massage’) or distracting (e.g., ‘encourages me to work on a hobby’) are considered in this paper. For each item, participants indicated support on a 7-point-Likert scale ranging from 0 (not at all) to 6 (very much). Preceding filtering questions ensured that the partner was present at the time of assessment and that the participant was experiencing pain. As a result, the number of social support events was limited.

2.3.2. Neuroendocrine Measures

During 7 days at 5 times per day, participants self-sampled their saliva into plastic collection tubes via passive drool technique and immediately stored each sample in their home fridges (samples for cortisol assessment) or freezers (samples for oxytocin assessment). After participation the saliva samples were stored at –80°C for no longer than six months before analysis in the biochemical lab at [anonymized for peer-review].

From these saliva samples, salivary oxytocin (sOxy) was analyzed from the last salivary sample per day, resulting in 7 oxytocin samples per participant. To analyze sOxy concentrations, saliva samples were thawed and centrifuged at 4°C at 1.500 × *g* for 15 min and subsequently analyzed without extraction (20% of the samples in duplicates) following the protocol of oxytocin enzyme-linked immunosorbent assay from Enzo Life Sciences (ELISA; ENZO Life Sciences, Switzerland). The detection limit was 15 pg/ml, and the intra- and inter-assay coefficients of variation (CVs) were 8.46 and 11.45%, respectively. 1% of values was too high or low to be analyzed correctly and was thus excluded.

Salivary cortisol (sCort) was analyzed from 5 saliva samples per day, resulting in 35 cortisol measures per participant. SCort was measured with an enzyme-linked immunosorbent assay (ELISA; Demeditec, DES6611) with 20% in duplicates and a reported detection limit between 0.1 and 30 ng/ml. The intra- and inter-assay CVs in our sample were 2.85 and 5.78%, respectively.

2.4. Data Analysis

Data were analyzed using R version 4.3.1 (R Core Team, 2023). To account for the nested structure of the data, the package “nlme” (version 3.1-163) (Pinheiro et al., 2023) was used to fit multilevel models (MLM) with a maximum likelihood method of estimation. Missing data were handled using Restricted Maximum Likelihood (REML), which inherently accommodates

missing data by using all available data points. Measurements within days (level 1; L1) were treated as nested in days (level 2; L2) which were treated as nested in person on level 3 (L3). To avoid violations of model assumptions (e.g., normality of residuals), distributional properties of all dependent variables were checked prior to fitting the models. In case of non-normality, data were transformed using box-cox transformations (Osborne, 2019). As pre-registered[2], all models included the following control variables: age, contraceptive pill intake, cycle day, analgesic intake, and time within days. All control variables (apart from time within days) were centered on their grand mean. Potentially nonlinear time trends were tested by comparing models with linear time and models with higher-order polynomials. Thereafter, random slopes were tested separately by comparing the baseline model (i.e., all covariates, including time within days, and random intercepts on L2 and L3) against the same model with one additional random slope an L2 or L3 (see Stoffel et al., 2021). Model comparisons were conducted using likelihood ratio tests and by interpreting the Bayesian Information Criterion (BIC; where a lower BIC indicates a better fit to the data). Following these steps, the focal predictors were entered into the models. Given that they were measured repeatedly on each day for each person, within- and between-person variances were disentangled (see Brincks et al., 2017) by person-mean centering each single measurement (within-person effects) and by grand-mean centering each person-mean (between-person effects). As a result, it was possible to draw conclusions regarding (a) whether overall higher/lower levels of the focal predictor would be associated with overall higher/lower levels of the dependent variable (between persons) and (b) whether within-person fluctuations (i.e., higher or lower levels of a predictor for a person as compared to their usual level of this predictor) would be associated with alterations in the dependent variable (on L1). For each final model, model assumptions were tested according to standard procedures (as in (Pinheiro & Bates, 2000; Stoffel et al., 2021). As a last step, sensitivity analyses were performed for each final model in which all observations for each variable in the model with values exceeding ± 3 SD from each respective grand mean were excluded. Graphical representations of model results were built using the packages effects (Fox & Weisberg, 2018) and ggplot2 (Wickham, 2016).

3. Results

Of all 66 participants, 35 participants (53%) were in a committed relationship. Seven participants (11%) used hormonal contraception, 11 participants (17%) had up to 10 years of schooling, 27 (41%) had 10-13 years of schooling, 21 (32%) had a university degree and the educational data of 7 (11%) was missing. In the 7-day-window of 66 participants, 45 menstrual onsets were reported. Thirty-five participants (53%) had a verified endometriosis diagnosis. Variation of pain ratings by daily measurement time and by cycle day is reported in Table 1, the latter is also depicted in Figure 2. Descriptive statistics of the outcome and predictor variables are reported in Table 2.

There were no severe violations of model assumptions in any of the models reported. Detailed results of each model, including number of observations and the random effect's structure, are shown in tables 3 to 7. The exclusion of outliers in sensitivity analyses did not change the magnitude or direction of any of the results reported.

[2] [anonymized for peer-review]

