Childhood Trauma, Interoception, and Impairments in Self and Interpersonal Functioning

Associations between psychological, neurophysiological and endocrinological processes

Inaugural-Dissertation

zur Erlangung des Doktorgrades der Philosophie

an der Ludwig-Maximilians-Universität München

Fakultät für Psychologie und Pädagogik

Lehrstuhl für Klinische Psychologie und Psychotherapie

vorgelegt von

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2023

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Tag der mündlichen Prüfung: 04. Mai 2023

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Danksagung

Von Herzen danke ich all denjenigen, ohne die diese Arbeit nicht zustande gekommen wäre, und die mich auf diesem Weg begleitet und unterstützt haben.

Der größte Dank gilt meiner Doktormutter, Prof. Dr. Katja Bertsch, die mir stets mit ihrer überaus kompetenten und empathischen Art, über meine Promotion hinaus, eine exzellente Betreuung, und persönliche sowie berufliche Weiterentwicklung ermöglicht hat. Ich bin so dankbar, von einer nicht nur ausgezeichneten Wissenschaftlerin, sondern auch menschlich so wertschätzenden Professorin betreut worden zu sein, von der ich unglaublich viel lernen durfte, und die mich so positiv geprägt hat.

Ebenso danke ich ganz herzlich Prof. Dr. Thomas Ehring sowie Prof. Dr. Frank Padberg für die Begutachtung und Ko-Betreuung dieser Dissertation.

Meine Arbeit am Lehrstuhl für Klinische Psychologie und Psychotherapie der LMU ist dank all meiner lieben KollegInnen überaus bereichernd – Danke (Julia, Milena, Celina, Mia, Britta, Mina und allen weiteren...), für die schönen Freundschaften, die entstanden sind! Ein besonderer Dank gilt Aleya sowie Verena, die zeitgleich mit mir am Lehrstuhl, genauer gesagt in Benediktbeuern, gestartet sind und im Laufe der Jahre zu engen Freundinnen wurden. Ebenso möchte ich mich bei Dr. Barbara Cludius bedanken, für ein stets offenes Ohr, Ihre unterstützende Art, die mich gestärkt hat.

Ein weiterer Dank gilt Dr. Marius Schmitz sowie Dr. Marianne Cottin, für die bereichernde Zusammenarbeit, die zu dieser Dissertation beigetragen hat.

Mein wissenschaftliches Interesse am Zusammenhang zwischen Kindheitstraumata, Interozeption und Psychopathologie verdanke ich Dr. Violetta Schaan, von und dank der ich nicht nur wichtige Kenntnisse lernen durfte, die früh zum Fundament dieser Arbeit beigetragen haben, sondern die mir außerdem eine Quelle von Unterstützung, Freundschaft und Inspiration war.

Un merci chaleureux à toutes mes amies tant aimées, en Allemagne, en France et en Suisse. Merci à Aline, non seulement pour la révision (linguistique) minutieuse de ce travail. Und danke, liebe WG, dass ihr mich in München wie zuhause fühlen lasst. Danke Clara, für deine unverzichtbaren Formatierungskünste.

Ich möchte mich bei meiner geliebten Familie bedanken, dafür, dass ihr mich stets aufbaut, immer an mich geglaubt habt, mich so bedingungslos unterstützt, und immer für mich da seid, was diese Arbeit erst ermöglicht hat. Zuletzt gilt mein Dank Max Zettl, meinem überaus geliebten und geschätzten Partner, im Leben wie in der Forschung. Du hast einen unverzichtbaren Teil zu dieser Arbeit beigetragen, keine Worte könnten meiner Dankbarkeit gerecht werden, und meine Gefühle zum Ausdruck bringen.

"*Emotional experience is coupled to the perception of bodily processes.*"

(Rainer Schandry, 1981)

List of Scientific Publications and Author Contributions

Study I

Back, S. N., Zettl, M., Bertsch, K., & Taubner, S. (2020). Persönlichkeitsfunktionsniveau, maladaptive Traits und Kindheitstraumata. *Psychotherapeut*, *65*(5), 374-382.

This chapter is a post-peer-review, pre-copyedited version of an article published in Psychotherapeut. The final authenticated version is available online at https://doi.org/10.1007/s00278-020-00445-7.

Author contributions: S.N. Back and M. Zettl developed the research question and design, collected the data, performed the data analysis and interpretation. S. Taubner provided the funding resources and administered the project. S.N. Back and M. Zettl drafted the manuscript, K. Bertsch and S. Taubner provided critical revisions. All authors approved the final version of the manuscript for submission.

Study II

Back, S. N., & Bertsch, K. (2020). Interoceptive processing in borderline personality pathology: a review on neurophysiological mechanisms. *Current Behavioral Neuroscience Reports*, 7(4), 232-238.

This chapter is a post-peer-review, pre-copyedited version of an article published in Current Behavioral Neuroscience Reports. The final authenticated version is available online at https://doi.org/10.1007/s40473-020-00217-2.

Author contributions: S.N. Back and K. Bertsch developed the study concept and design. S.N. Back conducted the literature research and drafted the manuscript, which K. Bertsch revised. All authors approved the final version of the manuscript for submission.

Study III

Schmitz, M., Back, S.N., Seitz, K.I. Harbrecht, N.K., Streckert, L., Schulz, A., Herpertz, S.C., Bertsch, K. (2022). The impact of traumatic childhood experiences on interoception: disregarding one's own body. Submitted for publication and currently under review in *Borderline Personality Disorder and Emotional Dysregulation*.

This chapter is a pre-copyedited version of a submitted article.

Author contributions: K. Bertsch developed the study concept, S.C. Herpertz provided funding and administered the project. K. Bertsch and M. Schmitz developed the study design. M. Schmitz and K.I. Seitz performed the data collection. M. Schmitz performed parts of the pre-processing, whereas S.N. Back performed the pre-processing of the psychophysiological and behavioural data. N.K. Harbrecht and L.Streckert assisted in the pre-processing of the data. M. Schmitz analysed the data, performed the data interpretation and drafted the manuscript. S.N. Back, K. Bertsch, K.I. Seitz, N.K. Harbrecht, L.Streckert and S.C. Herpertz provided critical revisions. All authors approved the final version of the manuscript for submission.

Study IV

Back, S.N., Cottin, M., Zettl, M., Bertsch, K. (2022). Childhood traumatic experiences and levels of personality functioning: The mediating role of body connection in community samples from Germany and Chile. Submitted for publication in *Child Abuse & Neglect*.

This chapter is a pre-copyedited version of a submitted article.

S.N. Back developed the study concept, S.N. Back and M. Cottin developed the design and performed the data collection. S.N. Back performed the data analysis and interpretation. S.N. Back drafted the manuscript, K. Bertsch, M. Zettl and M. Cottin provided critical revisions. All authors approved the final version of the manuscript for submission.

Study V

Back, S. N., Schmitz, M., Koenig, J., Zettl, M., Kleindienst, N., Herpertz, S. C., & Bertsch, K. (2022). Reduced vagal activity in borderline personality disorder is unaffected by intranasal oxytocin administration, but predicted by the interaction between childhood trauma and attachment insecurity. *Journal of Neural Transmission*, *129*(4), 409-419.

This chapter is a post-peer-review, pre-copyedited version of an article published in Journal of Neural Transmission. The final authenticated version is available online at https://doi.org/10.1007/s00702-022-02482-9.

K. Bertsch and S.C. Herpertz developed the study concept, design and provided funding. Data collection was performed by K. Bertsch, S.C. Herpertz, and M. Schmitz. S.N. Back, M. Zettl and J. Koenig performed the data pre-processing, and S.N. Back performed the data analysis and interpretation. S.N. Back drafted the manuscript, M. Schmitz, M. Zettl, N. Kleindienst, S.C. Herpertz, and K. Bertsch provided critical revisions. All authors approved the final version of the manuscript for submission.

Outline

Current scientific developments in the taxonomy of mental disorders entail a transition from diagnosis-specific nolosgy to a transdiagnostic, dimensional conzeptualization of psychopathology (Dagleish et al., 2020). As mental health difficulties emerge from a complex interplay between biological, behavioral, psychosocial and cultural processes that transcend established diagnostic boundaries (Dagleish et al., 2020), transdiagnostic frameworks are thought to provide a more accurate and informative approach to classifying psychopathological phenomena (e.g., Kotov et al., 2017). This paradigm shift is exemplified by new evidence-based, dimensional models of personality disoders (PDs) in the 5th version of the Diagnostic Statistial Manual of Mental Disorders (DSM-5; APA, 2013) and International Classification if Mental Disease in its 11th version (ICD-11; WHO, 2019). The Alternative Model for Personality Disorder (AMPD) within Section III of the DSM-5 defines personality pathology along dimensional levels of personality functioning. Summarized as Criterion A, personality functioning represent a hierachical model of PD severity composed of impairments in self and interpersonal functioning. Self functioning is further subdivided into identity and self-direction whereas interpersonal functioning is partitioned into empathy and intimacy. More severe impairments in personality functioning are characterized by distorted representation and regulation of oneself in relation to one's social environment, a core dysfunction common to all types of PDs (Sharp & Wall, 2021). In fact, Borderline Personality Disorder (BPD) has been extracted as the most prototypical PD and general factor of all PDs, tapping into more severe deficits in personality functioning (Sharp et al., 2015). Building on the progress of the AMPD, the World Health Organization adapted a dimensional classification of personality pathology for clinical practice within the eleventh version of the ICD-11 (WHO, 2019). Moving forward, a severity dimension of impairments in self and interpersonal functioning replaces all former categorical PD types, whilst keeping an optional, additional categorical BPD pattern (WHO,

2019). Despite the replacement of the traditional PD conceptualization, the DSM-5-AMPD has no explicit theory or treatment implications (see Bach et al., 2018), and research on processes associated with impairments in personality functioning is still sparse. There is little research regarding underlying biopsychosocial processes that affect personality functioning, studies regarding associated constructs in individuals with and without mental disorders are missing.

Numerous theoretical models suggest that that various forms of traumatic interpersonal childhood experiences (TCE) might be important psychosocial risk factors for the development of transdiagnostic psychopathology (McLaughlin et al., 2020), including BPD (Porter et al., 2019). However, no study to date has examined the relationship between levels of personality functioning and TCE in young adults.

Besides interpersonal TCE as a distal, social risk factor, interoceptive processing has been proposed as a more proximal, psychobiological process mediating the relationship between TCE and impairements in self and interpersonal functioning (see Fotopoulou & Tsakiris, 2017 and Löffler et al., 2018 for a review). The efficient sensing, integration, and regulation of body signals during the navigation of one's social environment has been theorized to be shaped by early sensitive caregivers (Fotopoulou & Tsakiris, 2017). Interoceptive processes are critical to maintain essential homeostatic bodily functions (e.g., breathing), as well as higher-order psychological functions, ranging from emotions or a stable and coherent sense of self, to socially adaptive behavior in adulthood (Chen et al., 2021). Recent theoretical approaches therefore propose that reduced sensing, integration and regulation of interoceptive signals may underly the association between TCE and common impairments in self and interpersonal functioning in BPD (see Fotopoulou & Tsakiris, 2017 and Löffler et al., 2018 for reviews). Besides BPD, atypical interoceptive processing has also been considered as a common, transdiagnostic risk factor for various forms of psychopathology (see Brewer et al., 2021 for a review). Interoception subsumes multifaceted processes along the brain-body axis

(Forkmann et al., 2016, Chen et al., 2021) ranging from objective physiological processing, accurate perception and subjective sensibility to meta-cognitive awareness for own bodily signals (Khalsa et al., 2018). Consequently, various interoceptive processes may mediate the relationship between TCE and impairments in self and interpersonal functioning according to DSM-5 AMPD (including lower-hierarchy processes such as emotional dysregulation) in individuals with and without different mental disorders. However, knowledge on which interoceptive processes may underly the association between TCE and impairments in self and interpersonal functioning across individuals with and without different mental disorders, is still lacking.

One hormone potentially implicated in modulating interoceptive processing (Jankowski et al., 2004) is oxytocin. Oxytocin is considered to provide the neuroendocrinological basis for intimate relationships between child and caregiver following pregnancy (Rilling & Young, 2014) and its intranasal administration as been investigated as a potential endocrinological moderator of social functioning in BPD (Herpertz & Bertsch, 2015). Recent theoretical accounts propose that oxytocin encodes the saliency and precision of interoceptive signals, enabling the enhancement of emotional awareness which is important in the development of a sense of self, and its regulation during social interactions (Quattrocki & Friston, 2014). Albeit first studies suggest that intranasal oxytocin administration may enhance objective physiological states of interoception (e.g., heart rate variability) at rest (Norman et al., 2011), no study to date has eximaned if intranasal oxytocin administration may also modulate objective interoceptive processing at rest in BPD.

The overarching aim of the current thesis is to identify biopsychosocial processes associated with personality functioning by examining the complex interplay between endocrinological, neurophysiological, and psychological processes involved in the relationship between TCE, interoception and impairments in self and interpersonal functioning. This thesis

examines personality functioning from the perspective of the AMPD and involves diverse populations, including individuals without mental disorders as well as different mental disorders.

The current thesis (1) investigates the relationship between childhood trauma and levels of personality functioning, (2) tests if and which facets of interoceptive process(es) mediate the association between childhood trauma and self as well as interpersonal impairments in personality functioning in individuals with and without mental disorders, and (3) examined if intranasal oxytocin administration modulates objective interoceptive states in BPD. To adress these objectives, four empirical studies and one literature review were conducted including individuals with and without different mental disorders. This thesis employed a mixed-method design, combining a narrative review of empirical literature, cross-sectional studies, a randomized, double-blind, placebo-controlled trial, and various methods of data collection (i.e., self-report, behavioral, and psychophysiological measures).

The following chapter describes the theoretical and empirical rationale for the endocrinological, neurophysiological, and psychological relationships between childhood trauma, interoception, impairments in self and interpersonal functioning, and oxytocin, divided into three subchapters hierarchically organized following the three aims of this thesis. In the last subchapter, the concrete research aims are summarized. The second chapter presents the five cumulative research studies that were conducted to adress the research objectives of this thesis. In the third chapter, the results of the five studies are summarized and the research aims are discussed based on strenghts and limitations with suggestions for future studies and potential clinical implications. Lastly, the final chapter summarizes this thesis in German.

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1. General Introduction

In the tradition of the longstanding and widely used categorical approach to the classification of psychopathology, mental disorder categories are organized on the basis of distinctions between different sets of signs and symptoms and compiled into compendia of mental disorders (Dagleish et al., 2020). These compendia include the Diagnostic and Statistical Manual of Mental Disorders (DSM, currently available in its 5th edition; APA, 2013) and the International Statistical Classification of Diseases and Related Health Problems (ICD; currently available in its 11th edition; WHO, 2019). However, there is growing consensus that the categorical nosology is of limited purpose in research and clinical practice (e.g., Dagleish et al., 2020; Kotov et al., 2017). The major classification schemes assume that mental disorders represent discrete entities. However, growing evidence suggests continuity between normal and abnormal psychological processes within the population, rather than being categorical, "all-or-none", phenomena (Dagleish et al., 2020). Limitations of categorical models of psychopathology are well documented and include, but are not limited to, extensive comorbidity (Clark, 2007), heterogeneity of symptoms among individuals with the same diagnosis (Johansen et al., 2004), temporal instability (Morey & Hopwood, 2013), and limited clinical utility (Conway et al., 2019; Hengartner & Lehmann, 2017). Consequently, polythetic-categorical models and their significant limitations impede clinical research, assessment, and clinical practice (Cuthbert & Insel, 2013; Dagleish et al., 2020). In response, diverse transdiagnostic approaches to mental health emerged, ranging from softer approaches - seeking commonalities among existing psychopathological entities - to more radical approaches, such as setting existing categorical boundaries completely aside to implement alternative symptom spaces (Dagleish et al., 2020). Radical transdiagnostic approaches include the Hierachical Taxonomy of Psychopathology (HiToP, Kotov et al., 2017) and the Research Domain Criteria (RdoC, Insel et al., 2010). Common goal of these two frameworks was to establish a dimensional classification of mental health difficulties with hierarchically organized series of

continua that promote the search for common biopsychosocial processes of different levels and hierarchies of impairments (Kotov et al., 2017; Insel et al., 2010). One major challenge in those radical transdiagnostic conceptualizations rests in the development of an appropriate theory, as most of these initiatives rely on atheoretical foundations (Dagleish et al., 2020). However, theory is important for translation of data-driven knowledge into appropriate clinical interventions (Ehring et al., 2022). Softer definitions of "transdiagnostic" (Dagleish et al., 2020) encourage the search for alterations and dimensional relationships within as well as across existing diagnostic groups (Barch, 2020). The current thesis combines components of traditional and dimensional approaches to psychopathology, allowing the identification of biopsychosocial processes implicated within disorders, relying upon disorder-specific theoretical models, and common, dimensional levels of impairments across disorders and diagnostic boundaries (Barch, 2020).

The limitations of a categorical classification of psychopathology, as well as the challenges of moving to a dimensional operationalization, are reflected in recent developments in the classification of PDs (see Krueger et al., 2011 for a review). Both clinicians and researchers have long been dissatisfied with the distinction between PD types and have argued for a dimensional operationalization of PD diagnoses (Bernstein et al., 2007; Hopwood et al., 2017; Morey et al., 2014; Tyrer et al., 2019). The classification of personality pathology has its early taxonomic roots in antiquity (when Galen linked the three maladaptive Hippocratic humors to personality types; Kagan et al., 2018) and is currently divided into ten distinct types in the DSM-5 and ICD-10. However, studies have repeatedly failed to replicate the factor structure of various PD types, emphasizing the call by experts for a dimensional system for assessing personality pathology (Clark, 2007; Hopwood et al., 2017). In response, the American Psychological Association's (APA) Personality and Personality Disorders Work Group proposed a hybrid categorical-dimensional model for DSM-5 that combines elements

of dimensional and categorical diagnostics (APA, 2013; Krueger & Markon, 2014). Compared to the DSM-IV PD system, two new dimensional criteria (Criterion A and Critrion B) were introduced. Criterion A defines personality pathology as impairments in personality functioning, assessed on a dimensional scale (APA, 2013). Criterion B determines the nature of pathology using an empirically derived model of 25 maladaptive personality trait facets (APA, 2013; Krueger & Markon, 2014). A threshold of impairment in personality functioning (Criterion A) and the presence of one or more maladaptive facets are used to diagnose the presence of a PD. Thus, personality pathology can be classified based on an individual personality profile, or the clinician can assign one of the six original PD types that the proposed model retains (i.e., schizotypical, antisocial, borderline, narcissistic, avoidant and obsessive-compulsive PD). From the perspective of the DSM-5 working group, the use of a hybrid model should ensure progress in research but also continuity with clinical practice, thus closing the gap in implementation (Morey and Skodol, 2013). However, the APA Board of Trustees ultimately rejected the introduction of the hybrid model into Section II. Consequently, the hybrid model was moved to the newly created Section III (“Emerging measures and models”) and given the name "The DSM-5 Alternative Model for Personality Disorders (AMPD)" (Morey and Skodol, 2013).

Another important step in the shift toward an evidence-based, dimensional taxonomy of personality pathology occurred in the course of the revision to the eleventh version of the ICD (see Mulder, 2021 and Tyrer et al., 2019 for an overview). In the course of the revision, WHO opted for a dimensional approach for assessing personality pathology and replaced former categorical PD types with a unidimensional severity scale of impairments in personality functioning (Mulder, 2021). Effective since 2022, impairments related to aspects of self and interpersonal functioning that may manifest in maladaptive patterns of cognition, emotions and behavior now constitute the entry and core criteria for the classification of personality

pathology (WHO, 2019). The ICD-11 model shares many similarities with Criterion A of the AMPD, also distinguishing between different levels of severity of personality impairment in the domains of self and other (Mulder, 2021). In addition, the presence of one or more personality traits can be marked, analogous to criterion B of the AMPD (Mulder, 2021). The only residual of the traditional PD types is the borderline pattern, which is retained as an optional trait qualifier in ICD-11 (Mulder, 2021).

Impairment in personality functioning according to Criterion A of the AMPD is a unidimensional, hierarchically structured model of PD severity (APA, 2013). Impairments in personality functioning may be conceptually independent of specific PD traits, by rather reflecting the common core of personality pathology as the delayed development of an intrapsychic system crucial to compete with adult duties (Morey et al., 2011; Sharp et al., 2021). This intrapsychic system consists of disturbances related to aspects of self (depicting identity and self-direction) and interpersonal functioning (including empathy and intimacy; APA, 2013). The concept of personality functioning within Criterion A is operationalized using the Level of Personality Functioning Scale (LPFS; APA, 2013). Besides the consistent quantitative empirical evidence of personality pathology divided into two higher-order factors (i.e., self and interpersonal functioning), Criterion A, as a general p-factor for personality pathology, reflects early theories of psychodynamic and developmental psychopathology (Sharp et al., 2021), such as core concepts of more recent approaches (e.g., schema therapy, see Bach et al, 2018 for an overview). Indeed, the DSM-5 working group reviewed several validated psychodynamic measures for the construction of the LPFS, such as the Psychodynamic Diagnostic Manual (Lingiardi & McWilliams, 2017; Sharp et al., 2021) and the Reflective Functioning Scale (Fonagy et al., 1998) (see Bender et al., 2011 for an overview of development). The psychodynamic and developmental framework of psychopathology (Cummings et al., 2020) draws on the role of developmental processes and mechanisms in

association to continuities and discontinuities between normality and psychopathology (Fonagy & Target, 2000). These traditions promote the idea that in order to understand symptoms of psychopathology, it is crucial to consider developmental factors (Cummings et al., 2020) and personality aspects of the person exhibiting those difficulties (Lingardi & McWilliams, 2017; Sharp et al., 2021).

Higher levels of impairment in personality functioning are characterized by distorted representation and regulation of self in relation to the social environment (Sharp et al., 2021). Although common to all types of personality pathology, BPD is considered the most prototypical disorder among the ten PD diagnoses in terms of impairments related to self and interpersonal functioning (Sharp et al., 2015). Albeit its theoretical 256 symptom combinations, and the associated extremely heterogeneous clinical presentation (APA, 2013), recent studies suggest a strong common factor in patients with BPD (Sharp et al., 2015; Smits et al., 2017). Indeed, this common factor strongly aligns with the AMPD's concept of personality functioning, i.e., the assumption that personality pathology can be defined as a central dimension of impairments in self and interpersonal functioning (Bender et al., 2011). In addition to the strong empirical overlap of BPD with various aspects of personality functioning impairments, one reason for retaining the borderline pattern in ICD-11 was to fill the translational gap with clinically effective treatment options (Herpertz & Renneberg, 2020). Contrary to most other PD diagnoses, dedicated therapeutic procedures have been developed for BPD that address the core personality impairments of patients with BPD symptomatology. Those treatments include Dialectic Behavioral Therapy (DBT), which was based on Linehan's Biopsychoscial Model of BPD (Linehan, 1993), and Mentalization-based therapy (MBT; Volkert et al., 2019), building upon mentalization and early attachment theories (see Gunderson et al., 2018 for an overview). Those evidence-based recommendations for treating BPD are applicable to the treatment of Criterion A (see Hopwood, 2018), and therefore, theoretical

models of BPD might also be relevant with regard to personality functioning. For these reasons, as well as due to the high prevalence, high societal costs, and high individual distress, studying relevant processes implicated in BPD in the context of ICD-11 and a dimensional framework of personality functioning is highly relevant.

Despite the replacement of the traditional categorical PD conceptualization, research on biopsychosocial processes associated with impairments in personality functioning, as captured in DSM-5 and ICD-11, is still sparse. There is little research regarding underlying distal and proximate processes that affect personality functioning, studies regarding associated constructs in individuals with and without mental disorders are lacking. Therefore, the present thesis uses a soft transdiagnostic approach, in order to examine hypotheses-driven biopsychosocial processes within BPD, as well as their associations with dimensional impairments in personality functioning across individuals with and without different mental disorders.

1.1 Childhood Trauma and Personality Functioning: Psychological processes

Multifinality, a central principle of developmental psychopathology, states that identical, distal environmental experiences can put individuals at risk for a variety of different developmental outcomes (Cicchetti & Rogosch, 1993), including different forms of mental disorders (see McLaughlin et al., 2020 for a review). *Traumatic childhood experiences* (TCE) are an important distal, lifelong risk factor for the emerge of psychopathology (McCrory et al., 2017). TCE compromise a variety of aversive interpersonal experiences up to 18 years, including, but not limited to, physical, sexual, and emotional abuse or physical and emotional neglect (Bernstein et al., 2003), involving emotionally and/or physically devaluing and/or threatening experiences by early caregivers (Bernstein et al., 2003). Studies suggest that approximately every second child worldwide is exposed to some form of TCE (Hillis et al.,

2016). In fact, TCE may impede early regulatory skills and profoundly impact personality development (Kolb & Gibb, 2014; McLaughlin et al., 2020). First studies observed that individuals who report higher TCE also report greater impairments in personality functioning (see Back et al., 2021 for a review). Especially emotional dysregulation and deficient social information processing have recently been conceptualized as central psychological mediators, besides biological alterations, in the relationship between TCE and transdiagnostic psychopathology (see MacLaughin et al., 2020 for a review). Similarly, a recent study suggests that the DSM-5 levels in personality functioning mediate the relationship between TCE and mental health problems in high-risk samples (d'Huart et al., 2022). The authors propose that personality (dys-)functioning might represent one mechanism potentially explaining observed trajectories of risk (i.e., emotional dysregulation, social information misprocessing through impairments in self and interpersonal functioning) for transdiagnostic psychopathology, and resilience (i.e., social support through higher levels of interpersonal functioning) for mental health following TCE (d'Huart et al., 2022).

The DSM-5 AMPD framework is empirically derived, without explicit theory or treatment implications (see Bach et al., 2018). However, several etiological models align with the concept of personality functioning (see Gunderson et al., 2018 and Bach et al., 2019 for reviews). Across those theories, TCE can be regarded as a distal environmental factor, which, besides biological vulnerability, puts individuals at risk for the emerge of personality pathology, whilst different theories highlight specific lower-hierarchy functions of personality as central concepts to this relationship (see Gunderson et al., 2018 and Bach et al., 2019 for reviews). Prominent theories include Linehan's biopsychosocial theory (1993), Fonagy and Bateman's mentalization theory (2008), such as schema modes (Young et al., 2003), upon which effective treatments options for BPD are based on (e.g., DBT, MBT and schema therapy; see Choi-Kain et al., 2017 for an overview). According to Linehan (1993), TCE primarly

entails invalidation of the child's emotional responses, increasing susceptibility to impaired emotion-, self-regulation and related behaviors such as impulsivity, besides genetic predisposition. Those impairments of the self subsequently lead to dysfunctional behaviors and impairments in interpersonal functioning that further exacerbate the disturbances in self (Linehan, 1993).

Following the schema mode concept (Young, 2003), personality disorders are classified according to underlying schema and modes, with the healthy adult part showing deficits in detecting own needs, regulate emotions and impulses, such as maintain a coherent and positive self-concept, and be self- directed. These deficits in adult mode have recently been hypothesized to aling with transdiagnostic impairments in personality functioning (see Bach et al., 2018 for a review).

Fonagy and Bateman's mentalization theory (2008) states that failed mentalization, as defined by the inability to identify mental states (including emotions, attitudes and preferences) in oneself (e.g., self-awareness) and in others (e.g. empathy), leads to impairments in Self and interpersonal functioning. Mentalization theory builds upon attachment theory (Bowlby, 1988) in that the development of the self and its subsequent regulation in the adult social environment is considered to be shaped early in life by empathetic caregivers, responding to the child's need, mirroring of inner mental states and behaviors and encouraging the child's individuation (Bowlby, 1988). This behavior provides an emotionally secure "basis" from which the child may learn own emotions, needs and preferences as distinct from those of others, reflected in secure adult's internal working models of interpersonal relationships that promote interpersonal intimacy (Bowlby, 1988). Experiencing TCE, in turn, may lead to interpersonal hypersensitivity in assessing and anticipating interpersonal threat or neglect. Although functional in a traumatizing environment, greater external attention for internal and behavioral guidance may reinforce and consolidate beliefs of being abused and neglected in future close

relationships into adulthood (i.e., insecure attachment, Bowlby, 1988). Thereby, TCE has been theorized to disrupt adult self-representations, mental states, and associated behaviors even in a non-traumatizing environment (Fonagy & Bateman, 2008). In support for this perspective on the association between TCE and impairments in personality functioning, Gander et al. (2020) first showed that insecure attachment style mediated the relationship between TCE and DSM-5 levels of personality functioning in clinical and non-clinical samples of young adolescents. However, studies on the relationship between TCE and adult personality functioning according to the AMPD are lacking.

To summarize, theories and empirical studies on TCE, personality functioning, and BPD suggests that higher levels of traumatic experiences are related to higher levels of impairment in personality functioning, in both clinical and nonclinical samples. However, research to date has predominantly relied upon BPD, and most studies on the AMPD to date have been devoted to Criterion B (Zimmernmann et al., 2019). Furthermore, no studies have been conducted on the relationships between different forms of TCE and personality functioning according to the AMPD in adult community samples.

1.2 Childhood Trauma, Interoception, and Impairments in Self and Interpersonal Functioning: Psychological and Neurophysiological Processes

Albeit TCE represent a potentially important risk factor in the emergence of transdiagnostic psychopathology, developmental models of psychopathology underline the pivotable role of more proximate biological and psychological trajectories, in interplay with distal risk factors, for the emergence of transdiagnostic psychopathology in adulthood following TCEs (see McLaughlin et al., 2020 for a review). Investigations on more proximate neurophysiological pathways, that may contribute to explain this association, remain sparse. It has been suggested that *Interoception* (i.e., multifaceted processes by which an organism

senses, interprets, integrates and regulates signals from within the body, Chen et al., 2021) might be one possible biopsychological mediator in the observed relationship between TCE, self and interpersonal (dys-)functioning (see Löffler et al., 2018, Khalsa et al., 2018 for reviews). In the following paragraph, the thesis' definition and conceptualization of interoception will first be introduced, followed by theoretical considerations and empirical evidence on the relationship between TCE, interoceptive processing and self as well as interpersonal functioning.

Interoception can be conceptualized as dynamic, multifaceted processes, covering unconscious interoceptive signal transmission, (sub-)cortical representation and conscious perception of bodily signals such as their integration with attentional, motivational and social processes (Veitl, 1996; Khalsa et al., 2018). Craig (2009) ascribes a crucial role to the insular cortex in the cortical representation and processing of higher order interoceptive signals. According to Craig (2009), the posterior insula is primarly responsible for vestigial visceral-afferent signal representation, whilst during signal transmission towards the anterior insular cortex, various additional information is integrated, including but not limited to motivational, social and cognitive states from the anterior cingulate cortex (ACC) and the ventromedial and dorsolateral prefrontal cortex (Schulz & Vögele, 2020). Similarly, according to Garfinkel et al. (2015) and Forkmann et al. (2016), interoception constitutes distinct facets, including (1) objective physiological states of interoception (measurable by, e.g., heart-beat evoked brain potentials, HEP), (2) interoceptive accuracy (correspondence between actual and perceived bodily signal; measurable by, e.g., heartbeat perception tasks, HBCT, Schandry, 1981), (3) interoceptive sensibility (subjective evaluation of own's own tendency to attend to and perceive bodily signals; measurable by self-report or questionnaires), and (4) interoceptive awareness (meta-cognitive awareness of bodily signals, measurable by correspondence between interoceptive accuracy and sensibility; see table 2 for a detailed overview). In fact, these facets

have been conceptualized as representing distinct dimensions of interoceptive processing, as the strength of associations between single facets ranges from none to medium (Garfinkel et al., 2015; Forkmann et al., 2016). Assessment of multiple interoceptive facets, especially in clinical samples, is therefore important in order to reliably capture the entirety of multifaceted interoceptive processes, when aiming at precise development of tailored treatments (Garfinkel et al., 2016; Schulz & Vögele, 2021).

The earliest research on interoception dates back 150 years and is based on the identification of a set of physiological parameters that define the normal internal state of an organism that the body attempts to maintain (e.g., breath; Cameron, 2001; Chen et al., 2021). This maintenance function was later first introduced as homeostasis (Cameron, 2001; Chen et al., 2021). Since then, interoception has been referred to as the process by which the nervous system perceives and integrates information about the inner state of the body in order to maintain homeostasis (Khalsa et al., 2018). Traditional research on interoception is based on the neurophysiological ascending (i.e., afferent) flow of information from the body (i.e., the periphery) to the brain (i.e., the central nervous system, CNS), with most of research devoted to the cardiac domain (i.e., HEP and HBCT, Garfinkel et al., 2016). However, there are several problems associated with this narrow definition of interoception. First, one-way communication from the body to the brain is assumed, although the flow of information between the body and the brain is bi-directional, constantly interacting and influencing each other depending on internal and external stimuli of an individual in the social environment (Forkmann et al., 2016; Chen et al., 2021). Moreover, interoception and exteroception (i.e., perceiving and processing stimuli outside of the body) cannot be reliably distinguished according to anatomical origins, because proprioceptive, interoceptive, and somatosensory signals may originate from multiple anatomical domains at the same time (Chen et al., 2021). Those concerns recently gave rise to more extensive and inclusive conceptualizations of

interoception (see Schulz & Vögele, 2021 for an overview) as a bi-directional, multisensory process by which an organism senses, interprets, integrates and regulates signals from within the body, in the context of external, social stimulation (Chen et al., 2021, Quigley et al., 2021). Key components of this unified interoception research framework include afferent and efferent neurophysiological tracts as well as non-neural pathways such as hormones. A regulatory efferent and descending pathway is the vagus nerve, which is centrally involved in homeostatic functions for body regulation (Chen et al., 2021). Vagal activity within the cardiac domain can be operationalized, measured, and quantified using heart rate variability (HRV). Several studies demonstrate an important interplay between vagal activity, as measured by HRV, and interoceptive processing (Owens et al., 2018; Schäflein et al., 2018). Moreover, interoceptive accuracy has been found to be improved after vagus nerve stimulation (Villani et al., 2019). In favor of the broader conceptualization of interoception used in the present thesis, HRV is therefore additionally considered an objectifiable indicator of efferent interoceptive states (see table 2).

Table 1

Adapted four facets of interoceptive processing based on Garfinkel et al. (2013), including modifications by Forkmann et al. (2016), Chen et al. (2021) and Price & Thomson (2007).

Facet of Interoception	**Object of physiological states**		**Interoceptive Accuracy**	**Interoceptive Sensibility**	**Interoceptive Awareness**
	Afferent physiological states	**Efferent physiological states**			
Definition	Visceral-afferent signal transmission (i.e., from body to brain)	Visceral-efferent signal transmission (i.e., from brain to body)	objective performance in the perception of interoceptive signals during behavioral tasks	Subjective evaluation of own's own tendency to attend to and perceive bodily signals	meta-cognitive awareness of bodily signals
Parameter/Measurement	Heart-beat evoked potential (HEP)	Heart-rate variability (HRV)	Heart-beat perception task (HBPT, Schandry, 1981)	Scale of Body connection (SBC, Price & Thomson, 2007) or confidence ratings	correspondence between interoceptive accuracy and sensibility
Operationalisation	Event-related electrocortical signal (> 450 ms after R-wave in the electrocardial signal)	The root-mean-square of successive R–R-interval differences in the electrocardiogramm (RMSSD)	Correspondance between actual and perceived heartbeats within specified time intervals	Sum scores of the subscales "body awareness" and "body dissociation" or average Self-reported confidence ratings in HBPT	extent of subjective confidence rating predicting objective interoceptive performance

Note. Table adapted from Garfinkel et al. (2015)

Efficient sensing, integration and regulation of body signals while navigating one's social environment, whether rising to the level of conscious awareness or not, is not only crucial

for maintaining homeostatic bodily functions (for example breathing, maintaining body temperature and blood pressure) but also suggested to serve higher-order psychological functions ranging from emotional needs and a sense of self to socially adaptive behavior (Chen et al., 2021, Smith et al., 2022). The association between interoceptive processing, emotion perception and regulation have first been assumed by James (1884) and Lange (1885), stating that emotional experiences depend on the perception of bodily processes (e.g., feeling sad as a function of crying). Schachter and Singer (1962) likewise assumed, that emotional experience emerges as a function of bodily signals, which are interpretated within a given context (e.g. feeling in love when perceiving elevated heart rate in the presence of a significant other). Since then, many studies linked interoceptive processes to emotion recognition and regulation. A recent meta-analysis showed that higher interoceptive accuracy is associated with higher emotional perception in samples without mental disorders (Parrinello et al., 2022). Füstös et al. (2013) demonstrated that during cognitive reappraisal of emotions, higher interoceptive accuracy was associated with downregulation of affect-related arousal in healthy participants. Multifaceted failure of interoceptive processing (i.e., reduced interoceptive sensitivity and -awareness) has been suggested to underlie alexithymia (i.e., deficits in identifying emotional experiences) in autism spectrum disorder (Brewer et al., 2016; Garfinkel et al., 2016). More recently, research has increasingly been considering the role of interoceptive processing for self-awareness and social functioning (see Chen et al., 2021 for a review). Following Damasio's theory of somatic markers (1996), emotion entails representation and regulation of complex homeostatic changes occurring in the body in a specific context. Extending previous theories on emotion, these 'somatic markers' are thought to influence not only emotion perception, but also decision-making, cognition and (social) approach and avoidance behaviors, especially in complex or uncertain situations (Damasio, 1996), with focus on the insula as neuroanatomical and functional center of self (Craig, 2009). Indeed, the anterior

insula cortex is not only supposed to be involved in conscious perception of bodily sensations (Craig, 2020), but also emotional experiences (Critchley & Garfinkel, 2017) and thought to form representations of the self (Craig, 2009).

