Role of Relaxation in Resilience and Health

Doctoral thesis for obtaining the academic degree

Doctor of Natural Sciences (Dr. rer. nat.)

submitted by

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at the

Universität Konstanz

Faculty of Sciences

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Konstanz, 2024

Konstanzer Online-Publikations-System (KOPS)
URL: http://nbn-resolving.de/urn:nbn:de:bsz:352-2-qzpf2q1v8hbu4

Tag der mündlichen Prüfung: 9.12.2024
1. Referent: Prof. Dr. Jens C. Pruessner
2. Referent: Prof. Dr. Andrea Hartmann-Firnkorn

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Acknowledgments

I want to express my deepest gratitude to all those who have supported me throughout my journey in the three years while completing this doctoral thesis.

First and foremost, I would like to thank my primary supervisor, Jens Pruessner, for his support and insightful feedback. Your expertise and encouragement to develop my ideas have been instrumental in shaping this work. I am immensely grateful to you for providing me with the freedom and flexibility to work at my own pace.

I am also grateful to my secondary supervisor, Andrea Hartmann-Firnkorn, whose guidance helped me see the potential of integrating scientific research with clinical practice.

A special thanks goes to all my colleagues at the SHINE lab. Whether it was troubleshooting R scripts, organizing conference travels, or simply providing a much-needed laugh, you all made this journey not just productive but genuinely enjoyable. In particular: Maria, Bernadette, and Ulrike, for listening to my ideas and scientific challenges, providing encouragement and feedback, Annika for sharing her experiences in combining a doctoral thesis with the training to become a psychotherapist, Elea for insightful debates about our shared research interests and facing the challenge of elaborate cake decorating together, and Stella and Nina for always having a sympathetic ear for challenges and celebrations.

To the students, participants, and patients who contributed to this research, I am deeply thankful for your willingness to be a part of my projects. Without your contribution, this work would not have been possible.

I also want to express my gratitude to the Bodenseeinstitut für Psychotherapie and Michael Odenwald for supporting me in the practical challenges of combining my doctoral thesis with my therapy training. I am also very grateful to Oliver Müller, Nadine Weber, Maike Hofsäß, and the team of Ward 61 for providing me with the opportunity to collect a clinical sample.

To my family, Mama, Papa, and Julian, thank you for your unconditional love and belief in my abilities, always encouraging me to do my own thing (as Udo would say). Your support has been my safety net during the highs and lows of this academic journey. To my godmother Barbara, whose enthusiasm for science, research, and excitement over discoveries has inspired me. To my friends, thank you for your understanding, and patience, and for providing much-needed moments of relaxation and laughter. To Flo, for your unwavering support in every aspect. Thank you for being on my team, celebrating my achievements, listening to my endless research rants, and carrying the 360° camera up the mountain.

Lastly, I would like to acknowledge the financial support from the University of Konstanz following the Landesgraduiertenförderungsgesetz, which made my thesis possible.

Abstract

In recent years, there has been a rise in the incidence of mental disorders, leading to decreased well-being in the population and increased expenses for the healthcare system. Understanding the mechanisms that lead to the development of mental disorders, including the protective factors improving resilience, is a prerequisite for developing targeted interventions aiming to improve health in the population. Generally, fast and adequate adaption to changing environmental demands was found to be a core aspect of health. This includes not only a rapid stress response when faced with a threat but also an effective relaxation response in safe environments to refill resources. This thesis, therefore, aims to investigate the possible role of the relaxation response in resilience and health.

Since a standardized relaxation protocol is needed to investigate this question, the first study of this thesis was a systematic literature review aiming to derive the properties of an effective (virtual) relaxation intervention. The findings revealed substantial heterogeneity across studies employing virtual relaxation interventions while also suggesting promising outcomes for interventions using virtual nature stimuli designed to enhance immersion. Based on these results, my colleagues and I developed a virtual nature relaxation intervention to investigate further possible factors influencing the relaxation response. Since experiencing early life adversity (ELA) is a known risk factor for developing mental disorders, we investigated the effects of ELA on the relaxation response in a healthy sample (ELA Relax study). We employed a virtual nature intervention based on the results from the systematic review and a paced breathing intervention. The results showed a blunted psychophysiological relaxation response associated with the experience of ELA. The following study explored the relaxation response in patients with borderline personality disorder (BPD Relax study). Comparing BPD patients with healthy participants showed lower psychophysiological relaxation parameters in the BPD patients at baseline but no significant differences in the relaxation response, even though the BPD patients reported high exposure to ELA.

The studies conducted allow conclusions about the optimal operationalization of relaxation, including insights into measurements, interventions, and study designs. Additionally, the findings from the intervention studies emphasize the importance of assessing ELA and the presence of mental disorders together since the effect of ELA

on the relaxation response seems to differ depending on the development of mental disorders.