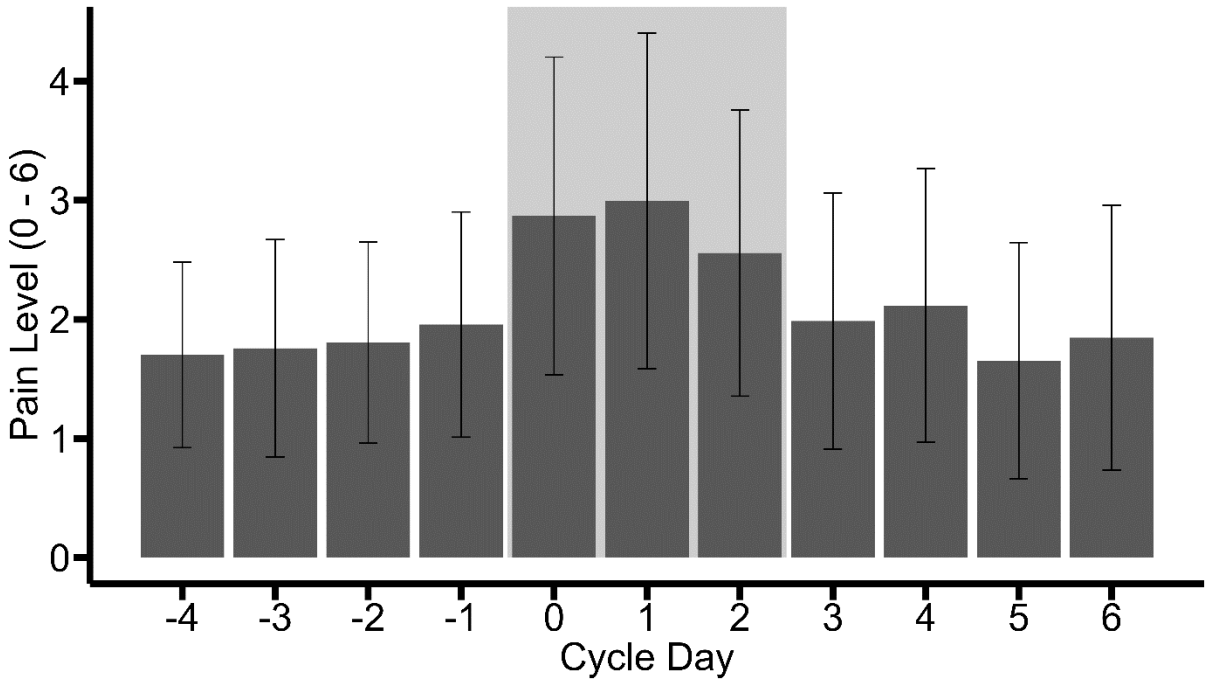

Fig. 2. Variation of pain ratings by cycle day. In Cycle Day, zero refers to menstrual onset.

Table 1
Variation in Pain Ratings by Time

Daily Measurement Time	*N*	*M*	*SD*
T1 - 45 min after awakening	65	1.97	1.21
T2 - 11:00	404	2.07	1.16
T3 - 14:00	409	2.12	1.23
T4 - 18:00	382	2.15	1.17
T5 – pre-sleep	403	2.18	1.19
Cycle Day			
-4	68	1.70	0.78
-3	106	1.76	0.91
-2	146	1.80	0.85
-1	191	1.96	0.95
0	226	2.87	1.33
1	215	3.00	1.41
2	215	2.56	1.20
3	148	1.99	1.08
4	106	2.12	1.15
5	78	1.65	0.99
6	39	1.85	1.11

Notes: T1 and T5 were self-initiated, for T2 - T4 data was included with a tolerance of +/- 15 min; in *Cycle Day*, zero refers to menstrual onset.

Table 2
Descriptive Statistics of Outcome and Predictor Variables

	N	*M*	*SD*	range
Pain	1985	2.1	1.19	1 - 7
Pain (transformed)	1985	0.74	0.72	0 - 2.94
Distracting Support	328	2.16	1.42	1 - 6.33
Solicitous Support	328	2.89	1.97	1 - 7
Stress	2100	2.41	1.48	1 - 7
sCort	2081	5.2	4.6	0.12 - 29.74
sOxy	396	116.21	129.07	4.4 - 1135.4

Notes: sCort = salivary cortisol; sOxy = salivary oxytocin.

Model 1. Pain as a Function of Distracting Support
Only data to which the following applies was used for this model: (a) the participant was in a relationship; (b) in that specific situation the partner was present; and (c) in that specific situation the participant was in pain. The results of this model showed that between-person variations (b = 0.15, p = .04), but not within-person variations (b = -0.03, p = 0.46), in distracting support were positively associated with pain. This suggests that individuals who on average experienced higher distracting support than others reported higher average levels of pain. In contrast, within these individuals, moments of distracting support receipt were minimally and non-significantly associated with lower levels of momentary pain. Figures 3 and 4 illustrate these effects.

Model 2. Pain as a Function of Solicitous Support
Only data to which the following applies was used for this model: (a) the participant was in a relationship; (b) in that specific situation the partner was present; and (c) in that specific situation the participant was in pain. The results of this model showed that between-person variations (b = 0.10, p = 0.03), but not within-person variations (b = 0.04, p = 0.31), in solicitous support were positively associated with pain. This indicates that those who on average experienced higher solicitous support reported higher average levels of pain. Within these individuals, moments of solicitous support receipt were not associated with momentary pain levels. Figures 5 and 6 illustrate these effects.

Model 3. Pain as a Function of perceived Stress
A continuous autoregressive correlation structure of order 1 (CAR-structure) based on time between assessment (3-hour intervals) was added to the final model, because the residual values of L1 were not distributed independently. The updated model (BIC = 2107.84) significantly improved the model fit ($X^2(2) = 17.57$, $p < .001$), as compared to the model without the CAR-structure (BIC = 2118.19). Thus, the results reported here are based on the model including the CAR-structure. The within- and between-person variations in stress were significantly and positively associated with pain (between-person: b = 0.19, p < .001; within-person: b = 0.08, p = .001). This indicates that individuals who on average experienced higher stress reported higher average levels of pain. On the other hand, higher levels of stress for a given person (in a given moment within days, as compared to the person average levels of stress) were associated with higher levels of momentary pain. Figures 7 and 8 illustrate these effects.

Model 4 and 5. Pain as a Function of Cortisol and Oxytocin

A CAR-structure based on time between assessment (3-hour intervals) was added to the final models predicting sCort and sOxy, because the residuals on L1 were not distributed independently. The updated model (sCort BIC = 2117.81; sOxy BIC = 1934.70) significantly improved the model fits (sCort $X^2(2) = 17.74$, $p < 0.001$; sOxy $X^2(2) = 10.26$, $p = .001$), as compared to the models without the CAR-structures (sCort BIC = 2128.35; sOxy BIC = 1937.82). Thus, the final results reported here are based on the models including the CAR-structures. There were neither within- nor between-person associations of sCort (5 daily measurements, between-person: $b = -0.06$, $p = .23$; within-person: $b < -0.01$, $p = .52$) or sOxy (1 daily measurement, between-person: $b < 0.01$, $p = .86$; within-person: $b < 0.01$, $p = .60$) with pain. Graphical representations of these effects are shown in the supplementary information (Figures S2, S3, S4, S5).