Therefore, it has been assumed that interoceptive processes may play a major role in mental health (Khalsa et al., 2018), with atypical interoceptive processing typically observed across several mental disorders, which also show high rates of deficits in emotion regulation, self-and/or social functioning (see Brewer et al., 2021 for a review). Those observations led to the more recent hypothesis that atypical interoception might constitute a transdiagnostic, biopsychological risk factor for psychopathology (see Brewer et al., 2021 for a review), albeit empirical studies examining multiple interoceptive facets across different mental disorders are lacking.

Regarding impairments in personality functioning, Löffler et al (2018) proposed an extension of Linehan's biopsychosocial theory, stating that reduced interoception plays a crucial role in the etiology of pathology related to self and interpersonal functioning. According to their proposed model, reduced interoceptive processing may result from interactions between genetics and TCE, and primarily relates to reduced emotional awareness and emotion regulation, further explaining low levels of self-functioning in BPD. Consequently, diminished interoceptive processing and emotional dysregulation are thought to interact with additional areas of self- (e.g., impulsivity) and, subsequently, with interpersonal domains of functioning (e.g., instable social relationships), resulting in the prototypical symptoms observed in BPD (Löffler et al., 2018). Indeed, there is preliminary evidence of associations between reductions in single interoceptive facets in BPD, self-reported emotional dysregulation and TCE, suggesting that reduced interoceptive processing may reflect neglection of internal sensations in the service of external hypervigilance for behavioral guidance (Müller et al., 2015, Schmitz et al., 2021). However, former studies on BPD concentrated on single facets of interoceptive

processing. Therefore, it remains unclear whether BPD may be characterized by specific alterations in interoceptive facets, and if these are related to TCE and emotional dysregulation. Likewise, Fotopoulou and Tsakiris (2017) emphasized a developmental extension of the mentalizing perspective, in which the connection between bodily processes and mental states, such as emotions, is realted to Self-Other distinction, minimal sense of self, the ability to understand the needs and feelings of others (i.e., empathize), and to form and maintain satisfying social relationships in adulthood. In fact, Fotopoulou and Tsakiris (2017) claim that reflective processes like "mentalizing" might represent higher-order forms of minimal processes of embodied sensations and perceptions (i.e. interoception). According to their theoretical perspective, these processes are importantly shaped by early embodied experiences with caregivers (Fotopoulou & Tsakiris, 2017). Sensitive parenting involves embodied aspects (e.g., physical proximity and touch) and mental capacities (e.g., empathy). Both aspects are thought to be crucial to the child's ability to achieve homeostasis, self-regulate in social environments, and foster higher-order representation of self (Feldman et al., 2014; Fonagy et al., 2002, Stern, 1985). Insensitive parenting and TCE have been theorized to impair the child's ability to form accurate representations of bodily sensations as concomitants of specific emotional states and own needs, that may promote deficits in self and interpersonal functioning until adulthood (Bowlby, 1979; Fonagy & Target, 2002).

Indeed, there is some empirical evidence for these theoretical models. First studies support the relationship between reduced interoceptive processing and impairments in (single domains of) self or interpersonal functioning in individuals with and without mental disorders: Tajadura-Jiménez & Tsakiris (2014) showed that healthy participants with low interoceptive accuracy demonstrated higher alterability of mental self-representations. Moreover, interoceptive sensitivity predicted self-reported levels of empathy in patients with autism spectrum disorder (Mul et al., 2018) and lower self-reported interoceptive sensitivity has been

associated to higher self-reported avoidance of intimate relationships (Oldroyd et al., 2019). Second, first studies suggest an association between TCE and reduced interoceptive processing: Schaan et al. (2019) showed that in healthy participants reduced interoceptive accuracy after an acute stressor was associated with higher self-reported TCE. However, explicit empirical evidence on the above-mentioned models, e.g., the mediating role of interoceptive processing in the relationship between TCE and impairments in self and interpersonal functioning in individuals with and without various mental disorders, taking into account multiple facets of interoception, are lacking.

To summarize, TCE has been theorized to potentially impair the child's ability to form accurate representations of inner bodily sensations, associated homeostatic bodily processes, their integration with emotional experiences, such as higher-order self and interpersonal functions (see Löffler et al., 2018 and Fotopoulou & Tsakiris, 2017 for reviews). According to these frameworks, reductions in interoceptive processes may potentially foster the neglect of internal sensations in service of external hypervigilance for behavioral guidance (see Löffler et al., 2018 and Fotopoulou & Tsakiris, 2017 for reviews). Therefore, reduced interoceptive processing, may mediate the relationship between TCE and impairments in self and interpersonal functioning, as operationalized in the AMPD (including lower-hierarchy processes such as emotional dysregulation and higher-hierarchy process of personality functioning) in individuals with and without different mental disorders. However, it remains unclear whether BPD (representing the most prototypical disorder of impairments in personality functioning, tapping into more severe levels of dysfunctioning) is characterized by specific alterations in interoceptive facets (2.1) and if the same altered interoceptive facet(s) may also explain the relationship between TCE, impairments in emotion regulation (2.2) and

higher-order domains of personality functioning (2.3) across individuals with and without different mental disorders.

1.3 Childhood Trauma, Interoception, and Oxytocin: Psychological, Neurophysiological, and Endocrinological Processes

Oxytocin is an important regulatory hormone specifically implicated in the neuroendocrinological link between sensitive caring and adult social functioning (Herpertz & Bertsch, 2015), which may modulate interoceptive processing (Jankowski et al., 2004). Oxytocin modulates homeostatic bodily functions within the parasympathetic arm of the autonomic nervous system and plays an important role in augmenting prosocial, affiliative behaviors (see Quattrocki and Friston, 2014 for a review). Oxytocin is implicated in providing the neuroendocrinological basis for intimate relationships between child and caregiver following pregnancy (Rilling & Young, 2014). According to an aetiological model of BPD by Herpertz and Bertsch (2015), deficits in self- and interpersonal functioning might interact with lower parental oxytocin levels to activate a neuroendocrine cascade associated with increased vulnerability for TCE, such as the intergenerational transmission of trauma. Indeed, women with BPD exhibit lower basal oxytocin levels compared with women without BPD (Bertsch et al., 2013).

Intranasal-oxytocin administration has been investigated as a potential endocrinological moderator of threat and stress processing in individuals with BPD (see Herpertz & Bertsch, 2018). Besides reducing stress and normalizing approach/avoidance behaviour in BPD (Herpertz & Bertsch, 2018; Schneider et al., 2020), intranasal oxytocin administration demonstrates a beneficial effect on self- (e.g., emotion recognition in autism spectrum disorder; Guastella et al., 2010) and interpersonal functioning (e.g., empathy in healthy individuals; Hurlemann et al., 2010). Moreover, the insula and cingulate cortex, central brain regions

commonly activated by intranasal administration oxytocin (Wigton et al., 2015), are also considered key brain regions for interoceptive processing (Khalsa et al., 2018). Indeed, oxytocin has been shown to modulate the interplay between interoceptive and exteroceptive salience processing within the insula (Yao et al., 2018). In a recent theoretical account, oxytocin has been proposed to encode the saliency and precision of interoceptive signals, enabling the enhancement of emotional awareness, essential for the development of a sense of self and its regulation during social interactions (Quatrokki & Friston, 2014). These empirical results and theoretical considerations suggest that oxytocin might play an important role in self and interpersonal functioning and that intranasal oxytocin administration may modulate and possibly enhance interoceptive processing. However, empirical findings have been mixed: In some studies, intranasal oxytocin administration did not modulate ascending objective physiological states of interoception at rest in patients with BPD (e.g., HEPs, Schmitz et al., 2020) nor interoceptive accuracy at rest in healthy male individuals (Yao et al., 2018). In contrast, in other studies, intranasal oxytocin administration increased descending interoceptive pathways at rest in healthy male subjects (e.g., higher HRV; Norman et al., 2011). More recent empirical studies on the effects of intranasal oxytocin administration on HRV in women even suggest important modulations by levels of self-reported TCE and attachment insecurity (e.g., domain of intimacy within interpersonal functioning) (Schoormans et al., 2020, Riem et al., 2021).

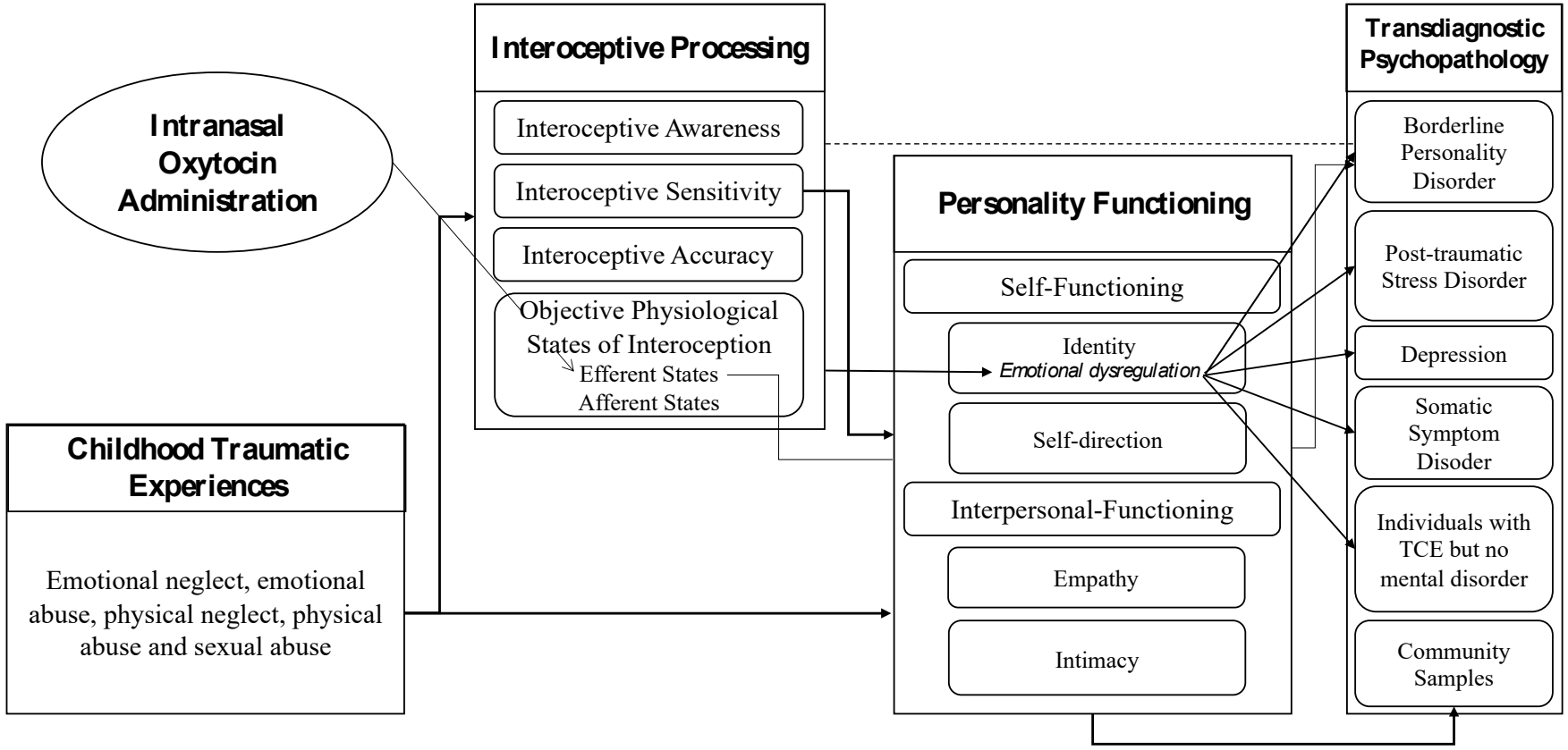
Taken together, evidence suggests that intranasal oxytocin administration may modulate and potentially enhance HRV, an objective indicator of efferent interoceptive states, an effect which might be modulated by TCE and attachment insecurity in women. However, no study investigated the effects of IN-OT on HRV at rest, and explored their interactions with TCE and attachment insecurity, in women with BPD, yet (3).

1.4 Summary and Aims

The taxonomy and nosology of mental disorders is currently facing a paradigm shift: recent developments in the classification of mental disorders mark a shift towards transdiagnostic, dimensional models of psychopathology. This shift is particularly evident in the classification of personality pathology, where the traditional categorical taxonomy of PD types is marked by transitions to quantitively-derived, more dimensional frameworks. However, despite moving towards levels of personality functioning, it lacks explicit empirical evidence on involved processes, enabling the research for causal mechanisms and tailored treatment implications. Therefore, the aim of the current thesis entails research regarding biopsychosocial processes associated with personality functioning, both within BPD and across individuals with and without different mental disorders. A detailed illustration of the biopsychosocial model tested in the current thesis is presented in table 2.

Table 2

Potential biopsychosocial pathways underlying the relationship between Childhood Trauma, Interoception and Personality Functioning



Theoretical and empirical findings suggest that (1) various forms of TCE are associated with impairments in personality functioning, (2) interoceptive processes might mediate the relationship between TCE and impairments in self and interpersonal functioning, and (3) intranasal oxytocin administration may modulate interoceptive processing. However, studies investigating the complex interplay between psychological, neurophysiological and endocrinological processes implicated in the relationship between TCE, interoception and impairments in personality functioning according to the AMPD are lacking. More precisely, studies are required that (1) investigate the associations between different forms of TCE and adult personality functioning from perspective of the AMPD. Concerning the potential mediating role of interoceptive processes for the above-mentioned association, (2) there is a lack of research on multiple interoceptive facets in the relationship between TCE and various lower and higher-order domains of personality functioning (i.e., identity, self-direction, empathy, and intimacy). Regarding potential endocrinological pathways, (3) studies on the modulatory role of intranasal oxytocin administration for efferent interoceptive states and potential moderations by TCE and impairments in interpersonal functioning (e.g., attachment insecurity) are needed.

The aims of the current thesis were threefold. The first aim (1) was to investigate the associations between childhood emotional and physical abuse, neglect, sexual abuse and adult personality functioning in a young-adult community sample. The second aim (2) was to hierarchically elicit the mediating role of multiple interoceptive processes in the relationship between TCE and adult impairments in personality functioning in individuals with and without different mental disorders. The second aim includes (2.1) a narrative review on empirical evidence concerning various multifaceted interoceptive processes in BPD, (2.2) an examination of multifaceted interoceptive processes that mediate the relationship between TCE and emotional dysregulation across different mental disorders (including Post-traumatic Stress

Disorder, PTSD; Major Depressive Disorder, MD and Somatic Symptom Disorder, SSD) and healthy individuals with TCE, and finally (2.3) an empirical test of the hypothesis that the same interoceptive process mediates the relationship between TCE and personality functioning in adult community samples. The third aim (3) was to study potential modulatory effects of intranasal oxytocin administration on HRV (e.g., efferent interoceptive states) at rest in adult women with BPD and its interaction with TCE and attachment insecurity (i.e., impairment in interpersonal functioning).

To achieve these aims, five studies were conducted. First, a cross-sectional online study was conducted to examine the latent associations between different self-reported forms of TCE and personality functions using structural equation modeling. For the second aim, a narrative review synthetized the psychological and neurophysiological evidence on various multiple facets of interoception (including objective physiological states, interoceptive -accuracy, -sensibility and -awareness) in BPD. Moreover, a laboratory study on individuals with TCE and either PTSD, MD, SSD, or no mental disorder was conducted. Multiple facets of interoception were measured by means of questionnaires (e.g., interoceptive sensibility, -awareness), behavioral ratings (i.e., interoceptive accuracy, -awareness) and physiological parameters (e.g., resting-state HRV). Using mediation analysis, the mediating role of interoception in the relation between self-reported TCE and emotional dysregulation was investigated. The fourth study was an online cross-sectional study on the latent mediation of self-reported interoceptive sensibility in the association between self-reported TCE and self and interpersonal functioning in two adult community samples from Germany and Chile. For the third aim, in a placebo-controlled, double-blind, randomized controlled trial, the influence of intranasal oxytocin administration on resting-state HRV in adult women with BPD and matched healthy women was investigated, and its interaction with self-reported TCE and attachment insecurity.

2. Cumulative Studies of this thesis

Study I: Persönlichkeitsfunktionsniveau, maladaptive Traits und Kindheitstraumata

Back, S. N., Zettl, M., Bertsch, K., & Taubner, S. (2020). Persönlichkeitsfunktionsniveau, maladaptive Traits und Kindheitstraumata. *Psychotherapeut*, *65*(5), 374-382. This chapter is a post-peer-review, pre-copyedited version of an article published in Psychotherapeut. The final authenticated version is available online at https://doi.org/10.1007/s00278-020-00445-7.

Persönlichkeitsfunktionsniveau, maladaptive Traits und Kindheitstraumata

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Angaben zur Einhaltung ethischer Richtlinien: Sarah Back, Max Zettl, Katja Bertsch und Svenja Taubner geben an, dass kein Interessenkonflikt besteht. Alle beschriebenen Untersuchungen am Menschen wurden mit Zustimmung der zuständigen Ethik-Kommission, im Einklang mit nationalem Recht sowie gemäß der Deklaration von Helsinki von 1975 (in der aktuellen, überarbeiteten Fassung) durchgeführt. Von allen beteiligten Studienteilnehmern liegt eine Einverständniserklärung vor.

Zusammenfassung

Traumatische Erlebnisse in der Kindheit gelten als bedeutsamer Risikofaktor für Persönlichkeitsstörungen (PS). Allerdings ist die empirische Befundlage zu verschiedenen Formen von Kindheitstraumata und PS inkonsistent. Darüber hinaus fehlt bislang der Einbezug dimensionaler Maße für PS trotz ihres gegenwärtigen Einzugs in diagnostische Manuale. Die vorliegende Studie untersucht die Beziehung zwischen selbstberichteten Kindheitstraumata, dem Funktionsniveau der Persönlichkeit (Kriterium A) sowie maladaptiven Traits (Kriterium B) mittels Strukturgleichungsmodellen in einer Stichprobe junger Erwachsener (N=473). Alle Assoziationen zwischen Traumata, Kriterium A und B sind signifikant. Traumatische Erlebnisse sind stärker mit der Schwere der Funktionsbeeinträchtigung (Kriterium A) assoziiert als mit spezifischen maladaptiven Traits (Kriterium B), wo sich die stärksten Zusammenhänge mit der Persönlichkeitsdomäne „Verschlossenheit“ zeigen. Während körperlicher Missbrauch und körperliche Vernachlässigung sowie sexueller Missbrauch vor allem mit Antagonismus und Enthemmtheit assoziieren, sind emotionaler Missbrauch und emotionale Vernachlässigung mit negativer Affektivität, Verschlossenheit und Psychotizismus assoziiert. Unsere Ergebnisse zeigen, dass einzelne Funktionsbereiche und Traits der Persönlichkeit differentiell mit retrospektiven Traumata assoziiert sind, was die Relevanz dimensionaler Maße von PS für ein differenziertes Verständnis der Beziehung von Persönlichkeitspathologie und Kindheitstraumata unterstreicht.

Stichwörter: Kindesmisshandlung, Kindheitstraumata, Persönlichkeitsstörungen, Persönlichkeitsfunktionsniveau, maladaptive Traits

Abstract

Childhood trauma is an important risk factor for the development of personality disorders (PDs), but the evidence on their differential associations is empirically inconsistent and heterogeneous. There is also a lack of studies on trauma and dimensional measures of PDs, which are currently introduced into the diagnostic manuals. The present study investigates the relationship between self-reported forms of childhood trauma, personality functioning (Criterion A) and maladaptive traits (Criterion B) using structural equation models in a sample of young adults (N = 473). All associations between childhood trauma, Criterion A and Criterion B are significant. Level of Personality Functioning (Criterion A) is more strongly associated with traumatic experiences than with maladaptive traits (Criterion B), which suggests that effects of maltreatment and neglect might be better conceptualized on a continuum of personality pathology rather than a specific type of PD. The association between detachment and childhood trauma is highest within Criterion B, a personality trait that taps into symptoms of post-traumatic stress disorder. Antagonism and disinhibition are mostly associated with physical and sexual abuse, whilst negative affectivity, detachment and psychoticism are mostly associated with emotional trauma and neglect. Our results show that specific levels of functioning and traits are differentially linked to retrospective reports of trauma, underlining the relevance of dimensional models of PDs for a better understanding of the association between childhood trauma and personality pathology.

Keywords: childhood maltreatment, childhood trauma, personality disorders, level of personality functioning, maladaptive traits

Trailer: Die empirische Relevanz dimensionaler Modelle von Persönlichkeitsstörungen (PS), mit der Einführung des alternativen Modells zur Diagnostik von PS im DSM-5 sowie den

Veränderungen mit ICD-11, birgt das Potential die Zusammenhänge zwischen Kindheitstraumata und Persönlichkeitsproblemen differenzierter zu explorieren und zu verstehen. In der vorliegenden Studie untersuchten wir die spezifischen Zusammenhänge zwischen verschiedenen Formen von Traumata, der kontinuierlichen Schwere der Persönlichkeitsbeeinträchtigung, sowie maladaptiven Persönlichkeitsfacetten mittels Strukturgleichungsmodellen.

Kindheitstraumata

Traumatische Erlebnisse in der Kindheit und Jugend umfassen sowohl aktive Handlungen in Form körperlicher, sexueller und emotionaler Misshandlung, als auch passive Erfahrungen wie körperliche und emotionale Vernachlässigung (Manly 2015). Die hohen Prävalenzen schwerer Körperlicher Vernachlässigung (10.8%), schwerer emotionaler Vernachlässigung (6.6%), gefolgt von körperlichem Missbrauch (2.8%), sexuellem Missbrauch (1.9%) und emotionaler Misshandlung (1.6%), unterstreicht die epidemiologische Relevanz von Kindheitstraumata in der deutschen Bevölkerung (Häuser et al. 2011)). Traumatische Kindheitserlebnisse stellen einen erheblichen Risikofaktor für psychische Störungen, chronische Erkrankungen, Suizidalität sowie eine insgesamt verkürzte Lebenserwartung dar (Brown et al. 2009, Felitti 1998, Gilbert et al. 2010, Metzler et al. 2017). Insbesondere Persönlichkeitsstörungen (PS) können mit traumatischer Kindesmisshandlung und -vernachlässigung in Verbindung gebracht werden: PS-Patienten berichten retrospektiv häufiger über körperlichen und sexuellen Missbrauch als Patienten, die nicht von einer PS betroffen sind (Modestin et al. 1998). Längsschnittstudien ergaben, dass junge Erwachsene mit einer Vorgeschichte von Vernachlässigung oder Misshandlung in der Kindheit, ein vierfach erhöhtes Risiko für eine PS aufweisen (Johnson et al. 1999) und zehn der zwölf kategorialen PS-Diagnosen sind mit Kindesmisshandlung und -vernachlässigung assoziiert (Tyrka et al. 2009). Vor allem Patienten mit der Diagnose einer Borderline-PS weisen in zwei von drei Fällen eine Vorgeschichte körperlicher oder sexueller Misshandlung auf (Johnson et al. 1999). Persönlichkeitsstörungen (insbesondere die Borderline-PS) als Traumafolgestörungen zu charakterisieren ist jedoch empirisch umstritten, da die Heterogenität in den Befunden hoch ist, die Effektstärken in meta-analytischen Untersuchungen klein bis moderat ausfallen und bisherige Untersuchungen zu Trauma und Borderline-PS als qualitativ unbefriedigend eingestuft wurden (Tyrka et al. 2009, Hyles et al. 2019). So konnte eine Längsschnittstudie

aufzeigen, dass weder körperlicher noch sexueller Missbrauch in der Kindheit prospektiv die Borderline-PS-Symptomatik signifikant vorhersagen (Zweig-Frank & Paris 2002). Zudem sind verschiedene Formen von Misshandlung nicht spezifisch für einen bestimmten PS-Typ (Brandon et al. 2001). Traumata in der Kindheit scheinen jedoch Persönlichkeitsbeeinträchtigungen zu begünstigen: Einige Befunde sprechen für die Assoziation traumatischer Erfahrungen und allgemeiner Persönlichkeitsbeeinträchtigung oder genereller Persönlichkeitsstörungssymptome (Brandon et al. 2001, Arata et al. 2005, Cohen et al. 2014, Scheffers et al. 2019, Berenz et al. 2013). Insbesondere subklinische Persönlichkeitsproblematiken (erfasst durch dimensionale Maße von PS) weisen einen Zusammenhang mit verschiedenen Formen von Kindheitstraumatisierungen auf, welche jedoch in der klassischen, kategorialen Diagnostik von PS nicht abgebildet werden (Brandon et al. 2001).

Dimensionale Modelle von Persönlichkeitsstörungen

Das Alternative Modell für die Diagnostik von Persönlichkeitsstörungen (AMPD; Krueger et al. 2015, American Psychological Association 2013) in Sektion III des DSM-5, sowie die bevorstehenden Modifikationen in der PS-Diagnostik nach ICD-11 (Tyrer et al 2015) eröffnen einen evidenzbasierten, dimensionalen Zugang zur Diagnostik und Erforschung von PS. Trotz der kontinuierlichen Weiterentwicklung der Diagnosemanuale ist die gegenwärtige kategoriale Diagnostik von PS umstritten, da es den PS-Diagnosen an Validität, Reliabilität und klinischer Nützlichkeit mangelt (Bernstein et al. 2017, Hoopwood et al. 2018; Hyman 2010; Kotov et al 2017; Krueger et al. 2014; Morey et al. 2014). Die Konsequenzen dieser Defizite für die klinische Praxis sind vielschichtig: Die große Zahl an Komorbiditäten (Clark 2007, Grant et al. 2005; Zimmermann et al. 2015), die sehr heterogenen Störungsbilder innerhalb

eines PS-Typus (Johansen 2004) sowie die fehlende zeitliche Stabilität von PS-Diagnosen (bei teilweise gleichbleibender Beeinträchtigung; Gunderson et al. 2011, Zanarini et al. 2012).

Das AMPD operationalisiert PS anhand zwei neuer dimensionaler Kriterien: Beeinträchtigungen im Funktionsniveau der Persönlichkeit (*Kriterium A*) und maladaptive („problematische“) Persönlichkeitsmerkmale (*Kriterium B*). Kriterium A dient der Erfassung der Schwere von Persönlichkeitsbeeinträchtigungen auf einer fünfstufigen Skala (0 = keine oder geringfügige Beeinträchtigung, 4 = extreme Beeinträchtigung). Kriterium B differenziert pathologische Persönlichkeitsdomänen (sogenannte „traits“) und deren Ausprägungen (Krueger et al. 2014). Kriterium B umfasst fünf Merkmalsdomänen: Negative Affektivität, Verschlossenheit, Antagonismus, Enthemmtheit und Psychotizismus, welche empirisch die „Big-Five“ Persönlichkeitsfaktoren als pathologische Gegenstücke komplementieren (Krueger et al. 2014). Das Modell ist hierarchisch gestaltet, jeder Domänenfaktor gliedert sich in zweiter Ebene in fünf Merkmalsfacetten (Zimmermann et al. 2015). Für die Diagnose einer PS nach AMPD muss neben einer mittelgradigen Beeinträchtigung im Funktionsniveau der Persönlichkeit (Kriterium A) mindestens eine maladaptive Merkmalsfacette oder Merkmalsdomäne vorliegen (American Psychological Association 2013). Die Validität dieses Modells wird durch eine beachtliche Anzahl an Studien gestützt (Siehe Zimmermann et al. 2019).

Kindheitstraumata, Persönlichkeitsfunktionsniveau und maladaptive „Traits“ – Gegenwärtiger Forschungsstand

Dimensionale Modelle, wie das AMPD, bergen eine Vielzahl an Vorteilen zur Erforschung der gegenwärtig uneindeutigen Effekte traumatischer Kindheitserfahrungen auf die Persönlichkeit. Die Konsequenzen von Missbrauch und Vernachlässigung können differenzierter im Hinblick auf Persönlichkeitsbeeinträchtigungen (Kriterium A) als auch

bezüglich pathologischer Merkmale der Persönlichkeit (Kriterium B) erfasst werden. Außerdem können aufgrund der dimensionalen Operationalisierung von PS ein breites Spektrum an Beeinträchtigungen abgebildet werden, so unter anderem auch subklinischen Merkmale von PS.

Die bisherige Forschung hat sich bisher ausschließlich traumatischen Kindheitserfahrungen und Kriterium B des AMPD gewidmet. Eine rezente Studie konnte belegen, dass vier der fünf „Traits“ (Negative Affektivität, Verschlossenheit, Antagonismus und Enthemmtheit) den Zusammenhang zwischen SM und internalisierender sowie externalisierender Symptomatik im Erwachsenenalter erklären (Veith et al. 2017). In einer italienischen Studie konnten außerdem die höchsten Zusammenhänge zwischen traumatischen Erfahrungen (Vernachlässigung und emotionaler Missbrauch) und Psychotizismus identifiziert werden, eine Merkmalsdomäne, die vor allem schizotype und dissoziative Charakterzüge abbildet (Borroni et al. 2019). In der gleichen Studie waren Vernachlässigung und emotionaler Missbrauch in der Kindheit stärker mit allen fünf Trait-Dimensionen assoziiert als körperlicher Missbrauch und sexueller Missbrauch. Dies unterstreicht die Relevanz emotionaler Traumata für die Persönlichkeitsentwicklung, was ebenfalls durch Langzeitstudien belegt wird (Zweig-Frank und Paris 2002).

Es fehlen jedoch bisher Nachweise zu traumatischen Kindheitserfahrungen und dem Schweregrad von Persönlichkeitsbeeinträchtigungen, obwohl Kriterium A das „Kernstück“ der PS-Diagnostik nach AMPD darstellt. Außerdem sind bisher keine Studien zu den Effekten emotionaler und physischer Vernachlässigung auf maladaptive Persönlichkeitsmerkmale nach Kriterium B verfügbar, obwohl Borroni und Kollegen (2019) die besondere Relevanz von Vernachlässigung in Assoziation zu kindlichen Traumata nachweisen konnten. Die gegenwärtige Studie untersucht mittels Strukturgleichungsmodellen die Beziehung zwischen verschiedenen Formen traumatischer Kindheitserfahrungen (sexueller Missbrauch, emotionaler

Missbrauch, körperlicher Missbrauch, emotionale Vernachlässigung, körperliche Vernachlässigung), dem Funktionsniveau der Persönlichkeit (Kriterium A) sowie maladaptiven Persönlichkeitsmerkmalen (Kriterium B) in einer deutschsprachigen Stichprobe.

Methodik

Stichprobe

Die Stichprobe wurde über Flyer und Online-Foren rekrutiert, die Datenerhebung erfolgte internetgestützt im Rahmen einer Studie zur dimensionalen Erfassung von Persönlichkeit. Die Gesamtstichprobe umfasst 473 Erwachsene (74.4% weiblich), das Alter betrug im Durchschnitt 24.2 Jahre (SD = 2.9). Die Stichprobe wies ein hohes Bildungsniveau auf: 45.5% verfügten über einen Studienabschluss, 37.2% Abitur, 15.2% über die fachgebundene Hochschulreife oder einen niedrigeren Schulabschluss, 2.1% besuchten noch die Schule. 15.9% der TeilnehmerInnen befanden sich in der Vergangenheit bereits einmal in stationärer oder ambulanter Behandlung aufgrund einer psychischen Störung. 16.3% litten zum Zeitpunkt der Teilnahme an einer psychischen Störung. Die häufigsten selbstberichteten Diagnosen in der Gesamtstichprobe waren affektive Störungen (9%), Persönlichkeitsstörungen (5.4%), Trauma- und stressbezogene Störungen (2.9%) und sonstige Störungen (3.9%).

Instrumente

Traumatische Kindheitserfahrungen. Misshandlung im Kindes- und Jugendalter wurden durch die deutsche Version des „Childhood Trauma Questionnaire“ (CTQ; Bernstein et al. 2003) erfasst. Der Selbstberichtfragebogen enthält 28 Items und besteht aus den fünf Subskalen: emotionale Misshandlung, körperliche Misshandlung, sexueller Missbrauch, emotionale Vernachlässigung und körperliche Vernachlässigung (Bernstein et al. 2003). Jede Subskala wird durch je fünf Items abgebildet, die auf einer 5-stufigen Skala beantwortet werden (1 = überhaupt nicht; 5 = sehr häufig). Der Fragebogen wurde in einer bevölkerungsrepräsentativen

Stichprobe validiert (Klinitzke et al. 2012). Normen für nicht-klinische Stichproben liegen vor (Scher et al. 2001).

Kriterium A. Das Funktionsniveau der Persönlichkeit wurde durch den „Level of Personality Functioning Scale – Self Report“ (LPFS-SR; Morey 2017), ein 80-Item Selbsteinschätzungsinstrument erfasst. Der Fragebogen misst den Schweregrad von Persönlichkeitsbeeinträchtigung in vier Bereichen (Identität, Selbststeuerung, Empathie und Nähe), die Items werden auf einer 4-stufigen Skala (1 = stimme überhaupt nicht zu; 4 = stimme voll und ganz zu) beantwortet (Morey 2017).

Kriterium B. Maladaptive Persönlichkeitsmerkmale wurden durch das „Personality Inventory for DSM 5-Brief Form” (PID-5-BF, Krueger et al. 2013) erfasst. Die 25 Items des Fragebogens werden auf einer 4-stufigen Skala (0 = trifft überhaupt nicht zu; 3 = trifft genau zu) beantwortet. Die fünf Subskalen bilden die 5 Persönlichkeitsdimensionen nach Kriterium B ab: Negative Affektivität, Verschlossenheit, Antagonismus, Enthemmtheit und Psychotizismus. Die deutsche Version des Instruments wurde in zwei Stichproben validiert (Zimmermann et al. 2014).

Statistische Analysen

Im ersten Schritt wurde die faktorielle Güte der verwendeten Fragebögen anhand konfirmatorischer Faktorenanalysen geprüft. Die Modell-Güte wurde mittels mehrerer Fit-Indizes bewertet: der Comparative Fit Index (> .95), der Tucker-Lewis Index (>. 95), und der Root Mean Square Error of Approximation (< .06). Alle Fragebögen wiesen eine zufriedenstellende faktorielle Struktur auf. Im nächsten Schritt wurden zwei Strukturgleichungsmodelle berechnet: Modell 1 besteht aus 6 latenten Faktoren: körperlicher Missbrauch, emotionaler Missbrauch, sexueller Missbrauch. körperliche Vernachlässigung,

emotionale Vernachlässigung (CTQ) sowie Kriterium A (LPFS-SR). Modell 2 bildet körperliche Vernachlässigung, emotionale Vernachlässigung, sexueller Missbrauch. körperliche Vernachlässigung, emotionale Vernachlässigung (CTQ) sowie die Persönlichkeitsdomänen nach Kriterium B ab (Negativer Affekt, Verschlossenheit, Antagonismus, Enthemmtheit und Psychotizismus) (PID-5-BF). In beiden Modellen wurde allen Faktoren gestattet frei zu korrelieren. Für die Berechnung der Strukturgleichungsmodelle wurde der DWLSMV-Schätzer verwendet.

Um die Komplexität und Anzahl zu schätzender Parameter in Modell 1 zu verringern, wurden aus den 80 Items des LPFS-SR jene mit der höchsten Ähnlichkeit zu mehreren Item-Paketen zusammengeführt. Es wurden schrittweise Items mit der höchsten Summe von Varianz und Kovarianz extrahiert. So wurden 25 Item-Pakete gebildet, die jeweils durch drei gemittelte Items abgebildet werden.

Multikollinearität wurde anhand des Variance Inflation Factor ausgeschlossen (< 5). Multivariate Ausreißer wurden mittels der Mahalanobis Distanz ermittelt und ergab für Kriterium A und Trauma sowie für Kriterium B und Trauma 6 signifikante Ausreißer. Von diesen 6 ProbandInnen befanden sich zum Zeitpunkt der Studienteilnahme 5 in Behandlung aufgrund einer psychischen Störung. Deshalb wurde hierbei nicht von einem Eingabefehler, sondern von plausiblen Werten ausgegangen und auf einen Ausschluss der Fälle verzichtet. Der Datensatz enthielt keine fehlende Werte. Sämtliche Analysen wurden in R 3.3.2 (R Core Team, 2017) mit dem Paket „lavaan“ (Rosseel 2012) durchgeführt.

Ergebnisse

Deskriptive Statistiken und Cronbach’s Alpha Werte für die verwendeten Fragebögen sind in Tab. 2 abgebildet. Die Stichprobe verfügte insgesamt über ein hohes Funktionsniveau: Nach Kriterium A wiesen 74% keine Beeinträchtigungen auf, 10% wurden als leicht

beeinträchtigt und 15% als moderat/schwer beeinträchtigt klassifiziert. Die durchschnittlichen Gesamtskalenwerte kindlicher Traumata sind als gering einzustufen. Die Beeinträchtigung im Funktionsniveau weißt einen signifikanten, negativen Zusammenhang zum Bildungsniveau auf ($r = -.32$; $p < .001$), ebenso wie der Gesamtwert maladaptiver Traitausprägung ($r = -.28$; $p < .001$) und der Gesamtwert kindlicher Traumata ($r = -.27$; $p < .001$). Der Gesamtwert maladaptiver Traitausprägung korreliert zudem geringfügig negativ mit dem Alter ($r = -.17$; $p < .001$). Es konnten keine Zusammenhänge zum Geschlecht festgestellt werden. Partielle Korrelationenskoeffizienten für kindliche Traumata und dem Funktionsniveau ($r = .52$; $p < .001$) als auch für kindliche Traumata und der maladaptiven Traitausprägung ($r = .49$; $p < .001$), bei Kontrolle für den Einfluss von sowohl Alter, Bildung als auch psychiatrischen Status, sind als hoch einzustufen. Dies zeigt, dass der überwiegende Anteil der Zusammenhänge auf frühkindliche Traumata und keine konfundierende Variablen zurückzuführen ist.