To summarize, it is postulated that the relaxation response is linked with health and resilience. The correlation between ELA and diminished relaxation response in healthy individuals highlights its involvement in the mechanisms connecting ELA with the development of mental disorders. BPD patients showing reduced baseline relaxation parameters and an intact relaxation response was an unexpected result. Possible explanations include the development of BPD as an adaptive process to experiencing ELA and BPD patients retaining the ability to relax in response to relaxation interventions but being unable to relax in everyday situations, resulting in decreased baseline relaxation parameters. Future studies should investigate those possible explanations and interventions for improving relaxation parameters in vulnerable populations and patients with mental disorders. In the long run, those interventions could bolster resilience or be included in the treatment and prevention of mental disorders.

Zusammenfassung

In den letzten Jahren hat die Häufigkeit psychischer Störungen zugenommen, was zu einer Beeinträchtigung des Wohlbefindens in der Bevölkerung und zu höheren Kosten für das Gesundheitssystem führte. Das Verständnis der Mechanismen, die zur Entwicklung psychischer Störungen führen, einschließlich der Schutzfaktoren, welche Resilienz stärken, ist eine Voraussetzung für die Entwicklung gezielter Maßnahmen zur Stärkung von Gesundheit in der Bevölkerung. Generell wurde festgestellt, dass eine schnelle und angemessene Anpassung an sich ändernde Umweltanforderungen ein zentraler Aspekt von Gesundheit ist. Dazu gehört nicht nur eine schnelle Stressreaktion bei Bedrohung, sondern auch eine wirksame Entspannungsreaktion in sicheren Umgebungen, um Ressourcen wieder aufzufüllen. Ziel dieser Arbeit ist es daher, die mögliche Rolle der Entspannungsreaktion für Gesundheit und Resilienz zu untersuchen.

Da zur Untersuchung dieser Frage ein standardisiertes Entspannungsprotokoll benötigt wird, war die erste Studie dieser Arbeit eine systematische Literaturübersicht mit dem Ziel, die Eigenschaften einer wirksamen (virtuellen) Entspannungsintervention abzuleiten. Die Ergebnisse zeigten eine deutliche Heterogenität zwischen den Studien, in denen virtuelle Entspannungsinterventionen eingesetzt wurden. Darüber hinaus zeigten sich vielversprechende Ergebnisse für Interventionen, die virtuelle Naturstimuli verwenden, und darauf ausgerichtet sind die Immersion zu verbessern. Auf der Grundlage dieser Ergebnisse habe ich gemeinsam mit meinen KollegInnen eine Entspannungsintervention in der virtuellen Natur entwickelt, um mögliche Faktoren, die die Entspannungsreaktion beeinflussen, weiter zu untersuchen. Da das Erleben belastender Kindheitserlebnisse (Early life adversity, ELA) ein bekannter Risikofaktor für die Entwicklung psychischer Störungen ist, untersuchten wir die Auswirkungen von ELA auf die Entspannungsreaktion in einer gesunden Stichprobe (ELA Relax Studie). Wir entwickelten eine Entspannungsintervention basierend auf virtueller Natur und den Ergebnissen aus der systematischen Literaturübersicht und verwendeten diese in den folgenden Studien. Als weitere Entspannungsintervention setzten wir eine Atemübung ein. Die Ergebnisse zeigten eine abgeschwächte psychophysiologische Entspannungsreaktion in Verbindung mit ELA. Die Folgestudie untersuchte die Entspannungsreaktion bei Patientinnen mit Borderline Persönlichkeitsstörung (BPD Relax Studie). Der Vergleich von BPD-Patientinnen mit gesunden Teilnehmerinnen

ergab niedrigere psychophysiologische Entspannungsparameter bei den BPD-Patientinnen zu Beginn der Studie, aber keine signifikanten Unterschiede in der Entspannungsreaktion, obwohl die BPD-Patientinnen in hohem Maße ELA erlebt hatten.

Die durchgeführten Studien lassen Rückschlüsse auf die optimale Operationalisierung von Entspannung zu, einschließlich gemessener Variablen, Interventionen und Studiendesigns. Darüber hinaus unterstreichen die Ergebnisse der Interventionsstudien die Bedeutung einer gemeinsamen Bewertung von ELA und dem Vorliegen psychischer Störungen, da die Wirkung von ELA auf die Entspannungsreaktion in Abhängigkeit von der Entwicklung psychischer Störungen unterschiedlich zu sein scheint.

Zusammenfassend wird postuliert, dass die Entspannungsreaktion mit Gesundheit und Resilienz zusammenhängt. Die Korrelation zwischen ELA und einer verminderten Entspannungsreaktion bei gesunden Personen unterstreicht deren Einfluss auf die Mechanismen, die ELA mit der Entwicklung von psychischen Störungen verbinden. Ein unerwartetes Ergebnis war, dass BPD-Patientinnen reduzierte Baseline Entspannungsparameter und eine intakte Entspannungsreaktion aufwiesen. Mögliche Erklärungen beinhalten die Entwicklung von BPD als Anpassungsprozess an das Erleben von ELA. Außerdem könnte es sein, dass BPD-PatientInnen die Fähigkeit zur Entspannung als Reaktion auf Entspannungsinterventionen beibehalten, aber nicht in der Lage sind, sich in alltäglichen Situationen zu entspannen, was verminderten Entspannungsparametern während der Baseline führt. Künftige Studien sollten diese möglichen Erklärungen und Interventionen zur Verbesserung der Entspannungsparameter in gefährdeten Bevölkerungsgruppen und bei PatientInnen mit psychischen Störungen untersuchen. Langfristig könnten diese Maßnahmen die Resilienz stärken oder in die Behandlung und Prävention von psychischen Störungen einbezogen werden.