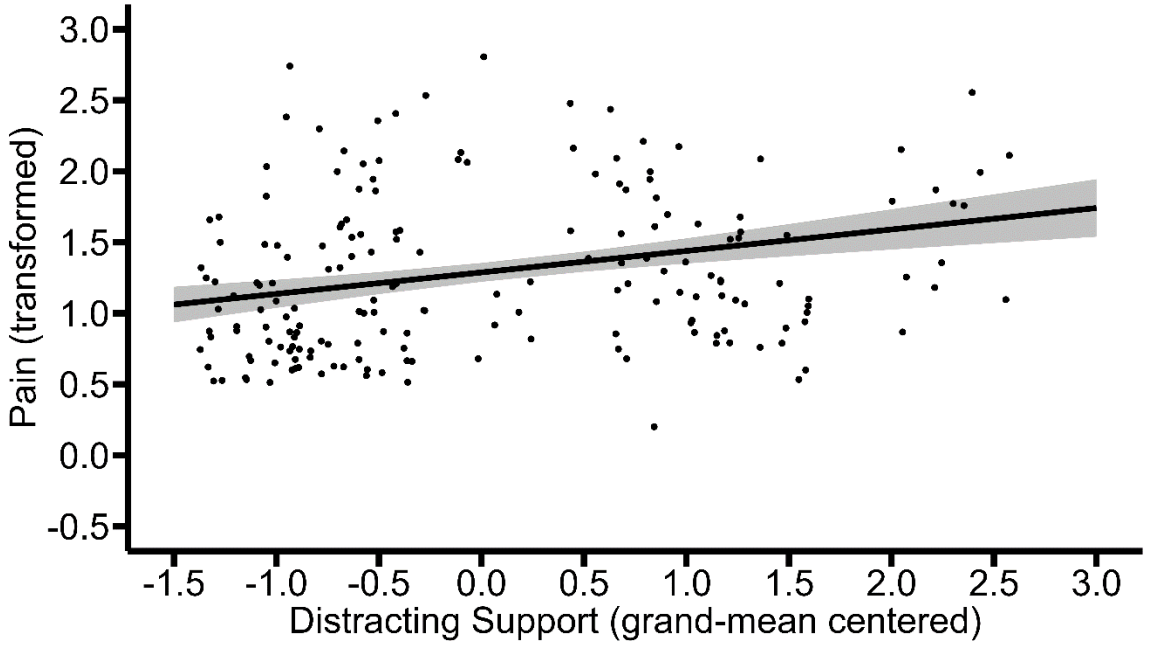

Fig. 3. Between-person association of distracting support with pain. The graph illustrates the average predicted values of pain (transformed) as a function of distracting support. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

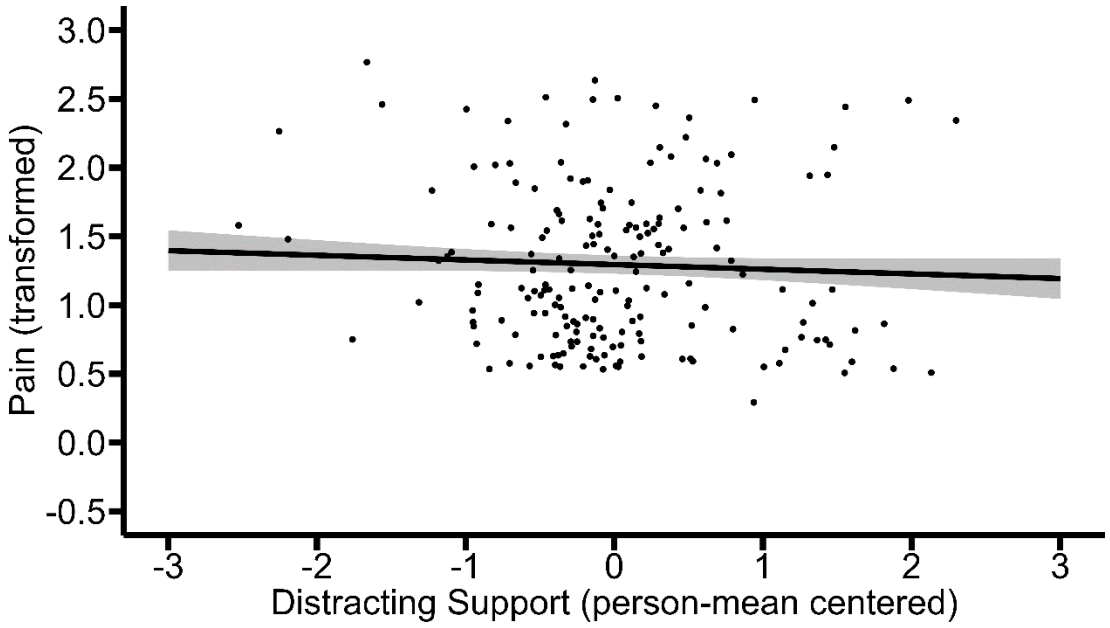

Fig. 4. Within-person association of distracting support with pain (non-significant). The graph illustrates the average predicted values of pain (transformed) as a function of distracting support. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

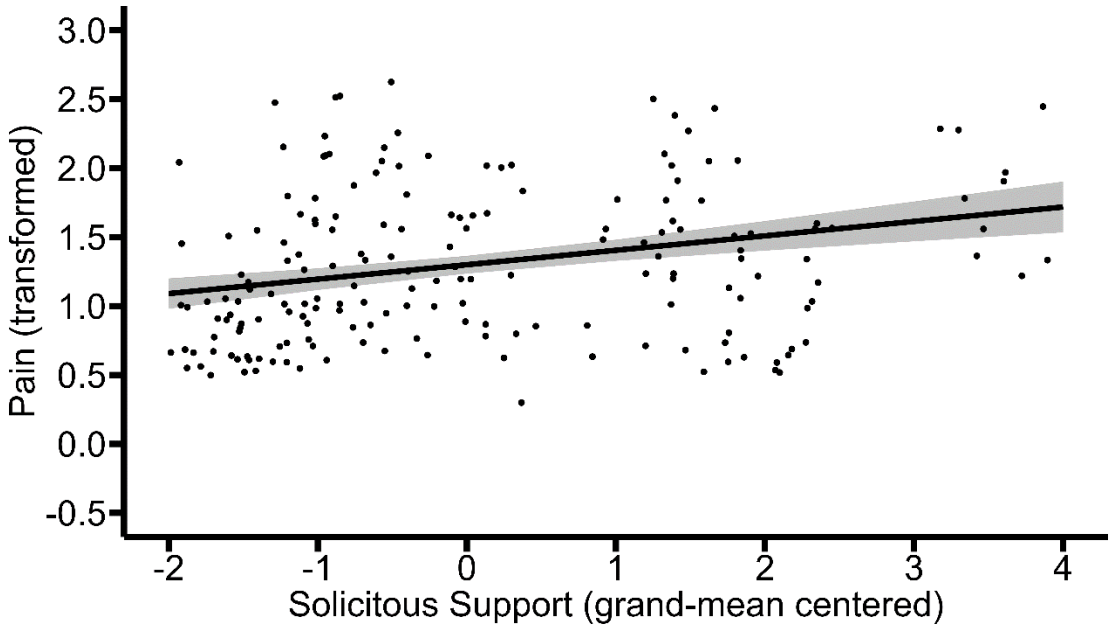

Fig. 5. Between-person association of solicitous support with pain. The graph illustrates the average predicted values of pain (transformed) as a function of solicitous support. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