Tabelle 2

Deskriptive Statistiken und Reliabilitätsanalysen für die Fragebögen CTQ, LPFS-SR und PID-5-BF

		Cronbach Alpha (α)	Mittelwert	Standartabweichung	Spannweite
CTQ	EM	.9	9.73	5.15	20
	EV	.9	10.8	4.92	20
	KV	.56	7.75	3.1	16
	KM	.9	6.3	3.1	20
	SM	.94	6.1	3.0	20
PID-5-BF	Negative Affektivität	.74	6.7	3.2	14
	Verschlossenheit	.72	4.6	3.1	14
	Antagonismus	.79	2.7	2.7	12
	Enthemmtheit	.7	4	2.75	13
	Psychotizismus	.76	4.4	3.1	15
LPFS-SR	Identität	.89	88.7	25.43	123.5
	Selbststeuerung	.87	60.62	20.4	92.5
	Empathie	.8	39.33	13.25	74
	Nähe	.82	73.9	20.46	109

Fußnote: EM = emotionaler Missbrauch, EV = emotionale Vernachlässigung, KV = körperliche Vernachlässigung, KM = körperlicher Missbrauch, SM = Sexueller Missbrauch, CTQ = Childhood Trauma Questionnaire, PID-5-BF = Personality Inventory for DSM-5-Brief Form, LPFS-SR = Levels of Personality Functionning Scale – Self Report

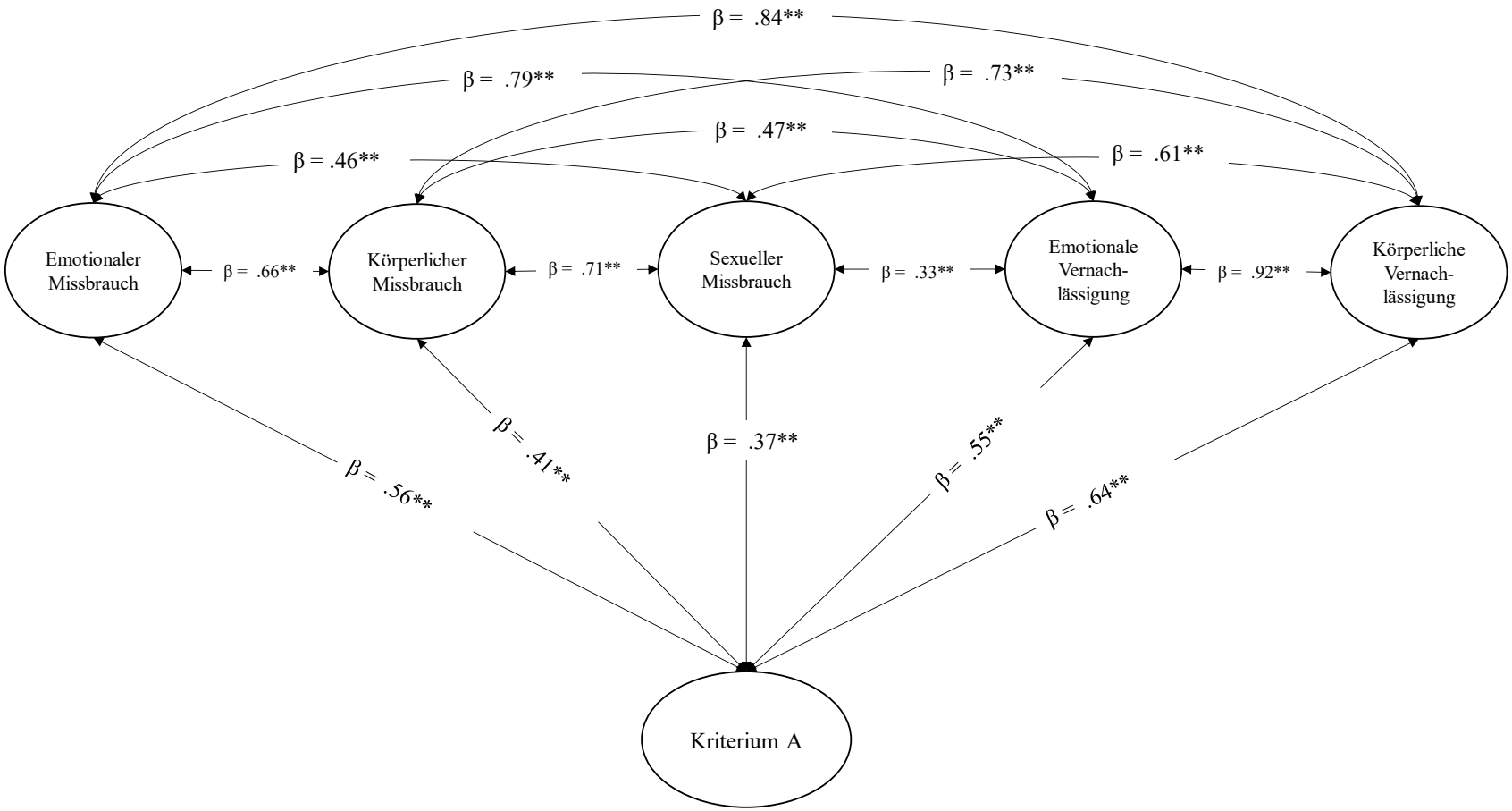
Trauma und Persönlichkeitsfunktionsniveau

Das Modell für körperlichen Missbrauch, emotionalen Missbrauch, sexuellen Missbrauch. körperliche Vernachlässigung, emotionale Vernachlässigung und Kriterium A wies eine gute Passung zu den Daten auf: χ^2 (*1160*) = 1823.990, $p < 0.001$, CFI = .984, TLI = .984, and RMSEA = .035 (.032 - .038). Das Strukturgleichungsmodell ist in Abb. 1 mit standardisierten Pfadkoeffizienten aufgeführt. Standardisierte Pfadkoeffizienten in einem Strukturgleichungsmodell sind mit Korrelationen gleichzusetzen, welche die Stärke der Beziehung zwischen latenten Faktoren widerspiegeln. Alle Pfadkoeffizienten waren signifikant bei $p < 0.01$ und wiesen durchweg moderate bis hohe Korrelationen auf.

Traumatische Erfahrungen sind im Mittel hoch mit dem Funktionsniveau der Persönlichkeit assoziiert (β_{MW} = .61). Der stärkste Zusammenhang zeigt sich zwischen dem Funktionsniveau der Persönlichkeit und körperlicher Vernachlässigung (β_{MW} = .64), gefolgt von emotionalem Missbrauch (β_{MW} = .56), emotionaler Vernachlässigung (β_{MW} = .55) und körperlichem Missbrauch (β_{MW} = .41). Der niedrigste Zusammenhang lässt sich zu sexuellem Missbrauch (β_{MW} = .37) nachweisen.

Abbildung 1

Assoziationen zwischen Funktionsniveau der Persönlichkeit und frühkindlichen Traumata



Fußnote: Die Werte repräsentieren die standardisierten Pfadkoeffizienten β_{MW}. Modelfitwerte: χ^2 (*1160*) = 1823.990, $p < 0.001$, CFI = .984, TLI = .984, and RMSEA = .035 (.032 - .038). Alle Pfadkoeffizienten waren signifikant bei $p < 0.01$ (**)

Trauma und maladaptive Persönlichkeitsmerkmale

Das Modell für körperlichen Missbrauch, emotionalen Missbrauch, sexuellen Missbrauch. körperlicher Vernachlässigung, emotionaler Vernachlässigung und den Persönlichkeitsdomänen nach Kriterium B wies ebenfalls eine gute Passung zu den Daten auf: χ^2 (*1130*) = 1331.887, $p < 0.001$, CFI = .992, TLI = .992, und RMSEA = .019 (.015 - .024). Das Strukturgleichungsmodell ist in Tabelle. 3 mit standardisierten Pfadkoeffizienten aufgeführt. Für eine bessere Übersicht wurden die Interkorrelationen der Trauma-Skalen nicht abgebildet und die latenten Trauma-Faktoren für jede Persönlichkeitsdomäne separat dargestellt. Alle Pfadkoeffizienten waren signifikant bei $p < 0.01$.

Der mittlere Zusammenhang zwischen Kriterium B und traumatischen Kindheitserfahrungen beträgt $\beta_{MW} = .5$, und ist somit niedriger als der berichtete Gesamtzusammenhang in 5.1, jedoch trotzdem als hoch einzustufen. Wie in 5.1 zeigen sich von allen Traumata bei körperlicher Vernachlässigung die stärksten Assoziationen zu maladaptiven Persönlichkeitsdomänen, darunter negativer Affektivität ($ß_{MW} = .4$), Verschlossenheit ($ß_{MW} = .59$), Enthemmtheit ($ß_{MW} = .49$) und Antagonismus ($ß_{MW} = .49$). Lediglich auf Psychotizismus trifft dies nicht zu, welcher den stärksten Zusammenhang zu emotionaler Misshandlung ($ß_{MW} = .49$) aufweist. Von allen Persönlichkeitsdomänen zeigte Verschlossenheit im Mittel den stärksten Zusammenhang zu Kindheitstraumata ($\beta_{MW} = 0.46$).

Tabelle 3

Assoziationen zwischen maladaptiven Traits (Kriterium B) und Kindheitstraumata.

Psychotizismus	Antagonismus	Enthemmtheit	Verschlossenheit	Negative Affektivität	
.69**	.4**	.63**	.63**		NA
.71**	.43**	.52**			V
.63**	.59**				E
.55**					A
					P
.41**	.32**	.37**	.56**	.36**	Emotionale Vernachlässigung
.49**	.34**	37**	.51**	.4**	Emotionaler Missbrauch
.42**	.49**	.49**	.59**	.4**	Körperliche Vernachlässigung
.39**	.42**	.41**	.31**	.26**	Körperlicher Missbrauch
.32**	.47**	.37**	.33**	.22**	Sexueller Missbrauch

Fußnote: Strukturgleichungsmodell für körperlichen Missbrauch, emotionalen Missbrauch, sexuellen Missbrauch. körperlicher Vernachlässigung, emotionaler Vernachlässigung und den fünf Persönlichkeitsdomänen nach Kriterium B (NA = Negative Affektivtät, V = Verschlossenheit, E = Enthemmtheit, A = Antagonismus, P = Psychotizismus). Die Werte repräsentieren die standardisierten Pfadkoeffizienten β_{MW}. Modelfitwerte: χ^2 (*1130*) = 1331.887, $p < 0.001$, CFI = .992, TLI = .992, and RMSEA = .019 (.015 - .024). Alle Pfadkoeffizienten waren signifikant bei $p < 0.01$ (**).

Diskussion

Die gegenwärtige Studie untersucht den Zusammenhang zwischen traumatischen Erfahrungen in der Kindheit, dem Funktionsniveau der Persönlichkeit (Kriterium A) sowie maladaptiven Persönlichkeitsmerkmalen (Kriterium B).

Die Strukturgleichungsmodelle legen nahe, dass traumatische Kindheitserlebnisse und allgemeine Persönlichkeitspathologie insgesamt moderate bis hohe Zusammenhänge aufweisen. Höhere Werte in körperliche Vernachlässigung, emotionale Vernachlässigung, emotionalen Missbrauch, körperlichen Missbrauch und sexuellen Missbrauch sind mit stärkeren Beeinträchtigungen im Persönlichkeitsfunktionsniveau, als auch mit der Ausprägung maladaptiver Persönlichkeitsmerkmale in allen Domänen assoziiert. Dass Vernachlässigung und Missbrauchserlebnisse in der Kindheit mit PS assoziiert sind, deckt sich mit einer Reihe an Untersuchungen (Zweig-Frank & Paris 2002, Borroni 2019).

Die Ergebnisse der Studie zeigen, dass *körperliche Vernachlässigung* (mit Ausnahme von Psychotizismus), konsistent über Kriterium A und B hinweg, am stärksten mit Persönlichkeitspathologie assoziiert ist. Dies legt nahe, dass die Unterlassung elterlicher Fürsorge einen bedeutsamen Risikofaktor darstellt, welcher die Entwicklung einer PS begünstigen kann. Wohingegen sich die meisten Studien mit dem Einfluss aktiven Missbrauchs beschäftigen, zeigen unsere Ergebnisse, dass körperliche Vernachlässigung die stärkste Beziehung zu Persönlichkeitspathologie aufweist, was den Ergebnissen von Borroni (2019) entspricht. Diese Beziehung deckt sich auch mit psychophysiologischen Befunden: Eine Vorgeschichte körperlicher Vernachlässigung ist, entgegen anderer Trauma-Formen, mit basalem Hyperkortisolismus assoziiert (Flory et al. 2009), was wiederum mit Symptomen der Borderline PS bei komorbiden kindlichen Traumata verbunden ist (Jogems-Kosterman et al. 2007). Somit könnte der starke Zusammenhang von körperlicher Vernachlässigung und PS im Sinne der Diathese-Stress-Pathogenese (Holey 2000) erklärt werden. Besonders die

dominierende Prävalenz von körperlicher Vernachlässigung unterstreicht die aktuellen Befunde. Demnach sollten sich Prävention und Intervention, neben Opfern von aktivem Missbrauch, ebenso passiv-vernachlässigten Kindern und Jugendlichen widmen, um schädigenden Effekten entgegenzuwirken.

Kriterium A

Traumatische Erfahrungen sind stärker mit dem Funktionsniveau der Persönlichkeit assoziiert (β_{MW} = .51) als mit maladaptiven Persönlichkeitsmerkmalen (β_{MW} = .5). Bei kontinuierlicher Abbildung der Persönlichkeitspathologie ist die Stärke des Zusammenhangs zu Traumata höher als in Studien welche PS kategorial erfasst haben (Zweig-Frank & Paris 2002) und stützt aktuelle Befunde zu Langzeitfolgen von Traumata in der Kindheit (Cohen et al. 2014, Scheffers et al. 2019). Dies unterstreicht die empirische Relevanz dimensionaler Maße von PS in Kontext von Traumatisierungen im Kindes- und Jugendalter.

Neben körperlicher Vernachlässigung sind noch emotionaler Missbrauch & emotionale Vernachlässigung bedeutsam mit Kriterium A assoziiert. Der Effekt emotionalen Missbrauchs und allgemeiner Vernachlässigung entspricht ebenfalls den Befunden von Borroni und Kollegen (2019) sowie Scheffers und Kollegen (2019). Im Bereich der aktiven Handlungen scheint emotionaler Missbrauch relevanter für den Schweregrad der PS zu sein als sexueller/körperlicher Missbrauch. Die Befunde zu emotionalen Traumatisierungen decken sich mit einem Teil der heterogenen Studienlage zu Trauma und PS (Zweig-Frank & Paris 2002), die inkonsistente Studienlage macht jedoch weitere Untersuchungen zur Relevanz emotionaler Traumata notwendig.

Kriterium B

Von allen Persönlichkeitsdomänen wurde Verschlossenheit im Mittel am stärksten durch kindliche Traumata vorhergesagt ($\beta_{MW} = 0.46$). Die Merkmalsdomäne Verschlossenheit ist charakterisiert durch *sozialen Rückzug*, *Affektarmut*, sowie *Vermeidung von Nähe* und *Depressivität* (29). Dies weist eine starke konzeptuelle Nähe zu Trauma-assoziierter Vermeidung (charakterisiert durch *Dissoziationen*, *Verleugnung* oder *emotionaler „Taubheit"*) auf, was ein typisches Symptom einer posttraumatischen Belastungsstörung darstellt (Zimmermann et al. 2015). Unsere Befunde legen nahe, dass sich die Folgen von Kindheitstraumatisierungen womöglich ebenfalls in einer durch Verschlossenheit geprägten Persönlichkeit abbilden könnten.

Negative Affektivität & Verschlossenheit, welche das Spektrum *internalisierender* Psychopathologie abbilden, sind am stärksten mit körperlicher Vernachlässigung, emotionaler Vernachlässigung & emotionalem Missbrauch assoziiert. Antagonismus & Enthemmtheit hingegen, welche dem *externalisierenden* Spektrum zuzuordnen sind, werden vor allem durch körperliche Vernachlässigung, körperlichen Missbrauch & sexuellen Missbrauch vorhergesagt. Die Befunde legen nahe, dass externalisierende Persönlichkeitssymptomatik vor allem mit physischer Traumatisierung- und internalisierender Symptomatik insbesondere mit emotionalen Traumata assoziiert ist. Dies deckt sich mit empirischen Studien zu kategorialen PS-Diagnosen (Brandon et al. 2001): Für die Antisoziale und Borderline PS, welche sich durch eine deutlich externalisierende Symptomatik von den anderen PS-Typen unterscheiden, wurde der stärkste Zusammenhang zu körperlichem Missbrauch sowie sexuellem Missbrauch berichtet. Für die Vermeidende PS, charakterisiert durch internalisierende Symptome, wurde in der gleichen Studie der stärkste Zusammenhang zu emotionalem Missbrauch gefunden. Zudem zeigen unsere Befunde, dass externalisierende Persönlichkeitspathologie insbesondere durch missbräuchliche Kindheitserfahrungen charakterisiert, internalisierende PS-Symptomatik

dagegen ist erhöht mit Vernachlässigung assoziiert. In Übereinstimmung dazu fanden Arata und Kollegen (2005), dass externalisierendes Verhalten, wie *Aggressivität* und *Ärger* im Erwachsenenalter am stärksten durch körperlichen Missbrauch in der Kindheit erklärt werden konnte, während *Einsamkeit*, *soziale Isolation* und *verringertes Selbstbewusstsein* am meisten durch emotionale Vernachlässigung vorhergesagt wurde, wenn für andere Formen von Trauma kontrolliert wird.

Körperliche Missbrauchserfahrungen, welche im Kern mit elterlicher Gewalt oder Aggressivität verknüpft sind, werden als soziale Lernerfahrungen durch das heranwachsende Kind in Form sozialer Skripte generalisiert und könnten somit externalisierende Verhaltensweisen als erlernte Form sozialer Interaktion erklären. Komplementär dazu fehlen emotional vernachlässigten Kindern emotionale Ressourcen und Lernerfahrung um soziale Interaktionen funktional zu bewältigen, was sich potentiell durch sozialen Rückzug äußern kann (Arata et al. 2014, Abbassi et al. 2010, Bandura 1977). Aus Sicht der Bindungstheorie bewirken ein missbräuchliches Bindungsumfeld und ein Mangel an emotionaler Unterstützung und Sicherheit beim betroffenen Kind Vermeidungstendenzen vor potentiell angstauslösenden sozialen Situationen. Diese wiederum sind langfristig mit einer Inhibition mentalisierungsbasierter Prozesse, fehlender affektiver Regulationsfähigkeit und potentiell psychopathischer Verhaltensneigungen im Erwachsenenalter assoziiert (Taubner et al. 2013, Fischer-Kern et al. 2010, Krischer & Sevecke 2008).

Limitationen

Die Ergebnisse sollten unter Berücksichtigung mehrerer Limitationen interpretiert werden. Zum einen ist die Stichprobengröße für Strukturgleichungsmodelle vergleichsweise klein. Folglich sind manche Parameterschätzungen möglicherweise instabil. Die Stichprobe verfügte über ein sehr hohes Bildungsniveau und beschränkte sich auf junge Erwachsene.

Zudem wies die Mehrheit der Stichprobe ein hohes Persönlichkeitsfunktionsniveau sowie vergleichsweise geringe traumatische Erfahrungen auf. Somit ist die Repräsentativität reduziert und Generalisierbarkeit der Ergebnisse eingeschränkt. Jedoch lässt sich feststellen, dass der partielle Zusammenhang zwischen sowohl Traumata und dem Funktionsniveau, als auch maladaptiven Traits, nachdem Kontrolle für Alter, Bildung und Geschlecht, immer noch substantiell hoch war. Dies spricht für die Bedeutsamkeit des einzigartigen Zusammenhangs zwischen Traumata und Persönlichkeitsstörung in der vorliegenden Stichprobe. Zur Sicherstellung der Validität unserer Ergebnisse sind jedoch weitere Studien mit klinischen Stichproben notwendig. Außerdem basieren die vorliegenden Ergebnisse auf retrospektiven Selbstberichten von Traumata, welche gedächtnisspezifischen Verzerrungen unterliegen können. Zuletzt verhindert das querschnittliche, korrelative Design der Studie kausale Rückschlüsse auf den Zusammenhang zwischen Trauma, Kriterium A und Kriterium B. Zuletzt wurden, im Gegensatz zu Kriterium B, nicht die Assoziationen zwischen Kindheitstraumata und den Subfacetten von Kriterium A im Rahmen des Strukturgleichungsmodells untersucht. Künftige Studien sollten sich demnach den differenzierten Zusammenhängen zwischen Kindheitstraumata und den einzelnen Funktionsbereichen der Persönlichkeit (Identität, Selbststeuerung, Empathie und Intimität) widmen.

Fazit für die Praxis:

- Retrospektive Berichte von körperlichem Missbrauch, emotionalem Missbrauch, sexuellem Missbrauch, körperlicher Vernachlässigung und emotionaler Vernachlässigung sind jeweils signifikant mit dem Funktionsniveau der Persönlichkeit (Kriterium A) und allen 5 Domänen maladaptiver Persönlichkeitsfacetten (Kriterium B) des AMPD assoziiert.

- Die kontinuierlich erfasste Schwere der Persönlichkeitsbeeinträchtigung (Kriterium A) ist stärker mit traumatischen Erlebnissen in der Kindheit assoziiert als mit spezifischen Persönlichkeitsfacetten (Kriterium B), was die empirische Relevanz kontinuierlicher Abbildungen von Persönlichkeitspathologie im Zusammenhang mit Trauma unterstreicht.
- Der hohe Zusammenhang zwischen Traumata und der Persönlichkeitsfacette „Verschlossenheit“ legt nahe, dass sich Kindheitstraumatisierungen potentiell in einer durch sozialen Rückzug, Affektarmut, sowie Vermeidung von Nähe geprägten Persönlichkeit abbilden könnten.
- Externalisierende Persönlichkeitsfacetten (Antagonismus & Enthemmtheit) wurden durchschnittlich vor allem durch körperliche und sexuelle Missbrauchserfahrungen vorhergesagt.
- Internalisierende Persönlichkeitsfacetten (Negative Affektivität & Verschlossenheit) sind insgesamt am stärksten mit emotionalen Traumata und Vernachlässigung assoziiert.

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Study II: Interoceptive processing in borderline personality pathology: a review on neurophysiological mechanisms

Back, S. N., & Bertsch, K. (2020). Interoceptive processing in borderline personality pathology: a review on neurophysiological mechanisms. *Current Behavioral Neuroscience Reports*, 7(4), 232-238. This chapter is a post-peer-review, pre-copyedited version of an article published in Current Behavioral Neuroscience Reports. The final authenticated version is available online at https://doi.org/10.1007/s40473-020-00217-2.

Interoceptive processing in borderline personality pathology: a review on neurophysiological mechanisms

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Katja Bertsch has received funding by the German Research foundation for her work on interoceptive processing in BPD (BE5292/3-2 and BE5292/5-1). The authors Sarah N. Back and Katja Bertsch declare that they have no conflict of interest.

Authors' contributions: S.N.B. has drafted the manuscript which was then revised and rewritten by K.B. Both authors have read and approved the final version of the manuscript. Human and Animal Rights and Informed Consent: All reported studies/ experiments with human subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines). This article does not contain any studies with animal subjects performed by any of the authors.

Abstract

Purpose of Review: This review summarizes empirical evidence on alterations in four distinct interoceptive facets, namely, objective physiological states, interoceptive accuracy, interoceptive sensitivity and interoceptive awareness in borderline personality disorder (BPD) and related conditions. We focus on psychological and neurophysiological mechanisms and discuss their possible relevance for the pathogenesis of BPD.

Recent Findings: Recent findings on objective physiological states suggest that patients with BPD likely exhibit reduced central representation of interoceptive signals as baseline, which might be related to diminished autonomic balance in these patients. Findings on interoceptive accuracy in BPD either suggest reduced or intact interoceptive processing during conscious attention towards inner sensations, eventually presenting a potential target of therapeutic intervention for particular subgroups. Although evidence is sparse, interoceptive sensitivity may be reduced in BPD.

Summary: Distinguishing levels of interoception according to Forkmann et al. (2016) revealed a severe pattern of disturbed neurophysiological processing, including difficulties in representing inner sensations and regulating emotions, such as a generally reduced trait to focus on bodily sensations. We propose a heightened attentional bias towards external cues to guide behavior together with a reduced integration of inner sensations, potentially resulting from a learning history of invalidation of own sensations and feelings in childhood.

Keywords: interoception, borderline personality disorder, heartbeat evoked potentials, heartbeat perception, neurophysiology

Introduction

Borderline personality disorder (BPD) is a severe, complex, and common mental disorder characterized by affective instability, impulsivity, chronic feelings of inner emptiness, and interpersonal problems [1]. The prevalence of BPD is about 1.7% in the general population and up to 15-28% in clinical populations [2].

According to prominent theories, deficits in the processing, recognition, and regulation of own and other peoples' emotions may be regarded as core feature of BPD [3; 4; 5] and there is agreement for the prominent role of early life adversity (ELA) – along with a biological vulnerability – in the etiology of BPD across theories [1]. In fact, ELA is more prevalent in BPD than in any other clinical condition [6] and has been linked emotion dysregulation [7; 3], deficits in mentalization [4], and interpersonal hypersensitivity [5]. It has recently been suggested that impaired interoception, a concept that refers to the processing, awareness, and recognition of own bodily signals, might play a mediating role between ELA and these core symptoms of BPD [8]. More than a century ago, James and Lange were there first to assume an interaction between interoceptive and emotion processes [9,10]. Since then, empirical evidence for an association between the ability to perceive and regulate own emotions and the correct attribution of inner physiological arousal to a specific emotional trigger is increasing – particularly in healthy samples [11]. With regard to the etiology of BPD, it has been assumed that consistent experiences of ELA may lead to a stronger focus on external stimuli as a natural protective strategy to prevent or be prepared for further potentially harmful events, setting the ground for an interpersonal hypersensitivity [1]. At the same time, little attention to own inner processes, feelings, and needs as well as their constant invalidation by caregivers is thought to contribute to emotion dysregulation. Emotion experiences are more strongly associated with external than internal cues and own competences to regulate emotions remain poor due to a lack of learning experiences and parental guidance (Linehan, 1993). If children do not learn that

own emotions are related to physiological reactions, this might also hinder the development of mentalization, i.e., the awareness of own and other peoples' emotions, intentions, and believes as well as the distinction of own inner states and emotions from those of others [4]. In fact, there is first evidence for negative effects of acute and chronic stress, including ELA on interoception [12; 13]. Interoceptive deficits could thus be an interesting mediator between ELA and core symptoms of BPD, including emotion dysregulation, interpersonal hypersensitivity, and poor mentalization, and therefore be a promising target for interventions [8]. However, interoception is not a unique construct, but rather subsumes a dynamic, complex system of several psychophysiological processes with at least four distinct facets [14;15] that should be investigated in detail for a better understanding and treatment of interoceptive deficits. In this review, we therefore first introduce four facets of interoception and their association to an individual's learning history of inner sensations. We will then present currently available evidence for each facet in BPD and related conditions. Finally, we will critically evaluate the existing evidence and discuss challenges and opportunities for future research.

Interoception: A process with multiple facets

Interoception is a dynamic system defined as the "processing of visceral-afferent neural signals by the central nervous system, which can finally result in the conscious perception of bodily processes" [12]. Visceral-afferent signals – information from inner organs – are continuously transmitted to the central nervous system via autonomic pathways. These signals may reach consciousness under certain circumstances, i.e., if a homeostatic threshold is exceeded or if attention is guided towards a certain body process requiring an evaluation of associated signals and their integration with ongoing psychological processes [14; 12]. Since the term "interoception" subsumes the whole system of afferent visceral feedback from unconscious

representations in the central nervous system to the integration of attentional, motivational, and social processes that are strongly associated with an individual's learning history, interoception may be better understood as a *multifaceted system.* In 2015, Garfinkel and Critchley [14] conceptualized three distinct interoceptive processes: (1) *interoceptive accuracy* (IA), the ability to perceive own bodily signals, e.g., one's own heartbeat, in behavioral tasks; (2) *interoceptive sensibility* (IS), a trait or dispositional tendency to focus on interoceptive bodily signals assessable with self-report questionnaires; (3) *interoceptive awareness* (IA), the meta-cognitive awareness about one's own performance measured by the correspondence of actual performance in interoceptive awareness tasks and subjective confidence about this performance. Lately, a fourth process, (4) the visceral-afferent signal transmission and representation has been added as a basic, psychophysiological indicator of interoceptive processing, and defined as *objective physiological states* [15]. Importantly, these four facets of interoception are correlated, but first results suggest that the strength of association may be reduced in some clinical conditions, such as autism spectrum disorder [17], and these reductions predicted clinical symptoms, such as anxiety and emotional deficits in individuals with autism spectrum disorder. Facet-specific interoceptive deficits have also been demonstrated in depersonalization-derealization disorder (DPD) [17] and abuse [18], supporting the importance of analyzing multiple interceptive facets in BPD particularly when aiming at the development of precise interventions.

Objective Physiological States and BPD

Following Forkman et al. [15], we consider objective psychophysiological indicators of visceral-afferent processing the most basic facet of interoception. Afferent neurons encode mechanical and chemical stimuli and transport information to the central nervous system to

maintain and regulate the organism's homeostasis. The vagus nerve contains about 80-85% of afferent fibers that project to the nucleus of the solitary tract (NTS) and further the brain stem and subcortical regions, including the hypothalamus and amygdala. Afferent baroreceptors in the heart and their vessels are responsible for cardiovascular regulation and reflexes, such as the generation of visceral sensations and concomitant emotional feelings [19].

The most prominent central representants of cardiac-afferent signal transmission are *heartbeat evoked potentials* (HEPs), electrocortical potentials which are continuously reaching higher-cortices, do not require conscious perception, and are assessed by electroencephalography (EEG) [20]. The advantage of HEPs compared to other objective measures of interoception is that HEPs do not require conscious attention allocation towards bodily sensations and are not dependent on motivation making HEPs particularly suitable for the study of clinical populations. In 2015, Müller and collegues [21]•• found reduced mean HEP amplitudes in the resting state EEG of 34 unmedicated patients with BPD compared to 31 healthy controls (HC), while HEPs of 17 patients with BPD in remission did not significantly differ from those of the HC. In this study, HEPs were significantly associated with grey matter volume in the left anterior insula and the anterior cingulate cortex (ACC), two prominent brain regions for both interoception and emotion processing. Moreover, HEPs were negatively associated with self-reported emotion dysregulation and emotional childhood abuse. The findings of reduced HEPs in resting state EEG and their association with emotion dysregulation have been recently replicated by the same group in an independent sample of 53 unmedicated BPD patients and 60 HC [22]•. Patients with DPD who, similar to those with BPD, are characterized by emotional numbness, disturbed identity and body ownership did not show an increase in HEP amplitudes from resting state to a condition in which they were asked to consciously focus on interoceptive signals [17]. Since this attentional modulation of HEP is usually found in HC, its lack in patients with DPD suggests difficulties in attending to their inner sensations in a disorder which shows

at least some symptomatic overlap with BPD. Diminished HEP amplitudes have also been reported in patients with major depression, who like patients with BPD frequently report ELA and are characterized by negative affectivity, compared to HC [23]. Together these studies provide first evidence for alterations in the central processing of interoceptive signals related to BPD symptomatology, particularly emotion dysregulation as well as to ELA.

With regard to the cortical representation of interoceptive signals, the association of HEPs with left anterior insular and ACC volume [21]•• are consistent to previous source localization studies [24] and neuroimaging experiments [25] according to which these two regions are crucially involved in the representation and multisensory integration of interoceptive signals. While the dorsal posterior insular cortex is mostly engaged in the mere representation of interoceptive signals, the anterior insula is involved in multisensory integration of interoceptive signals with higher-order cognitive and affective information. The connectivity between ACC and insula has been related to the integration of internal and external stimuli for behavioral guidance [26]. The finding of Müller et al. [21]•• may hence suggest that reduced HEP in BPD rather result from reduced integration and interpretation of interoceptive, emotional, and external signals. This in line with the above mentioned learning history characterized by emotional invalidation and ineffective reflection of the child's emotions by caregivers and a child learning to rely on external emotional cues on the cost of developing an inner understanding of emotional states as behavioral guidance [3], an ability to properly self-other differentiation, an important antecedent of mentalization [4] and eventually deficits in self- and emotion regulation, identity disturbance, feelings of emptiness, and other BPD symptoms.

Despite the attentional modulation of HEPs in HC [20] and the similarity of HEPs between remitted patients with BPD and HCs [21]•• making them a plausible target for interventions, so

far, only one studies has tried to pharmacologically modify BPD patients' resting-state HEPs by intranasal oxytocin administration, however, without significant effects [22]•. Oxytocin has been previously discussed to play an important role in the pathogenesis of BPD being a possible link between ELA and core BPD symptoms, such as interpersonal hypersensitivity, emotion dysregulation, and deficient mentalization [27]. In fact, reduced baseline oxytocin levels have been reported in serum of women with BPD compared to HC [28] and in cerebrospinal fluid of women with ELA compared to women without ELA [29]. Moreover, intranasal oxytocin administration may reduce threat hypersensitivity [30], threat approach [31], and amygdala and insular reactivity to emotionally negative stimuli [30; 32] in individuals with BPD. Since first results in HC indicate an oxytocinergic modulation of interoceptive processing, i.e., reduced interoceptive accuracy, increased right anterior insular activity and connectivity to posterior insula, only in a socio-emotional context, but not at rest [33], further research is needed to explore context-dependent oxytocinergic modulation of interoceptive processing as well as the switching between intero- and exteroception in BPD.

Beside HEPs that are bidirectionally linked with information processing on the brain-body axis, other indicators of efferent signal transmission, such as heartrate variability (HRV) or cortisol levels, might be considered representing the (para-)sympathetic branches and hypothalamus-pituitary-adrenal (HPA) stress axis and, thus, objectifiable physiological indicators for interoceptive processes [12]. Despite heterogenous results, a meta-analysis revealed lower baseline vagally-mediated HRV indices for time and frequency domains with medium effect size in patients with BPD compared to HC [34]. HRV is a common indicator of emotional processing [35] and lower vagal tone has been associated with affective instability and emotion dysregulation [36]. Alterations have also been reported in HPA axis functioning [37]: Across studies, patients with BPD showed elevated continuous cortisol levels at baseline and decreased

cortisol reactivity to social stressors, maybe due to a decreased responsiveness to endogenous ACTH.

Taken together, the results suggest deficits in afferent and efferent information processing along the brain-body axis in patients with BPD which may be a consequence of chronic early stress experiences or ELA although many more studies are needed to elucidate context-specific alterations and the association between different physiological markers in BPD.

Interoceptive Accuracy and BPD

Interoceptive accuracy is usually assessed in "objective" behavioral tests in which participants have to consciously focus on a particular interoceptive signal [25]. Oftentimes, interoceptive accuracy is solely assessed for the cardiovascular domain using either a tracking and a signal detection method. Tracking, also known as heartbeat counting or "Schandry tasks" assesses an individual's accuracy in detecting his/her heartbeats by counting them in a given time interval [38], while discrimination or "Whitehead tasks" present a serious of external auditory, visual, or tactile stimuli and an individual has to judge whether these stimuli are synchronic or not with his/her own heartbeat [39].

So far, evidence on interoceptive accuracy in BPD remains weak with heterogenous findings from a very small number of studies. Using a tracking task, Mussgay and collegues [40] compared interoceptive accuracy of different patient groups, amongst others a group of 26 patients with diverse personality disorders including BPD with 48 HC and found reduced interoceptive accuracy in the personality disorder group vs. HC. However, in a more recent study, Hart and collegues [41] reported no significant difference between 24 patients with BPD

and 30 HC in a tracking and a discrimination task. Although the interpretation of results remains limited due to the small sample size and lack of standardized interview-based diagnostic assessments, they may point to an intact interoceptive accuracy in BPD which is consistent to non-significant differences in heartbeat tracking and discrimination between patients with DPD and HC [42]. As mentioned above, interoception is a multifaceted process and correlations between the facets have been found to be particularly weak in individuals with low interoceptive accuracy [14]. If confirmed by other studies, an intact ability to consciously allocate attention towards interoceptive stimuli may have important therapeutic implications being a potential target for interventions which may also affect other interoceptive facets. In any case, the results underline the importance of understanding and assessing interoception as a multifaceted process particularly when studying its involvement in mental disorders, such as BPD.

The relationship between ELA and interoceptive accuracy has been recently investigated in 66 HC by Schaan and colleagues [43]•: Heartbeat tracking was significantly negatively related with self-reported childhood trauma after a psychosocial stress induction. There was no effect of ELA on heartrate or cortisol levels and these physiological indicators were not significantly related with interoceptive accuracy [43]•. Interestingly, participants who reported higher negative affect at baseline, showed post-stress lower accuracy and baseline negative affect mediated the effects of childhood trauma on interoceptive accuracy after stress [43]•. Negative affect at baseline might rather represent a trait or chronic emotional state following threatening early experiences that hinders the processing of bodily information [43]•. Similar findings of reduced interoceptive accuracy have also been reported in patients with major depression underlining the importance of negative affectivity [44].

Taken together, evidence is still too small and heterogenous to draw any conclusion with regard to BPD and interoceptive accuracy. Further research needs to elucidate whether patients with

BPD are able to and may actually benefit from training the conscious allocation of attention on interoceptive signals.

Interoceptive Sensibility and BPD

Interoceptive sensibility refers to a trait or dispositional tendency to focus on internal signals which may be captured with self-report questionnaires, such as the Multidimensional Assessment of Interoceptive Awareness [45].