List of Abbreviations

ACT	Acceptance and Commitment Therapy
ANS	Autonomic Nervous System
ApEN	Approximate Entropy
BDI	Becks Depression Inventory
BF	Biofeedback
BMI	Body Mass Index
BPD	Borderline Personality Disorder
BR	Breathing rate
BSL	Borderline Symptom List
CTQ	Childhood Trauma Questionnaire
DBT	Dialectic Behavioral Therapy
EDA	Electrodermal Activity
ELA	Early Life Adversity
FuzzEN	Fuzzy Entropy
GDS	Geriatric Depression Scale
GRADE	Grading of Recommendations Assessment Development and Evaluation
HC	Healthy controls
HF	High-frequency heart rate variability
HMD	Head-mounted display
HPA	Hypothalamic-pituitary-adrenal axis
HRV	Heart rate variability
ICC	Intraclass Correlation Coefficient
IPQ	Igroup Presence Questionnaire
LF	Low-frequency heart rate variability
MDBF	Mehrdimensionaler Befindlichkeitsfragebogen
MDD	Major Depression Disorder
MRJPQ	Modified Reality Judgment and Presence Questionnaire
NN50	Successive RR intervals differing by more than 50 ms
NRS	Numeric rating scale
PANAS	Positive And Negative Affect Schedule
PBI	Parental Bonding Instrument
PFC	Prefrontal Cortex
pNN50	Proportion of successive RR intervals that are larger than 50ms

PNS	Parasympathetic Nervous System
POMS	Profile of Mood States
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRISMA-P	Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
RMSSD	Root mean square of successive differences
RRI	Time interval between consecutive R-peaks
RSA	Respiratory Sinus Arrhythmia
RSQ	Relaxation State Questionnaire
SampEN	Sample Entropy
SDNN	Standard deviation of all normal-to-normal intervals
SDSD	Standard deviation of successive differences
ShanEN	Shannon Entropy
SNS	Sympathetic Nervous System
STAI	State-Trait-Anxiety Scale
VAS	Visual analog scale
VLF	Very low-frequency heart rate variability
VR	Virtual reality

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1. General Introduction

Impairments in health, be they mental or physical, affect us every day. Even a minor cold can impact well-being, interpersonal relationships, and productivity, emphasizing the importance of good health for every aspect of life (Åsbring, 2012). In particular, impaired mental health was found to negatively impact well-being and life satisfaction (Dear et al., 2002) and is even proposed to have a more profound impact on mental well-being than physical health (Waters et al., 2008). In recent years, the prevalence of mental illnesses has increased around the globe (Barr et al., 2015; Mojtabai & Jorm, 2015; Tkacz & Brady, 2021; Wiens et al., 2020). Mainly, the Covid-19 pandemic has led to an increase in psychological diseases, particularly depression and anxiety disorders (World Health Organization, 2022). The gap between healthy and ill people appears to have widened since predominantly vulnerable people experienced a decrease in mental health during and after the pandemic, for example, adolescents, pregnant women, and people with preexisting mental disorders (Blendermann et al., 2023; Bower et al., 2023; World Health Organization, 2022). Even before this recent increase, mental illnesses accounted for 125.3 million disability-adjusted life-years in 2019 worldwide, a noticeable increase from 80.0 million in 1990 (Mental Disorders Collaborators, 2022). In Germany, mental diseases are the most common reason for occupational disability (34.50%), well ahead of diseases of musculoskeletal disorders (20.10%; Morgen & Morgen, 2024).

Even though there are various theories and etiological models for the development of mental diseases, their origin is complex, and many questions remain (Mallard et al., 2023; Smith et al., 2020). Various factors were found to influence the development of mental disorders, such as genetics and personality (Mallard et al., 2023; Smith et al., 2020). On the one hand, some factors increase the risk of developing mental disorders, like exposure to (early life) trauma, social rejection, and a lack of social support (Isaksson et al., 2021; Sayed et al., 2015; Sigrist et al., 2021a). On the other hand, there are also factors associated with resilience, defined as recovering from adverse experiences while maintaining mental health (Herrman et al., 2011). Those factors include optimism, cognitive and behavioral flexibility, secure attachment, a supportive social network, physical health, high levels of education, and functional coping strategies (Chbeir & Carrión, 2023; Hart et al., 2014; Juster et al., 2010). Especially considering the recent increase in mental diseases, a better understanding of risk factors and protective factors can contribute to a better understanding of good health and well-being in the population.

1.1 Importance of adaptability

Everyday life is filled with cues of threat and safety. Even when sitting at the desk in the office, one encounters a multitude of impressions every second. Those rage from external ones, like the sound of a car passing the building or the laughter of colleagues from the office next door, to internal ones, like a growing hunger just before lunch break. Interpreting those signals, distinguishing between important and unimportant, adapting, and acting quickly and adequately are prerequisites for survival and health (Brosschot et al., 2017; Porges, 2001; Ulrich-Lai & Herman, 2009). For example, the sound of a car probably does not warrant a response while sitting in the office but is essential for survival when crossing the street.