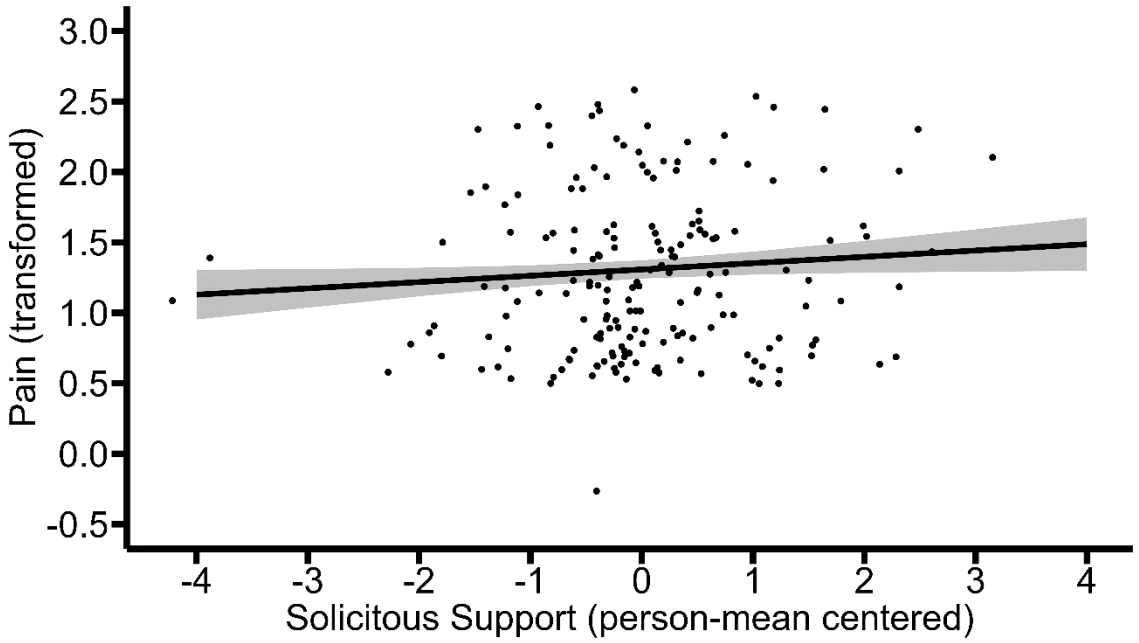

Fig. 6. Within-person association of solicitous support with pain (non-significant). The graph illustrates the average predicted values of pain (transformed) as a function of solicitous support. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

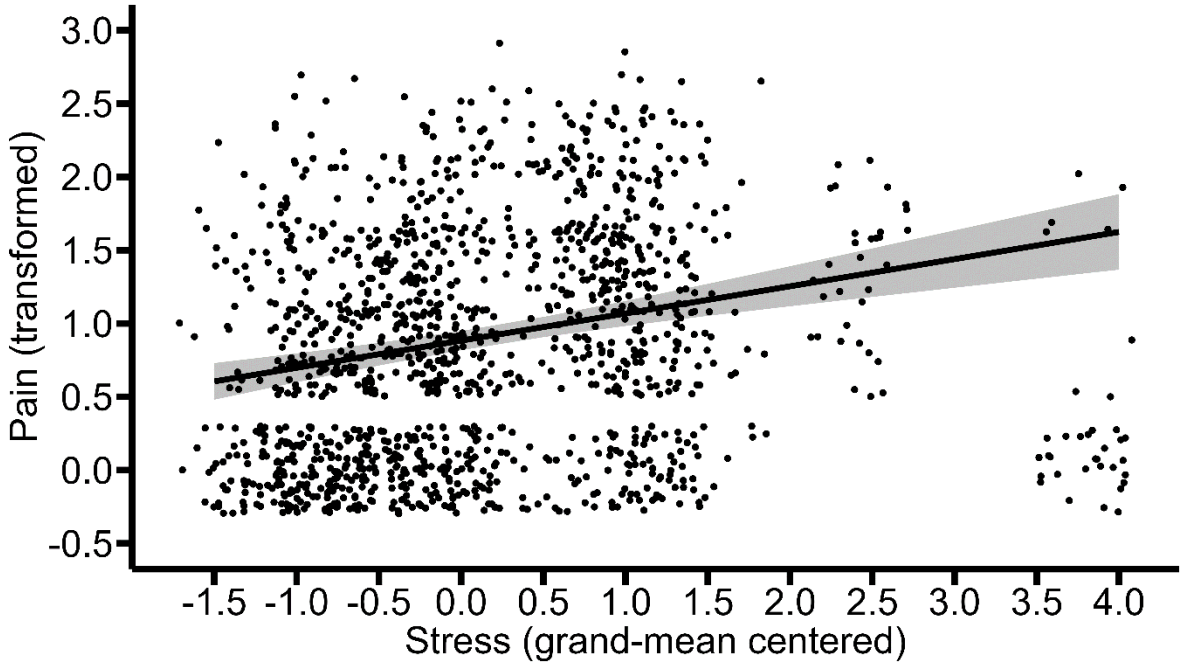

Fig. 7. Between-person association of stress with pain. The graph illustrates the average predicted values of pain (transformed) as a function of stress. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

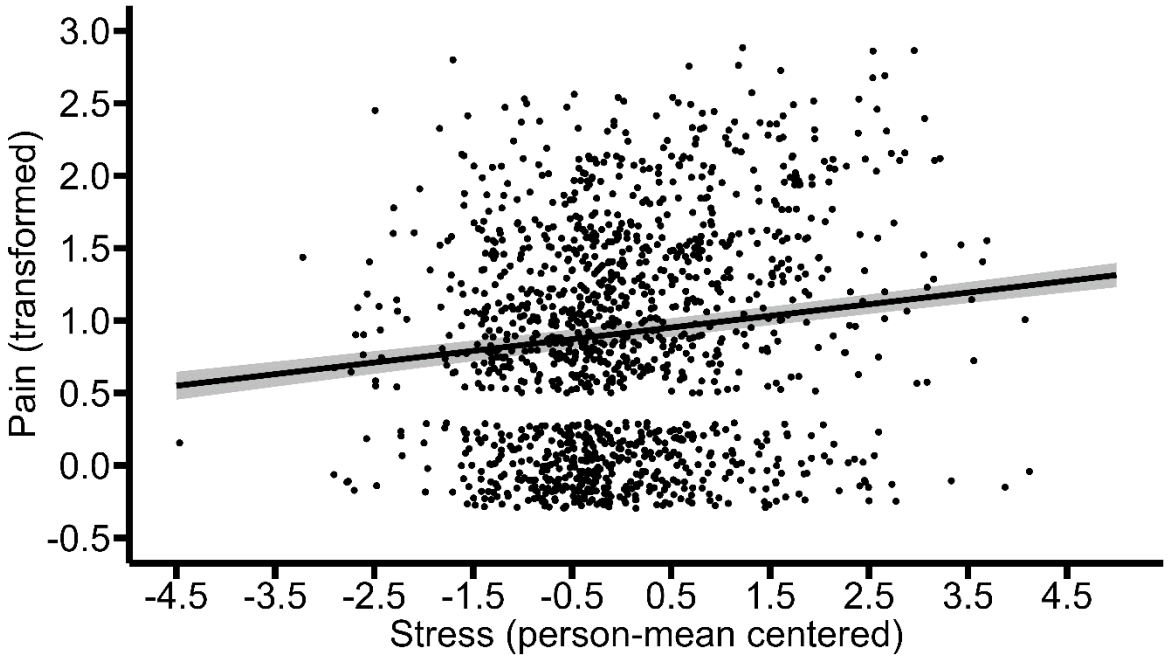

Fig. 8. Within-person association of stress with pain. The graph illustrates the average predicted values of pain (transformed) as a function of stress. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