So far, only one published study has investigated interoceptive sensibility and BPD [46]. Comparing patients with bulimia nervosa and comorbid BPD to those suffering from bulimia nervosa alone revealed significantly higher disturbances in interoceptive sensitivity (subscale "interoceptive awareness of the Eating Disorder Inventory-2) [47] as well as higher body dissatisfaction for bulimic patients with BPD. Even though the interpretation of this effect is limited due to the comorbid eating disorder, the lack of a HC group, and the small number of items for the interceptive sensibility assessment, it is in line with deficits in body perception as part of BPD diagnosis, amongst others dissociation, chronic feelings of emptiness and inner numbness, depersonalization and derealization. Patients with BPD also evaluate their body more negatively in general [48; 49; 50; 51]. Particularly sexually connotated body parts were negatively associated by patients with BPD and also by those with BPD in remission in whom the difference in evaluations of sexually connotated and neutral body parts were predicted by the severity of sexual abuse in childhood (Kleindienst et al., in press). Finally, in a still unpublished study with Schmitz et al. (submitted) investigated body awareness and body dissociation in 94 patients with a current and 19 with a former BPD diagnosis a well as 96 HC using the Scale of Body Connection [52]. Replicating previous results of Zeeck and collegues [46] they found reduced body awareness and increased body dissociation in BPD. Furthermore,

body dissociation mediated the association between self-reported ELA and emotion dysregulation in the patient sample. Interestingly and contrary to BPD, patients with DPD do not show reduced interoceptive sensibility compared to HC [42].

Together these results provide some first indications for disturbed interoceptive sensibility in BPD. Considering the frequent reports of physical and sexual abuse in BPD, one could speculate that reduced interoceptive sensibility represents a general coping style helping to avoid any kind of bodily sensations that could reactivate traumatic experiences. Moreover, reduced interoceptive sensibility seems inherently linked to identity disturbances and chronic feelings of emptiness – as a lack of general focus on inner processing.

Interoceptive Awareness in BPD

Interceptive awareness is understood is the metacognitive judgment on interoceptive accuracy and refers to the extent of an individual's confidence ratings predicting their own actual interoceptive accuracy (Garfinkel & Critchley, 2013). So far, there are no studies available on interoceptive awareness in BPD.

Conclusion

In this review, we summarized research on interoceptive processes in BPD and related disorders. Based on the presented studies, we conclude that up to now evidence for disturbed interoception is strongest when objective physiological states are assessed. Here, evidence is based on few, but relatively large, well-controlled studies (HEPs) or even meta-analyses including the control of possible confounding variables (HRV, cortisol levels). With regard to

interoceptive accuracy, only two studies with conflicting results and several limitations including small or unspecific samples are available. Although interoceptive sensibility has only been directly investigated in one published study so far which is confounded by a comorbid eating disorder that also influences interoception and does lack a healthy control group, there is accumulating evidence for deficits by studies assessing body evaluation and new, unpublished findings in a large and well-characterized sample of patients with BPD. To date, no data are available on interoceptive awareness in BPD.

From these results, a number of scientific and clinical implications may be drawn: (a) more studies which assess multiple facets of interoception in large samples of patients with BPD in whom BPD symptomatology as well as ELA are assessed with validated measures and who are compared to healthy controls as well as other clinical conditions. The latter is needed in order to assess (b) transdiagnostic and/or disorder-specific alterations in interoceptive processes and their association with ELA. Furthermore, (c) the correlation between different facets of interoceptive processes may help to elucidate specific deficits. In case of a divergence between objective performance, subjective sensibility, and objective physiological markers, this may provide first hints for effects of attention allocation. If patients with BPD are able to accurately perceive their heartbeat when instructed to do so, this could provide a first target for intervention that may eventually also affect other facets of interoception. One should note that mindfulness interventions, such as body scans are already an element of some effective treatment programs for patients with BPD [3]. Furthermore, allocating attention towards interoceptive signals is known to influence objective interoceptive processes (i.e., leading to elevated HEPs in HC). Lastly, (d) research has primarily focused on the cardiovascular domain and the generalizability of these result on interoceptive processes for other domains, such as the respiratory or gut activity is still debated particularly amongst clinical samples.

Taken together, currently available evidence at least partly confirms our hypothesis of deficits in interoceptive processing in BPD. With regard to the hypothesized mediating role of interoception between ELA and emotion dysregulation as the core symptom of BPD, there is first supportive evidence from objective physiological markers in BPD [21]**, interoceptive accuracy in HC [43] and body dissociation and evaluation that are closely related to interoceptive sensibility in BPD (Kleindienst et al., in press; Schmitz et al., submitted.). Theoretically, this closely fits to prominent models of BPD according to which core symptoms of BPD such as emotion dysregulation, interpersonal hypersensibility, and mentalization are closely linked to chronic experiences of invalidation and abuse resulting in a focus on external signals as behavioral guidance instead of listening to inner signals, emotions, and needs [3]. If children do not learn to connect own emotions with physical reactions and if the child's emotions, needs and physiological signals are constantly ignored or invalidated, an external focus is more likely and inner signals will receive less and less attention. Such individuals may learn that the more attention they spend on potential external threats, the more likely they may avoid or escape such threat eventually leading to an interpersonal hypersensitivity as seen in BPD. Furthermore, the development of mentalization requires the mirroring and reflection of a child's emotions by caregivers which amongst others helps building up a stable self-other differentiation as well as the successful recognition and differentiation of own and other people's emotional states [4]. Again, this could involve the processing of interoceptive signals or, in other words, if own bodily signals are not adequately processed, this might interfere the development of self-other distinction and hence mentalization. From a neuroscientific point of few, the anterior insular cortex and the ACC which are both known for their involvement in both representation and integration of interoceptive signals and emotional states with close associations amongst each other as well as with many other brain areas involved in the

processing and regulation of emotion as well as down-stream loops back to the body via amygdala and hypothalamus [24;25].

To conclude, interoception is a multifaceted process that should, in our view, receive further research attention as a possible mediator between ELA and BPD symptomatology as well as target for new interventions.

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Study III: The impact of traumatic childhood experiences on interoception: disregarding one's own body

Schmitz, M., Back, S.N., Seitz, K.I. Harbrecht, N.K., Streckert, L., Schulz, A., Herpertz, S.C., Bertsch, K. (2022). The impact of traumatic childhood experiences on interoception: disregarding one's own body. Submitted for publication and currently under review in *Borderline Personality Disorder and Emotional Dysregulation*. This chapter is a pre-copyedited version of a submitted article.

The impact of traumatic childhood experiences on interoception: disregarding one's own body

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The study was approved by the ethics review board of the Medical Faculty Mannheim, Heidelberg University, and adhered to the Declaration of Helsinki in its current form. All participants gave written informed consent before study participation. The authors report no relevant conflicts of interest. This work was funded by a grant from the German Research Foundation (Deutsche Forschungsgemeinschaft [DFG]), awarded to Sabine C. Herpertz and Katja Bertsch within the GRK2350/1–324164820 (speaker: Christian Schmahl). The data that support the findings of this study are available on reasonable request from the corresponding

author. We thank the team of the research training group GRK2350 for collaboration in participant recruitment and organization.

Authors' contribution: SH, and KB designed the study. MS, and KS recruited the participants. MS collected the data, conducted data analyses, and prepared the first draft of the manuscript. SB conducted HRV analysis. MS, KB, and AS interpreted the results. All authors provided substantive feedback and revisions to the manuscript. The final version of this paper has been approved by all authors.

Abstract

Background**:** Deficient interoception, the processing and perception of internal bodily signals, has been discussed as a mechanism underlying various mental disorders. First results indicate a mediating role of interoception in the interplay of traumatic childhood experiences and adult mental disorders. Traumatic childhood experiences may hinder the adequate processing, integration, and trust in bodily signals that are important in order to understand and regulate own needs and emotions, thereby increasing the vulnerability for mental disorders. However, an overarching study investigating alterations in different interoceptive measures and trauma-related disorders as well as their mediating role between early trauma and emotion dysregulation is still missing.

Methods**:** One hundred thirty-six individuals with varying levels of traumatic childhood experiences who either had a current diagnosis of major depression, posttraumatic stress disorder, or somatic symptom disorder, or no mental disorder, took part in a multidimensional assessment of interoceptive processes, including interoceptive accuracy, sensibility, and awareness. Kruskal-Wallis tests were used to compare groups regarding interoceptive processes and associations with traumatic childhood experiences and emotion dysregulation were analyzed with Spearman correlations. Furthermore, mediation analyses were computed to examine and compare interoceptive processes as potential mediators between traumatic childhood experiences and emotion dysregulation.

Results: Only body dissocation, a measure for interoceptive sensibility, was significantly reduced in individuals with a current mental disorder. Body dissocation was also the only interoceptive measure significantly associated with traumatic childhood experiences and emotion dysregulation and the only significant mediator in the relationship between traumatic childhood experiences and emotion dysregulation across groups.

Conclusion: Results suggest body dissocation, but not other interoceptive measures, as an important feature linking traumatic childhood experiences to current emotion dysregulation, an important transdiagnostic feature. As body dissociation refers to a habitual non-attendance or disregard of interoceptive signals, integrative therapeutic interventions could help affected individuals to overcome difficulties in emotion perception and regulation.

Trial registration: The general study design was preregistered; see the German Clinical Trials Register (DRKS-ID: DRKS00015182). This study's analysis plan was not preregistered.

Keywords: dissociation, stress, trauma, emotion dysregulation, beliefs

Background

Traumatic childhood experiences (TCEs) are an important singular risk factor for mental disorders later in life [1-3]. TCEs include a variety of adverse experiences in childhood, including emotional or physical neglect as well as emotional, physical, and sexual abuse [4]. Despite tremendous progress, the mechanisms and pathways by which TCEs lead to later psychopatholgy are still not fully clear [5-8]. One possible mediator for the observed link between TCEs and psychopathology might be alterations in interoception, i.e. the processing and perception of signals from inside the body [9].

Ranging from afferent signal transmission and its cortical representation to conscious perception of own bodily signals [10, 11], interoceptive processes constitute a multifaceted system. Three important facets include (1) conscious interoceptive processes, which can be operationalised by the correspondence between perceived and actual body signal, e.g., assessed using heartbeat perception tasks (Brener & Ring, 2016) and are referred to as interoceptive accuracy, (2) self-reported evaluation of one's own interoceptive abilities which is known as interoceptive sensibility, and (3) meta-cognitive interoceptive awareness, i.e., the convergence between interoceptive accuracy and sensibility [12].

It has been assumed that interoceptive processes play a major role for mental health [9]. Moreover, it has recently been suggested that TCEs, besides a biological vulnerability, might lead to impaired interoception and thereby to reduced emotional awareness and heightened emotion dysregulation, such as in borderline personality disorder (BPD) [13]. The importance of interoception for emotion perception and regulation has been stated since early emotion theories [14-19]. Interoception includes both the ability and willingness to attend to own inner processes, feelings, and needs. Based on the active inference framework [20-23], interoceptive deficits have been proposed to occur when afferent interoceptive evidence is no longer integrated in inner models of bodily states. The disrepancy between predicted bodily state and

interoceptive evidence results in the emergence of error signals. In the case of adaptive functioning, such error signals are resolved by updating inner models and used to informing actions to (re-)maintain homeostasis [24]. However, inadequate adjustment can lead to a persistent presence of error signals. This may either be due to (1) the afferent signalling itself, such as weak or unprecise interoceptive signals, (2) overly strong inner models, or (3) context rigidity, i.e., the same inner model is maintained even when the context changes. Since interoception is important for homeostasis [25, 26] and emotion regulation [27, 28], with emotion regulation representing strategies to (re-)maintain emotional homeostasis and body-related symptoms, deficient interoception might represent a possible mediating pathway between TCEs and emotion dysregulation.

Indeed, there is first evidence for this assumption. First, alterations in interoceptive processes have been reported in trauma-related disorders, which also show deficits in emotion regulation. Such disorders encompass, but are not limited to, posttraumatic stress disorder (PTSD), BPD, major depression (MD), and somatic symptom disorder (SSD), all of which show high prevalence of TCEs (Chandan et al., 2020; Choi et al., 2019; de Aquino Ferreira et al., 2018; Humphreys et al., 2020; Nelson et al., 2012; Turniansky et al., 2019; Vallati et al., 2020) and exhibit emotion regulation deficits [29-33]. Interoceptive impairments which have been investigated so far yielded inconsistent results of reduced to normal interoceptive signal processing [34-36], as well as reduced to normal interoceptive accuracy [37-40] and reduced interoceptive sensibility [41, 42]. However, it must be noted that, up to now, not all interoceptive dimensions have been studied in all presented disorders. Second, first studies suggest an association between TCEs and interoceptive processes. Interoceptive accuracy and TCEs were negatively associated after an acute stressor in healthy individuals [43] and sympatho-adreno-medullary (SAM) axis activation led to decreased interoceptive accuracy in healthy individuals with TCEs [44]. Third, a first mediation model in women with BPD showed

that body dissociation, a measure for interoceptive sensibility, mediated the link between TCEs and emotion dysregulation in patients with BPD [42]. However, it remains unclear whether altered interoception is limited to trauma-related mental disorders or represents a transdiagnostic feature related to TCEs [28]. This differentiation is crucial to develop new diagnostic and treatment approaches targeting interoceptive dysfunctions.

The current study sought to close this gap. Following a multidimensional conceptualization of interoception [10, 12], we assessed interoceptive accuracy, sensibility, and awareness in a relatively large well-characterized sample of patients with MD, PTSD, or SSD as well as healthy controls with varying levels of TCEs. Additionally, we measured heart rate variability (HRV), i.e., the beat-to-beat variability of heart rate, which represents an index of cardiac control through the autonomic nervous system (ANS) [45] and actual sympathetic and parasympathetic output [46], which has been shown to be reduced in trauma-related disorders [47] and associated with interoceptive processing [48-51].

The aims of the study were threefold. First, we investigated alterations in interoceptive processes among three different mental disorders and healthy individuals. Second, we investigated associations between TCEs, interoceptive processes, and emotion dysregulation across diagnostic categories. Finally, we studied the proposed mediating role of interoceptive processes between TCEs and emotion dysregulation as an important transdiagnostic feature.

Based on previous studies, we expected to replicate interoceptive impairments in trauma-related disorders and explored the specificity of previous findings compared to clinical controls. Moreover, since previous studies included heterogenous samples of patients with and without TCEs, we were able to further inspect the impact of TCEs on interoceptive processes. We expected negative associations between interoceptive processes and both TCEs as well as emotion dysregulation, and that interoceptive processes significantly mediate the relationship between TCEs and emotion dysregulation across groups.

Methods

Design

This research was part of a larger study on the shared effects of TCEs on social information processing across different mental disorders with high prevalence of TCEs, consisting of patients with MD, PTSD, and SSD, as well as HC (German Clinical Trials Register: DRKS00015182). Therefore, a multiple-group cross-sectional design was employed, including participants with varying levels of TCEs following a further dimensional conceptualization. The original study is part of the German Research Foundation's Research Training Group 2350, dedicated to investigating the impact of adverse childhood experiences on psychosocial and somatic conditions across the life span [52]. All participants gave written informed consent before their participation and were reimbursed for their participation. The study was approved by the ethics review board of the Medical Faculty Mannheim, Heidelberg University.

Recruitment and enrollment

Participants were recruited from online announcements, flyers, and through a clinical referral from inpatient and outpatient departments. All participants were fluent in the German language.

Inclusion and exclusion criteria: General exclusion criteria for all participants were (a) age under 18 years or over 60 years; (b) neurological disorders; (c) current substance abuse, assessed via urine toxicology screening and clinical interview; (d) severe medical illness; (e) pregnancy, and (f) left-handedness due to fMRI measurements (not reported here). Additional general exclusion criteria for participants with mental disorders were lifetime diagnoses of schizophrenia, schizoaffective, or bipolar disorder and severe substance use disorder in the last two years. Inclusion of psychotropic medications for participants with mental disorders were

limited to regularly prescribed antidepressants, antipsychotics (sleep-inducing effect only), and/or anticonvulsants (i.e., pregabalin, pain-relieving effect only) (see Table S1 in the Supplement).

Participants with mental disorders had to fulfill diagnostic criteria for a diagnosis of PTSD, MD, or SSD, with diagnostic group allocation based on the current diagnosis that had been made first during the participant's lifetime. Therefore, participants could be diagnosed with up to three of these disorders of interest (i.e., MD, PTSD, SSD), but were excluded if the current diagnosis was not determined as first lifetime disorder. Mental disorders were assessed with the Structured Clinical Interview for DSM-5 (SCID-5) [53].

The inclusion criterion for *healthy controls (HC)* was the absence of any mental disorder, either current or lifetime, as assessed using the SCID-5.

Out of 140 adult participants, four individuals were excluded from the current analysis due to cardiac arrhythmia (n=1) or missing of both behavioral and self-reported data on interoception (technical problems and non collecting self-reports, n=2; dropout due to aberrant neurological finding, n=1), resulting in a final sample of 136 participants (see Table 1 and Table S1 in the Supplement for details). All participants experienced at least one TCE and were classified into the four diagnostic groups MD (N=35 [24 female], M_{age}=31.74, SD=12.09 years), SSD (N=34 [26 female], M_{age}=30.09, 11.59 years), PTSD (N=33 [28 female], M_{age}=34.33, SD=12.48 years), and HC (N=34 [27 female], M_{age}=29.56, SD=9.64 years). The groups did not differ in age ($F_{3,132}$=1.17, p=.326), body-mass-index ($F_{3,132}$=1.23, p=.303), highest school degree (Kruskal-Wallis test: H[3]=5.41, p=.144), or sex distribution ($\chi^2_{df=3}$=2.68, p=.447).

Table 1

Sample Characteristics

Data	Mean±SD (Mdn; IQR)				*H* Value	*p* Value[a]	*p* Value[b]					
	MD (*n*=35) (24 women)	**SSD (*n*=34) (26 female)**	**PTSD (*n*=33) (28 female)**	**HC (*n*=34) (27 female)**			***MD vs SSD***	***MD vs PTSD***	***MD vs HC***	***SSD vs PTSD***	***SSD vs HC***	***PTSD vs HC***
Depression severity (BDI-II)[c]	32.74±9.65 (31.00; 18.00)	16.26±9.49 (17.50; 17.75)	25.33±11.57 (25.00; 19.00)	5.12±4.52 (4.00; 8.25)	78.96	<.001	<.001	.283	<.001	.039	.002	<.001
SSD-12 [c]	18.46±10.91 (18.00; 16.00)	30.56±6.58 (31.00; 8.25)	19.52±9.81 (20.00; 13.00)	7.91±8.07 (5.00; 11.00)	60.90	<.001	<.001	1.00	.001	.001	<.001	<.001
PHQ-15 [c]	11.43±5.00 (11.00; 6.00)	12.62±4.79 (13.00;6.00)	12.45±5.53 (13.00; 7.00)	6.65±5.07 (6.00; 7.50)	25.10	<.001	1.00	1.00	.007	1.00	<.001	<.001
PCL-5	27.46±19.13 (29.00; 32.00)	17.03±15.29 (12.50; 17.25)	41.36±13.16 (41.00; 22.00)	8.56±11.01 (3.50; 12.00)	55.68	<.001	.160	.027	<.001	<.001	.200	<.001
Early Traumatization (CTQ)	47.34±13.46 (45.00; 18.00)	40.79±12.37 (37.50; 17.25)	69.82±22.84 (71.00; 33.00)	47.65±17.95 (44.00; 28.50)	33.69	<.001	.401	.001	1.00	<.001	.893	<.001
Emotional Abuse	12.91±5.46 (13.00; 9.00)	10.29±4.71 (9.00; 5.25)	17.97±6.20 (20.00; 11.00)	12.18±5.71 (11.00; 10.50)	25.57	<.001	.340	.015	1.00	<.001	1.00	.002
Physical Abuse	7.20±2.92 (6.00; 3.00)	6.56±2.96 (5.00; 2.25)	11.94±6.10 (10.00; 9.50)	9.09±5.21 (7.50; 6.00)	26.22	<.001	1.00	<.001	1.00	<.001	.062	.115
Sexual Abuse	6.17±2.92	5.59±2.06	10.85±6.50	6.18±2.90	35.65	<.001	1.00	<.001	1.00	<.001	1.00	<.001

	(5.00; 1.00)	(5.00; 0.00)	(9.00; 8.00)	(5.00; 0.00)								
Emotional Neglect	13.74±5.34 (13.00; 6.00)	11.44±5.05 (11.00; 8.00)	18.06±5.53 (20.00; 9.00)	12.38±4.93 (12.00; 9.00)	23.96	<.001	.545	.020	1.00	<.001	1.00	.001
Physical Neglect	7.31±2.61 (7.00; 3.00)	6.91±2.37 (6.00; 4.00)	11.00±4.58 (11.00; 8.00)	7.82±3.13 (7.00; 4.25)	20.47	<.001	1.00	.003	1.00	<.001	1.00	.020
DERS [c]	116.60±22.68 (117.00; 32.00)	99.09±20.82 (97.50.00; 29.00)	116.39±22.04 (119.00; 28.50)	78.79±19.66 (80.00; 25.00)	47.76	<.001	.025	1.00	<.001	.024	.014	<.001
FDS [d]	13.95±9.91 (12.50; 12.05)	10.81±8.22 (7.73; 10.51)	16.73±12.22 (12.27; 10.68)	6.39±6.28 (4.55; 6.19)	24.62	<.001	1.00	1.00	.001	.187	.074	<.001
BSI	1.41±0.53 (1.36; 0.51)	0.80±0.42 (0.75; 0.78)	1.26±0.67 (1.17; 1.19)	0.31±0.35 (0.22; 0.15)	66.87	<.001	.002	1.00	<.001	.059	.001	<.001

Abbreviations: BDI-II, Beck Depression Inventory revised; BSI, Brief Symptom Inventory; CTQ, Childhood Trauma Questionniare; DERS, Difficulties in Emotion Regulation Scale; FDS, German adaptation of the Dissociative Experience Scale (DES); H, test statistic of the Kruskal-Wallis test; HC, healthy controls; IQR, interquartil range; MD, major depressive disorder; Mdn, median; p Value, probability value; PCL-5, PTSD Checklist for DSM-5; PTSD, posttraumatic stress disorder; PHQ-15, Patient Health-Questionnaire-15; SD, standard deviation; SSD, somatic symptom disorder; SSD-12, Somatic Symptom Disorder B-Criteria Scale. [a] Uncorrected for multiple testing; [b] Corrected for multiple testing via Bonferonni; [c] *n*=2 missings replaced by group mean values; [d] *n*=3 missings replaced by group mean values

Materials and Methods

In this section, measures of all relevant constructs are presented. For details, please refer to the Supplement.

Traumatic childhood experiences

TCEs were assessed with the *Childhood Trauma Questionnaire* (CTQ) [54]. The CTQ measures physical, sexual, and emotional abuse as well as physical and emotional neglect. A total sum score was calculated, ranging from 25 to 125, with higher values indicating a higher frequency of traumatic experiences.

Psychopathology

Mental health disorders were assessed using the *Structured Clinical Interview for DSM-5* (SCID-5) [53] (Interrater reliability: κ=1.00). The severity of common somatic symptoms was assessed using the *Patient Health-Questionnaire-15* (PHQ-15) [55] and the *Somatic Symptom Disorder - B Criteria Scale* (SSD-12) [56] was used to assess SSD symptomatology. PTSD symptom severity was assessed using the *Posttraumatic Stress Disorder Checklist for DSM-5* (PCL-5) [57]. Severity of depressive symptoms was assessed with the *Beck-Depression-Inventory II* (BDI-II) [58]. General symptom severity was assessed with the *Brief Symptom Inventory* (BSI) [59]. Due to its overlap with body dissociation, a measure of trait dissociation was administered in order to investigate the specifity of body dissociation in the current study [42]. Thus, the German adaptation of the *Dissociative Experience Scale*, the *Fragebogen zur Erfassung Dissoziativer Symptome* (FDS) [60, 61] was used.

Emotion dysregulation

Emotion regulation deficits were assessed with the *Difficulties in Emotion Regulation Scale* (DERS) [62]. The DERS comprises six subscales: *nonacceptance of negative emotions*,

difficulties engaging in goal-directed behaviors when distressed, *difficulties controlling impulsive behaviors when distressed*, *limited access to effective emotion regulation strategies*, *lack of emotional awareness*, and *lack of emotional clarity*. A total sum score was calculated, ranging from 36 to 180, with higher values indicating more severe deficits in emotion regulation.

Interoceptive processes

Interoceptive sensibility was measured both via self-reported interoceptive task-confidence and self-report questionnaire. The mean score of the confidence ratings across heartbeat counting trials was calculated as a global measure of interoceptive sensibility pertaining to self-reported heartbeat perception [12]. The *Scale of Body Connection* (SBC) [63] was used to assess self-reported *body awareness* and *body dissociation* during the last two months. *Body awareness* measures attention to bodily signals in everyday situations and the perception of bodily responses to emotions. *Body dissociation* refers to the avoidance or disregard of internal bodily experiences and the feeling of seperatedness from one's own body. Mean scores, ranging from 0 to 4, were calculated for each scale, with higher values indicating higher body awareness and body dissociation, respectively.

Interoceptive accuracy was assessed by means of the heartbeat counting task [64]. A heartbeat perception score was calculated, across seven consecutive time intervals of varying length unknown to the participants (20, 25, 35, 45, 55, 65, 75 seconds), by comparing the perceived number of heartbeats (HB) and the actual number of heartbeats, with higher values (maximum of 1) indicating higher interoceptive accuracy (overall internal consistency α=.96):

$$\mathrm{IAc} = \frac{1}{7}\sum_{k=1}^{7} 1 - \frac{|\sum \mathrm{HB\ actual}_k - \sum \mathrm{HB\ perceived}_k|}{\sum \mathrm{HB\ actual}_k}$$ [65].

Interoceptive awareness was calculated as the within-participant Pearson correlation *r* [12], between interoceptive accuracy and confidence averaged across trials, resulting in an interoceptive awareness score ranging from -1 to +1. Negative values indicate a discrepancy between confidence and objective interoceptive accuracy, while positive values indicate an accordance and values near zero indicate low interoceptive awareness:

$$\frac{\frac{\sum_{i=participant}^{N=7}(x_{in=trial}-\bar{x}_i)(y_{in=rating}-\bar{y}_i)}{N-1}}{s(x_i)*s(y_i)}.$$

HRV was operationalised using the root-mean-square of successive R–R-interval differences (RMSSD). RMSSD was chosen as it is claimed to be a comparably robust and statistically reliable indicator of vagally-mediated short-term HRV [66], which is mostly unaffected by breathing artefacts [67].

Procedure

Participants completed a 5-minute resting-state electrocardiogram (ECG) measurement before performing the heartbeat counting task. The ECG was recorded using Einthoven II electrode placement. HRV-Analysis was based on resting-state RMSSD values as HRV index. For details, see the Supplement.

Statistical analysis

Analyses were performed using IBM SPSS v26.0 (descriptives and correlation analyses) and R v3.5.0 via R plug-in for SPSS (mediation analysis). To account for deviations from normality, non-parametric analyses were performed. Two-tailed $p<.05$ was employed for all analyses.

***Aim 1: Group comparisons for interoceptive processes*.**

Kruskal-Wallis tests were used to compare groups regarding interoceptive measures. Dunn-Bonferroni-tests were conducted as post-hoc tests following significant effects (r as effect size) [68].

Aim 2: Correlation analysis between TCEs, interoceptive dimensions and emotion dysregulation.

Spearman correlations were used to investigate the relationship between interoceptive dimensions and both TCEs and emotion dysregulation for the whole sample.

Aim 3: Analysis of the mediating role of interoceptive processes between TCEs and emotion dysregulation.

Mediation analysis was performed using the ROBMED macro with robust bootstrap for SPSS (v0.6.0; bootstrapping procedure: 10,000 samples, confidence intervals: 95%, unstandardized coefficients, adjusted robust R^2 as effect size) [69]. The mediation model included interoceptive accuracy (heartbeat counting task), interoceptive sensibility (mean confidence, body awareness, body dissociation), interoceptive awareness, and RMSSD as HRV index. Only complete cases (*N*=99) were included (missings: *n*=26 technical recording issues, *n*=9 missing self-report, *n*=2 physiological aberrant finding, *n*=1 task difficulties).

Results

Group comparisons for interoceptive processes.

There was a significant group difference in all three measures of interoceptive sensibility (see Table 2): Patients with MD had significantly lower levels of mean confidence than HC (effect size *r*=-.37), patients with SDD had significantly higher levels of body awareness than patients with MD and patients with PTSD (MD: *r*=.33, PTSD: *r*=.46), and all

three patient groups reported significantly higher body dissociation than HC (MD: r=.44, SSD: r=.37, PTSD: r=.68). However, groups did not differ significantly in interoceptive accuracy or interoceptive awareness. With regard to HRV, patients with MD showed lower RMSSD as HRV index, compared to patients with SSD (r=-.40) and HC (r=-.45). The groups did not differ in heart rate ($H[3]$=0.58, p=.901).

Correlation analysis between TCEs, interoceptive dimensions and emotion dysregulation.

Both TCEs (CTQ score) and emotion dysregulation (DERS score) were positively correlated with self-reported body dissociation (see Table 3). No further significant correlations were obtained for the remaining interoceptive measures after controlling for multiple testing.

Analysis of the mediating role of interoceptive processes between TCEs and emotion dysregulation.

The mediation analysis revealed a significant indirect effect of TCEs (CTQ total score) on emotion dysregulation (DERS total score) through body dissociation (b=0.304, 95% CI [0.139, 0.534]), including interoceptive accuracy, confidence ratings, interoceptive awareness, body awareness, and HRV (RMSSD) as parallel mediators (see Fig. 1). While the total effect of TCEs on emotion dysregulation was significant (b=0.393 p=.001), the direct effect was not after including the mediators (b=0.089, p=.455, adjusted robust R^2=0.325). In the current mediation model, body dissociation, but not the other interoceptive measures, mediated the association between TCEs and emotion dysregulation.

Table 2

Sample Characteristics for Interoceptive Dimensions

Interoceptive dimensions	Mean±SD (Mdn; IQR)				*H* Value	*p* Value[a]	*p* Value[b]					
	MD	SSD	PTSD	HC			*MD vs SSD*	*MD vs PTSD*	*MD vs HC*	*SSD vs PTSD*	*SSD vs HC*	*PTSD vs HC*
Interoceptive accuracy	0.65±0.19 (0.70; 0.33)	0.60±0.18 (0.60; 0.30)	0.62±0.16 (0.61; 0.23)	0.62±0.26 (0.66; 0.26)	1.39	.708						
Confidence	3.64±1.87 (2.86; 1.93)	4.35±1.54 (4.00; 2.89)	4.02±2.08 (3.21; 3.18)	4.94±1.75 (5.14; 3.00)	9.57	.023	.446	1.00	.018	1.00	1.00	.308
Interoceptive awareness	0.17±0.39 (0.19; 0.52)	0.26±0.44 (0.40; 0.68)	0.21±0.42 (0.18; 0.65)	0.41±0.43 (0.51; 0.89)	6.80	.079						
Body Awareness (SBC)	2.40±0.53 (2.38; 0.56)	2.75±0.52 (2.83; 0.65)	2.15±0.68 (2.33; 0.83)	2.46±0.57 (2.50; 0.92)	14.87	.002	.046	1.00	1.00	.001	.275	.706
Body Dissociation (SBC)	1.45±0.65 (1.25; 0.75)	1.33±0.59 (1.38; 0.88)	1.82±0.69 (1.87; 1.09)	0.82±0.63 (0.63; 1.00)	27.53	<.001	1.00	.379	.004	.089	.022	<.001
HRV (RMSSD)	27.77±19.22 (20.70; 13.69)	40.73±20.33 (33.57; 25.67)	32.54±15.43 (28.17; 20.13)	49.21±30.92 (44.48; 53.25)	16.22	.001	.010	.667	.002	.730	1.00	.269

Abbreviations: H, test statistic of the Kruskal-Wallis test; HC, healthy controls; HRV, heart rate variability; IQR, interquartil range; MD, major depressive disorder; Mdn, median; p Value, probability value; PTSD, posttraumatic stress disorder; RMSSD, Root Mean Square of Successive Differences; SBC, Scale of Body Connection; SD, standard deviation; SSD, somatic symptom disorder.

[a] Uncorrected for multiple testing; [b] Corrected for multiple testing via Bonferonni

Table 3

Associations between traumatic childhood experiences, emotion dysregulation, and interoceptive dimensions

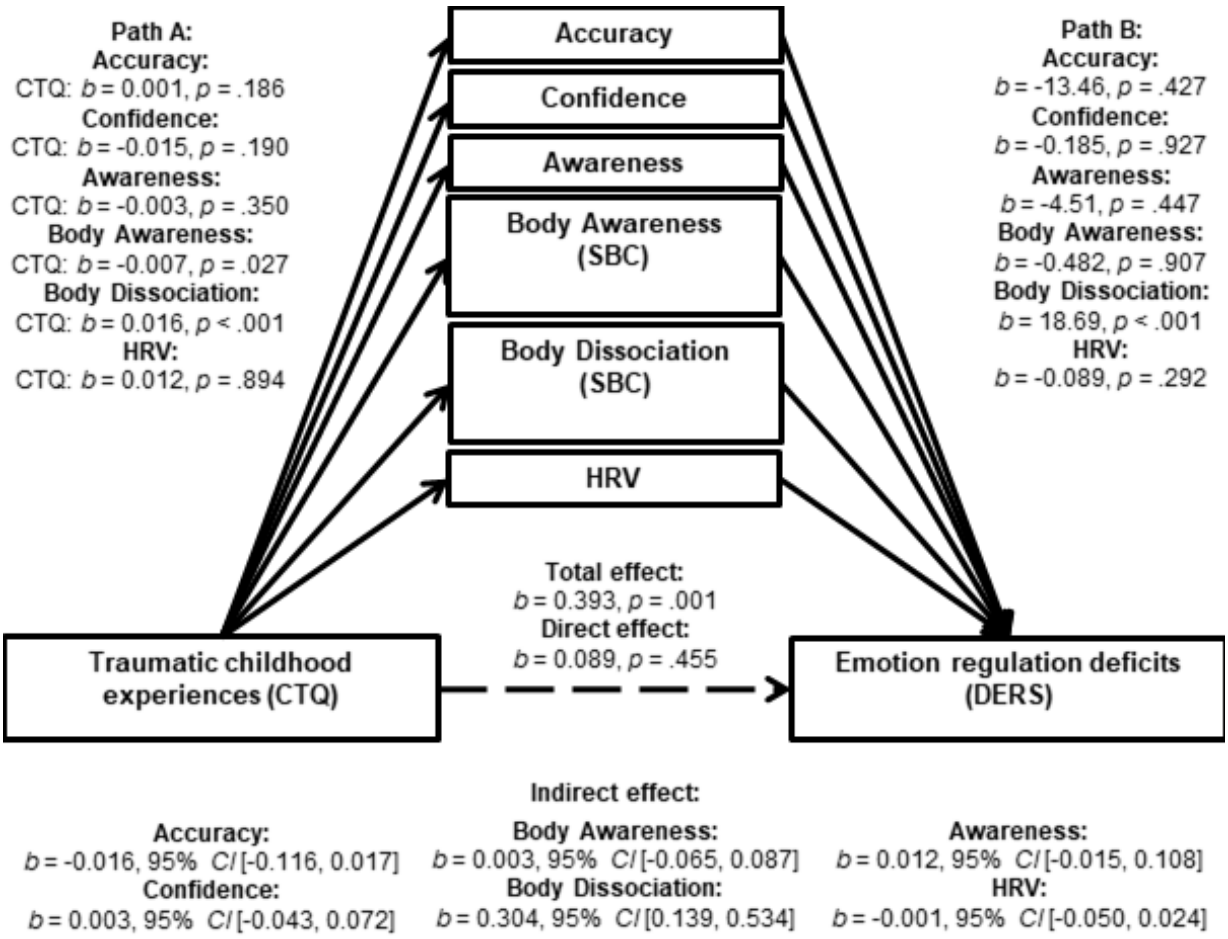
	Traumatic childhood experiences	Emotion Dysregulation	Interoceptive accuracy	Confidence	Awareness	Body Awareness (SBC)	Body Dissociation (SBC)	HRV (RMSSD)
Traumatic childhood experiences (CTQ)	1							
Emotion Dysregulation (DERS)	**.333*** <.001 *N*=136	1						
Interoceptive accuracy	.073 .437 *N*=116	.023 .805 *N*=116	1					
Confidence	-.196 .035 *N*=116	-.170 .068 *N*=116	-.005 .956 *N*=116	1				
Awareness	-.098 .298 *N*=116	-.198 .033 *N*=116	-.211 .023 *N*=116	.069 .463 *N*=116	1			
Body Awareness (SBC)	-.203 .024 *N*=124	-.209 .020 *N*=124	**-.281*** .004 *N*=105	.261 .007 *N*=105	.042 .674 *N*=105	1		
Body Dissociation (SBC)	**.372*** < .001 *N*=124	**.555*** < .001 *N*=124	.007 .940 *N*=105	-.216 .027 *N*=105	-.194 .048 *N*=105	-.199 .027 *N*=124	1	
HRV (RMSSD)	-.077 .392 *N*=126	-.211 .018 *N*=126	.170 .076 *N*=110	-.094 .330 *N*=110	.159 .097 *N*=110	-.024 .803 *N*=114	**-.310*** .001 *N*=114	1

Abbreviations: CTQ, Childhood Trauma Questionniare; DERS, Difficulties in Emotion Regulation Scale; HRV, heart rate variability; RMSSD, Root Mean Square of Successive Differences; SBC, Scale of Body Connection. *Note:* Critical alpha values are set to (0.05/8=.006) with significant values highlighted via asterisk.

The observed pattern remained even when trait dissociation was entered as an parallel mediator as can be seen in the Supplement (see Fig. S1).