1.1.1 Role of the autonomic nervous system in adaptability

Filtering information and adapting by reacting adequately is a constant and primarily subconscious process mediated by the autonomic nervous system (ANS). The ANS consists of three parts: the sympathetic nervous system (SNS), the parasympathetic nervous system (PNS), and the enteric nervous system. Various areas in the forebrain, the brain stem, and the spinal cord are associated with the ANS, combined with afferent and efferent pathways, forming a feedback loop (Gibbons, 2019; Porges, 2003). The prefrontal cortex (PFC) is essential for the feedback loop, linking input with output and enabling flexibility in responding to external and internal changes (Thayer et al., 2009). The basis for ANS activation is distinguishing between safe and unsafe environments and adapting to environmental demands (Thayer et al., 2012). If the environment is perceived as safe, the PFC inhibits the activity of the amygdala, not necessarily reducing fear but including a higher level appraisal of the situation (Thayer et al., 2012). An active amygdala is associated with the emotional response of the ANS when faced with a threat and, therefore, the stress response driven by the SNS (Gibbons, 2019). An active PFC inhibiting the amygdala and, therefore, the stress response to foster a calm state that enables restoration, emotion regulation, and social interaction is associated with activation of the PNS (Porges, 2015; Thayer et al., 2012). The most important pathway for the PNS is the vagus nerve, which quickly disinhibits SNS influence on heart activity when faced with a threat, increasing heart rate within milliseconds (Brosschot et al., 2016; Gibbons, 2019). In addition to heart rate, the ANS controls a variety of physiological functions like blood pressure, gastrointestinal function, bladder function, temperature regulation, sexual function, and pupillary function. Responses from the ANS can be categorized as either belonging to the *rest/digest* response, the *fight/flight* response, or the *freeze/hide* response, with every response fulfilling a function that is vital for survival (Del Giudice et al., 2011; Gibbons, 2019). While the rest/digest response gets activated in situations perceived as safe, thereby promoting physiological growth and restoration, the fight/flight response frees metabolic resources in the face of a threat to enable defending ourselves or fleeing. The freeze/hide response gets activated in situations perceived as life-threatening, for example, freezing after extensive injury to limit movement and, therefore, blood loss (Del Giudice et al., 2011; Gibbons, 2019; Porges, 2003).

The interplay between SNS and PNS to enable those diverse responses is complex and proposed to follow a hierarchical structure. Phylogenetically newer areas (e.g., PFC, myelinated vagus) actively inhibit older ones (e.g., amygdala), enabling the build-up of resources, social behavior, and emotion regulation. When faced with threats, the older areas are rapidly disinhibited, enabling responses focused on survival, such as fighting or fleeing. Older areas are associated with the fight/flight response, while the newer ones are associated with the rest/digest response (Brosschot et al., 2017; Del Giudice et al., 2011; Porges, 2001, 2003, 2015). It is important to emphasize that SNS and PNS are not rigid antagonists. Therefore, a decrease in one does not necessarily lead to an increase in the other (Berntson et al., 1993a). While reciprocal activation is possible, in which an increase in one leads to a decrease in the other, so is coinhibition where both exhibit a decreased activity. A further possibility is a coactivation with SNS and PNS showing increased activity, which can be induced, for example, by skydiving (Del Giudice et al., 2011).

1.1.2 Interplay of sympathetic and parasympathetic nervous system

Various theories focus on the interplay between SNS and PNS and the adaptive qualities that follow. For example, the *Polyvagal Theory* (Porges, 2001, 2003, 2015, 2022) emphasizes the hierarchical organization of the ANS. When reacting to environmental changes, the phylogenetically newer part of the ANS inhibits the phylogenetically older regions until a threat is detected. The phylogenetically youngest part of the ANS is the myelinated vagus nerve, belonging to the PNS. It is associated with the rest/digest response. It inhibits the SNS influence on the sinoatrial node, leading to physiological changes like a decrease in heart rate and a lowering of blood pressure. This process is called the vagal break. If the vagal brake is activated, it allows growth and restoration and activates the social engagement system, leading to prosocial behavior and regulation of emotions. It enables quick adaption to changes in environmental demands by slowing or speeding up heart rate within milliseconds (Porges, 2001, 2003). The myelinated part of the vagus is not fully developed at birth but develops within the first months of life, promoted by skin-to-skin contact with the primary caregiver, for example, the mother (Porges & Furman, 2011). Vagal inhibition of the "older" branches of the ANS driven by the myelinated vagus is not only crucial for a fast response to changes in the environment but also since ongoing sympathetic activation can harm mammals in the long run (Porges, 2001, 2003). Therefore, the Polyvagal Theory emphasizes the importance of safety cues, primarily associated with social interaction, to activate the vagal break (Porges, 2015). While some studies support the Polyvagal Theory (e.g., Quintana et al., 2012), it has also faced various criticisms, particularly regarding its limited empirical evidence, especially in adults (e.g., Egizio et al., 2008), and concerns about the fundamental neuroanatomical assumptions on which the theory is based (Grossman, 2023).