Table 3. Pain as a Function of Distracting Support.

	Fixed Effects	
	Estimates (se)	*p*
Intercept	1.217(0.112)	< .001***
Time	0.00(0.000)	.971
Age	-0.013(0.011)	.255
Contraceptives	-0.460(0.362)	.224
Analgesic Intake	0.198(0.112)	.080
Cycle Day	0.049(0.023)	.037*
Distracting Support		
Between-Person Level	0.151(0.068)	.043*
Within-Person Level	-0.034(0.045)	.456
	Random Effects (SD)	
Level 3 (across persons)		
Intercept	0.202	
Distracting Support Within-Person Level	0.005	
Level 2 (across days)		
Intercept	0.296	
Distracting Support Within-Person Level	0.125	
Residual	0.332	

Note. Table depicts point estimates (standard errors for fixed effects in brackets). Distracting support was centered on the person mean (within-person level) and on the grand mean (between-person level); time was not centered and represents the amount of time (in minutes) since midnight; all other predictors were centered on the grand mean. Covariances between random effects within a level were estimated (unstructured random effect matrices). Number of participants = 18; total number of observations = 184. *p < .05; ** p < .01; ***p < .001.

Table 4. Pain as a Function of Solicitous Support.

	Fixed Effects	
	Estimates (se)	*p*
Intercept	1.289(0.109)	< .001 ***
Time	-0.000(0.000)	.776
Age	-0.009(0.011)	.406
Contraceptives	-0.178(0.333)	.600
Analgesic Intake	0.159(0.111)	.155
Cycle Day	0.051(0.024)	.033 *
Solicitous Support		
Between-Person Level	0.105(0.045)	.034 *
Within-Person Level	0.045(0.044)	.308
	Random Effects (SD)	
Level 3 (across persons)		
Intercept	0.190	
Solicitous Support Within-Person Level	0.085	
Level 2 (across days)		
Intercept	0.315	
Solicitous Support Within-Person Level	0.002	
Residual	0.328	

Note. Table depicts point estimates (standard errors for fixed effects in brackets). Solicitous support was centered on the person mean (within-person level) and on the grand mean (between-person level); time was not centered and represents the amount of time (in minutes) since midnight; all other predictors were centered on the grand mean. Covariances between random effects within a level were estimated (unstructured random effect matrices). Number of participants = 18; total number of observations = 184. *p < .05; ** p < .01; ***p < .001.

Table 5. Pain as a Function of Stress.

	Fixed Effects	
	Estimates (se)	*p*
Intercept	0.815(0.0749)	< .001 ***
Time	0.013(0.007)	.082
Age	0.001(0.011)	.932
Contraceptives	-0.055(0.221)	.805
Analgesic Intake	0.402(0.060)	< .001 ***
Cycle Day	0.018(0.020)	.378
Stress		
Between-Person Level	0.185(0.065)	.001 **
Within-Person Level	0.080(0.013)	< .001 ***
	Random Effects (SD)	
Level 3 (across persons)		
Intercept	0.370	
Cycle Day	0.101	
Stress (Within-Person Level)	0.026	
Level 2 (across days)		
Intercept	0.508	
Time	0.072	
Stress (Within-Person Level)	0.045	
Residual	0.382	

Note. Table depicts point estimates (standard errors for fixed effects in brackets). Stress was centered on the person mean (within-person level) and on the grand mean (between-person level); time was not centered and represents the amount of time (in minutes) since midnight; all other predictors were centered on the grand mean. Covariances between random effects within a level were estimated (unstructured random effect matrices). Number of participants = 41; total number of observations = 1366. *p < .05; ** p < .01; ***p < .001.

Table 6. Pain as a Function of Cortisol.

	Fixed Effects	
	Estimates (se)	*p*
Intercept	0.912(0.084)	< .001 ***
Time	0.002(0.009)	.830
Age	-0.000(0.013)	.995
Contraceptives	0.089(0.232)	.705
Analgesic Intake	0.422(0.061)	< .001 ***
Cycle Day	0.023(0.021)	.272
Cortisol		
Between-Person Level	-0.060(0.048)	.227
Within-Person Level	-0.002(0.004)	.517
	Random Effects (SD)	
Level 3 (across persons)		
Intercept	0.407	
Cycle Day	0.107	
Cortisol (Within-Person Level)	0.010	
Level 2 (across days)		
Intercept	0.523	
Time	0.071	
Cortisol (Within-Person Level)	0.000	
Residual	0.392	

Note. Table depicts point estimates (standard errors for fixed effects in brackets). Cortisol was centered on the person mean (within-person level) and on the grand mean (between-person level); time was not centered and represents the amount of time (in minutes) since midnight; all other predictors were centered on the grand mean. Covariances between random effects within a level were estimated (unstructured random effect matrices). Number of participants = 41; total number of observations = 1334. *p < .05; ** p < .01; ***p < .001.

Table 7. Pain as a Function of Oxytocin.

	Fixed Effects	
	Estimates (se)	*p*
Intercept	0.908(0.081)	< .001 ***
Time	0.003(0.008)	0.699
Age	0.013(0.013)	0.290
Contraceptives	0.179(0.243)	0.466
Analgesic Intake	0.367(0.062)	< .001 ***
Cycle Day	0.016(0.023)	0.485
Oxytocin		
Between-Person Level	0.000(0.001)	0.858
Within-Person Level	0.000(0.000)	0.602
	Random Effects (SD)	
Level 3 (across persons)		
Intercept	0.396	
Cycle Day	0.111	
Oxytocin (Within-Person Level)	0.001	
Level 2 (across days)		
Intercept	0.538	
Time	0.000	
Residual	0.382	

Note. Table depicts point estimates (standard errors for fixed effects in brackets). Oxytocin was centered on the person mean (within-person level) and on the grand mean (between-person level); time was not centered and represents the amount of time (in minutes) since midnight; all other predictors were centered on the grand mean. Covariances between random effects within a level were estimated (unstructured random effect matrices). Number of participants = 39; total number of observations = 1247. *p < .05; ** p < .01; ***p < .001.