Figure 1

Parallel Mediation Model in a Sample of Patients with Major Depression, Somatic Symptom Disorder, Posttraumatic Stress Disorder, and Healthy Controls (N=99)



Discussion

In the current study, we investigated whether interoceptive processes are altered in disorders related to TCEs, are associated with TCEs and emotion dysregulation, and do mediate the relationship between TCEs and emotion dysregulation, an important transdiagnostic feature. Interestingly, in partial support of aim 1, we found consistent alterations in only one measure of interoceptive sensibility, namely body dissocation with higher scores in patients with PTSD, SSD, and MD compared to healthy controls. Furthermore, with regard to aims 2 and 3, body dissocation also appeared to be the only measure significantly associated with TCEs as well as significant mediator of the association between TCEs and emotion dysregulation in this large and well-characterized sample of individuals with varying TCEs.

Our findings of higher body dissociation in three different groups of patients with trauma-related disorders as well as positive associations to TCEs and emotion dysregulation are in line with earlier studies showing higher body dissociation in individuals with a history of TCEs [63, 70]. Likewise, the observed associations correspond to similar findings of heightened dissociation [71-73], for which we controlled for. Importantly, body dissociation, a measure of reduced or impaired interoceptive sensibility in terms of habitual disregard or non-attendance of interoceptive signals [74, 75], was found to mediate the association between TCEs and emotion dysregulation amongst all measured interoceptive processes. The current finding replicates and expands an earlier mediation analysis in women with BPD [42].

An explanation for its putative clinical importance in individuals with TCEs and mediating role might be that body dissocation represents an inner attitude toward one`s own body and a non-adaptive emotion regulation attempt due to TCEs. Whereas interoceptive signal transmission seems to be sufficient during an attention state, such as a heartbeat counting task, body dissociation might indicate a coping style. A habitual avoidance or disregard of internal bodily experiences and the feeling of seperatedness from one’s own body might reflect a focus

on external stimuli as a protective strategy due to a history of TCEs. This kind of strategy may have important implications. First, individuals with TCEs and higher body dissociation might not be able to accurately detect and monitor bodily signals without a conscious state of attention in everyday life. Second, individuals with TCEs might have learned to mistrust their own bodily signals, either because they regard them as dangerous or simply as unhelpful for determining one's own emotional state, and therefore choose to disregard them. Third, individuals with TCEs might have difficulties integrating and using bodily signals as internal cues for their own emotions and needs. Given the importance of bodily signals for homeostasis [25, 26] and emotion regulation [27, 28], body dissociation might represent a clinical variable of interest for psychological interventions. Furthermore, it highlights the need to assess interoceptive processes more closely to everyday in life in order to be able to determine and disentangle the causes and mechanisms underlying heightened body dissociation in individuals with TCEs.

One such mechanism might be stress. Stress responses form a complex neuro-behavioral cascade, which includes physiological changes and corresponding physical symptoms [76]. While acute stress reflects a response to a potentially harmful stimulus of limited duration, chronic stress can be elicited either by prolonged exposure or perpetuated in the aftermath of severe stressors. Both acute and chronic stress have been shown to impact interoceptive processes [76]. Of note, interoceptive accuracy and TCEs have been shown to be only associated during states of acute stress [43, 44]. Chronic stress as experienced through TCEs might induce malfunctions in the body-brain communication which become prominent in states of acute stress, wherein deficient processing of physical symptoms might hinder regulative processes [76, 77]. One might speculate that the recurrence of such experiences and failed adaptive regulations leads to persistent internal error signals which in turn may lead to heightened body dissociation. Whether body dissociation alters the perception of interoceptive signals during acute stress needs to be investigated in further studies. Error signals should

become prominent during acute stress, in an attempt to restore homeostasis instead of a general background noise of interoceptive dysfunction. Such error signals might even replace habitual disregard of bodily symptoms by perceptions of physical symptoms in a positive feedback loop [78], thereby representing interoceptive regulation attempts [77].

Although interoceptive accuracy has been studied intensively, we did not find neither a mediation effect nor significant group differences at rest in the current sample. Of note, potential methodological shortcomings of the heartbeat counting task have been debated in the literature, some of which may compromise its validity. One account is that the original task is contaminated by non-interoceptive processes, such as estimating one's own heartbeats and under-reporting [79]. However, in order to be able to compare current findings with previous studies, the original setup of the heartbeat counting task was administered, resulting in a ratio of 13.79% of of 'good' heartbeat perceivers (based on a score greater than 0.85) [80], a finding which has has been reported in previous studies [49, 81]. Although, average interoceptive confidence and interoceptive accuracy were not significantly associated, all groups showed on average positive values of interoceptive awareness, suggesting that most participants were able to judge their actual accuracy in the heartbeat counting task. Therefore, we conclude that the participants were able to form metacognitive beliefs, which corresponded on average to the achieved task performance. However, the current mediation analysis and group comparisons suggest that the heartbeat counting task and measures building upon it (i.e., confidence ratings and interoceptive awareness), did not contribute to reveal interoceptive deficits and mediators in the current sample. Similarly, performance on the heartbeat counting task did not show associations to mental health outcomes in a recent meta-analysis [82], further suggesting that other operationalisations of interoceptive accuracy might be more suitable to reveal interoceptive approaches to treatment [83].

Likewise, RMSSD as HRV index did not emerge as a significant mediator in our current mediation analysis. The lacking finding of a direct link between TCEs and HRV is in line with a recent meta-analysis [84]. HRV, as indexed by RMSSD, represents both parasympathetic tone [85], which can serve as an indicator of cardiac activation and afferent bodily signal strength [86], as well as cardiac adaptability and control. Lower HRV has been shown to be related to adverse physical health outcomes [46] and found to be typically reduced in trauma-related disorders [47]. The current findings suggest that parasympathetic regulation does not necessarily play a major role for the link between TCEs and emotion dysregulation. This was unexpected, since dysfunctions of the ANS, as reflected by altered HRV, have been associated with stress [87]. In contrast, significantly lower RMSSD was found only in the MD group. Although not statistically significant, the observed pattern of lower HRV in the three patient groups are in line with previous research [47] indicating, on average, a tendency of autonomic dysregulation in the trauma-related patient groups. Interestingly, RMSSD as HRV index in the current study was negatively correlated with body dissociation but uncorrelated with interoceptive accuracy. The latter finding is inconsistent with a previous study from [49], wherein a positive relationship was found. However, further studies with higher sample sizes are needed in order to disentangle symptom severity, psychotropic medication load, and HRV, and to control for possible confounding variables [88] before strong conclusions can be drawn. In addition, as HRV has been linked to dissociative experiences [89, 90], associations between HRV and body dissociation need to be further examined in the future.

Of importance, the current study revealed interoceptive deficits in interoceptive sensibility within the sample of trauma-related disorders. Whereas patients with SSD tended to exhibit higher body awareness, which might be indicative of an habitual attention tendency as reflected in the SBC [75] and could interact with bodily distress [91], patients with MD reported lower levels of mean confidence. Although this finding needs further replication especially in

moderately depressed patients [39, 92], patients with MD might show a general tendency of lower task performance confidence but are able to adequatly judge their performance in a trial-by-trial evaluation. Patiens with PTSD showed higher body dissociation alongside the other two clinical groups. As body awareness was not significantly altered in patients with PTSD, it needs to be further examined whether heightened body dissociation might be interpreted as a form of experiental avoidance in PTSD.

In summary, the findings of the current study underline the importance of interoceptive sensibility and metacognitive beliefs such as the disregard of one's bodily signals due to body dissociation. The results are in line with the notion that physiological interoceptive states and interoceptive accuracy, as mostly measured in interoceptive studies, might not sufficiently capture relevant (higher-order) interoceptive processes [10, 12]. As outlined by [93] in their 2 x 2 factorial model of interoceptive abilities, the measurement of interoceptive sensibility (representing 'beliefs') can be subdivided concerning interoceptive accuracy (e.g., confidence ratings) and interoceptive attention (e.g., self-reports such as the SBC), with the latter providing the most distinct findings in the current study. As the term 'beliefs' in a broader meaning has been adopted on the neural basis in the active inference framework, interoceptive dysfunctions might be characterised by overly strong expectations (or 'beliefs') shaping the perception of interoceptive signals [24]. When such expectations are not updated in case internal or external changes occur, resulting error signals prevail, further hindering adaptive homeostatic processes. One intriguing, yet speculative assumption is that patients with TCEs form interoceptive beliefs which (sub)-consciously disregard internal bodily experiences due to persistent internal error signals, which in turn leads to difficulties in emotion regulation. However, since interoceptive processes represent a complex cascade and further stress-mediating systems such as the immune system need to be investigated [76], the involved mechanisms mediating the impact of TCEs

on interoception remain largely unaddressed, with the current study indicating altered interoceptive beliefs as a possible final result.

Limitations

Several limitations should be acknowlegded: First, TCEs were assessed via self-report questionnaire. Although the CTQ self-report questionnaire has been shown excellent convergent validity with an clinical interview measure recently [94], subjective experiences of TCEs rather than actual exposure have been investigated as the low agreement between retrospective and prospective measures of TCEs indicates [95, 96]. Since the cross-sectional design does not allow for causal inferences, longitudinal studies are needed which investigate the association between interoception and prospective measures of TCEs.

Second, TCEs, body dissociation, and emotion dysregulation were all measured via self-report. Therefore, the observed relationship between solely self-report measures might be affected by monomethod bias. Whether the observed relationships extend to other measures of body dissociation and emotion dysregulations needs to be adressed in future studies.

Third, due to the dimensional approach and matching rationale, HC and patients without the (self-reported) presence of TCEs were not investigated. By combining the groups, we were able to investigate and replicate a parallel mediation model of different interoceptive processes for the first time across individuals with TCEs in a large sample, thereby overcoming shortcomings of previous studies. Of note, patients with PTSD showed higher scores on the CTQ. Besides possible interaction effects of TCEs and clinical diagnosis, the HC group in the current study could be categorised as ‘resilient’ to a certain degree, in a sense that they adapted in the face of TCEs without developing a trauma-related disorder. Future studies are needed to investigate generalizability of the current findings.

Fourth, to the current state of knowledge, the validity of interoceptive accuracy based on the heartbeat counting task [64] is currently debated in the literature. Although reliability and convergent and discriminant validity have been recently investigated [97-99], comparisons between studies are difficult. Importantly, the results obtained in the current study were comparable to previous studies. However, future studies should adapt and compare different interoceptive tasks which incorporate different interoceptive organ systems and physical arousal states [100-103], instead of the original heartbeat counting task.

Fifth, we did not control for sex, comorbidities, and medication which might have affected the results [83, 85, 88, 104-106].

Conclusion

TCEs represent an important risc factor for psychopathology such as emotion dysregulation, and might also impact certain interoceptive processes. The present findings confirmed self-reported body dissociation as a possible mediator between TCEs and emotion dysregulation. Developing psychotherapeutic interventions targeting interoceptive beliefs might prove to be a promising complement to existing interventions for patients affected by TCEs.

Abbreviations

ANS: Autonomic nervous system; BDI-II: Beck Depression Inventory revised; BPD: Borderline personality disorder; BSI: Brief Symptom Inventory; CTQ: Childhood Trauma Questionnaire; DERS: Difficulties in Emotion Regulation Scale; ECG: Electrocardiogram; FDS: German adaptation of the Dissociative Experience Scale (DES); HB: Heartbeats; HC: Healthy controls; HRV: Heart rate variability; MD: major depressive disorder; PCL-5: PTSD Checklist for DSM-5; PHQ-15: Patient Health-Questionnaire-15; PTSD: posttraumatic stress

disorder; RMSSD: Root-Mean-Square of Successive R–R-interval Differences; SAM: Sympatho-adreno-medullary; SBC: Scale of Body Connection; SCID-5: Structured Clinical Interview for DSM-5; SSD: somatic symptom disorder; SSD-12: Somatic Symptom Disorder B-Criteria Scale; TCE: Traumatic childhood experiences.

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Supplementary Information

Supplementary sample characteristics

Current comorbid and lifetime mental disorders, and psychotropic medication load are depicted in Table S1.

Current psychotropic medication was restricted to regular medication with antidepressants, antipsychotics (sleep-inducing effect only) and anticonvulsants (i.e., pregabalin, pain-relieving effect only) for patients with mental disorders. Psychotropic medication load was calculated as a composite measure following procedures outlined in previous studies [1-3]. Daily dosages for each medication were coded as absent=0, low-dose=1, or high-dose=2. The composite measure was calculated as the sum score of number and dosages of all medications taken by an individual participant. Antidepressants were categorized as low- (levels 1 and 2) or high-dose (levels 3 and 4) [4]. Chlorpromazine dose equivalents were used for scoring of antipsychotic medication. Chlorpromazine dose equivalents equal or below, or above the mean effective daily dose of chlorpromazine represent low- or high-dosings, respectively [5, 6]. Pregabalin dosing was coded as low (≤300 mg) or high (>300 mg) [7, 8].

Supplementary Table S1

Current Comorbid and Lifetime Diagnoses of Mental Disorders and Psychotropic Load

	MD (*n*=35) (24 women)	SSD (*n*=34) (26 female)	PTSD (*n*=33) (28 female)	HC (*n*=34) (27 female)
Current comorbid Diagnoses[a]				
MD	35 (35)	7 (21)	8 (24)	0 (0)
SSD	1 (1)	34 (34)	2 (4)	0 (0)
PTSD	2 (3)	1 (1)	33 (33)	0 (0)
Other affective disorders	3 (2)	2 (3)	3 (3)	0 (0)
Other somatization disorders	0 (0)	0 (0)	0 (0)	0 (0)
Other anxiety disorders	8 (10)	4 (7)	5 (9)	0 (0)
Eating disorders	2 (4)	1 (7)	3 (9)	0 (0)
Substance use disorders	0 (5)	0 (5)	0 (12)	0 (0)
Psychotropic medication load[b]	1.31 (1.37)	0.50 (1.02)	0.76 (1.00)	0.00 (0.00)

Note. HC, healthy controls; MD, major depressive disorder; PTSD, posttraumatic stress disorder; SD, standard deviation; SSD, somatic symptom disorder.
[a] Data are presented as current (lifetime) diagnosis
[b] Data are presented as mean (SD)

Supplementary information on Materials and Methods

Traumatic childhood experiences

The *Childhood Trauma Questionnaire* (CTQ) [9] assesses *traumatic childhood experiences* (TCEs). Participants rate frequency of TCEs on a 5-point scale (ranging from 'never true' to 'very often true') for the five scales *physical* (e.g., 'People in my family hit me so hard that it left me with bruises or marks'), *sexual* (e.g., 'Someone molested me'), and *emotional abuse* (e.g., 'I thought that my parents wished I had never been born'), and *physical* (e.g., 'I had to wear dirty clothes') and *emotional neglect* (e.g., 'I felt loved' [reverse coded]) with five items each (resulting in corresponding scores from 5 to 25). A total sum score can be calculated from the scales, ranging from 25 to 125 (overall internal consistency α=.90).

Psychopathology

Specifically trained diagnosticians assessed mental health disorders using the German version of the *Structured Clinical Interview for DSM-5* (SCID-5) [10]. Interrater reliability was based on 12 randomly selected video-taped diagnostic interviews rated by five independent raters and the head of the diagnostic unit, and yielded an excellent [11] score of κ=1.00.

The *Patient Health-Questionnaire-15* (PHQ-15) [12] was used to assess the presence and severity of common somatic symptoms within the last 4 weeks using 15 items. Each symptom can be scored from 0 ('not bothered at all') to 2 ('bothered a lot') with sum scores ranging from 0 to 30 (overall internal consistency α=.82).

The *Somatic Symptom Disorder - B Criteria Scale* (SSD-12) [13] consists of 12 items, with 4 items for each of the three psychological sub-criteria comprising cognitive, affective and behavorial aspects. Item scores range between 0 ('never') and 4 ('very often') and the total sum score ranges between 0 and 48 (overall internal consistency α=.94).

The *Posttraumatic Stress Disorder Checklist for DSM-5* (PCL-5) [14] was used to assess the presence and severity of PTSD symptoms over the past month. Item scores range between 0 ('not at all') and 4 ('extremely') and sum scores the total sum score ranges between 0 and 80 (overall internal consistency α=.95).

Severity of depressive symptoms was assessed with the *Beck-Depression-Inventory II* (BDI-II) [15]. Each of the 21 items represents an affective or somatic symptom related to depression, with statement scales ranging from 0 ('no disturbance') to 3 ('maximal disturbance'), and corresponding sum scores ranging from 0 to 63 (overall internal consistency α=.95).

General symptom severity was assessed with the *Brief Symptom Inventory* (BSI) [16]. Nine primary symptom dimensions are measured with 53 items ranging from 0 'not at all' to 4 'extremely'. In the current study, the *BSI Global Severity Index* (BSI GSI), which is the mean score of all items, was used (overall internal α=.96).

The German adaptation of the Dissociative Experience Scale, that is, the Fragebogen zur Erfassung Dissoziativer Symptome (FDS) [17, 18] was used to assess trait dissociation. The FDS consists of 44 items measuring the frequency of dissociative experiences (in 10% increments, ranging from 0 to 100) on the dimensions amnesia (e.g., 'Some people find evidence that they have done things that they do not remember doing'), absorption/imaginative involvement (e.g., 'Some people have the experience of not being sure whether things that they remember happening really did happen or whether they just dreamed them'), derealisation/depersonalization (e.g., 'Some people sometimes have the experience of feeling that other people, objects, and the world around them are not real') and conversion (e.g., 'Some people sometimes have difficulties with their eyes, e.g., double or blurred vision, blind in one or both eyes, without a doctor being able to find a physical cause'). A mean score can be calculated, ranging from 0 to 100 (internal consistency in the present study α=.94).

Emotion dysregulation

The *Difficulties in Emotion Regulation Scale* was used to assess emotion regulation deficits (DERS) [19]. The DERS comprises six subscales: *nonacceptance of negative emotions* (6 items; e.g., 'When I'm upset, I become angry with myself for feeling that way'), *difficulties engaging in goal-directed behaviors when distressed* (5 items; e.g., 'When I'm upset, I have difficulty focusing on other things'), *difficulties controlling impulsive behaviors when distressed* (6 items; e.g., 'When I'm upset, I become out of control'), *limited access to effective emotion regulation strategies* (8 items; e.g., 'When I'm upset, I believe there is nothing I can do to make myself feel better'), *lack of emotional awareness* (6 items; e.g., 'When I'm upset, I acknowledge my emotions' [reverse coding]) and *lack of emotional clarity* (5 items; e.g., 'I have difficulty making sense out of my feelings') [20]. Participants rate each item on a 5-point scale ranging from 1 ('almost never') to 5 ('almost always'). A total sum score can be calculated, ranging from 36 to 180 (overall internal consistency α=.94).

Interoceptive sensibility

The *Scale of Body Connection* (SBC) [21] was used to assess self-reported *body awareness* and *body dissociation* during the last two months. The subscale *body awareness* (12 items; overall internal consistency α=.79) measures attention to bodily signals in everyday situations and the perception of bodily responses to emotions (e.g., 'I take cues from my body to help me understand how I feel'). The subscale *body dissociation* (8 items; (overall internal consistency α=.80) refers to the avoidance or disregard of internal bodily experiences and the feeling of seperatedness from one's own body (e.g., 'I distract myself from feelings of physical discomfort'). The SBC has been proposed to reflect confidence in interoceptive ability and preferential or habitual attendance to interoceptive signals [22], which has later been

incorporated in the *Multidimensional Assessment of Interoceptive Awareness* (MAIA) [23] a further well-established measure of interoceptive sensibility. Each item of the SBC is scored on a 5-point scale, ranging from 0 ‘not at all’ to 4 ‘all of the time’, with higher values indicating higher body awareness and body dissociation, respectively.

Additional measures

Demographic details, height, and weight were assessed with a standardized questionnaire. Education was assessed based on years completed in the stardard German school system (9 years=certificate of secondary education, 10 years=general certificate of secondary education, 13 years=university entrance diploma).

Supplementary information on Procedure

Heartbeat counting task

Participants were instructed to sit still and relaxed in a sound-attenuated, dimly lit room for a 5-minute resting-state electrocardiogram (ECG) measurement. After the resting state measurement, participants were asked to silently count their own heartbeats without manually checking. Start and stop times were defined by an acoustic signal. After two practice trials of 30 seconds, the task was repeated in seven consecutive time intervals (20, 25, 35, 45, 55, 65, 75 seconds each), whereby the duration of the time intervals was unknown to the participants. After each time interval, participants were asked to indicate the number of counted heartbeats via keyboard. In addition, participants were asked to judge how confident they were with regard to their own counting abilities (‘How well do you think you perceived your heartbeat?’ with scores ranging between 1 (‘not at all’) and 9 (‘very well’)).

Additional information on ECG Recording and Processing

For the electrocardiogram, three skin electrodes (Red DotTM Ag/AgCl, Micropore tape and solid gel, 3 M Health Care), were attached to the front of the subject's body (right anterior: below the right collarbone, left low: left bottom centered on the 7th rib, right low: right lower abdomen) and a reference electrode (standard ECG electrode, Ag/AgCl) under the right shoulder opposite the right anterior electrode. The electrodes had a diameter of 45mm and contained an inner gel layer with a diameter of 2mm. The ECG was recorded using an AccuSync® 71 trigger monitor in combination with a QuickAmp Amplifier (Brain Products GmbH; pass-band filter: 0.01-200 Hz; sampling rate: 1000 Hz) for the reference electrode. The signal was recorded with a differential amplifier and a high-pass filter at 0.5Hz for offline analysis. The R-spikes for pulse detection were identified online via the AccuSync® 71 monitor and BrainVision Recorder 1.20 and offline using an ECG marker macro and manual inspection in the BrainVision Analyzer 2.1.

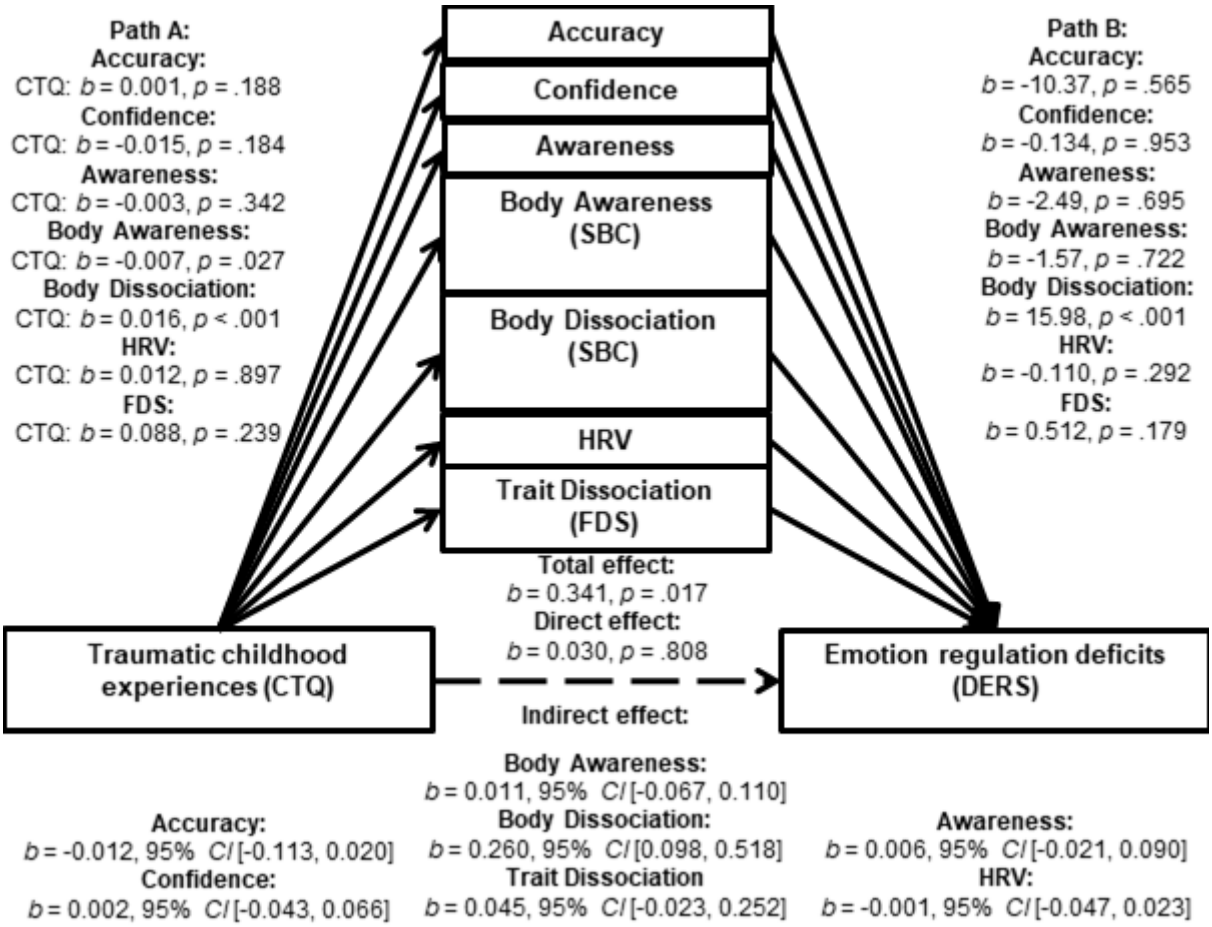
For HRV-Analysis, heart rate (HR) and R-peaks were detected offline with EDF-Browser Software employing combined adaptive thresholding [24], followed by a visual inspection for artifacts and correct R-trigger location. Inter-beat-intervals (IBI) were then computed and further processed using the RHRV package, a widely used HRV analysis in R [25]. Cleaned and processed IBIs were additionally visually reviewed by the researcher for artifacts and, in case of presence, manually removed. In a final step, RMSSD indices were derived automatically and transferred to SPSS (IBM SPSS 26). RHRV-extracted HRV-parameters show high reliability and validity compared to respective parameters as retrieved by Kubios (rs > 0.8), a “gold standard software” for HRV analysis [26].

Mediation analysis

In order to further validate the mediating role of body dissociation, trait dissociation (FDS total score) was included in the mediation model as presented in the manuscript. Including trait dissociation as parallel mediator did not change the pattern of results (b=0.260, 95% CI [0.098, 0.518] for body dissociation and b=0.045, 95% CI [-0.023, 0.252] for trait dissociation). Again, the total effect was significant (b=0.341, p=.017), whereas the direct effect was statistically not significant (b=0.030, p=.808, adjusted robust R^2=.343), suggesting that body dissociation fully mediated the association between traumatic childhood experiences and emotion dysregulation even after controlling for trait dissociation (see Fig. S1).

Supplementary Figure S1

Parallel Mediation Model including Trait Dissociation in a Sample of Patients with Major Depression, Somatic Symptom Disorder, Posttraumatic Stress Disorder, and Healthy Controls (N=99)



Note. Path A represents the effect of the predictor on each mediator, path B represents the combined relationship of each mediator with the outcome, with the direct effect representing the effect of the predictor on the outcome after inclusion of all mediators and the total effect representing the basic relationship between the predictor and the outcome. The indirect effect represents the combined effect of path A and path B and therefore the mediation. Significance inferences at the 0.05 α level are based upon the notion whether confidence intervals include zero.

Abbreviations. CTQ, Childhood Trauma Questionnaire; DERS, Difficulties in Emotion Regulation Scale; FDS, German adaptation of the Dissociative Experience Scale; HRV, heart rate variability; SBC; Scale of Body Connection

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Study IV: Childhood traumatic experiences and levels of personality functioning: The mediating role of body connection in community samples from Germany and Chile

Back, S.N., Cottin, M., Zettl, M., Bertsch, K. (2022). Childhood traumatic experiences and levels of personality functioning: The mediating role of body connection in community samples from Germany and Chile. Submitted for publication in *Child Abuse & Neglect*. This chapter is a pre-copyedited version of a submitted article.

Childhood traumatic experiences and levels of personality functioning: The mediating role of body connection in community samples from Germany and Chile

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The authors report no relevant conflicts of interest. This work was funded by grants from the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG), awarded to Katja Bertsch for her work on interoceptive processing in Borderline Personality Disorder (BE5292/ 3-2 and BE5292/5-1). The data supporting this study's findings are available on request from the corresponding author. Author contribution: S.N. Back developed the study concept, S.N. Back and M. Cottin developed the design and performed the data collection. S.N. Back performed the data analysis and interpretation. S.N. Back drafted the manuscript, K. Bertsch, M. Zettl, and M. Cottin provided critical revisions. All authors approved the final version of the manuscript for submission.

Abstract

Background: Childhood traumatic experiences (TCE) are a major risk factor for adult psychopathology, including levels of personality functioning based on the Alternative Model of Personality Disorders (AMPD). However, studies on processes mediating this relationship are sparse. One such process might be reduced body connection, which has been shown to mediate the relationship between TCE and impairments in subdomains of self (e.g., emotional dysregulation) and interpersonal functioning (e.g., intimate relationships) in individuals with and without mental disorders. However, evidence regarding higher-order deficits in personality functioning is lacking.

Objective: The present study investigated if body connection mediates the association between TCE and personality functioning according to the AMPD.

Participants and Setting: 1,313 adult community-dwelling individuals from Germany ($N = 794$) and Chile ($N = 519$) were included in an Online-survey.

Methods: Participants completed TCE, personality functioning, and body connection questionnaires. The role of body connection, i.e., body awareness and body dissociation, in the relationship between TCE and personality functioning (including domains of self and interpersonal functioning) was tested using parallel mediation models.

Results: TCE explained 26% of the variance in impairments of personality functioning while controlling for age, sex, and nationality. 60% of this effect was explained by body connection, particularly body dissociation. Body dissociation and, to a much lesser extent, body awareness accounted for 64% of the variance in self functioning, and 55% of the variance in interpersonal functioning explained by TCE.

Conclusion: This study highlights the role of TCE in disturbed body processing for impairments in personality functioning.

Keywords: Childhood trauma, personality functioning, personality disorder, body dissociation, interoception

Introduction

Traumatic childhood experiences (TCE) are an important risk factor for psychopathology later in life (McCrory et al., 2017). TCE comprises a variety of aversive interpersonal experiences up to 18 years, including physical, sexual, and emotional abuse or physical and emotional neglect (Bernstein et al., 2003). Studies suggest that more than half of all children worldwide are exposed to some form of TCE (Hillis et al., 2016). Due to the increased brain plasticity in childhood and adolescence (reflecting the brain's ability to adapt to external experiences), TCE may not only impede early regulatory skills, but also have a profound impact on psychobiological processing and personality development (Kolb & Gibb 2014; McLaughlin et al., 2020). Several studies demonstrated that individuals who report higher TCE also report greater impairments in self and interpersonal functioning, as well as more maladaptive personality traits (Back et al., 2022).

The concept of levels of personality functioning (ranging from none to severe impairments in self and interpersonal functioning) serves as the major diagnostic criterion for the dimensional classification of personality pathology according to the DSM-5 Alternative Model of Personality Disorders in Section III '*Emerging Models'* (AMPD; APA, 2013), and was recently incorporated into the eleventh version of the ICD (WHO, 2019). Within the AMPD, impairments in self hierarchically map to deficits in identity (e.g., unclear boundaries between oneself and others, unstable self-worth, and deficits in emotion recognition and regulation), and self-direction (e.g., incoherent or unstable personal goals, evaluation standards, and self-reflection). Impairments in interpersonal functioning subsume deficits in empathy (e.g., difficulties comprehending and appreciating foreign experiences, perspectives, and the effect of own behaviour on others), and intimate relationships (e.g., desire and capacity for intimate, stable, and mutual interpersonal relationships; APA 2013). The dimensional conceptualization of levels of personality functioning according to DSM-5 and ICD-11

integrate various processes which have recently been conceptualized as mediators in the relationship between TCE and transdiagnostic psychopathology (especially emotion dysregulation and deficits in social information processing, see MacLaughin et al., 2020 for a review). A recent study confirms that levels in personality functioning mediate the relationship between TCE and mental health problems in high-risk samples (d'Huart et al., 2022).

Albeit first evidence suggests a significant relationship between TCE and the AMPD's levels of personality functioning in clinical as well as community samples (see Back et al., 2022 for a review), knowledge on processes that may explain this association is sparse. Recently, deficits in body connection, that is, the connection between bodily and mental processes, have been proposed and studied as one such mediating process between TCE and impairments in self and interpersonal functioning in borderline personality disorder (BPD) (Schmitz et al., 2021; for reviews, see Back & Bertsch, 2020 and Löffler et al., 2018). TCE are assumed to promote lower awareness and integration of own bodily signals with higher-order psychological functions, e.g., reduced sensitivity and attention for own inner needs and emotions, an insufficient development of capacities to regulate own feelings, and, eventually, impairments in all subdomains of self and interpersonal functioning (see Löffler et al., 2018, Back & Bertsch, 2020 for reviews). Likewise, Fotopoulou and Tsakiris (2017) emphasized a developmental perspective in which the connection between bodily and mental processes in adulthood is important to a) distinguish oneself from others, b) to develop a minimal sense of self, c) the ability to understand the needs and feelings of others (i.e., empathize), as well as d) to form and maintain satisfying social relationships. These processes are importantly shaped by early embodied experiences with caregivers (Fotopoulou & Tsakiris, 2017).

There is some empirical evidence from cross-sectional and experimental studies supporting the relationship between body connection and personality functioning in individuals without mental disorders: Tajadura-Jiménez & Tsakiris (2014) showed that healthy participants with

low sensitivity to internal bodily processes experiences showed higher alterability of mental self-representations. Moreover, bodily awareness was positively associated with sensitivity to other peoples' emotions (Terasawa et al., 2014) and the dissociation from bodily processes has been related to the avoidance of intimate relationships (Oldroyd et al., 2019).

Considering clinical interventions, improving body connection has interestingly been an important element of many psychotherapeutic interventions in the treatment of patients with trauma- or stress-related disorders (e.g., body scans in mindfulness-based interventions; Dreeben, Mamberg & Salmon, 2013). Supporting the necessity of such interventions, Schmitz et al., recently found that the association between TCE and emotion dysregulation is fully mediated by body dissociation in individuals with borderline personality disorder (Schmitz et al., 2021), major depression, posttraumatic stress disorder, somatic symptom disorder, as well as individuals with TCE but without mental disorders (Schmitz et al., submitted). However, to date, a study investigating the role of body connection in the association between TCE and personality functioning according to DSM-5 AMPD is still missing.

The aim of the present study was to examine body connection, including body dissociation and body awareness, as potential mediators in the relationship between TCE and personality functioning. In addition, this study sought to investigate if this mediation effect occurred for both domains of personality functioning: self such as interpersonal functioning. Based on the above-outlined evidence, we hypothesized that especially body dissociation might be a mediator in the relationship between TCE and personality functioning, and that this effect might be present with regard to self as well as interpersonal functioning.

Methods

Participants

In total, *N* = 1,313 individuals participated in the current online survey study. *N* = 800 were recruited from the German general population via PsyWeb (https://psyweb.uni-muenster.de/), a scientific survey panel, and *N* = 519 from Chile via online announcements, advertisements on social media, university, as well as via clinical websites. All samples were pooled for the current analyses and, hence, comprehend a wide range of variance in TCE and personality functioning across national boundaries. Inclusion criteria were an age of at least 18 years, sufficient knowledge of the respective (German or Spanish) language and documented informed consent. Within the Chilean sample, a clinical subsample (N = 296) was recruited with an additional self-reported diagnosis of a personality disorder at any moment of their life and concurrent psychological or psychiatric treatment to participate in the survey to further increase clinical symptom range.

Study Design

Data from both countries was collected online using the SoSciSurvey platform, and the recruitment lasted from February 2021 to April 2021. All data were collected anonymously using self-report questionnaires. After completing the survey, which took in total around 30 minutes, participants had the opportunity to participate in a lottery for ten €25-Amazon gift cards. The present study was designed in accordance with the ethical principles of the Declaration of Helsinki, reviewed and approved by the ethics committees of Ludwig-Maximilians-University in Munich, Germany, and Universidad de Chile, in Santiago, Chile.

Questionnaires

Childhood Trauma Questionnaire - Short Form (CTQ-SF)

The CTQ-SF (Bernstein et al., 2003) is the most widely used self-report instrument assessing childhood traumatic experiences. The 28 items depict five forms of childhood trauma within separate subscales: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. Items are rated on a 5-point Likert-scale (1 = *never true*; 5 = *very often true*). As a short form of the original CTQ version (Bernstein & Fink, 1998), the CTQ-SF demonstrates good convergent validity (Bernstein et al., 2003), factor validity, reliability (Scher et al., 2005), and measurement invariance across diverse populations (Bernstein et al., 2003). The current study employed the validated German (Wingenfeld et al., 2010) and Spanish versions (Behn et. al, 2020) of the questionnaire, with a Cronbach's alpha of .83 for the total sample, indicating good reliability, respectively.

Scale of Body Connection (SBC)

The Scale of Body Connection (Price & Thomson, 2007) is intended to measure two components of body connection during the last two months: Body awareness and body dissociation. Whereas the body awareness subscale (12 items) assesses the attention to and perception of bodily signals in everyday life, such as bodily reactions to emotions, the body dissociation subscale (8 items) depicts the tendency to avoid and/or ignore internal bodily experiences, including the feeling of detachment or disconnection from the own body. On a five-point Likert scale, items are answered from 0 'not at all' to 4 'all of the time', and subscale values represent the mean scores of the respective number of items per subscale. The SBC was validated in several countries, indicating good reliability and validity. The current study employed the German translation (Schmitz et al.,2021) of the original English version (Price &

Thomson, 2007) as well as the validated Spanish version (Quezada-Berumen et al., 2014). Cronbach's alpha indicated acceptable reliability at 0.71 in the current study.

Level of Personality Functioning Scale – Brief Form 2.0 (LPFS-BF 2.0)

The LPFS-BF 2.0 (Weekers et al.,2018) is a 12-item self-report measure of personality functioning according to criterion A of the AMPD. Items 1-6 capture the dimension of self functioning, whereas items 7-12 depict interpersonal functioning. Items are rated on a 4-point Likert-scale (0 = *very false or often false*; 3 = *very true or often true*). Latent factor structure, convergent validity, and reliability of the LPFS-BF 2.0 have been confirmed in several studies (Weekers et al.,2018; Bach & Hutsebaut, 2017). The current study employed the validated German version (Spitzer et al.,2021) and the measurement-invariant Spanish version of the questionnaire (Cottin et al., in preparation, as employed in Natoli et al.,2022). Cronbach's alpha indicated acceptable reliability at 0.79 for the current total sample.