Safety signals are also the core aspect of the *Social Safety Theory* (Slavich, 2020). It postulates that social safety has been of evolutionary importance to humans. Therefore, social safety is beneficial, and social threat is harmful to human health and behavior. Social safety is associated with connection, inclusion, and a sense of belonging, similar to the social engagement system included in the Polyvagal Theory (Porges, 2001). During childhood, social safety schemas are formed, representing cognitions about oneself, the environment, and the future (e.g., "You can handle things on your own") that influence physiology and behavior throughout the lifespan (Slavich, 2020).

The absence of threat is insufficient to perceive a situation as safe, as stated by the *Generalized Unsafety Theory Of Stress* (Brosschot et al., 2016, 2017). Following the principle of hierarchical inhibition, this theory postulates that the stress response is the default response and needs to be actively inhibited by the vagal break. For that to happen, the environment must be perceived as safe, and the simple absence of threat is considered uncertain.

The *neurovisceral integration model* agrees that the stress response is activated by default and needs to be actively inhibited by the PNS in a safe environment (Thayer et al., 2012; Thayer & Lane, 2000, 2009). It also emphasizes the role of an active PNS in detecting and adequately reacting to fast changes in the environment since the PNS influence on heart activity happens faster than the SNS influence (Thayer & Lane, 2000). This model adds adaptive emotion regulation, voluntary attention, and goal-directed behavior to the functions enabled by an active PNS (Thayer et al., 2009, 2012; Thayer & Lane, 2000).

Successful adaptation to external or internal changes not only refers to the response evoked by specific stimuli. The *Vagal Tank Theory* (Laborde et al., 2018) postulates that resting levels and recovery after the response also hold essential information about the adaptability of an organism. For example, returning to baseline after a stressor is as essential for health and survival as a quick response when exposed to the stressor. Delayed recovery from an acute stressor was found to be associated with a hyporeactive PFC in patients with mental disorders (anxiety disorders, depression, posttraumatic stress disorder, and schizophrenia). Additionally, a hyporeactive PFC is associated with a failure to recognize safety signals and increased negativity bias, which describes a heightened sensitivity to threats and negative outcomes. In turn, an active PFC is a sign of an adaptive vagal break (Thayer et al., 2012). This line of argumentation associates mental disorders with the inflexibility of the ANS, which implies that mental disorders might make it more difficult to detect and adapt to fast changes in the environment (Porges, 2003; Thayer & Lane, 2000). This inflexibility is not only linked to stress and relaxation responses but also to the performance of executive functions, indicating impaired functioning in general (Thayer et al., 2009).

Another theory proposes that chronic disinhibition of the SNS over time increases the allostatic load, leading to potential damages (Brosschot et al., 2017; Porges, 2003; Thayer & Lane, 2009). Allostatic load describes the cost of imbalances in the systems that promote adaptation to a changing environment. Allostatic load can lead to overworking of the adaption systems (e.g., leading to chronic stress), a failure to shut down after an acute stressor, or failure to respond adequately to environmental demands (McEwen, 1998). This results in unfavorable consequences for physical health (e.g., hypertension) and behavior (e.g., irritability; Guidi et al., 2020; Porges, 2001). Looking at the behavioral aspects, an inability to detect (social) safety signals locks the ANS in the fight/flight response, limiting the range of social behavior and impeding the ability to inhibit the stress response after an acute stressor (Brosschot et al., 2016, 2017; McEwen, 2008; Porges, 2001, 2022; Slavich, 2020). This leaning of the ANS towards SNS activation gives a possible explanation for interindividual differences in response to the same stimulus (Porges, 2022). Going back to the initial example of the various stimuli existing in an office, a person with an active vagal break will most likely interpret the laughter of colleagues as non-threatening or even positive. However, someone with a disinhibited vagal break and, therefore, activated SNS will probably interpret the laughter as a threat stemming from colleagues laughing about him or her, which in turn limits prosocial behavior. One explanation for those differences in ANS activity focuses on early life experiences. Social safety cues are learned from the primary caregiver during childhood and adolescence. Therefore, children raised in adverse environments might not learn to adequately detect those cues, fixating the ANS in the fight/flight response as a consequence (Brosschot et al., 2016; Porges, 2015, 2022). The Adaptive Calibration Model (Del Giudice et al., 2011) postulates that those interindividual changes are based on the adaption of the ANS to threat and safety during childhood. Much sympathetic activation in early years serves as a cue for mortality and morbidity, shifting the ANS toward strategies based on disinhibited SNS activity (e.g., aggressive behavior; Del Giudice et al., 2011). Since the primary goal of adaption processes by the ANS is survival and not well-being, the system tends to err on the side of caution, needing more time and effort to rate an environment as safe (Brosschot et al., 2017; Del Giudice et al., 2011). In addition to early experiences, various other factors are associated with a chronically disinhibited SNS and allostatic load, for example, lifestyle (e.g., smoking), socioeconomic status, education, and social support (Guidi et al., 2020).