4. Discussion

The present study investigated the effects of different types of social support on momentary pain perception in women suffering from CPP and associations with stress and stress-related neurohormonal markers in daily life. Study participants were assessed during a time when pain variability was highest: during the late premenstrual and early follicular phase of their menstrual cycle.

Data suggest that overall, both distracting as well as solicitous support are related to *higher* pain ratings on a between-person level. Reported stress was found to be related to higher pain ratings on a within- and between-person level. This relation did not emerge for the association between cortisol or oxytocin with pain.

4.1. Social Support

While social support is consistently assumed to be beneficial for health, associations with chronic pain are more complex. More precisely, close and loving others usually show supportive behavior in response to pain expression, and this might be immediately helpful on a momentary level (Che et al., 2018). However, sadly these initially intuitive and positive interaction patterns might result in an increased focus on the pain, operant conditioning processes of avoidance behavior and increasing disability in the long-term.

The present results on distracting support are in line with this notion: On a between-person level, distracting support was associated with higher pain levels. In contrast, on a within-person level, distracting support was slightly (and non-significantly) associated with decreased pain levels. This shift from a positive association of distracting support and pain on the overall level to a negative association on a momentary level suggests complex interpersonal dynamics and there are different possibilities to interpret this finding: Firstly, on the individual level, self-distraction alone does not seem to be an effective technique to lower pain intensity or pain distress over time (Van Ryckeghem et al., 2018). Secondly, on the interpersonal level, distracting support may be weakly, but negatively correlated with pain acceptance (McCracken, 2005). Thirdly, while on a momentary level distraction can immediately alleviate pain symptoms, social support overall might increase focus on the symptoms in the long-term.

For solicitous support, results imply that this support style may be pain increasing on both, the between- and within-person level – although the within-person effect was not significant and should thus be interpreted cautiously. This interpretation is in line with recent findings by Nees et al. (2022) showing that chronic pain patients had stronger pain-related neural responses and higher pain ratings when a partner with a solicitous support style was present. The results suggest that operant learning mechanisms are involved and that a partner with a solicitous support style might unintentionally serve as a cue to process pain stimuli differently. Above this, solicitous support may decrease the patients' feeling of agency. Agency and the threat thereof are an important topic in chronic pain in general, but also in endometriosis-related chronic pelvic pain (van Stein et al., 2023). Furthermore, in a chronic pain context solicitous support may compromise patients' sense of competence (Martire et al., 2002) and may even prevent patients from autonomously performing tasks (2002). A review by Rafaeli and Gleason (Rafaeli & Gleason, 2009) discusses further how comparable kinds of social support may threaten the recipients' feeling of autonomy.

Of note, endometriosis-related CPP presents a distinctive profile among pain conditions due to its high hormonal dependence and thus cyclically recurring pain. Also, via its effects on

sexual interaction, CPP might affect interactions in romantic relationships differently than other chronic pain conditions and may thus be fundamentally negative for intimate relationships.

4.2. Stress

Matching our hypotheses, we found higher stress ratings to be related to higher pain ratings. This is in line with laboratory studies (Crettaz et al., 2013) as well as ecological momentary assessments (Fischer et al., 2016). Although stress and pain are similar constructs in psychophysiological terms, the medium size B coefficients suggest that conceptually different constructs were measured. The present data support the notion, that stress and pain are strongly intertwined and can result in a vicious circle: Stress can influence pain signaling, possibly leading to increased pain experience, while pain may evoke feelings of threat which in turn facilitate HPA activity, increase alertness and attention to potential threat, and facilitate threat learning, all resulting in the experience of stress (Timmers et al., 2019).

4.3. Cortisol

Although reported stress and pain levels were positively related on the moment-to-moment level, salivary cortisol and pain levels were not. This finding contradicts the hypothesis and parts of previous research (Thieme et al., 2005).

However, this is not the first time that a study finds a mismatch in the degree of psychophysiological correspondence. E.g., in a review on the Trier Social Stress Test, in only 25% of studies cortisol response and self-reported stress were significantly correlated (Campbell & Ehlert, 2012). One important mediating factor in this inconclusive data might be found in sex hormone variability: Studies have found cortisol responses to fluctuate across the menstrual cycle with cortisol reactivity being weaker in phases with low estrogen (like in this study; (Montero-López et al., 2018)). Furthermore, in the early follicular phase (low estrogen) individuals reported increased psychosocial distress in comparison to the periovulatory phase (high estrogen)(Albert et al., 2015).

4.4. Oxytocin

Higher oxytocin levels were expected to be associated with lower pain levels. However, the presented data does not suggest any significant relation between oxytocin and pain on a moment-to-moment level.

Most studies in this field predominantly involve healthy male participants, utilize externally administered oxytocin, and employ experimentally induced pain stimuli (Boll et al., 2020b; Pfeifer et al., 2020; Tracy et al., 2017). Focusing on studies that are more comparable to ours, the findings concerning the relation between endogenous oxytocin and spontaneous pain are mixed. Schneider et al. (Schneider et al., 2023) found oxytocin to be significantly negatively related to emotional pain. For physical pain, they found a non-significant trend for a negative association, matching findings by (Anderberg & Uvnäs-Moberg, 2000). Research suggests that oxytocin levels fluctuate across the day (Engel et al., 2019) and while in our study oxytocin was measured only in the evenings, Schneider et al. (Schneider et al., 2023) took several measures per day enabling them to analyze diurnal variations of the oxytocin-pain-relation. Further research is needed to determine if spontaneous physical pain and endogenous oxytocin merely aren’t related, or if more in-depth studies of diurnal variation are necessary.

4.5. Strengths and Limitations

The design of this study has considerable strengths. The EMA method allowed an assessment of pain processes in a repeated fashion and with great detail, resulting in data of high ecological validity and reliability. Assessing spontaneous real-life pain in relation to daily social interactions and endogenous salivary cortisol and oxytocin during pre-scheduled menstrual cycle phases of high pain variability also contribute to the high ecological validity.