Data Analysis

First, bivariate correlations among all variables of interest (i.e., CTQ sum score, LPFS-BF 2.0 sum score, self and interpersonal functioning subscales, and the SBC subscales body awareness and body dissociation) were examined using Spearman correlations. Second, a parallel mediation model was conducted to investigate the direct and indirect effects of TCE (CTQ score) on personality functioning (LPFS-BF 2.0 total score) through body dissociation and body awareness (SBC subscales) as parallel mediators simultaneously. Third, we explored the same direct and indirect effects of TCE on impairments in self functioning (LPFS-BF 2.0 subscale) and in interpersonal functioning (LPFS-BF 2.0 subscale) through body dissociation and body awareness as parallel mediators in two additional, separate mediation models. Since visual and statistical inspection revealed a violation of the assumption of normality for all

variables of interest, we applied a bootstrapping sampling procedure to robustly estimate all effects (with 10,000 bootstrapped samples), a non-parametric approach allowing for more accurate inferences in case of not-normally distributed data (Mooney & Duval, 1993). This approach is in line with official recommendations for mediation analysis as provided by Hayes (2013) and McKinnon et al., (2007). Significance at the level of $\alpha = 0.05$ was only considered significant if zero was not included within respective confidence intervals. We included age, sex, and nationality as control variables in all mediation models in order to adjust for their influence. Statistical analysis were conducted in R and SPSS, using the process macro (version 4.1) for mediation analysis by Hayes (2013).

Results

Descriptive Data and Sample Characteristics

From the *N*=1,399 individuals enrolled in the study, *N* = 29 participants responded at least twice as fast as the average participant based on the Relative Speed Index (Leiner 2019), a reliable indicator for meaningless data based on relative completion times, and were subsequently excluded from any analysis. *N* = 2 participants reported an age below 18 years, *N* = 55 participants did not provide information on the Childhood Trauma Questionnaire and were equally removed from any further analysis. The final sample for the descriptive and inferential statistics included *N* = 1,313 individuals. *N* = 31 participants from Chile did not provide demographic data and were therefore excluded from respective parts of the descriptive and mediation analysis. Consequently, mediation analysis was based on a subsample consisting of *N* = 1,282.

Descriptive analysis for the total sample, as well as separately for the German and Chilean samples are provided in table 1. Our sample mostly consisted of women (76.6% female,

M = 32.9 years old, *SD* = 9.76), who were either actively pursuing a job, an academic or a vocational training (85%), and 42.2% reported a current or past mental disorder. The mean score of levels in personality functioning (*M* = 13.47, *SD* = 8.12) equals to a T-score of 48 for the general German population, indicating a rather low severity level, as expected in a population-based sample (Spitzer et al.,2021). According to the classification by Walker et al., (1999), 68.6% of the sample reported at least one clinically significant experience of childhood abuse or neglect. Among all forms of TCE, according to the CTQ, clinically significant emotional abuse was most frequently reported (in 53.3% of the sample), followed by physical neglect (41.6%), emotional neglect (29.4%), sexual abuse (28.1%) and physical abuse (25.4%). From the 68.6% of the sample indicating clinically relevant TCE, 19.2% reported one form of TCE, 15.8% reported two concurrent forms of TCE, 14.9% indicated three concurrent forms of TCE, 11.3% emphasized four concurrent forms of TCE, and 7.4% presented clinically significant history in all forms of TCE.

Table 1

Sample Description

	Total (N = 1.313)	Chile (N = 519)[1]	Germany (N = 794)
Gender *n* (%)			
Female	981 (76.59)	379 (73.02)	602 (79.00)
Male	288 (22.47)	108 (20.81)	180 (23.62)
divers	13 (1,0)	1 (0.02)	12 (1.57)
Age *years*			
Mean (*SD*)	32.9 (9.76)	31.37 (10.59)	33.79 (9.10)
Range	18-74	18-74	18-55
Occupation[2] *n (%)*			
Employed	613 (47.82)	115 (23.57)	498 (62.72)
Student/Trainee	467 (36.43)	255 (49.13)	212 (26.7)
Unemployed	202 (15.76)	118 (22.73)	84 (10.5)
Clinical *n (%)*			
Mental disorder[3]	540 (42.12)	296 (60.66)	244 (32.02)
No Mental disorder	742 (57.88)	192 (39.34)	550 (72.18)
TCE			
Mean (*SD*)	44.47(17.3)	43.22 (16.52)	46.37 (18.29)
Range	25-125	25-125	25-125
LPF			
Mean (*SD*)	13.47 (8.12)	11.76 (8.78)	14.59 (7.45)
Range	0-36	0-36	0-36
Self			
Mean (*SD*)	8.00 (4.95)	6.95 (5.19)	8.68 (4.67)
Range	0-18	0-18	0-18
Interpersonal			
Mean (*SD*)	5.48 (3.9)	4.81 (4.26)	5.91 (3.59)

Range	0-18	0-18	0-18
Body connection			
Body Dissociation			
Mean (*SD*)	1.22 (.74)	1.17 (.75)	1.26 (.74)
Range	0-4	0-4	0-4
Body Awareness			
Mean (*SD*)	2.4 (.7)	2.49 (.74)	2.35 (.74)
Range	0-4	0-4	0-4

Abbreviations: TCE (Traumatic Childhood experiences measured by the sum score of the Childhood Trauma Questionnaire), LPF (Levels of Personality Functioning measured by the Levels of Personality Functioning Scale-Brief Version 2), Body connection (Body awareness and dissociation measured by the Scale of Body Connection).

Note. [1]N = 31 participants from Chile did not indicate age, gender, occupation, or clinical status. Therefore, descriptive data was based on $N = 488$ for the respective variables.

[2]Employed = actively and primarly pursuing a financially compensated job, including salaried employees, civil servants, self-employed persons, and contract-based work on an honorary basis; Student/Trainee = actively and primarily pursuing vocational or academic training, including university students and vocational trainees (pre- and postgraduate), Unemployed = not pursuing actively any financially compensating job or vocational/academic training.

[3]Self-reported official record of a mental disorder diagnosed by a licensed psychotherapist or medical doctor; For the Chilean sample = diagnosis of a personality disorder at any moment of their life and a concurrent psychological or psychiatric treatment; For the german sample = diagnosis of any current mental disorder (most frequent self-reported diagnoses were affective disorders (20.2%), personality disorders (9.3%), anxiety disorders (7.3%), post-traumatic stress disorder (7.2%) and eating disorders (4.3%)).

Bivariate Correlations

Correlational analyses revealed substantial, significant associations between most of the assessed variables (see Table 2 for a list of all associations). TCE (CTQ sum score) demonstrated a moderate, positive association with body dissociation (r = .426, p < .001), as opposed to a very low, negative correlation to body awareness (r = -.082, p < .01), and a moderate positive correlation with personality functioning (r = .435, p < .001), as well as it's two subscales, self functioning (r = .382, p < .001), and interpersonal functioning (r = .420, p < .001). Personality functioning demonstrated a very strong, positive correlation to body dissociation (r = .728, p < .001), and a small, negative correlation with body awareness (r = -.230, p < .001).

Mediation Analyses

In the next step, we analyzed whether the two facets of body connection, namely, body dissociation and awareness mediated the association between TCE and personality functioning (see also Figure 1). TCE explained 26% of the variance in personality functioning after adjusting for age, sex, and nationality (R^2 = .261). Furthermore, there was a significant indirect effect of TCE on personality functioning through body dissociation (b = .128, 95% *CI* [.111, .147]), and, albeit to a much smaller degree, through body awareness (b = -.003, 95% *CI* [-.001, -.006]). The direct effect (c') remained significant after the mediators were included, but its effect was substantially reduced. The total mediating effect of body dissociation and awareness accounted for 60% of the total effect between TCE and personality functioning. The total model explained 58% of the variance in personality functioning (R^2 = .579).

In a further step, we investigated the mediating role of body connection in the relationship between TCE and the two domains of personality functioning, namely, self and interpersonal functioning, by calculating two separate mediation analyses (also see Figure 2).

After adjusting for the control variables, TCE explained 24% of the variance in self functioning (see Figure 2), and 21% of the variance in interpersonal functioning (see Figure 3). There was a significant indirect effect of TCE on self functioning (*b* = .075, 95% *C I*[.065, .089]) and interpersonal functioning (*b* = .053, 95% *CI* [.045, .062]) through body dissociation, and, to a smaller degree, through body awareness (Self: *b* = 001, 95% *CI* [.001, .003], Interpersonal: *b* = 002, 95% *CI*[.001, .003]). The direct effect (c') of TCE on both self and interpersonal functioning remained significant after including the two mediators. The mediating effect of body dissociation and awareness accounted for 64% of the total effect between TCE and self functioning, and for 55% of the total effect between TCE and interpersonal functioning. In sum, the models explained up to 53% in self (R^2 = .53) and up to 45% in interpersonal functioning (R^2 = .45).

Figure 1

Parallel Mediation Model on TCE, Body Dissociation, Body Awareness, and Personality Functioning

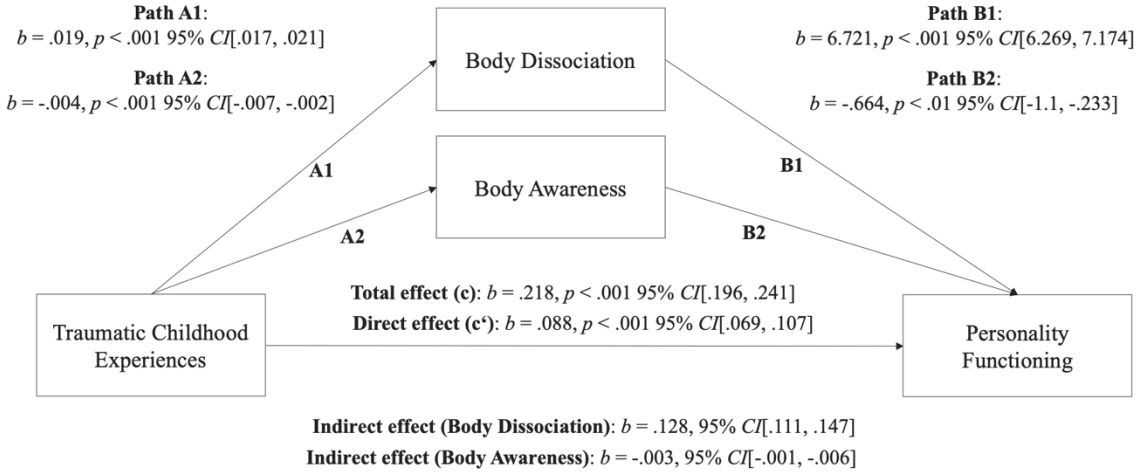


Figure 2

Parallel Mediation Model on TCE, Body Dissociation, Body Awareness, and Self-Functioning

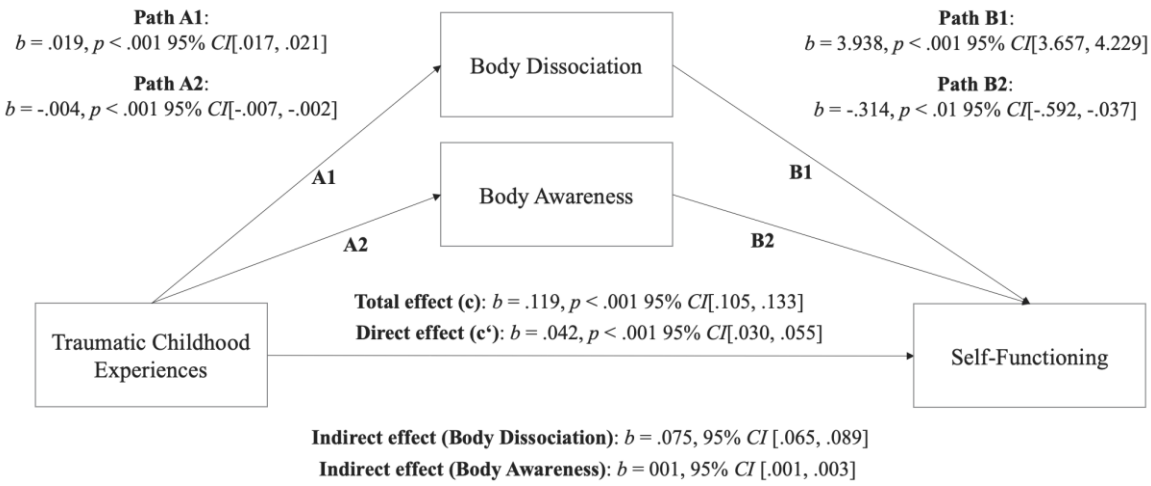
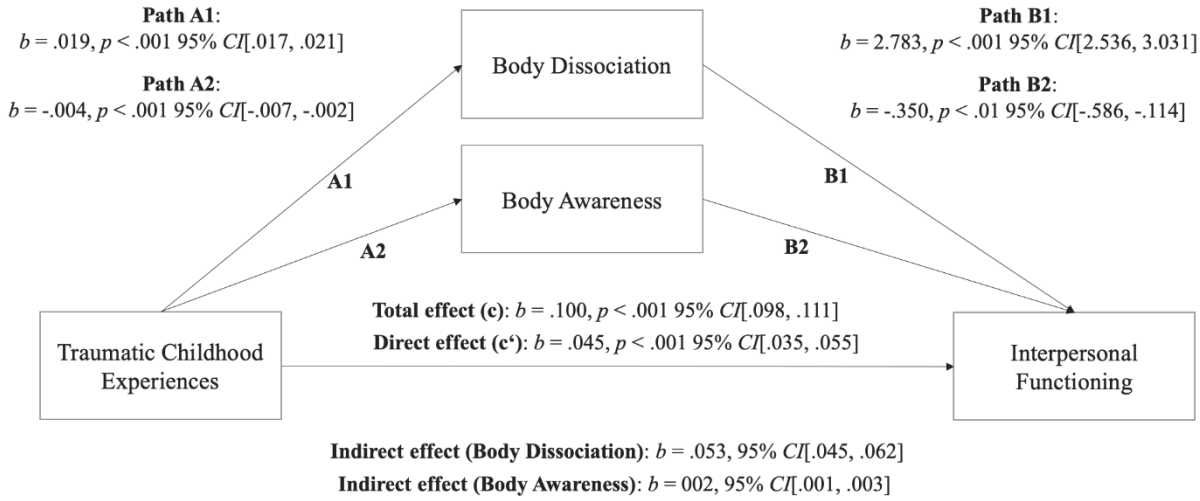


Figure 3

Parallel Mediation Model on TCE, Body Dissociation, Body Awareness, and Interpersonal Functioning



Discussion

The current study investigated the mediating role of self-reported body connection in the relationship between TCE and personality functioning in a heterogeneous sample including participants from two countries, from a community sample as well as a clinical sample. The results confirm the central role of TCE for impairments in personality functioning, accounting for 26% of the variance. Interestingly, 60% of this effect was explained by body connection, and in particular by body dissociation. Our additional analyses showed that this was true for both domains of personality functioning: body dissociation (and, to a much smaller degree, body awareness) accounted for 64% of the variance in self functioning explained by TCE and 55% of the variance in interpersonal functioning explained by TCE. Thus, the current study provides further evidence for the crucial role of body dissociation, i.e., disturbed integration between bottom-up bodily and top-down mental processes, associated with impairments related to self and interpersonal functioning and TCE.

In all of our mediation analyses, body dissociation was found to be a substantial and significant mediator in the association between TCE and personality functioning. Body awareness showed a significant, but very modest and almost negligible effect, across all mediation analyses. These results are in line with and confirm the findings of Schmitz et al., (2021) and Schmitz et al., (submitted): Only body dissociation fully mediated the association between TCE and emotional dysregulation (a lower-order domain of self functioning) in individuals with BPD (Schmitz et al., 2021) and across individuals with PTSD, MD, SSD and individuals without a mental disorder, in contrast to body awareness and related processes (Schmitz et al.,submitted).

Taken together, our results suggest that especially the avoidance and non-attendance of bodily sensations could contribute to impairments in self and interpersonal functioning following TCE, in contrast to the mere perception of body sensations (i.e., body awareness),

across individuals with and without various mental disorders. Higher levels of body dissociation are indicative of lower integration of aversive body sensations in emotional states (Price & Thompsom, 2007) and may be a proxy for sensitivity to interoceptive processing (e.g., in terms of habitual disregard or non-attendance of signals from inner bodily signals; Khoury et al., 2018). Comparable to our results, research on interoception in BPD point towards a reduced subjective tendency to attend to inner bodily sensations (i.e., reduced interoceptive sensitivity), and a reduced cortical representation of interoceptive signals (i.e., reduced objective physiological states) alongside with an unaltered ability to accurately perceive interoceptive signals (i.e., interoceptive accuracy; see Back & Bertsch 2020, for a review). These findings on reduced subjective and physiological interoceptive processing might reflect an overly strong focus on external stimuli (instead of internal bodily information), in order to earlier detect and prevent traumatic harm (as seen in survivors of TCE, see Back & Bertsch, 2020 for a review; Schmitz et al., 2021). In line with the theoretical model for BPD (Löffler et al., 2018) and the developmental perspective on interoception for the sense of self (Foutopouli & Tsakiris, 2017), learned habitual disregard of inner bodily signals in adulthood resulting from TCE might contribute to higher-order deficits in identity, self-direction, empathy and intimacy in relationships. In favor of the current results, Mindfulness-based interventions, aiming at restoring the willingness to perceive and conscious attention location towards inner bodily and associated psychological sensations, are already important elements in transdiagnostic, third-wave psychotherapy programs (such as dialectic behavioral therapy, mindfulness-based cognitive therapy), including body-oriented modules such as body scan (Dreeben, Mamberg & Salmon 2013).

Limitations and future directions

Despite some intriguing advantages of the current study, such as the inclusion of a relatively large and heterogenous sample including participants from two different countries (and continents) from the general population as well as clinical settings, some limitations need to be regarded. First, our cross-sectional, correlational, mono-method design does not allow for causal inference. Furthermore, using mediation modeling on cross-sectional data has been criticized (Maxwell & Cole, 2007). We tested mediation models as recommended by Hayes (2013) and MacKinnon et al. (2007). Therefore, our results should be interpreted as a preliminary proposed model, with further experimental and longitudinal research warranted for a conclusive test of effects.

The partial mediation effect suggests that other processes not depicted in our mediation model are also implicated in the relationship between TCE and personality functioning. Other processes might include transdiagnostic protective and resilience factors, such as social support (Seitz et al., 2022). Following recent evidence on transdiagnostic models of psychopathology, TCE likely represent a differential susceptibility factor, increasing affected individual's vulnerability to stressors and subsequent emerge of psychopathology, but also sensitivity to improvements in stress-regulation in population-based samples (Albott et al., 2018). As personality functioning depicts the entire spectrum from none to severe impairment, it may be important to also include resilience and protective factors promoting sensitivity to improvements in everyday (early) stress-regulation, especially in those samples characterized by lower clinical symptom severity (as expected in community or population-based samples). This might be especially true for the current sample, with levels of personality functioning equal to the mean value expected within a representative general population, (i.e., representing rather higher ranges of functioning; Spitzer et al., 2021).

We solely relied on self-report measures, limiting the validity of the clinical characterization of our subsamples, and with the retrospective report of childhood traumata being affected by recall bias and state-dependent memory. On the other hand, retrospective and prospective measures of childhood trauma have been shown to be of good comparability (Scott, McLaughlin, Smith & Ellis, 2012) and the CTQ shows equal psychometric properties compared to interview-based assessments (Seitz et al., 2022). Future studies should replicate our findings employing experimental and longitudinal designs and assess clinical status by means of standardized interviews.

Third, we cannot prove that our effects on body dissociation are independent of other, more general forms of dissociation, which have been shown to be highly prevalent in BPD (Scalabrini et al., 2017). Therefore, our effects on body dissociation may be conflated with those of other forms of dissociation that eventually might better explain or complement our proposed model. However, Schmitz et al., (2021) and Schmitz et al., (submitted) were able to demonstrate that the effects of bodily dissociation are robust when levels of trait dissociation were statistically controlled for. Future studies should also control for other forms of acute and chronic dissociation when studying the specific effects of dissociation from bodily processes.

Conclusion

Our results suggest a mediating role of body dissociation in the relationship between TCE and personality functioning. Further research on body connection and complementing processes as potential mechanisms of change in personality functioning temporarily following TCE is needed.

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Study V: Reduced vagal activity in borderline personality disorder is unaffected by intranasal oxytocin administration, but predicted by the interaction between childhood trauma and attachment insecurity

Back, S. N., Schmitz, M., Koenig, J., Zettl, M., Kleindienst, N., Herpertz, S. C., & Bertsch, K. (2022). Reduced vagal activity in borderline personality disorder is unaffected by intranasal oxytocin administration, but predicted by the interaction between childhood trauma and attachment insecurity. *Journal of Neural Transmission*, *129*(4), 409-419. This chapter is a post-peer-review, pre-copyedited version of an article published in Journal of Neural Transmission. The final authenticated version is available online at https://doi.org/10.1007/s00702-022-02482-9.

Reduced vagal activity in Borderline Personality Disorder is unaffected by intranasal oxytocin administration, but predicted by the interaction between childhood trauma and attachment insecurity

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All participants provided their written informed consent prior to study participation. The study was approved by the Ethics Committee of the Medical Faculty of the University of Heidelberg. The study was supported by financial grants from the German Research Foundation (DFG) awarded

to K. Bertsch and S.C. Herpertz within the Clinical Research Unit 256 (KFO-256, BE5292/2-1, HE2660/14-1 and HE2660/16-2). The authors have no conflict of interest to declare that are relevant to the content of this article. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgements: We kindly thank Dr. Jan Dörendahl for his expertise in statistical analysis. We also thank the team of the Clinical Research Group on Mechanisms of Disturbed Emotion Processing in Borderline Personality Disorder (KFO 256) for participant recruitment and organization.

Authors' contributions: Conceptualization: Katja Bertsch, Sabine C. Herpertz; Funding Acquisition: Katja Bertsch, Sabine C. Herpertz; Resources: Katja Bertsch, Sabine C. Herpertz; Project Administration: Katja Bertsch, Sabine C. Herpertz; Data Curation: Marius Schmitz; Investigation: Marius Schmitz; Methodology: Sarah N. Back, Katja Bertsch; Software: Sarah N. Back, Max Zettl, Julian Koenig; Formal Analysis: Sarah N. Back; Validation: Max Zettl, Marius Schmitz, Julian Koenig, Nikolaus Kleindienst, Sabine C. Herpertz; Writing - Original Draft: Sarah N. Back; Writing – Review & Editing: Sarah N. Back, Marius Schmitz, Julian Koenig, Max Zettl, Sabine C. Herpertz, Nikolaus Kleindienst, Katja Bertsch; Supervision: Katja Bertsch

Abstract

Individuals with borderline personality disorder (BPD) show self-regulatory deficits, associated with reduced heart-rate variability (HRV). However, results on reduced HRV in BPD remain heterogeneous, thus encouraging the search for developmental constructs explaining this heterogeneity. The present study first examined predictors of reduced resting-state HRV in BPD, namely the interaction between self-reported adult attachment insecurity and childhood trauma. Secondly, we investigated if alterations in resting-state HRV are modified by intranasal oxytocin administration, as oxytocin may enhance HRV and is implicated in the interaction between childhood trauma and disturbed attachment for the pathogenesis of BPD. In a randomized, placebo-controlled trial, 53 unmedicated women with BPD and 60 healthy controls (HC) self-administered either 24 I.U. of oxytocin or placebo and underwent a 4-minute electrocardiogram. Our results replicate significantly reduced HRV in women with BPD, explained up to 16% by variations in childhood trauma and attachment insecurity. At high levels of acute attachment insecurity, higher levels of childhood trauma significantly predicted reduced HRV in BPD. However, our results do not support a significant effect of oxytocin on mean HRV, and no interaction effect emerged including childhood trauma and attachment insecurity. Our findings highlight a complex interaction between reduced vagal activity and developmental factors in BPD.

Keywords: Heart-rate Variability, Vagal activity, Borderline Personality Disorder, Attachment, Oxytocin, Early Life Adversity, Childhood trauma

Introduction

Borderline personality disorder (BPD) is a severe mental disorder, which affects around 15-28% patients in clinical populations (APA 2001). Core symptoms of BPD are emotional dysregulation, impulsivity, and interpersonal hypersensitivity, all of which have been shown to be associated with alterations in heart-rate-variability (HRV; Lane et al. 2009; Thayer & Brosschot 2005; Ottaviani et al. 2018; Weise et al. 2020a).

HRV is defined as the beat-to-beat variability of heartrate (Berntson et al. 1997) indicating different autonomic states (i.e., higher variability indicating majorly vagal and lower variability reflecting majorly sympathetic predominance of the autonomic nervous system; ANS). While the sympathetic system is associated with energy mobilization during stress, the parasympathetic system reflects vegetative and restorative functions (Thayer & Brosschot 2005). According to the model of neurovisceral integration, these two states are in dynamic balance and interplay with different environmental demands (Thayer & Brosschot 2005). Chronic autonomic imbalance, in which the sympathetic stress system is hyperactive and the parasympathetic system is hypoactive (e.g., lower HRV at rest), in turn, is theorized to be associated with various pathological conditions (Thayer & Brosschot 2005), including BPD (for meta-analysis, see Koenig et al. 2016). Indeed, unaltered HRV has been proposed as a biomarker of self-regulation and mental health (Beauchaine & Thayer 2015). With regard to the aetiology of BPD, various results on reduced HRV point to a chronic reduction of the vagal ANS component, potentially reflecting a lack for efficient self-regulation (Thayer 2009; Koenig et al. 2017; Weise et al. 2020). Longitudinal studies suggest that changes in adolescent resting-state HRV are associated with changes in BPD symptomatology (Koenig et al. 2018; Sigrist et al. 2021), and even predicted clinical symptom reduction in adolescent BPD patients receiving dialectical behavioural therapy (Weise et al. 2020b).

However, findings on resting-state HRV in BPD remain heterogeneous: Several studies failed to find a significant reduction of resting HRV in women with BPD as compared to healthy controls (Austin et al. 2007; Gratz et al. 2013; Meyer et al. 2016; Krause-Utz et al. 2019). Mixed findings can be attributed to the high heterogeneity of resting-state HRV among individuals with BPD (Koenig et al. 2020), as compared to healthy (Koenig et al. 2016) and other clinical conditions, such as post-traumatic stress disorder (Meyer et al. 2016). High heterogeneity in physiological baseline activity within groups of BPD and across studies seems to be a common phenomenon, equally observed when inspecting other biobehavioral indices linked to stress physiology (Scott et al. 2013; Wingenfeld et al. 2010; Ehrenthal et al. 2019). In a recent review, Koenig et al. (2020) concluded that these alterations in ANS function within individuals with BPD might be linked to severe experiences of early maltreatment and trauma.

Heart-rate variability, childhood trauma and the moderating role of attachment insecurity

A history of *childhood traumatic experiences* and *attachment insecurity* are the most studied developmental risk factors of BPD (Gunderson et al. 2018; Ehrenthal et al. 2019), both being linked to disturbed vagal activity (Ostermann et al. 2010; Sigrist et al. 2020).

Childhood trauma is associated with a higher risk to develop BPD (see Gunderson et al. 2018 for review), with affected individuals being more than four times more likely to report childhood adversity as compared to non-clinical individuals (Porter et al. 2020; Kleindienst et al. 2020). Childhood trauma has been shown to exhaust early self-regulatory capacities and therefore contribute to the pathogenesis of dysregulated autonomic- and endocrine- functions in critical developmental periods, epigenetically priming physiological functioning towards heightened stress sensitivity (McLaughlin et al. 2015; Oosterman et al. 2010; Ferrer 2021).

Meyer et al. (2016) supported this strain of research concerning HRV as marker of ANS functioning, by showing that levels of childhood trauma were negatively associated with resting-state HRV in a sample including women with BPD. Childhood trauma might therefore generally prime the ANS towards higher sympathetic dominance, with different levels of early traumatization contributing to different HRV resting-states within BPD women (Meyer et al. 2016). Although childhood trauma can be considered a robust risk factor for BPD, early research already showed that some affected individuals nonetheless display a history of little or no traumatic experiences (Herman et al. 1989; Zanarini & Frankenburg 1997), thus childhood trauma does not necessarily and robustly precede BPD development (Gunderson et al. 2018). This suggests that additional mechanisms than only childhood trauma might be implicated in BPD pathogenesis.

A growing number of studies emphasizes that interindividual differences in *attachment insecurity* importantly contextualize the impact of childhood trauma on BPD symptoms (Crow et al. 2019; Baryschnikow et al. 2017; Peng et al. 2021), such as on personality functioning (Gander et al. 2020) as well as on pathophysiological mechanisms of BPD related to sympathetic hyperactivity/stress sensitivity (Ehrenthal et al. 2019; Simeon et al. 2011). Children living in conditions with severe disruptions in the parent–child relationship (e.g., relational childhood trauma) are at greater risk to develop and maintain unresolved internal working models of social interactions, contributing to attachment insecurity and personality pathology until adulthood (Bowlby 1982; Liotti 2004; Cyr et al. 2010). Internal working models are conceptualized as cognitive self-regulatory mechanisms (Mikulincer et al. 2009). Therefore, individuals with very low levels of integration and coherence of internal working models (i.e. higher attachment insecurity) may have also developed an altered biological predisposition to stress regulation (Ehrenthal et al. 2019). Empirically, subgroups of severely insecure attached individuals with BPD show heightened cortisol activity related to heightened sympathetic

activity in an interpersonal context (Ehrenthal et al. 2019). Concerning ANS functioning, insecurely attached individuals show reduced HRV when confronted with traumatic experiences, indicative for heightened sympathetic activity (Farina 2015; Decarli et al. 2020). Although former psychophysiological studies support the moderating role of attachment insecurity when inspecting cortisol activity in women with BPD (Ehrenthal et al. 2019; Simeon et al. 2011), no study tested the moderating role of attachment security on the association between childhood trauma and resting-state HRV in individuals with BPD yet.

Heart-rate variability, childhood trauma, attachment insecurity and oxytocin

A potential pharmacological intervention for reduced vagal activity as a physiological target mechanism underlying inefficient self-regulation in BPD might be intranasal administration of oxytocin (IN-OT; Herpertz & Bertsch 2015; Norman et al. 2011; Kemp et al. 2012). Oxytocin may especially impact the relationship between HRV, childhood trauma and attachment insecurity, as being conceptually and empirically linked to (1) the interaction between early-life stress and disturbed attachment in the pathogenesis of BPD (Herpertz & Bertsch 2015) and (2) IN-OT in dampening sympathetic activity at rest in order to facilitate capacity for adaptive self-regulatory behaviour (Norman 2011; Kemp et al. 2012; Porges 2007).

Oxytocin is an important regulator of social cognition and behaviour (Kemp et al. 2012), implicated in successfully establishing early attachment relationship between child and caregivers following pregnancy (Rilling & Young 2014). According to a pathophysiological model of BPD (Herpertz & Bertsch 2015), BPD could both result from and result in low parental oxytocin levels, activating a neuroendocrine cascade associated with elevated risk for childhood stress, poor parental attachment, promoting attachment insecurity, hypersensitivity to stress, and impeding regulation capacities until adulthood. Indeed, reduced baseline oxytocin levels have been found in serum of women with BPD compared with HC (Bertsch et al. 2013a)

and in cerebrospinal fluid of women with childhood trauma compared to women without childhood trauma (Heim et al. 2009).

IN-OT has been shown to reduce threat hypersensitivity and approach (Bertsch et al. 2013b; Schneider et al. 2019), such as amygdala and insular reactivity to stimuli of negative valence in women with BPD (Lischke et al. 2012). Oxytocin receptors are especially dense in specific limbic regions and their connections to the prefrontal cortex (Bartels & Zeki 2004), which may also modulate ANS activity (Fatisson et al. 2016). Peripherally, oxytocin receptors are located in the heart and surrounding vagal pathways. Thereby, oxytocin may upregulate parasympathetic and downregulate sympathetic responses, with IN-OT showing an enhancing effect on HRV at rest in healthy male individuals (Norman et al. 2011, Kemp et al. 2012). Although former studies support a beneficial effect of IN-OT on interpersonal pathology in BPD, no study investigated effects of IN-OT on intrapersonal mechanisms reflecting self-regulatory capacities, i.e. resting-state HRV in females with BPD, yet.

The current study

Within the central project of the Clinical Research Unit 256 (Schmahl et al. 2014), the current study presents a secondary analysis of the subproject „Social Perception II", encompassing a randomized-controlled trial studying the effects of oxytocin on social perception in BPD (Trial Registration Number: DRKS00009815). The aim of the present secondary investigation was to (1) replicate reduced baseline vagal activity in unmedicated BPD women as indexed by reduced time-domain measures of HRV (i.e. the root-mean-square of successive R–R-interval differences, RMSSD). RMSSD has been shown to be one of the most robust and reliable indicators of vagally-mediated HRV and to be mostly unaffected by breathing artefacts (Penttilä et al. 2001). In order to further resolve the high level of heterogeneity in resting-state HRV activity within BPD women and across studies, we examined (2) the moderating role of adult attachment insecurity in the association between

childhood trauma and RMSSD. However, we expect a smaller or no moderation effect within the sample of healthy women, in line with recent meta-analytic results showing a lack of relationship between CT and HRV in the absence of a concomitant psychopathological status (Sigrist et al. 2021). Lastly, we investigated (3) potential modulatory effects of oxytocin on RMSSD in women with BPD and healthy controls (HC) and (4) explored interactive effects of childhood trauma, attachment and clinical group with oxytocin on RMSSD.

Method

Participants

A total of 53 medication-free adult female women with a current DSM-IV diagnosis of BPD (M_{age}=30.02, SD=7.42, range=30) and 60 healthy female controls (M_{age}=27.82, SD=7.1, range=34) participated in the study. Recruitment and diagnostic assessment were performed by the central project of the Clinical Research Unit 256 (Schmahl et al. 2014). The study was approved by the Ethics Committee of the Medical Faculty of the University of Heidelberg. All participants provided their written informed consent prior to study participation and were paid for their participation. All projects from this research group include participants from a joint database. Therefore, the BPD and HC sample was included in a publication of Schmitz et al. (2020) and Schneider et al. (2020) which, however, did not include investigation of HRV of patients with BPD compared to HC, which is the focus of the current study.

BPD women and healthy controls were matched for age ($t_{(111)}$=1.61, p=.109), and Body-Mass-Index (BMI; calculated as body weight (kg) / body height $(m)^2$) ($t_{(111)}$=1.5, p=.137) and did not differ in heart rate (mean=69.4 bpm; $t_{(111)}$=1.8, p=.075). Both groups neither encountered any neurological disease, severe physical or psychiatric condition (including cardiac condition, pregnancy, current alcohol and/or drug abuse, drug and/or alcohol dependency two months prior testing, lifetime diagnosis of schizophrenia, schizoaffective or

bipolar disorder), nor took any acute medication (except contraceptives and need-based medication, maximum one day prior to laboratory testing). Additionally, healthy controls did neither receive any lifetime psychiatric diagnosis, nor underwent any psychotherapeutic/psychiatric treatment.

Materials

Qualified and trained diagnosticians assessed BPD and other psychiatric diagnoses with semi-structured interviews, i.e. the Structured Clinical Interview for DSM IV for Axis I disorders (SCID-VI-I; First et al. 1995) and the International Personality Disorder Examination for Axis II disorders (IPDE; Loranger et al. 1997).

Childhood traumatic experiences were assessed using the Childhood Trauma Questionnaire (CTQ; Bernstein et al. 2003). Participants rated the frequency of traumatic experiences on a 5-point Likert scale (ranging from "never true" to "very often true"), for 5 scales ("physical abuse", sexual abuse", "emotional abuse", "physical neglect" and "emotional neglect"). The total sum score was calculated, ranging from 25 to 125, with a Cronbach's α of .87 in the present sample.

Adult romantic attachment style was operationalised by the Experiences in Close Relationships Scale (ECR-R; Ehrenthal et al. 2009), with the two subscales of anxiety and avoidance of attachment. A total mean score of the two scales was calculated, ranging from 1 to 7, indicative for the overall level of attachment insecurity, with a Cronbach's α of .97 in the present sample.

A standardised questionnaire was used to measure demographic information, age, weight, height and BMI (see Table 1).

Procedure

After an extensive telephone screening, participants underwent a face-to-face clinical diagnostic interview. On the day of the experiment, participants were instructed not to smoke, take caffeine or analgesics and to relinquish eating 2h prior to the experimental session. Testing took place in a sound-attenuated, dimly-lit room, followed by the collection of biological samples (not reported here). In a double-blind design, participants were randomly assigned via block randomisation (computerized algorithm, performed by an independent person not involved in the study), either to a single intranasal dose of 24 I.U. of oxytocin (six puffs of 2 I.U. to each nostril) or a placebo condition (spray with the same inactive ingredients but without oxytocin). The oxytocin and placebo nasal sprays were prepacked in identical bottles and consecutively numbered with each number being subdivided in "A" and "B" according to the randomisation schedule. The allocation sequence was concealed from both participant and the researcher conducting the study. Sealed and stapled envelopes, containing information about the allocation between number and content of the nasal spray, were locked and only opened after the last participant had completed the study. Electrodes were applied and participants performed several experimental tasks (see Schneider et al. 2020 and Schmitz et al. 2020 for a detailed description). 85 min after spray administration, 4 minutes of ECG measurement were taken in a comfortable upright position, and participants were instructed to sit still and stay awake.