1.2 Importance of relaxation

Recovering after a stressor is an important aspect of flexibility and health. Physiologically, this is associated with an increased PNS activity and inhibition of the SNS, which leads, for example, to a decrease in heart rate, blood pressure, and respiratory rate (Benson et al., 1981; Dusek & Benson, 2009; Hernandez-Ruiz et al., 2020). On a behavioral level, it allows us to exhibit prosocial behavior, foster social connections, and detect as well as send safety signals (Porges, 2022). These aspects are associated with health, social connection, restoration, and growth (Porges, 2022). Adequate disinhibition of the SNS is not only crucial for a flexible response to changes in the environment but also to avoid the negative effects of allostatic load, which are associated with a chronic disinhibit SNS and a failure to activate the vagal break (Brosschot et al., 2017). The listed changes in the ANS, namely a decrease in SNS and an increase in PNS activity are defined as the relaxation response, also called rest/digest response, and postulated to be the counterpart to the fight/flight response (Benson et al., 1981; Dusek & Benson, 2009; Hernandez-Ruiz et al., 2020; Smith, 2007). The physiological relaxation response is not only associated with physiologically beneficial states (e.g., reduced blood pressure) but was also found to have positive effects on aspects of physiological health like hypertension and headaches as well as behavioral aspects like a reduced consumption of drugs, alcohol, and nicotine (Benson et al., 1975; Dusek & Benson, 2009). The relaxation response also affects subjective qualities, namely leading to an increase in well-being and positive emotions (e.g., joy; Benson et al., 1975; Dusek & Benson, 2009; Steghaus & Poth, 2021).

While the fight/flight response is needed to survive acute threats, the relaxation response is needed to refill resources in safe environments and protect against the negative consequences of prolonged SNS disinhibition. This makes an adaptive relaxation response a vital aspect of a healthy life (Bhasin et al., 2013; Dusek & Benson, 2009). Similarly to defining health as more than the absence of illness (Callahan, 1973) and safety as more than the absence of threat (Brosschot et al., 2016), relaxation is more than the absence of stress. Instead, it is linked to a unique combination of physiological (e.g., heightened PNS activity) and affective changes (e.g., increase in positive emotions; Benson et al., 1975; Dusek & Benson, 2009; Steghaus & Poth, 2021). It is also likely linked to resilience, which includes the ability of the ANS to recover rapidly after an acute threat by returning to baseline levels through the activation of the PNS. This enables prosocial behavior and the detection of safety cues and is associated with mental and physical health (McEwen, 2008; Porges, 2022).

A lack of resilience when encountering adverse events might contribute to the development of mental illnesses. While there are multiple factors contributing to the development of mental illnesses, the current consensus describes an interaction between genetics and the environment (Schlossberg et al., 2010). Twin studies have shown that even with a shared genetic vulnerability, it is the nonshared experiences that differentiate between health and developing mental diseases (Lahey et al., 2011). On a physiological level, reduced activity in the PFC and the PNS and, therefore, limited inhibition of the amygdala and sympathetic activity are associated with mental illnesses (Thayer et al., 2012; Thayer & Lane, 2009). These physiological characteristics are linked to a greater negativity bias, failure to recognize safety signals, less functional emotion regulation abilities, and delayed recovery from a stressor (Brosschot et al., 2016; Thayer et al., 2012; Thayer & Lane, 2009). Learning to detect safety signals happens during infancy, which might be compromised in adverse childhoods leading to a chronically disinhibited SNS which in turn is a risk factor for developing mental and physiological diseases (Berman et al., 2022; Brosschot et al., 2016; Del Giudice et al., 2011; Maccari et al., 2014; Porges, 2015, 2022; Slavich, 2020; Smith & Pollak, 2021). Experiencing early life adversity (ELA), for example, abuse, absent parents, or bullying, requires a child to adapt to survive. Physiologically, this can lead to a chronic disinhibition of the SNS, shifting towards strategies that focus on survival instead of social connection and well-being (Del Giudice et al., 2011). A consequence of the chronic disinhibition of SNS activity is compromised PNS activity, which is not only a risk factor but also associated with mental diseases (Del Giudice et al., 2011; McEwen & Akil, 2020; Porges, 2022).

1.3 Operationalization of relaxation

1.3.1 Measurements

When planning to operationalize relaxation, one aspect that needs to be discussed is the identification of valid markers to measure relaxation. As described above, relaxation has physiological and subjective properties that both should be considered when measuring relaxation. Physiological relaxation increases PNS activity, which can be measured by heart rate variability (HRV). HRV describes the beat-to-beat variance of the heart rhythm, is influenced by SNS and PNS, and is discussed to be a general marker of adaptability (Acharya et al., 2006; Shaffer & Ginsberg, 2017). Since various options exist to calculate HRV, choosing the suitable marker requires care as not all adequately represent PNS activity (Pham et al., 2021). While respiratory sinus arrhythmia (RSA) describes the speeding and slowing of heart rate influenced by the vagus, it is very dependent on the breathing cycle, only representing PNS activity when breathing with nine to 25 breaths per minute (Laborde et al., 2018). Another HRV marker adequately indicating PNS activity is the high-frequency (HF) band, representing frequencies of .15 to .40 Hz. Fast Fourier transformation can separate HRV into different components based on frequency.