However, the following limitations must be considered: In this study, only distracting and solicitous support were considered. However, other social support styles may also play important roles in the context of chronic pain. While EMA approaches bring many advantages, they rely on real-time self-report data that can be susceptible to mood fluctuations and situational influences. Moreover, participants may change their behavior or responses simply due to feeling monitored. Although individuals were pre-screened for high pain levels, their everyday pain ratings were surprisingly low. This discrepancy may be attributed to the strong wording of the label at the scale maximum (“the most extreme pain I have ever experienced”). Potentially, this caused a bias towards lower pain ratings. The number of measurements of oxytocin were limited (396 observations). These measures were taken at the last measure per day with low variance in the data. Likewise, the number of moments, when actual social support was reported, was limited (328 observations). Interpreting the (missing) link between each measure and pain thus requires caution and confirmation through larger sample sizes and more measurement points.

5. Conclusion and Implications for Future Research

Distracting as well as solicitous social support were found to be related to higher pain ratings on a between-person level, suggesting a long-term effect within the dyad. More research on different social support styles and their impact is due, especially in CPP/endometriosis samples, where intimate relationships are particularly burdened. Also, there is a need for detailed analyses of the long-term effects of social support styles on recurrent or chronic pain syndromes and how these might be used for pain management and psychosocial interventions.

In summary, this study expands previous research suggesting that both stress and social support can have an adverse impact on pain experience in a gynecological/ pelvic pain population. This knowledge is crucial when designing interventions for CPP patients: While stress management may be helpful, social support does not appear to be helpful in improving pain symptoms. Rather, when translating psychosocial interventions to use in patients' daily lives, particularly close or romantic others need more specific advice on how to respond to pain expressions. Here, some guidance on how to exchange immediate and intuitive supportive behavior with positive feedback on agentic behavior might be beneficial.

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[anonymized for peer-review]

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Electronic Supplement

EMA-schedule for one day

prompt	time	items used				
T1	upon awakening	saliva sample (cortisol)	control questions + sleep quality			
T2	T1 + 30min	saliva sample (cortisol)	control questions			
T3	T1 + 45min	saliva sample (cortisol)	control questions	mood, social situation, stress, pain		
T4	11:00	saliva sample (cortisol)	control questions	mood, social situation, stress, pain		
T5	14:00	saliva sample (cortisol)	control questions	mood, social situation, stress, pain		
T6	18:00	saliva sample (cortisol)	control questions	mood, social situation, stress, pain		
T7	when going to sleep	saliva sample (cortisol + oxytocin+ Progesterone + estradiol)	control questions	mood, social situation, stress, pain	Catastrophizing, fear of pain, anxiety, activity, coping, partner worries	sexual health (only on day 4+7)

→ on 7 consecutive days

Fig. S1. Schedule for ecological momentary assessment (EMA).

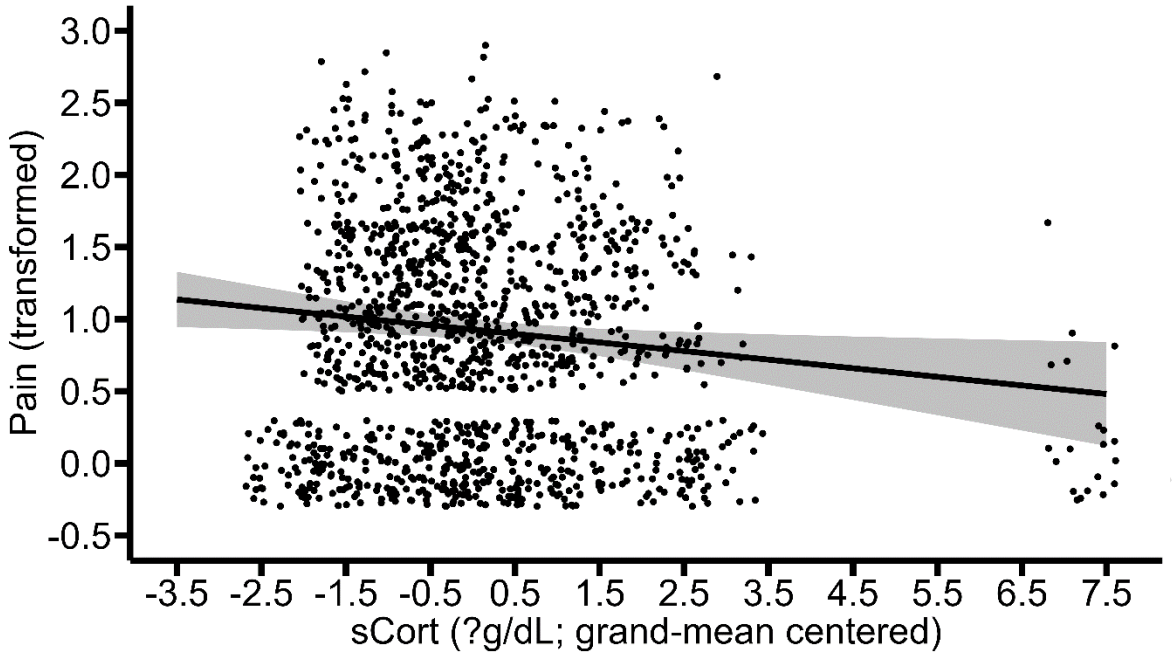

Fig. S2. Between-person association of salivary cortisol (sCort) with pain (non-significant). The graph illustrates the average predicted values of pain (transformed) as a function of sCort. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