Physiological Data Acquisition and Processing

ECG was measured using 2 Ag/AgCl electrodes with micropore tape and solid gel (3M Health Care) according to Eindhoven II configuration and stored at a sampling rate of 1000 Hz (72-chanel QuickAmp amplifier; Brain Products GmbH). Heart rate (HR) and R-peaks were detected offline with EDF-Browser Software employing combined adaptive thresholding (Christov 2004). Raw ECG was visually inspected for artefacts and correct R-trigger location.

Three participants (BPD=1, HC=2) had to be excluded from further HRV-Analysis due to poor raw ECG signal quality and concomitant fail of automatic R-Trigger detection. Inter-beat-intervals (IBI) were transferred to ASCII format, cleaned and processed using the RHRV package, an automatic tool for HRV analysis in R (Martinez et al. 2017). Cleaned and processed IBIs were additionally visually reviewed for potential artefacts. In a final step, RMSSD indices were derived automatically and transferred to SPSS (IBM SPSS 26). Zhang and colleagues suggested that RHRV-extracted indices for HRV display high reliability and validity ($r > 0.8$) compared to respective indices retrieved from the gold-standard software Kubios (Zhang et al. 2020).

Statistical Analysis

Group differences in RMSSD (*hypothesis 1*) as well as effects of oxytocin administration on RMSSD (*hypothesis 3*) were analysed using a 2x2 analysis of variance (ANOVA; SPSS 26), with the between-subject factors group (BPD, HC) and substance (oxytocin, placebo). A moderated linear regression analysis using the PROCESS plug-in for SPSS was performed (model number 1, version 3.4.1; Hayes 2017) in order to test for a potential moderating effect of attachment insecurity score on the association between the childhood trauma score and mean RMSSD score in the BPD group, and in the HC group (all predictors were mean centred; *hypothesis 2*). Moreover, we exploratory tested for potential interactions of childhood trauma, attachment insecurity, substance and clinical status on RMSSD (exploratory question *4*) by running an ANCOVA with the between-subjects factor group (BPD, HC), substance (oxytocin, placebo) as well as childhood trauma (continuously) and attachment (continuously) as covariates, checking for every specific interaction with substance (childhood trauma*substance, attachment*substance, childhood trauma*attachment*substance, childhood trauma*attachment*group*substance). Partial eta-

squared (η^2) are reported as effect size (.01, .06, .14 are considered small, medium, and large effects, respectively (Cohen, 1988))

Table 1

Demographic, psychometric and self-reported data of women with borderline personality disorder (BPD) and healthy controls (HC) in the oxytocin (oBPD, N = 26; oHC, N = 30) and placebo condition (pBPD = 27; pHC, N = 30)

	oBPD (n = 26)	**pBPD (N = 27)**	**oHC (N = 30)**	**pHC (N = 30)**	**BPD vs HC**		**oBPD vs. pBPD**		**oHC vs. pHC**	
	M + *SD*	*M* + *SD*	*M* + *SD*	*M* + *SD*	*t*	*p*	*t*	*p*	*t*	*p*
Age (years)	29.0 + 7.9	31.0 + 6.9	27.6 + 7.8	28.0 + 6.4	1.62	.109	- 1.02	.313	- 0.20	.842
Body Mass Index (BMI)	24.0 + 5.0	25.4 + 6.0	22.5 + 2.6	24.1 + 5.3	1.49	.139	- 0.93	.358	- 1.5	.140
Heart Rate (bpm)	69.0 +8.4	73.0 + 9.6	65.2 + 9.2	70.3 + 10.5	1.80	.075	- 1.58	.121	- 2.03	.048
BPD Dimensional Score (IPDE)	*14.7 + 1.8*	14.6 + 1.6	0.0 + 0.0	0.0 + 0.0	62.1	.000	0.92	.532	-	-
Early Traumatization (CTQ)	58.9 + 22.2	63.0 + 18.1	31.2 + 6.3	31.4 + 9.3	9.96	.000	- 0.73	.467	- .10	.921
Adult Attachment Style (ECR-R)	4.5 + 0.6	4.2 + 1.4	1.8 + 0.2	1.8 + 0.3	16.2	.000	1.17	.250	- .42	.673

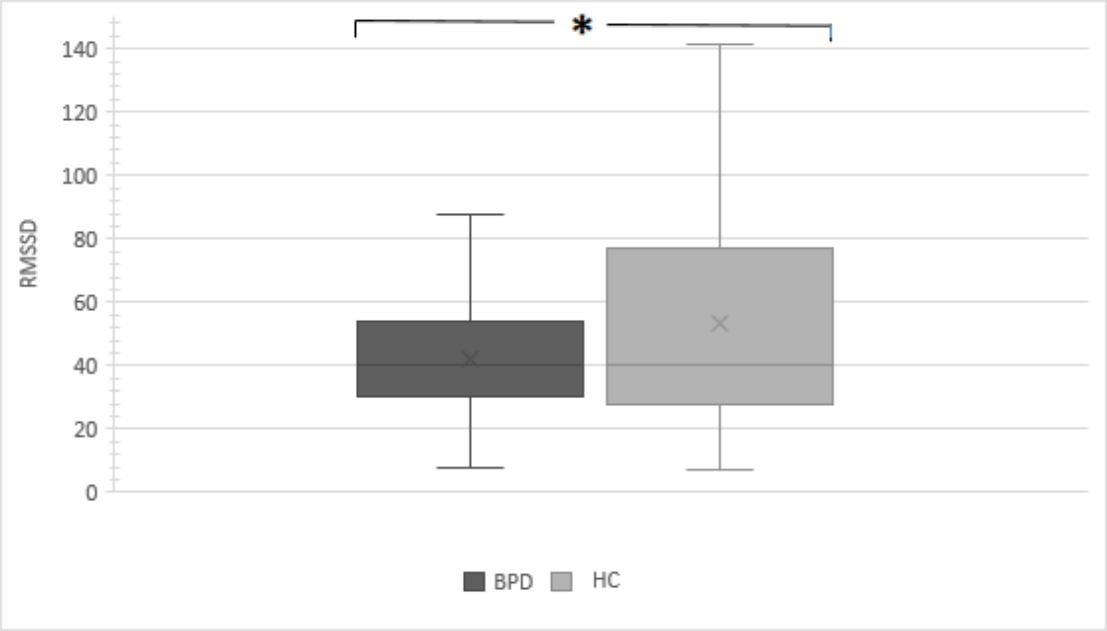
Abbreviations: BMI, body mass index; BPD, women with borderline personality disorder; CTQ, Childhood Trauma Questionnaire; ECR-R, Experiences in Close Relationships Scale; HC, healthy controls; IPDE, International Personality Disorder Examination. Explanatory note: Heart rates were calculated via ARTIIFACT.

Results

As expected (*hypothesis 1*), women with BPD had significantly lower mean RMSSD values than HC ($F(1,107)=4.6$; $p=.034$, $\eta^2=.04$, see Figure 1). Concerning *hypothesis 2*, neither the main effect of substance ($F(1,107)=2.4$, $p=.121$, $\eta^2=.02$) nor the group by substance interaction ($F(1,107)=0.5$; $p=.475$, $\eta^2=.01$) reached statistical significance. Thus, contrary to *hypothesis 3*, there was no evidence that IN-OT modulated HRV activity in the current study, neither in women with BPD, nor HC.

Figure 1

*Box-plot diagram of the RMSSD of women with current borderline personality disorder (BPD; N = 52), and healthy controls (HC; N = 58). *p > 0.05*



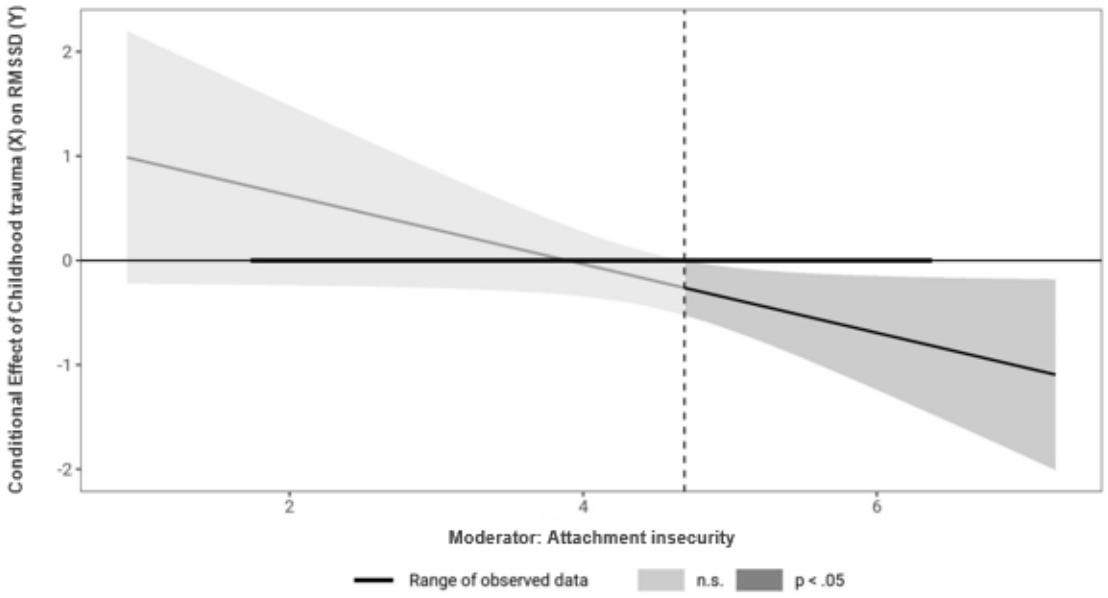
Concerning *hypothesis 2*, moderated regression analysis for the BPD group revealed that the R^2 for the overall model within the BPD group was $R^2=.16$ (adjusted $R^2=.11$), indicative for a medium goodness-of-fit ($R^2=.16$, $F(3,48)=3.15$, $p=.033$) according to Cohen (1988). Hence, the model including the three variables "childhood trauma", "attachment" and

"childhood trauma*attachment" explained 16% of the total variance in RMSSD in BPD women. At the individual level of the predictors, "attachment" (R^2=.16, F(3, 48)=3.15, p=.033, b=.18, t(48)=2.08, p=.042) and the interaction "childhood trauma*attachment" (R^2=.16, F(3, 48)=3.15, p=.03, b=-.01, t(48)=2.03, p=.048) significantly predicted RMSSD in the BPD group. Concerning the predictor "attachment", the regression indicated that higher levels of attachment insecurity were linearly associated with lower basal HRV levels in women with BPD. The interaction term between childhood trauma and attachment accounted significantly for 7% of the total variance in RMSSD (ΔR^2=.07, ΔF(3, 48)=3.15, p=.03, b=-.01, t(48)=2.03, p=.048). Johnson-Neyman technique revealed a significant interaction between childhood trauma and RMSSD only when attachment values exceeded a total mean score of 4.69 (p=.05; 40.38% of BPD sample, see Fig.2). When the mean attachment score is below the respective interval [4.69; 6.36], the slope of childhood trauma on RMSSD was non-significant (p=.110-.900). Therefore, the moderation analysis revealed that the association between childhood trauma and HRV levels was significant in those women with BPD demonstrating high levels of attachment insecurity. Thus, in accordance with *hypothesis 2*, attachment insecurity moderated the relationship between childhood trauma and HRV in women with BPD.

The respective moderated regression model for the HC group did not reach statistical significance (R^2 = .09, F(1, 55) = 7.2, p = .540). As expected, (see *hypothesis 2*), the predictive model between CT, attachment insecurity and HRV does not seem to apply for healthy women, due to a lack of variance within the predictors.

Figure 2

Conditional effect of X (= Childhood Trauma, CTQ) on Y (= HRV, RMSSD) of moderator (= Attachment Insecurity, ECR). The dashed black vertical line (mean attachment score = 4.69) represents the point where the relationship between Childhood Trauma and RMSSD transitions from statistically non-significant (light grey) to significant (dark grey) and is determined using the Johnson-Neyman technique



Note. The range of observed values of attachment insecurity (ECR) is [1.73; 6.36].

With regard to *exploratory hypothesis 4*, we found no interaction including the factor substance: neither the interaction substance by childhood trauma ($F(2,108)=1.019$; $p=.365$), substance by attachment ($F(2,108)=.121$; $p=.886$), substance by childhood trauma by attachment ($F(2,108)=.538$; $p=.585$), or substance by childhood trauma by attachment by group ($F(2,108)=.345$; $p=.709$). Thus, there was no evidence that IN-OT modulated HRV depending on different levels of attachment insecurity, childhood trauma, or having a diagnosis of BPD or not.

Discussion

The aim of the current study was to (1) replicate findings on reduced HRV at rest in women with BPD compared to HC, and to test if the (2) interaction between childhood trauma and attachment insecurity predicted reduced HRV in women with BPD and HC. Moreover, we investigated (3) modulations of oxytocin administration on HRV at rest and (4) explored interactions with childhood trauma, attachment insecurity and clinical status.

Most importantly, a significantly diminished HRV at rest in women with BPD compared to healthy women was predicted by interactions between high attachment insecurity and increased childhood trauma in the current sample. Only individuals with BPD and high attachment insecurity showed a significantly negative association between childhood trauma and HRV at rest. We found no evidence for linear relationships between CT and attachment insecurity predicting HRV, neither when accounting for a potential modulation between those predictors, in healthy women. Moreover, (3) IN-OT had no effect on HRV at rest, neither in the BPD, nor in the HC group and this lack of effect remained stable after (4) exploring interactions with childhood trauma and attachment insecurity.

In line with *hypothesis 1*, women with BPD showed significantly reduced vagally-mediated HRV as indexed by a commonly reported time domain measures RMSSD, compared to HC. Our result of reduced resting HRV in BPD women is in line with the results of Koenig et al. (2016), but the effects of the current study were smaller than the medium-sized effects as proposed by meta-analysis (Koenig et al. 2016). Reduced baseline autonomic functioning in BPD could display a chronic state of physiological imbalance towards less vagal activity, reflecting reduced biological capacity for efficient self-regulatory mechanisms (Thayer & Brosschot 2005; Austin 2007). Whereas we found a small but significant difference in HRV, many other studies reported no significant differences in HRV between BPD and HC (Meyer

et al. 2016; Austin et al. 2007; Gratz et al. 2013). The differences in results and effect sizes might be explained by the inconsistency in study design, assessed confounding factors (e.g., physical activity), BPD sample characteristics (e.g., medication) and size, as well as indices of HRV throughout the studies, calling for more replicability in HRV and BPD research designs.

The current results provide evidence for childhood trauma and attachment insecurity as relevant predictors explaining 16% of HRV variance in women with BPD. In line with *hypothesis 2*, we found that higher reports of childhood trauma predicted lower basal HRV in BPD, but only in those individuals with high levels of acute attachment insecurity, and no linear relationship between those constructs within the HC sample.

In the light of the neurovisceral integration model (Thayer & Brosschot 2005), a chronic state of sympathetic stress mobilization may represent a maladaptive physiological threat adaptation resulting from a combination of very early traumatic experiences and the presence of insecurity in current relationships. These interpretations are in line with previous research suggesting an interactive influence of childhood trauma and adult attachment insecurity on BPD symptoms (Carlson et al. 2009; Baryschnikow et al. 2017; Godbout et al. 2018), as well as the psychophysiological results pointing to the specific role of unresolved attachment on heightened stress sensitivity in BPD (Simeon et al. 2011). The lack of significant regressions within the HC group provides further evidence for the above-mentioned moderation to interact with psychopathological status. This is in line with the results of a current meta-analysis (Sigrist et al. 2020) which outlined the evidence of the negative relationship between childhood trauma and HRV only in the presence of psychopathology. Due to the almost absence of traumatic childhood experiences and attachment insecurity in the healthy control group (see *Table 1*), the variance in those predictors might have most likely been too low in order to explain sufficient variance within HRV for the regression model to become significant.

In conclusion, our results provide further support for the relevance of developmental constructs in contextualizing biobehavioural mechanisms and interindividual variations in BPD (Ehrenthal et al. 2019). Following the interpretations of Sigrist et al. (2020), we suppose that CT might potentially contribute to alterations within ANS development in childhood, as indexed by low vagal activity (low HRV), eventually perpetuating into adulthood as a function of acute insecurity in current relationships, and increasing the risk for psychopathology related to self- and interpersonal dysfunctioning (e.g., BPD).

Contrary to *hypothesis 3*, resting-state HRV was not modulated by oxytocin administration, as there was neither a significant main effect of substance, nor an interaction effect with clinical status. In contrast to our results, intranasal administration of oxytocin has been found to enhance baseline HRV in male HC (Norman et al. 2011; Kemp et al. 2012) as well as in a male clinical sample (Martins et al., 2020). As recent studies point to a pattern of interactive effects with childhood trauma and attachment insecurity (Schoormanns et al. 2020; Riem et al., 2021), we conducted exploratory analysis (*hypothesis 4*) but found no significant interaction of neither childhood trauma, attachment insecurity nor clinical group with oxytocin on RMSSD at rest. In contrast, it has been suggested that oxytocin is involved in attachment security and that methylation of the oxytocin receptor may be involved in the epigenetic modulation of childhood trauma (see Brüne 2015 for a review).

The lack of IN-OT effect is generally obedient with the *social salience hypothesis*, which states that oxytocin solely impacts neurophysiological activity under circumstances of salient social cues (Wigton et al. 2015). Our findings match those reported by Schmitz et al. (2020), who did not find alterations in heartbeat evoked brain potentials at rest following oxytocin administration in BPD women within the same sample. Moreover, our results match the interpretations by Riem et al. (2021), attributing altered HRV after oxytocin administration

to an increased attentional salience as induced by the social presence during the experiment. Concerning the interactive effects with early trauma, in accordance to our results, childhood trauma did not modulate IN-OT on salivary oxytocin in male adolescents (Fragkaki et al., 2020) and HRV was unaffected by IN-OT in individuals with adverse childhood experiences (Schoormans et al., 2020). Matching the conclusions as initially drawn by Herpertz und Bertsch (2015), IN-OT might therefore be more suited in improving BPD associated symptoms/mechanisms (including disturbed vagal activity) in the context of *social interactions* with and attachment to familiar people (e.g., before seeing a psychotherapist). Study designs following this hypothesis would be of interest.

Several limitations should be considered. First, we did not control for physical activity, smoking and menstrual cycle, as well as age and BMI, despite official recommendations for their inclusion into HRV research (Quintana et al., 2016). Therefore, we cannot exclude the possibility that differences in HRV between groups and their interaction with oxytocin and developmental constructs might be influenced by the above-mentioned intervening variables. Nevertheless, the groups were matched according to age, gender, and did not differ in terms of heart rate or BMI. Moreover, we only investigated RMSSD as indicator of HRV activity, although frequency domain indicators (such as high-frequency HRV) are also adequate, especially in capturing vagal activity (Task Force of the European Society of Cardiology, 1996). As we only measured ECG for 4 minutes, and did not control for breathing artifacts, we decided to rely on a relatively robust, single indicator of HRV (e.g., RMSSD, Penttilä et al. 2001; Quintana et al. 2016). The interpretations concerning the lacked oxytocin effect should be treated with caution: Most studies which found an effect of IN-OT on resting HRV relied on male individuals (Norman et al. 2011; Kemp et al. 2012), and those studies on females controlled for menstrual cycle (Schormanns et al. 2020), which we did not. Therefore, possible

effects of oxytocin on HRV in females with BPD might eventually be present, as a function of menstrual cycle. Last, we employed a cross-sectional design, including the well documented limitations for reporting past traumatization (Maughan & Rutter 1997), hindering causal inference.

We conclude that reduced vagal activity (e.g., reduced HRV) in BPD might be a promising target of intervention, as being associated with severity of early traumatic experiences in insecurely attached females with BPD. Future studies should aim to replicate our findings controlling for important covariates influencing HRV (e.g., physical activity, smoking, breath) employing longitudinal research designs. Moreover, our results suggest that IN-OT may not be a suitable intervention in enhancing autonomic functioning at rest in women with BPD. Further research on female individuals with BPD, controlling for menstrual cycle and employing interpersonal contexts are needed in order to draw clear conclusions on oxytocin's pharmacological potential.

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3. General Discussion

As mental health difficulties emerge from complex interactions between biological, behavioral, psychosocial and cultural processes that transcend diagnostic boundaries, dimensional, transdiagnostic models increasingly enter nosology and classification of mental disorders (Dagleish et al., 2020). Common to the emerging models in DSM-5 and ICD-11 is the emphasis on levels in personality functioning as the core concept of personality pathology. The overarching aim of the current thesis was to identify biopsychosocial processes associated with personality functioning. Therefore, this thesis addresses the relationship between TCE, interoception, self and interpersonal functioning in individuals with and without mental disorders, to advance our understanding of the endocrinological, neurophysiological, and psychological processes involved in this relationship.

The overarching aim of this thesis was therefore split into several sub aims: (1) to investigate the associations between various forms of TCE and personality functioning in a young-adult community sample, (2) to elicit the mediating role of multi-facetted interoceptive processes in the relationship between TCE and impairments in personality functioning in individuals with and without different mental disorders, and (3) to investigate potential modulatory effects of intranasal oxytocin administration on efferent interoceptive states (i.e., HRV) at rest in adult women with BPD considering the interaction with TCE and interpersonal functioning (i.e., attachment insecurity).

With regard to the first aim, the results of the first study indicate that retrospectively reported exposure to various forms of TCE was strongly associated with impairments in personality functioning in young adults. Concerning the second aim, the second study demonstrated deficits in afferent and efferent physiological states of interoception (i.e., reduced HEP and reduced HRV) and reduced self-reported interoceptive sensibility in women with BPD. Reduced afferent physiological states and interoceptive sensibility were associated with higher levels of TCE and impaired emotional dysregulation in BPD. Moreover, in the second,

third and fourth study, deficits in self-reports of interoceptive sensibility consistently emerged as a mediator in the relationship between TCE and self and interpersonal functioning in individuals with a variety of mental disorders (i.e., BPD, MD, SSD and PTSD) or without a mental disorder. With reference to the third aim, intranasal oxytocin administration did neither show modulatory effects on HRV at rest in women with BPD or healthy women, nor did this effect interact with TCE or attachment insecurity. Considering the overaching aim, the results from the studies suggest that childhood emotional and physical neglect such as abuse as well as sexual abuse might represent distal psychosocial risk factors, potentially increasing the vulnerability for the emerge of impairments in adult personality functioning. Subjective evaluation of decreased attendance and perception of bodily signals (i.e., interoceptive sensibility) emerged as one possible, more proximal risk factor, potentially contributing to the explanation of the relationship between TCE and adult impairments in self as well as interpersonal functioning across individuals with and without various mental disorders. Oxytocin, however, might not exhibit endocrinological effects on heart-rate variability at rest (i.e., objective physiological states of interoception) in women with BPD. The results of the studies with regard to the thesis' aims, strengths and limitations as well as future directions and potential clinical implications will be presented in the following sections.

3.1 Associations between Childhood Trauma and Levels of Personality Functioning

The results of the first study suggest that retrospective reports of emotional and physical neglect as well as emotional, physical, and sexual abuse in childhood and adolescence are strongly associated with higher levels of personality impairment in young adulthood. Considering the high levels of personality functioning in the recruited community sample, dimensional assessment suggest that this relationship might also apply for not meeting the criteria for a mental disorder, which aligns with recent advances towards dimensional

conceptualization and nosology of personality pathology. Some studies on categorical PD models support our results by showing that TCE is associated with general and subclinical PD symptoms in people without a personality disorder (Arata et al., 2005, Cohen et al., 2014). A strong dimensional relationship between TCE and personality functioning in community samples could be replicated by the results of study four of this thesis, also with regard both subdomains of self and interpersonal functioning. Consistent with the only previous study that also explicitly included Criterion A of the AMPD, self-reported TCE and levels of personality functioning show a similarly strong association in young adolescents with and without a mental disorder (Gander et al., 2019). The relevance of emotional and physical neglect and abuse in childhood for the emerge of personality pathology is depicted in theoretical models by Linehan (1993), Fonagy and Bateman (2008) such as the schema mode model by Young (2003). According to these models, experience of various forms of abuse and/or neglect may increase susceptibility to impaired emotion- and self-regulation through learned heightened attention towards potential interpersonal threat at the expense of attention to own feelings and needs (Linehan, 1993). TCE has been hypothesized to promote the representation of being abused and neglected in intimate relationships in adulthood, further contributing to unstable social relationships (Fonagy and Bateman, 2008; Young, 2003). In accordance, Gander et al. (2019) showed that insecure attachment style partly mediates the relationship between TCE and levels of personality functioning in individuals with and without a mental disorder. However, whether specific subdomains of self and interpersonal functioning (e.g., emotion dysregulation) show similar or different degree(s) of association to TCE, as suggested by some theoretical models (Linehan, 1993), remains unanswered.

Albeit, the retrospective design of the studies precludes causal inferences, the results from study one and four suggests that TCE might represent an important distal, psychosocial risk factor, potentially increasing the vulnerability for the emerge of dimensional impairments

in adult personality functioning in individuals without a mental disorder, which should be investigated longitudinally in future studies. Consistent with the hierarchical approach of Criterion A and supporting the assumption that TCE is highly related to a common dimensional factor of personality pathology, recent evidence suggests that TCE displays a stronger association with higher-order common factors of psychopathology than with individual distinct disorder categories (Keyes et al., 2012). Similarly, transdiagnostic approaches to TCE point to impairments in domains of self (e.g., emotional dysregulation) and interpersonal functioning (e.g., social threat hypervigilance) as key mediators in the relationship between TCE and adult transdiagnostic psychopathology. As d'Huart et al. (2022) recently showed that personality functioning partly mediated the effects of TCE on mental health difficulties in high-risk samples, it remains an open question whether the strong relationship between TCE and personality functioning might further contribute to explain the emergence of transdiagnostic psychopathology.

3.2 Interoception as mediator in the relationship between Childhood Trauma, Self and Interpersonal Functioning

Targeting specific alterations in multifaceted interoceptive processes (i.e., objective physiological states, interoceptive accuracy, -sensibility and -awareness) in BPD, the most prototypical disorder in terms of impairments in self interpersonal functioning (2.1), study two reviewed that previous literature suggests that BPD might exhibit reduced objective physiological processing (e.g., HEP and HRV) and reduced interoceptive sensibility, and mixed results regarding interoceptive accuracy which may potentially be intact. Considering the mediating role of multifaceted interoceptive processes (i.e., HRV, interoceptive accuracy, -sensibility and -awareness) in the relationship between TCE and impairments in emotion regulation (2.2) results from study two and three suggest that subjective evaluation of decreased

attendance of and focus to bodily signals (i.e., interoceptive sensibility) may fully explain certain domains of self-functioning, e.g., emotional dysregulation, across various mental disorders (BPD, PTSD, MD and SSD) and individuals who reported TCE but no mental disorder. Finally, testing interoceptive sensibility as a mediator of the relationship between TCE and higher-order domains of personality functioning (2.3), a similar relationship as observed in 2.2. also applies to and partially contributes to explain deficits in higher-order impairments in self and interpersonal functioning, such as general personality functioning, in community samples.

Regarding objective 2.1, the literature review performed within the second study revealed that former studies outlined reduced basal HEPs, HRV, and self-reported attention and attendance to bodily signals in individuals with BPD compared with healthy controls (Müller et al., 2015, Schmitz et al., 2020, Koenig et al., 2016, Schmitz et al., 2021). The finding of reduced HRV in women with BPD could be replicated by the results of study five of this thesis. In contrast, results from previous studies employing behavioral tasks were mixed, indicating either intact (Hart et al., 2013) or reduced objective attention and attendance of bodily signals in BPD (Mussagay, 1999). Those results suggest neurophysiological deficits in afferent interoceptive signal integration and efferent autonomic regulation at rest and self-reported habitual non-attendance of bodily sensations in individuals with BPD, but potentially intact interoceptive accuracy. If actual interoceptive signal perception might be preserved in BPD, even though afferent signal integration and attendance or focus to these may be reduced, intact interoceptive accuracy might be indicative of intact attentional allocation and preserved attendance to bodily signals in objective behavioral tasks at rest. One possible explanation for this discrepancy might be modulations by stress, which affects interoceptive processes (Schulz et al., 2020). Interoceptive accuracy and TCE have been shown to be linked only during states of acute stress (Schaan et al., 2019). Chronic stress, as experienced by TCE, could induce

deficits in afferent-efferent interoceptive processing that disturb the objective attendance of interoceptive signals, especially in states of acute stress where diminished processing of associated physical symptoms could impede regulative processes (Joshi et al., 2021; Schulz et al., 2020, Schmitz et al, submitted). During resting-state, preserved attendance through, for example, heightened attentional efforts to interoceptive signals might explain preserved objective interoceptive accuracy in BPD (Schmitz et al., submitted). Consistent with this interpretation, reduced HEPs in BPD correlated with grey matter volume in the anterior insula and anterior cingulate cortex in the study of Müller et al. (2015), mainly responsible for multisensory integration of interoceptive signals with cognitive-affective, internal, and external stimuli, for behavioral control (Craig, 2009). However, the dorsal insula is primarily responsible for the representation of interoceptive signals (Craig, 2009). Therefore, reduced HEPs in the anterior insula and anterior cingulate cortex in BPD patients might eventually be indicative for deficits in multisensory integration of interoceptive signals with higher-order processes rather than differences in lower-order interoceptive representation per se. This interpretation may be consistent with Flasbeck et al. (2020), who recently demonstrated that individuals with BPD display higher HEP amplitudes on frontocentral sides than healthy control. Flasbeck and colleagues (2020) suggested that the cumulative evidence indicates specific deficits in multisensory integration of interoceptive signals rather than reduced interoceptive signal representation per se. Moreover, the lack of a mediating effect of subjective attention to bodily signals (i.e., body awareness), in favor of habitual disregard of bodily signals during emotionally valanced situations (i.e., body dissociation) as observed in the study of Schmitz et al. (2021), may also be interpretated in favor of this interpretation. In addition, the cumulative results may support recent efforts in interoception research to move towards broader (higher order) definitions of interoception that also consider the integration of internal with contextual information processing (see Schulz & Tsakiris, 2022 for a review). However,

whether interoceptive accuracy is intact and stress-induction might potentially affect interoceptive accuracy and explain discrepancies in different interoceptive facets in individuals with BPD remains objective for future investigations. Moreover, studies investigating interoceptive awareness in BPD are still missing, preventing any conclusions on a potential role of this facet.

The studies summarized within study two suggest that reduced HEPs correlated with self-reported TCE and emotional dysregulation (Müller et al., 2015; Schmitz et al., 2020). Moreover, deficits in interoceptive sensibility fully mediated the relationship between TCE and emotional dysregulation in individuals with BPD (Schmitz et al., 2021). Reduced integration of afferent stimuli and subjective disregard of interoceptive signals have been theorized to potentially represent TCE-related neurophysiological and psychological coping mechanisms of externalized attention that come at the expense of internal bodily information processing (Linehan, 1993; Fonagy & Bateman, 2008). These interoceptive alterations might thereof contribute to emotional dysregulation, a central feature of BPD and impairments in areas of self-functioning. In accordance with theoretical extensions of Linehan's biopsychosocial model by Löffler et al. (2018), as well as the concept of interoceptive mentalization by Fotopoulo & Tsakiris (2017), TCE could potentially be associated with attentional and bodily coping strategies that increase the shift from one's own bodily signals to external cues. Therefore, individuals with BPD may have difficulties interpreting their own body signals and understanding and regulating the emotions associated with them (Linehan, 1993, Fonagy & Bateman, 2008).

Taken together, the results from the second study suggest deficits in neurophysiological and psychological processing, potentially reflecting specific deficits in attending and integrating bodily signals with higher-order cognitive, affective, internal, and contextual information. Regarding implicated biopsychosocial processes, the present findings suggest that

reduced attendance of and focus to interoceptive signals and reduced neurophysiological higher-order integration of bodily signals may be related to emotion regulation difficulties, representing areas of self-functioning.

Regarding objective 2.2, the results of the third study suggest that subjective non-attendance and dissociation from bodily processes (dissociation subscale of the SBC) emerged as full mediator in the relationship between TCE and emotional dysregulation in individuals with PTSD, MD, SSD, and individuals without a mental disorder. In contrast, HRV, interoceptive accuracy, interoceptive awareness, and other measures of interoceptive sensibility showed no comparable effect. The results of the third study are consistent with and extend the findings of the second study: the findings suggest that subjective reports of habitual disregards and non-attendance of bodily signals (i.e., interoceptive sensitivity) may potentially serve as a transdiagnostic factor in the relationship between TCE and emotional dysregulation in various mental disorders (BPD, PTSD, MD and SSD) as well as in healthy individuals. This is line with recent considerations of interoception as a transdiagnostic factor for psychopathology (Brewer et al., 2021). However, whether and how afferent physiological states of interoception (i.e., HEP) might contribute to this relationship, as suggested by studies in BPD (Müller et al., 2015; Schmitz et al., 2020), remains unanswered.

The findings are again consistent with theoretical assumptions by Löffler et al (2018) as well as the concept of interoceptive mentalization by Fotopoulo & Tsakiris (2017). This suggests the interpretation that TCE may affect psychological and bodily externalization strategies for behavioral control that potentially promote emotional dysregulation and impaired self-functioning in individuals across diagnostic boundaries. The results may be further interpreted in favor of emerging theories on interoception, i.e., active interoceptive inference theories of emotions, which suggests that deficits in higher order interoceptive integration is characterized by strong expectations or beliefs that shape the perception of interoceptive signals

across diagnoses (Paulus et al., 2019, Schmitz et al., submitted). Resulting from lacked integration and updating with internal or external changes, the resulting error signals might predominate at the expense of homeostatic processes (Schmitz et al., submitted).

The lack of observed effect of objective interoceptive processing (i.e., HRV) in the relationship between TCE and emotional dysregulation is consistent with a recent meta-analysis showing that the relationship between TCE and HRV depends on additional moderators such as psychopathological status, age, and developmental processes (Sigrist et al., 2021). The results are also in line with the fifth study, demonstrating that the relationship between TCE and HRV in patients with BPD is only observable in the context of high insecurity in intimate relationships. One potential explanation for this finding is that the relationship between TCE and deficits in regulatory efferent pathways of interoception might depend upon socially salient, external information processing, as outlined in objective 2.1 of this thesis. Consistent with this interpretation, Krause-Utz and colleagues (2022) found that TCE predicted reduced HRV only during an emotional working memory task in BPD patients, but not at rest, and thus suggested that TCE may promote neurophysiological deficits in reorienting attention towards internal bodily signals in the presence of salient social cues. However, if higher levels in interpersonal dysfunctioning might be related to higher deficits in objective physiological states of interoception, as suggested by the observed deficits in BPD, remains unanswered by the current results.

In summary, the results from the second and third study suggest that subjective non-attendance and dissociation from bodily processes, which might capture subjective attitudes about internal bodily sensations (i.e., interoceptive sensitivity), may explain TCE-associated emotion dysregulation in individuals with BPD, PTSD, MD, SSD, and individuals without mental health difficulties. In contrast, the objective attendance and meta-cognitive awareness to bodily signals and efferent regulation at rest may not contribute to this relationship in neutral

contexts at resting-state. Reduced interoceptive sensitivity may capture theoretical considerations on external focus at the expense of attention allocation towards internal sensations for emotion regulation (Linehan, 1993; Fonagy and Bateman, 2008).

Finally, regarding the aim 2.3, results of the fourth study suggest that subjective non-attendance and dissociation from bodily processes (dissociation subscale of the SBC) partially mediates the association between self-reported TCE and self and interpersonal functioning. This partial mediation effect was observed in community samples from two different continents, Germany and Chile. The results extend the findings of study two and three by highlighting the potential relevance of self-reported TCE and deficits in interoceptive sensibility in relation to higher order impairments in personality functioning.

Consistent with the present findings, deficits in interoceptive processing have been linked not only to emotional dysregulation but also other domains of impairments in personality functioning (see Löffler et al., 2018 for a review). This is further consistent with empirical research highlighting the important role of conscious attendance of one's own internal bodily signals in self-regulatory behaviors and social interactions necessary for the maintenance of homeostasis in early and adult life (Ciaunica & Crucianelli, 2019; Filippetti, 2021; Mundy & Jarrold, 2010). Extending theories on mentalization (Fonagy and Bateman, 2008), perception and integration of contingent multisensory information from within the body and the social environment are hypothesized to play an important role in successfully distinguishing between self and others, an important prerequisite for personality functioning (Bahrick, 2013; Jacquey et al., 2020). This is consistent with a meta-analysis of magnetic resonance imaging studies by Adolfi et al (2017), which supports the presence of a neurologically converging model of interoception, emotion regulation, and social cognition in the anterior insula and fronto-temporal regions (Adolfi et al., 2017). Moreover, the current results highlight the relevance of TCE-related dissociation from body processes for personality functioning, also in non-clinical

samples, matching conclusion drawn in the first aim of the thesis. However, conclusions regarding multiple facets of interoception, such as facet-specific alterations in personality functioning according to the AMPD, remains unanswered by the current results. Moreover, conclusions drawn regarding community samples may not be transferable to mere clinical samples, requiring further studies on multiple interoceptive processes in individuals with higher impairments in personality functioning. The partial mediation effect suggests that additional processes than interoceptive sensibility might be implicated in the observed mediation. One such process might be social support, which has been shown to be an important protective mechanism in the relationship between TCE and psychopathology (see McLaughlin et al., 2020 for a review).