Since the influence of PNS on heart rate is faster than that of SNS, the high-frequency band is an adequate measure of PNS activity. However, like with RSA, the respiratory pattern impacts HF (Acharya et al., 2006; Shaffer & Ginsberg, 2017; Thayer et al., 2012). Nevertheless, another marker often used to assess PNS activity is the root mean square of successive differences (RMSSD). While RMSSD correlates highly with RSA and HF, therefore estimating the vagally mediated influence on heart rate, it is less influenced by the breathing cycle (Acharya et al., 2006; Pham et al., 2021; Shaffer & Ginsberg, 2017). All HRV markers share a common disadvantage: beyond breathing patterns, there are various factors from different areas affecting HRV. Personal characteristics like age or sex, physiological health (e.g., diabetes, lung diseases), mental health (e.g., affective disorders, depression, personality disorders), medication (e.g., beta-blockers), and lifestyle (e.g., physical fitness, alcohol and nicotine consumption) to name just a few (Acharya et al., 2006; Quintana & Heathers, 2014; Sammito & Böckelmann, 2016; Shaffer & Ginsberg, 2017). Nevertheless, HRV is discussed to be a transdiagnostic marker, linking low baseline values not only with mental and physiological disease but also with stress, panic, anxiety, and worry, and high baseline values with health, adaptability, positive emotions (e.g., cheerfulness), and intact executive functions (Beauchaine & Thayer, 2015; Pham et al., 2021; Shaffer & Ginsberg, 2017).

Subjectively, relaxation is associated with a sense of well-being, an increase in positive emotions (e.g., calmness), and a decrease in mental arousal (Benson et al., 1975; Dusek & Benson, 2009; Hernandez-Ruiz et al., 2020; Steghaus & Poth, 2021). Defining relaxation as more than a decrease in stress and arousal emphasizes that the subjective changes linked to relaxation should be assessed directly (e.g., using the *Relaxation State Questionnaire* by Steghaus and Poth, 2021). Therefore, assessing subjective relaxation indirectly, for example, via a decrease in anxiety, is inadequate. A decrease in anxiety could still be linked to an increase in unpleasant subjective states like boredom instead of an increase in relaxation. Since physiological and subjective measures are not always correlated, relaxation should be measured on both levels (Hernandez-Ruiz et al., 2020).

1.3.2 Interventions

After discussing appropriate markers for physiological and subjective relaxation, the next question regards the methodology of relaxation interventions. So far, there is no successful standardized relaxation protocol (Meier et al., 2020), which limits the standardized investigation of relaxation. Existing protocols differ in interventions used, like massages (Meier et al., 2020), yoga (Klainin-Yobas et al., 2015), guided imagery (Bigham et al., 2014), breathing exercises (Russo et al., 2017), nature exposure (Farrow & Washburn, 2019), or music (Hernandez-Ruiz et al., 2020). Successful relaxation interventions are postulated to need the following characteristics: (I) a quiet environment with minimal stimulation often achieved by closed eyes, (II) a comfortable position associated with decreased muscle tonus, (III) a constant and repetitive stimulus, and (IV) a passive attitude to return attention the repetitive stimulus if distractions occur (Benson et al., 1975).

While some of the mentioned interventions fit these criteria, the standardization of those interventions ranges from challenging to impossible. For example, even if the same massage protocol is implemented, the interindividual differences between the persons giving the massage cannot be eliminated. In contrast, breathing exercises are easy to implement and standardize. As described above, breathing rhythm is linked closely to PNS activation via the vagus nerve, and especially paced breathing exercises have been found to increase HRV and subjective relaxation (Russo et al., 2017; Szulczewski, 2019). Changes in HRV associated with slow breathing (e.g., six breaths per minute) and an extended exhalation phase as compared with the inhalation phase were found to be caused by an increase in PNS activity (Kromenacker et al., 2018; Russo et al., 2017; Szulczewski, 2019).

While the mechanisms behind the effectiveness of paced breathing exercises are physiological, the mechanisms behind the relaxing effects of nature exposure are postulated to be more psychological. Spending time in natural environments is linked to a variety of positive effects, for example, a decrease in blood pressure, heart rate, and negative affect and an increase in HRV, positive affect and immune system activity (Farrow & Washburn, 2019; Li et al., 2007; Payne & Delphinus, 2019). Various theories propose the relaxing effects of nature. The *Biophilia Hypothesis* (Kellert & Wilson, 1993) postulates an innate need for contact with flora and fauna, which is visible, for example, in aesthetic preferences (Kahn Jr, 1997). While the *Psychoevolutionary Theory* (Ulrich, 1983) agrees with innate aesthetic preferences for natural scenes, it adds that recovering and relaxing quickly in a safe, natural environment has an evolutionary benefit (Ulrich, 1983). Hence, natural environments are postulated to capture attention effortlessly, a theme also found in the *Attention Restauration Theory* (Kaplan, 1995). This theory defines four characteristics needed to capture involuntary attention (i.e., Fascination, Being Away, Extent, and Compatibility) often possessed by natural scenes. However, even though real-life nature can successfully induce relaxation (Payne & Delphinus, 2019), standardizing is impossible. Ranging from weather, temperature, or pollution to accessibility of nature, many factors cannot be influenced. Therefore, virtual representations of nature have gained interest in recent years since they are easy to implement and standardized. Previous findings on the effectiveness of virtual nature-based relaxation interventions are heterogeneous, sometimes finding an effect on physiological relaxation (e.g., Annerstedt et al., 2013) and sometimes reaching nonsignificant results (e.g., Snell et al., 2019).