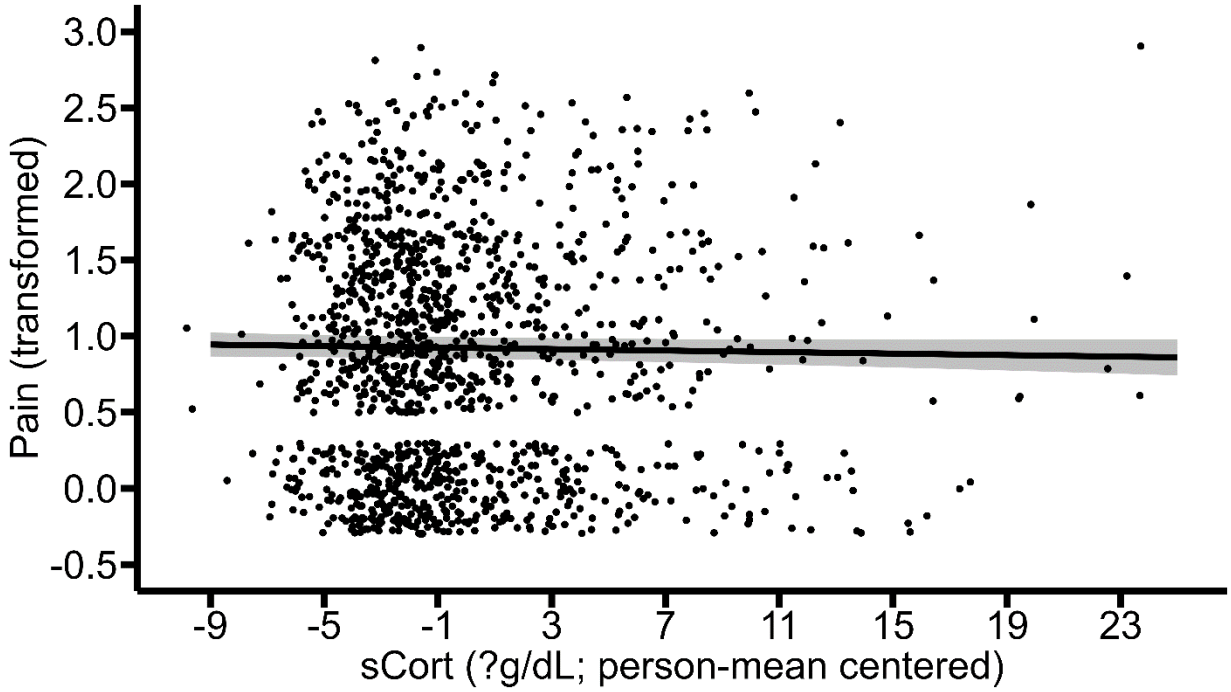

Fig. S3. Within-person association of salivary cortisol (sCort) with pain (non-significant). The graph illustrates the average predicted values of pain (transformed) as a function of sCort. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

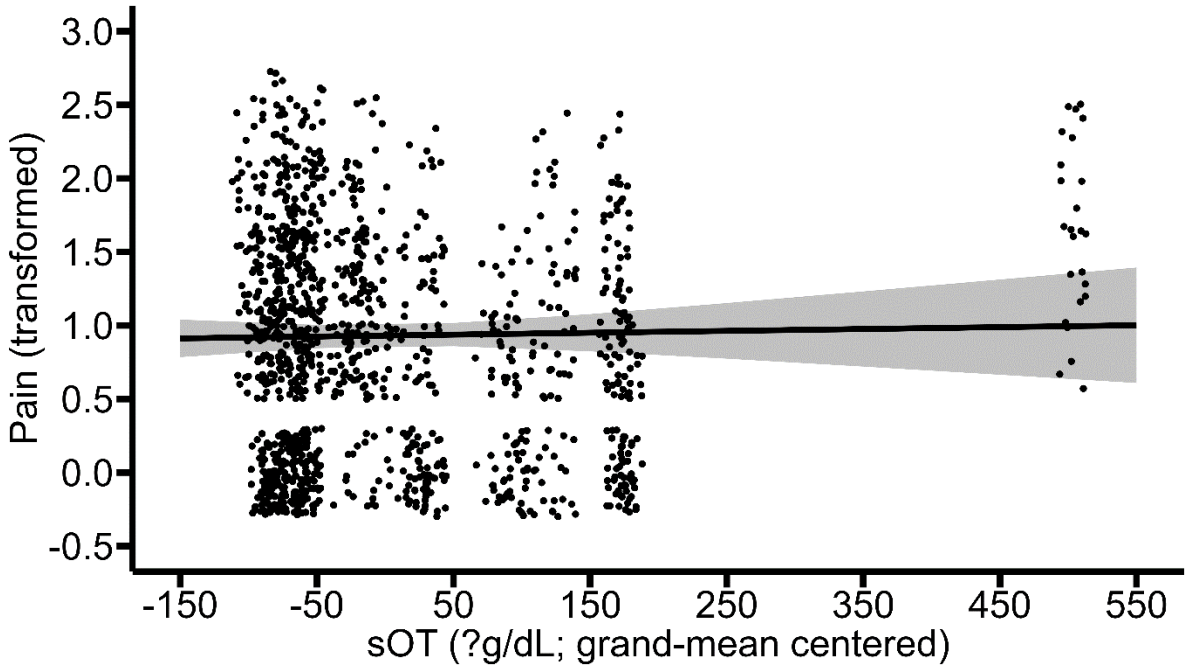

Fig. S4. Between-person association of salivary oxytocin (sOT) with pain (non-significant). The graph illustrates the average predicted values of pain (transformed) as a function of sOT. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

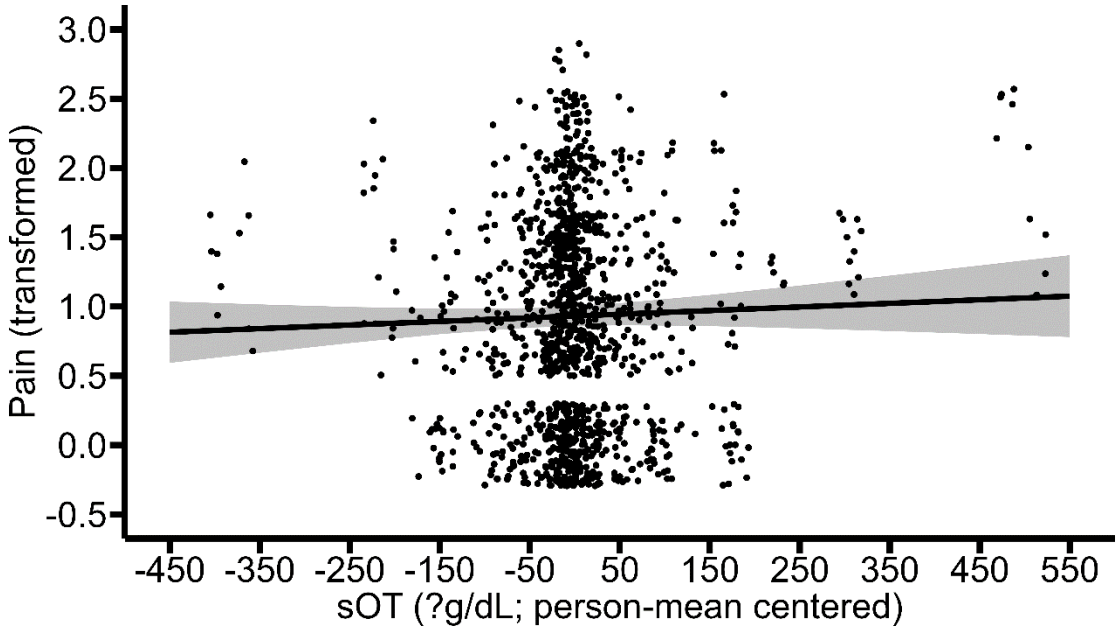

Fig. S5. Within-person association of salivary oxytocin (sOT) with pain (non-significant). The graph illustrates the average predicted values of pain (transformed) as a function of sOT. The ribbon indicates the standard error for the fixed effect. To avoid overlapping data points, they were jittered (adding small random noise) along the x- and y-axis.

Declaration in accordance to § 8 (1) c) and d) of the doctoral degree regulation of the Faculty

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