In summary, the cumulative results of studies two, three, and four demonstrate that reduced self-reported interoceptive sensibility fully explained the association between TCE and deficits in emotional dysregulation and partially explained impairments in self and interpersonal functioning in individuals with and without various mental disorders. One explanation for the TCE-associated subjective disregard of interoceptive signals in BPD and other mental disorders may confer with theoretical considerations by Linehan (1993) and Löffler et al. (2018), i.e., an external focus at the expense of attention allocation towards internal sensations for emotion regulation, being ignored in contexts requiring emotional information, and potentially further contributing to deficits in self and interpersonal functioning. It remains up to future studies to test if objective attention and attendance to interoceptive signals in neutral contexts might be preserved in BPD and impairments in personality functioning, and if other facets of interoception might contribute to explaining impairments in personality functioning following TCE. Importantly, the strength of the relationship between TCE and efferent states of interoception at rest in BPD might depend on the current degree of deficits in interpersonal functioning. Our results provide preliminary support for the mediating role of subjective

interoceptive processes in the transdiagnostic relationship between TCE and lower-order domains of self (e.g., emotional dysregulation) such as higher-order domains of personality functioning across diagnostic boundaries.

3.3 The modulatory role of intranasal oxytocin administration on efferent states of Interoception

The results of the fifth study revealed that resting state HRV was not modulated by intranasal oxytocin administration, either by a significant main effect of the substance or by an interaction effect with BPD diagnosis. These results contrast with those of Norman et al. (2011) and Martins et al. (2020), who suggest that intranasal oxytocin administration enhances resting state HRV in men at clinical high risk for psychosis. Additional exploratory analysis also revealed the absence of an interactive effect between TCE, attachment insecurity, and clinical status with intranasal oxytocin administration on HRV at rest. In contrast, Schoormans et al. (2020) and Riem et al. (2021) found interactive effects between TCE, attachment insecurity, and HRV in women. However, the lack of effect of intranasal oxytocin administration on HRV as an efferent marker of interoceptive processing is consistent with the lack of intranasal oxytocin administration effects on afferent markers of interoception (Schmitz et al., 2020) and interoceptive accuracy at rest (Yao et al., 2018). Consistent with the social significance hypothesis, the influence of oxytocin on interoceptive processing is complex and, in particular, may increase the significance of social cues. (Shamay-Tsoory & Abu-Akel, 2016). Therefore, the lack of effect on efferent states of interoception could be explained by the absence of salient external stimulation as present in a resting-state condition. In accordance with the social salience hypothesis, Yao et al. (2018) were able to show that during a face-recognition task, intranasal oxytocin administration decreased interoceptive accuracy and increased right anterior insula activation, pointing to oxytocin's potential in the multisensory modulation between

interoceptive and exteroceptive attention. The authors suggested that intranasal oxytocin administration may facilitate precise shifts of information integration in the anterior insula towards external social stimuli to effectively guide behavior during social interactions, but only when confronted with salient social cues (Yao et al., 2018). In addition, first evidence suggests that intranasal oxytocin administration increases interoceptive accuracy in a heartbeat discrimination task (requiring multisensory integration of interoceptive with exteroceptive stimuli) in individuals with higher alcohol consumption (Betka et al., 2018). Consistent with the social salience of intranasal oxytocin administration, Riem et al. (2021) attributed altered HRV after intranasal oxytocin administration to increased attentional salience triggered by social presence during the experiment. However, evidence to date is too mixed to draw clear conclusions about the potential for intervention of intranasal oxytocin administration for interoceptive processing in BPD (Amad et al., 2015). Nevertheless, evidence suggests that intranasal oxytocin administration may potentially modulate efferent interoceptive states in the light of external, salient social interactions in individuals with BPD. Thus, matching the conclusions by Herpertz & Bertsch (2015), intranasal oxytocin administration may be more suited in modulating the multisensory integration between interoceptive and exteroceptive information processing during social salience rather than interoceptive processing at rest per se (Betka et al., 2018; Yao et al., 2019).

3.4 Strengths of the current thesis

A strength of the present work entails the transdiagnostic approach including varying samples across diagnosis, diagnostic spectra and non-clinical individuals (Fusar-Poli et al., 2019). By complementing diagnosis-specific with dimensional approaches to psychopathology, this work has contributed to a more comprehensive understanding of how TCE and interoceptive processes relate to impairments in personality functioning in BPD and other

mental disorders such as healthy populations. Exploring the biopsychosocial components of personality functioning beyond existing diagnosis is of great importance given the transition of the current conceptualization of personality pathology with DSM-5' AMPD (APA, 2013) and ICD-11 (WHO, 2019).

By combining multiple methods of data collection (e.g., self-report, behavioral, and psychophysiological measures), multiple levels of observations could be integrated, particularly important in the context of interoception, a multifaceted construct that requires a comprehensive assessment (Garfinkel et al., 2013). Indeed, most clinical studies on interoception focus on alterations in single facets and use few measures. By integrating findings on several facets of interoception (Forkman et al., 2016) within study two and three, this thesis advances the current understanding of specific deficits in interoceptive processing in the relationship between TCE and impairment in self functioning. The identification of specific effects also provides the basis for identifying targets and developing fitting interventions (Forkman et al., 2016). Another methodological strength in the processing of the psychophysiological data in study three and five is a fully open-source approach to the analysis of HRV based on the raw electrocardiogram. While many investigations have relied on paid programs with limited access (e.g. Kubios; Tarvainen et al, 2014), the present studies employed fully replicable, unlicensed approaches to data analysis (Beelen, 2013; Martinez et al., 2017) in light of open science.

Besides the cross-sectional approaches of study one to four, study five includes a randomized-controlled, double-blind, placebo-controlled trial, the gold standard for effectiveness research (Hariton & Locascio, 2018) and the first study to investigate the effects of IN-OT on efferent interoceptive states in women with BPD. In contrast, other studies on the effects of IN-OT on HRV concentrated on male individuals (Norman et al., 2011; Martins et al., 2020). This is also relevant given the fact that in the past, clinical trials have not always adequately represented women or analyzed sex differences (Liu & DiPietro Mager, 2016).

Another strength includes the rigorous diagnostic assessment employed in study three and five. Structured clinical interviews were used to assess the presence of mental disorders. Interviews were conducted only by qualified researchers with a master's or doctoral degree in clinical psychology or medicine who had completed standardized diagnostic training before being recruited for the study. Lastly, the first study employed structural equation modeling, supplementing factor analysis with latent modeling (Kline, 2015). This method of analysis allows for accurate measurement of specific relationships and assurance of construct validity of the assessed questionnaires while modeling measurement error in the latent relationship between TCE and personality functioning.

3.5 Limitations and suggestions for future studies

However, the present results must be interpreted considering several important limitations that require further study. Albeit advantages of softer definitions on transdiagnostic to mental health and illness, there is also consensus amongst experts that a transition to “harder definitions of transdiagnostic psychopathology” in clinical research is necessary to ensure a proper transition to transdiagnostic nosology (Dagleish et al., 2020). A suggestion for future personality pathology studies might be to base recruitment on balanced groups with varying degrees of impairment (from none to severe) in personality functioning, whilst also measuring BPD pattern. This is important regarding the recruited samples in study one and four, that mainly reflected lower levels of personality impairments, as expected in the general population of individuals largely pursuing a job or higher education. However, for future studies, it is necessary to represent a broader range of impairments in personality functioning level, to evaluate the mediating role of interoceptive sensibility across the entire spectrum of personality pathology. Related to the notion of varying levels of functioning, it might be important to also consider resilience-associated constructs when investigating the relationship between TCE and

personality functioning in subclinical impaired and highly functioning samples. Importantly, not everyone who experiences TCE develops psychopathology, and it has been suggested that resilience may be an important mediator in that relationship (e.g., high social support; Seitz et al., 2021). Future studies could therefore also consider measures resilience in the mediating relationship between TCE and levels of personality functioning.

Another limitation is the mono-method reliance on cross-sectional and retrospective self-reports for the assessment of TCE, personality functioning, and interoceptive sensibility. In fact, retrospective and prospective reports of TCE display so little agreement that it has been suggested to capture separable constructs (Baldwin et al., 2019). Retrospective reports of trauma may underlie memory-specific bias, limiting the validity of the CTQ as a measure of prospective trauma. Consequently, the conclusions drawn in this thesis are limited to retrospective reports of childhood trauma. At the same time, the current thesis highlights the reliability and factor validity of the CTQ, which shows comparable psychometric properties to interview-based assessment (Seitz et al., 2022). Moreover, retrospective reports of TCE may have the advantage of capturing subjective traumatic experiences more sensitively, which may be especially important given the high association between emotional trauma and personality functioning (Back et al., 2022). Future studies should therefore retrospectively and prospectively report TCE to ensure greater measurement validity. Regarding self-reports of personality functioning, structured-diagnostic interviews should be applied as well in future studies, especially if a more precise assessment of personality functioning is sought. This is in accordance with studies suggesting higher prognostic validity of interview-based assessments of personality pathology compared to self-report questionnaires (Samuel et al., 2013). Regarding the AMPD, several validated interviews are available, for example the structured clinical interview for the alternative DSM-5 model for personality disorders (Ohse et al., 2021).

Regarding self-reports on interoception, we mostly relied on the SBC, with its two subscales of body awareness and dissociation (Price & Thomson, 2007). Although the validity of the SBC is well documented in several languages (Price & Thomson, 2017), we relied exclusively on a German translation of the SBC, which has not yet been officially validated in that language. On the other hand, the SBC shows acceptable reliability and measurement invariance across several countries (Price & Thomson, 2017) and has been served as a basis for the construction of the Multidimensional Assessment of Interoceptive Awareness (MAIA; Mehling et al., 2012), the most widely used questionnaire to measure interoceptive sensibility. Future studies should consider employing further questionnaires to measure interoceptive sensibility, such as the MAIA (Reis et al., 2019).

Another methodological issue in measuring interoception relates to recent concerns about the validity of the HBC-task (Schandry, 1981), the most widely used behavioral measure of interoceptive accuracy (Desmedt et al., 2020). Interoception research is currently evolving in terms of theoretical foundations and conceptualizations, which has important implications for its measurements (see Schulz & Vögele, 2021 for an extensive overview). We operationalized the concept of interoception based on the multiple facets approach (Forkmann et al. 2016; Chen et al., 2021), applying a broad assessment by including afferent and efferent, bi-directional indicators along the brain-body axis (Chen et al., 2021). As our results point to transdiagnostic deficits in higher order interoceptive integration, it seems important to complement the HBCT with measures of exteroception, such as the Whitehead task (Whitehead, 1977). Moreover, prospectively investigations are needed that track changes in interoceptive processing during neutral and socially salient contexts to consider the role of social stress in the relationship between interoceptive integration and it links to TCE and personality functioning.

Lastly, regarding the design of the studies, no causal inferences concerning the mediating role of interoception in the association between TCE and personality functioning can be drawn (Maxwell & Cole, 2007). Rather, this thesis provides first preliminary evidence for processes implicated in impairments in personality functioning. These findings clearly require further longitudinal evidence, including high-risk samples and longitudinal measurements of interoception in infants after exposure to TCE. In the light of translational research (Ehring et al., 2022), more experimental studies that causally link changes in interoceptive processing to transient changes in personality functioning are needed that considering an individuals' levels of TCE. In a further step, investigations on interoception as mechanism of change in personality functioning are still lacking. Therefore, future research may investigate higher order interoceptive integration before, during, and after psychotherapeutic treatment.

3.6 Potential Clinical Implications

Although further steps within the translational research process must be taken to draw definite clinical implications (Ehring et al., 2022), the current findings provide preliminary ideas for clinical practice.

Measures of TCE are extensively used in clinical research and practice (Klinitzke et al., 2011). As measures and interviews of personality pathology are not routinely performed and are often lengthy, evidence of TCE may be important for early detection of impairments in personality functioning. However, further longitudinal evidence is necessary before prospective conclusions may be drawn.

Moreover, the results on transdiagnostic deficits in higher-order interoceptive processing regarding emotional dysregulation and higher-order deficits in personality functioning in the presence of TCE might have several clinical implications. First, the training of attentional reallocation towards inner bodily sensations through mindfulness-based and body-oriented modules is already an integral component of third-wave CBT therapies,

including DBT (Linehan, 1993), but also schema therapy (Kellog & Young, 2006). Our results may suggest that attentional reallocation towards own bodily signals may be beneficial approach to promote emotion regulation and personality functioning by linking these experiences to further cognitive and affective experiences (e.g., prescribing meaning and value to bodily experiences for the self and its regulation in social contexts). Indeed, attentional interoceptive training has been shown to promote adaptive use of emotion regulation strategies and the flexible use of appropriate strategies in response to external triggers (e.g., integration and regulation of interoceptive signals with exteroceptive signals; Tan et al. 2023). The integration of interoceptive attention training could benefit not only patients with BPD, but potentially patients with other mental disorders who exhibit deficits in emotion regulation related to subjective experiences of TCE. Furthermore, interventions aiming at integrating bodily experiences in the cognitive-affective context of social situations may not only improve emotion regulation but also contribute to other areas of personality functioning. Given the broad prevalence of TCE in the general population (Klinitzke et al., 2011) and in light of the recent implementation of "personality difficulty" in ICD-11 (WHO, 2019), this may also apply to individuals who fall below the diagnostic threshold of common mental disorders. Understanding the meaning of bodily sensations within a specific social situation, the emotions and cognitions associated with them, could potentially contribute to personality functioning by promoting identity formation, regulation of emotions (i.e., self-direction), understanding others in terms of mental representations (i.e., empathy), and the pursuit of social affiliation (i.e., intimacy). However, further longitudinal studies and experiments are needed before firm clinical conclusions can be drawn.

Psychotherapeutic treatments may be complemented by physiological interventions, such as neuro- or biofeedback, which aim to enhance physiological states of interoception (Chen et al., 2021). This may be particularly important in the presence of combined deficits in

physiological states of interoception and impairments in interoceptive sensitivity, as observed in some individuals with BPD. The results from study five hint that biofeedback of efferent interoceptive states in BPD may be a beneficial approach indicated in individuals with higher impairments interpersonal functioning (e.g., attachment security). Concerning the potential of oxytocin to target interoceptive processing, the present results suggest that IN-OT at rest might not be an appropriate intervention to enhance efferent regulatory states of interoception. Future studies involving interpersonal salient contexts are needed to investigate whether IN-OT may facilitate efficient interoception attention reallocation in social contexts.

3.7 Conclusion

In the present work, various biopsychosocial processes related to personality functioning were investigated. The findings contribute to a better understanding of the complex relationship between endocrinological, neurophysiological, and psychological processes involved in the relationship between TCE, interoception, and impairments in self and interpersonal functioning. First, strong associations between TCE and levels of personality functioning were found in the present work. Regarding interoception as a possible mediator of this relationship, this thesis demonstrated that individuals with BPD show impairments in bi-directional, objective physiological states of interoception and interoceptive sensibility that are linked to TCE and impairments in self functioning (i.e., emotional dysregulation). In the present work, including healthy individuals and samples of various mental disorders, deficits in interoceptive sensibility mediated the relationship between TCE and lower-to-higher domains self and interpersonal functioning. In addition, the present thesis revealed that IN-OT may not modulate efferent interoceptive states (i.e., HRV) in patients with BPD at rest. The results provide preliminary evidence for (higher order) interoceptive attention allocation as a possible mediator in the relationship between TCE and impairments in personality functioning. The

effort of the current thesis further the exploration of additional processes implicated in the relationship between TCE and personality functioning.

4. Deutsche Zusammenfassung

Traumatisierende Kindheitserfahrungen, Interozeption und Einschränkungen im Funktionsniveau der Persönlichkeit: Zusammenhänge zwischen psychologischen, neurophysiologischen und endokrinologischen Prozessen

Da psychische Probleme aus einem komplexen Zusammenspiel zwischen biologischen, verhaltensbezogenen, psychosozialen und kulturellen Prozessen entstehen, die über die etablierten diagnostischen Grenzen hinausgehen (Dagleish et al., 2020), wird davon ausgegangen, dass transdiagnostische, dimensionale Ansätze einen präziseren und informativeren Ansatz für die Klassifizierung psychopathologischer Phänomene bieten können (Dagleish et al., 2020). Das Alternative Model for Personality Disorder (AMPD) in Abschnitt III des DSM-5 definiert die Persönlichkeitspathologie entlang dimensionaler Ebenen des Funktionsniveaus der Persönlichkeit (APA, 2013). Zusammengefasst als Kriterium A, stellt das Funktionsniveau der Persönlichkeit ein hierarchisches Modell des Schweregrads der Persönlichkeitsstörung dar, das sich aus Beeinträchtigungen der Selbst- und der zwischenmenschlichen Funktionen zusammensetzt (APA, 2013). Die Selbstfunktion besteht aus den Subdomänen Identität und Selbststeuerung, während die zwischenmenschliche Funktion in Empathie und Intimität unterteilt wird (APA, 2013). Schwerwiegendere Beeinträchtigungen der Persönlichkeitsfunktion sind durch eine verzerrte Selbstdarstellung und -regulierung in Bezug auf das soziale Umfeld gekennzeichnet, eine zentrale Störung, die allen Persönlichkeitsstörungen gemeinsam ist (Sharp et al., 2021). Tatsächlich wurde die Borderline-Persönlichkeitsstörung (BPD) als die prototypischste Störung und der allgemeinste Faktor aller PDs extrahiert (Sharp et al., 2015), die stärkere Defizite im Funktionsniveau der Persönlichkeit abbilden (Hopwood, 2018). Aufbauend auf den Fortschritten der AMPD hat die Weltgesundheitsorganisation in der elften Version des ICD eine dimensionale Klassifikation der Persönlichkeitspathologie für die klinische Praxis angepasst (WHO, 2019). Trotz der zunehmenden Ablösung der traditionellen kategorialen PD-Konzeptualisierung ist das DSM-5-AMPD weder theoriebasiert noch enthält es explizite therapeutische Implikationen (siehe Bach et al., 2018), und die Forschung zu biopsychosozialen Prozessen, die mit Beeinträchtigungen der Persönlichkeitsfunktion einhergehen, ist noch weitgehend unerforscht. In der vorliegenden

Arbeit wird daher ein transdiagnostischer Ansatz verwendet, um hypothesengeleitete biopsychosoziale Prozesse innerhalb der BPD sowie deren Assoziationen mit dimensionalen Beeinträchtigungen der Persönlichkeitsfunktion bei Personen mit und ohne unterschiedlichen psychischen Störungen zu untersuchen. Rezente empirische Befunde legen nahe, dass verschiedene Formen traumatischer interpersoneller Kindheitserfahrungen (TCE) wichtige lebenslange Risikofaktoren für die Entwicklung transdiagnostischer Psychopathologie sein könnten (siehe McLaughlin et al., 2020 für eine Review). Die Bedeutsamkeit von TCE als psychosozialer Risikofaktor, neben biologischer Vulnerabilität und weiteren Risikofaktoren, deckt sich mit frühen theoretischen Modellen zur Ätiologie von Persönlichkeitsstörungen, insbesondere der BPD (Gunderson et al., 2018; Porter et al., 2019). Bislang hat jedoch keine Studie den Zusammenhang zwischen dem Persönlichkeitsfunktionsniveau und TCE bei jungen Erwachsenen aus der allgemeinen Bevölkerung untersucht. Neben interpersonellem TCE als distalem, sozialem Risikofaktor wurde die interozeptive Verarbeitung als proximalerer, psychobiologischer Prozess vorgeschlagen, der die Beziehung zwischen TCE und Beeinträchtigungen des Selbst und der interpersonellen Funktionsfähigkeit vermitteln könnte (siehe Fotopoulou & Tsakiris, 2017 und Löffler et al., 2018 für eine Review). Die effiziente Wahrnehmung, Integration und Regulierung von Körpersignalen neben der Navigation in Interaktion mit der sozialen Umwelt (Chen et al., 2021) ist entscheidend für die Aufrechterhaltung wesentlicher homöostatischer Körperfunktionen (z. B. Atmung) sowie psychologischer Funktionen höherer Ordnung, die von Emotionen über ein stabiles und kohärentes Selbstgefühl bis hin zu sozial adaptivem Verhalten im Erwachsenenalter reichen (Chen et al., 2021, Smith et al., 2022). Neuere theoretische Ansätze hypothetisieren daher, dass eine verminderte Wahrnehmung, Integration und Regulierung interozeptiver Signale dem Zusammenhang zwischen TCE und allgemeinen Beeinträchtigungen der Selbst- und zwischenmenschlichen Funktionen bei BPD zugrunde liegen könnte (siehe Fotopoulou &

Tsakiris, 2017 und Löffler et al., 2018 für Reviews). Neben der BPD wird eine atypische interozeptive Verarbeitung auch als gemeinsamer, transdiagnostischer Risikofaktor für verschiedene Formen der Psychopathologie angesehen (siehe Brewer et al., 2018 für eine empirische Übersicht). Interozeption umfasst vielfältige Prozesse entlang der Gehirn-Körper-Achse (Forkmann et al., 2016, Chen et al., 2021), die von der objektiven physiologischen Verarbeitung, der genauen Wahrnehmung, der subjektiven Empfindung bis hin zum metakognitiven Bewusstsein für eigene Körpersignale reichen (Khalsa et al., 2018). Nach Garfinkel et al. (2015) und Forkmann et al. (2016) setzt sich die Interozeption aus verschiedenen Facetten zusammen, darunter (1) objektive physiologische Zustände der Interozeption (messbar z.B. durch Herzschlag evozierte Hirnpotentiale, HEP), (2) interozeptive Genauigkeit (Übereinstimmung zwischen tatsächlichem und wahrgenommenem Körpersignal; messbar z.B. durch Herzschlagwahrnehmungsaufgaben, HBCT; Schandry, 1981), (3) interozeptive Sensibilität (subjektive Bewertung der eigenen Tendenz, auf Körpersignale zu achten und sie wahrzunehmen; messbar durch Selbstbericht oder Fragebögen) und (4) interozeptives Bewusstsein (metakognitives Bewusstsein für Körpersignale, messbar durch Übereinstimmungsgrad zwischen interozeptiver Genauigkeit und Sensibilität). Nach konzeptionellen Änderungen auf der Grundlage von Chen et al. (2021) sowie Price & Thomson (2007) wurde die Herzratenvariabilität (HRV) als weiteres Maß für efferente objektive physiologische Zustände der Interozeption hinzugefügt (als Quantifizierung der absteigenden Bahnen vagaler Aktivität), so wie der Fragebogen der Körperverbundenheit (SBC) als Proxy für interozeptive Sensibilität. Da diese Facetten als unabhängig voneinder verstanden werden und Korrelationen oftmals gering ausfallen (Forkmann et al., 2016), können verschiedene interozeptive Prozesse den Zusammenhang zwischen TCE und Beeinträchtigungen der Selbst- und zwischenmenschlichen Funktionsfähigkeit gemäß DSM-5 AMPD (einschließlich hierarchisch untergeordneter Prozesse wie emotionaler Dysregulation) bei Personen mit und

ohne verschiedenen psychischen Störungen vermitteln. Es fehlen jedoch noch Untersuchungen darüber, welche interozeptiven Prozesse dem Zusammenhang zwischen TCE und Beeinträchtigungen des Selbst und der zwischenmenschlichen Funktionsfähigkeit bei Personen mit und ohne verschiedenen psychischen Störungen zugrunde liegen könnten. Ein Hormon, das speziell in den neuroendokrinologischen Zusammenhang zwischen sensibler elterlicher Fürsorge, dem Funktionsniveau der Persönlichkeit und der Modulation der interozeptiven Verarbeitung eingebunden ist (Jankowski et al., 2004), ist Oxytocin. Neuere theoretische Modelle gehen davon aus, dass Oxytocin die Bedeutung und Präzision interozeptiver Signale kodiert und so die Verbesserung des emotionalen Bewusstseins ermöglicht, das für die Entwicklung des Selbst und dessen Regulierung während sozialer Interaktionen wichtig ist (Quatrokki & Friston, 2014). Obwohl erste Studien darauf hindeuten, dass die intranasale Verabreichung von Oxytocin objektive physiologische Zustände der Interozeption (z. B. die HRV) in Ruhe verbessern kann (Norman et al., 2011; Martins et al., 2020), wurde bisher in keiner Studie untersucht, ob die intranasale Verabreichung von Oxytocin auch die objektive interozeptive Verarbeitung in Ruhe bei BPD modulieren kann.

Das übergeordnete Ziel der vorliegenden Arbeit ist es, biopsychosoziale Prozesse zu identifizieren, die mit dem Funktionsniveau der Persönlichkeit assoziiert sind, indem das komplexe Zusammenspiel zwischen endokrinologischen, neurophysiologischen und psychologischen Prozessen untersucht wird, die an der Beziehung zwischen TCE, Interozeption und Beeinträchtigungen des Selbst und der zwischenmenschlichen Funktionen beteiligt sind. In vorliegenden Arbeit wurden drei Ziele verfolgt. Das erste Ziel (1) war die Untersuchung der Zusammenhänge zwischen emotionalem und körperlichem Missbrauch, Vernachlässigung und sexuellem Missbrauch in der Kindheit und dem Funktionsniveau der Persönlichkeit im Erwachsenenalter an einer Stichprobe junger Erwachsener aus der Allgemeinbevölkerung. Das zweite Ziel (2) bestand darin, die vermittelnde Rolle multipler interozeptiver Prozesse in der

Beziehung zwischen TCE und Beeinträchtigungen im Funktionsniveau der Persönlichkeit bei erwachsenen Personen mit und ohne unterschiedlichen psychischen Störungen zu ermitteln. Das zweite Ziel umfasst (2.1) einen narrativen Überblick über die empirische Evidenz zu verschiedenen interozeptiven Prozessen bei BPD, (2.2) eine Untersuchung der verschiedenen interozeptiven Prozesse, die die Beziehung zwischen TCE und emotionaler Dysregulation bei verschiedenen psychischen Störungen (einschließlich Posttraumatischer Belastungsstörung, PTSD; Depression, MD und Somatischer Belastungsstörung, SSD) und gesunden Personen mit TCE vermitteln, und schließlich (2.3) eine empirische Untersuchung, ob dieselben interozeptiven Prozesse die Beziehung zwischen TCE und den Persönlichkeitsfunktionen in erwachsenen Stichproben aus der Allgemeinbevölkerung vermitteln. Das dritte Ziel (3) war die Untersuchung potenziell modulierender Effekte einer intranasalen Oxytozin-Verabreichung auf die HRV (als objektive interozeptive Zustände) in Ruhe bei erwachsenen Frauen mit BPD und deren Interaktion mit TCE und Bindungsunsicherheit. Um diese Ziele zu erreichen, wurden vier empirische Studien und eine Literaturübersicht durchgeführt. In dieser Arbeit wurde ein Mixed-Methods-Design angewandt, das einen narrativen Überblick über die empirische Literatur, Querschnittsstudien, eine randomisierte, doppelblinde, placebokontrollierte Studie und verschiedene Methoden der Datenerhebung (d.h. Selbstauskunft, Verhaltens- und psychophysiologische Messungen) kombiniert.

In Bezug auf das erste Ziel (1) deuten die Ergebnisse der ersten Studie darauf hin, dass die retrospektiv berichtete Erfahrung verschiedener Formen von TCE insgesamt stark mit Beeinträchtigungen im Persönlichkeitsfunktionsniveau bei jungen Erwachsenen assoziiert sind. In Bezug auf das zweite Ziel (2) zeigen die kumulativen Ergebnisse der Studien zwei, drei und vier, dass eine verringerte selbstberichtete interozeptive Sensibilität den Zusammenhang zwischen TCE und Defiziten bei der selbstberichteten Emotionsregulation vollständig und dem Funktionsniveau der Persönlichkeit, in den Bereichen Selbst und der zwischenmenschlichen

Funktionen, bei Personen mit und ohne verschiedenen psychischen Störungen, teilweise erklärt. Eine Erklärung für die TCE-assoziierte subjektive Missachtung interozeptiver Signale bei BPD und anderen psychischen Störungen könnte mit theoretischen Überlegungen von Linehan (1993) und Löffler et al. (2018) übereinstimmen, d.h. eine externe Fokussierung auf Kosten der Aufmerksamkeitszuweisung auf interne Empfindungen zur Emotionsregulation, die z.B. in Kontexten, die emotionale Informationen erfordern, ignoriert werden und so möglicherweise zu Defiziten in der Selbst- und interpersonellen Funktionsfähigkeit beiträgt. Zukünftige Studien müssen prüfen, ob die objektive Aufmerksamkeit und die Beachtung interozeptiver Signale in neutralen Kontexten bei BPD und Menschen mit Beeinträchtigungen des Persönlichkeitsfunktionsniveau erhalten sind und ob andere Facetten der Interozeption weiter zur Erklärung von Beeinträchtigungen der Persönlichkeitsfunktionen nach TCE beitragen könnten. Wichtig ist, dass die Stärke der Beziehung zwischen TCE und efferenten Zuständen der Interozeption in Ruhe bei BPD vom aktuellen Grad der Defizite in der zwischenmenschlichen Funktion (d.h. der Bindungsunsicherheit) abhängen könnte. Unsere Ergebnisse liefern vorläufige Befunde für die vermittelnde Rolle subjektiver, interozeptiver Prozesse in der transdiagnostischen Beziehung zwischen TCE und Bereichen des Selbst (d.h. emotionale Dysregulation) wie auch weiteren Bereichen des Persönlichkeitsfunktionsniveaus über diagnostische Grenzen hinweg. In Bezug auf das dritte Ziel zeigte die intranasale Verabreichung von Oxytocin weder modulierende Effekte auf die HRV in Ruhe bei Frauen mit BPD noch bei gesunden Frauen, noch interagierte dieser Effekt mit TCE oder Bindungsunsicherheit. In Anbetracht des übergeordneten Ziels deuten die Ergebnisse der Studien darauf hin, dass emotionale und körperliche Vernachlässigung bzw. Missbrauch in der Kindheit, sowie sexueller Missbrauch, distale psychosoziale Risikofaktoren darstellen könnten, die möglicherweise die Anfälligkeit für die Entstehung von Beeinträchtigungen der Persönlichkeitsfunktionen im Erwachsenenalter erhöhen. Die subjektive Bewertung einer

verminderten Anwesenheit und Wahrnehmung von Körpersignalen (d.h. interozeptive Sensibilität) erwies sich als ein potenziell proximaler Risikofaktor, der möglicherweise zur Erklärung des transdiagnostischen Zusammenhangs zwischen TCE und erwachsenen Beeinträchtigungen des Selbst und der zwischenmenschlichen Funktionen beiträgt. Oxytocin könnte jedoch bei Frauen mit BPD keine endokrinologischen Auswirkungen auf die Herzfrequenzvariabilität in Ruhe (d.h. objektive physiologische Zustände der Interozeption) haben, weder in Abhängigkeit von selbstberichteter TCE noch der Bindungsunsicherheit.

Eine Stärke der vorliegenden Arbeit ist der transdiagnostische Ansatz, der unterschiedliche Stichproben über Diagnosen, diagnostische Spektren und nicht-klinische Personen einschließt (Fusar-Poli et al., 2019). Durch die Kombination mehrerer Methoden der Datenerhebung (z.B. Selbstbericht, verhaltensbezogene und psychophysiologische Maßnahmen) konnten mehrere Beobachtungsebenen integriert werden. Neben den Querschnittsansätzen der Studien eins bis vier umfasst Studie fünf eine randomisiert-kontrollierte, doppelblinde, placebokontrollierte Studie, den Goldstandard der Wirksamkeitsforschung (Hariton & Locascio, 2018) und die erste Studie, die die Auswirkungen von intranasaler Oxytozin Vergabe auf efferente interozeptive Zustände (d.h. HRV) bei Frauen mit BPD untersucht. Eine weitere Stärke ist die rigorose klinische Diagnostik, die in den Studien drei und fünf eingesetzt wurde. Schließlich wurde in der ersten Studie ein Strukturgleichungsmodell erhoben, das die Faktorenanalyse durch eine latente Modellierung ergänzte (Kline, 2015). Bei der Interpretation der vorliegenden Ergebnisse müssen jedoch mehrere wichtige Einschränkungen berücksichtigt werden, die weitere Untersuchungen erfordern. Trotz der Vorteile der verwendeten Definition von transdiagnostischer Psychopathologie in der vorliegenden Arbeit besteht unter Experten Konsens darüber, dass ein Übergang zu "härteren Definitionskriterien" in der klinischen Forschung notwendig ist, um einen angemessenen Übergang zur transdiagnostischen Nosologie zu gewährleisten (Dagleish

et al., 2020). Ein Vorschlag für künftige Studien zur Persönlichkeitspathologie könnte darin bestehen, die Rekrutierung auf ausgewogene Gruppen mit unterschiedlichen Graden der Beeinträchtigung im Persönlichkeitsfunktionsniveau zu stützen. Im Zusammenhang mit dem Konzept der dimensional angelegten Funktionsniveaus der Persönlichkeit könnte es wichtig sein, auch mit Resilienz assoziierte Konstrukte zu berücksichtigen (wie in Seitz et al., 2022), wenn die Beziehung zwischen TCE und Persönlichkeitsfunktion in subklinisch beeinträchtigten und hoch funktionsfähigen Stichproben untersucht wird. Eine weitere Limitation ist die Tatsache, dass sich die Untersuchung von TCE, dem Persönlichkeitsfunktionsniveau und interozeptiver Sensibilität auf Querschnittstudien und retrospektiver Selbstberichte stützt. Die in dieser Arbeit gezogenen Schlussfolgerungen sind auf retrospektive Berichte über Kindheitstraumata beschränkt. Zukünftige Studien sollten daher auch prospektiv TCE erfassen, um eine größere Messvalidität zu gewährleisten (Baldwin et al., 2019). Schließlich können aufgrund des Studiendesigns keine kausalen Rückschlüsse auf die mediierende Rolle der Interozeption, sowie des Zusammenhangs zwischen TCE und dem Funktionsniveau der Persönlichkeit gezogen werden. Vielmehr liefert diese Arbeit erste vorläufige Belege für Prozesse, die mit Beeinträchtigungen im Funktionsniveau der Persönlichkeit einhergehen. Diese Ergebnisse erfordern eindeutig weitere Längsschnittuntersuchungen, einschließlich Hochrisikostichproben und Längsschnittmessungen der Interozeption bei Kindern und Jugendlichen nach Exposition gegenüber TCE. Die aktuellen Ergebnisse liefern ebenfalls erste Ideen für die klinische Praxis. Der Nachweis von TCE könnte für die Prävention und Intervention von Beeinträchtigungen des Persönlichkeitsfunktionsniveau wichtig sein. Bevor jedoch prospektive Schlussfolgerungen gezogen werden können, sind weitere Längsschnittuntersuchungen erforderlich. Unsere Ergebnisse deuten darauf hin, dass die Aufmerksamkeitsumlenkung auf eigene Körpersignale ein vorteilhafter Ansatz zur Förderung der Emotionsregulation und des Persönlichkeitsfunktionsniveaus sein könnte, indem

körperliche Erfahrungen mit weiteren kognitiven und affektiven Erfahrungen verknüpft werden (z.B. indem Körpererfahrungen Bedeutung und Wert für das Selbst und seine Regulierung in sozialen Kontexten zugeschrieben werden). Die Integration eines interozeptiven Aufmerksamkeitstrainings (e.g., Tan et al., 2023) könnte nicht nur Patienten mit BPD zugutekommen, sondern möglicherweise auch Patienten mit anderen psychischen Störungen, die Defizite in der Emotionsregulation im Zusammenhang mit subjektiven Erfahrungen von TCE aufweisen, sowie für Personen, die unter die diagnostische Schwelle der üblichen psychischen Störungen fallen. Das Training der Aufmerksamkeitsumlenkung auf innere Körperempfindungen durch achtsamkeitsbasierte und körperorientierte Module ist bereits ein integraler Bestandteil kognitiv-behavioraler Therapien der dritten Welle, einschließlich der Dialektisch-behavioralen Therapie (Linehan, 2003) und Schematherapie (Young, 2023). Psychotherapeutische Behandlungen können durch physiologische Interventionen wie Neuro- oder Biofeedback ergänzt werden, die darauf abzielen, den physiologischen Zustand der Interozeption zu verbessern (Chen et al., 2021). Dies könnte besonders wichtig sein, wenn kombinierte Defizite im physiologischen Zustand der Interozeption und Beeinträchtigungen der interozeptiven Sensibilität vorliegen, wie sie bei einigen Personen mit BPD beobachtet werden. Hinsichtlich des Potenzials von Oxytocin, die interozeptive Verarbeitung zu beeinflussen, deuten die vorliegenden Ergebnisse darauf hin, dass die intranasale Gabe von Oxytozin in Ruhe möglicherweise keine geeignete Intervention ist, um efferente Regulationszustände der Interozeption zu verbessern. Zukünftige Studien, die zwischenmenschlich bedeutsame Kontexte einbeziehen, sind notwendig, um zu untersuchen, ob intranasale Gabe von Oxytozin eine effiziente Umverteilung der Interozeptionsaufmerksamkeit in sozialen Kontexten erleichtern kann.

Zusammenfassend lässt sich festhalten, dass die Ergebnisse der Studien erste Rückschlüsse auf unterschiedliche biopsychosoziale Prozesse zulassen, welche mit dem Funktionsniveau der Persönlichkeit bei Menschen mit und ohne verschiedene psychische Störungen, zusammenhängen. Emotionale und körperliche Vernachlässigung bzw. Missbrauch in der Kindheit, sowie sexueller Missbrauch, die psychosoziale Risikofaktoren darstellen, könnten möglicherweise die Anfälligkeit für die Entstehung von Beeinträchtigungen der Persönlichkeitsfunktionen im Erwachsenenalter erhöhen. Die subjektive Bewertung einer verminderten Aufmerksamkeit auf und Wahrnehmung von Körpersignalen (d. h. interozeptive Sensibilität) erwies sich als ein potenziell proximaler Faktor, der möglicherweise zur Erklärung des transdiagnostischen Zusammenhangs zwischen TCE und erwachsenen Beeinträchtigungen des Selbst, insbesondere der emotionalen Dysregulation, und der zwischenmenschlichen Funktionen beiträgt. Oxytocin könnte jedoch bei Frauen mit BPD keine endokrinologischen Auswirkungen auf die HRV in Ruhe (d.h. objektive physiologische Zustände der Interozeption) haben, weder in Abhängigkeit von selbstberichteter TCE noch der Bindungsunsicherheit.

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