1.3.3 Study design

In addition to the heterogeneity between employed measures and interventions, there is also a great heterogeneity between study designs. Only focusing on short-term virtual nature relaxation interventions yields interventions ranging from 90 seconds (Tang et al., 2017) to 15 minutes (Anderson et al., 2017), some with a preceding stressor (Annerstedt et al., 2013) and some without (Browning et al., 2020), some with simultaneous physical activity (Calogiuri et al., 2018) but most assessed while sitting (Snell et al., 2019). Those differences make it hard to compare the yielding results.

A fundamental difference exists between assessing the relaxation parameters at baseline and the relaxation response. As described above, rest, response, and recovery are important aspects of physiological processes like the relaxation response and should, therefore, be assessed separately (Laborde et al., 2018). So far, previous studies have primarily focused on relaxation parameters at baseline or after an acute stressor. However, after an acute stressor, it is impossible to distinguish the recovery response after the stressor and the possible additional relaxation response induced by relaxation interventions. A standardized relaxation protocol should, therefore, assess rest, response, and reactivity induced by a relaxation intervention without the influence of an acute stressor.

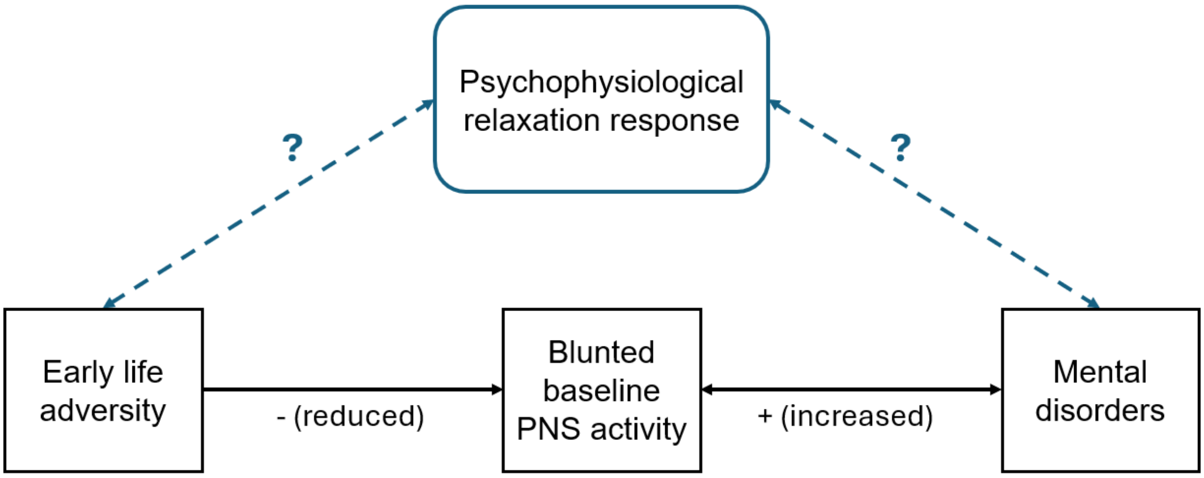
The current lack of a successful standardized relaxation protocol leads to many open questions concerning the relaxation response. First, mechanisms behind a successful activation of the relaxation response are still unclear, partly due to the great variety of relaxation interventions. Second, while studies show differences between responders and non-responders, it is unclear which interindividual differences are linked to the benefits of relaxation interventions (Hernandez-Ruiz et al., 2020; Jo et al., 2019).

1.4 Previous findings and open questions

As described above, blunted baseline PNS activity is associated with mental disorders (anxiety disorders, autism, depression, panic disorder, schizophrenia), severity of psychological symptoms, attention problems, callousness, and emotion dysregulation (Beauchaine & Thayer, 2015; Eikeseth et al., 2020; Koenig et al., 2016; Sigrist et al., 2021a). Baseline PNS activity is also discussed as a transdiagnostic marker for mental diseases and vulnerability (Beauchaine & Thayer, 2015). For example, low resting state HRV was shown to be associated with the development of mental diseases after experiencing ELA (Jin et al., 2018; Sigrist et al., 2021a). On the other hand, high baseline PNS activity seems to be associated with various factors linked to health and resilience, like social competence, attachment security, less negativity bias, and functional emotion regulation strategies (Beauchaine & Thayer, 2015; Thayer et al., 2012).

The current literature suggests a link between experiencing ELA and low resting vagally mediated HRV (Jin et al., 2018; Sigrist et al., 2021a; Stone et al., 2018; Thurston et al., 2020). However, some studies have found this relationship to be only significant if mental disorders are controlled for (Sigrist et al., 2021a; Stone et al., 2018). Different mechanisms are postulated to explain the links between ELA, low resting HRV, and the development of mental disorders. A meta-analysis concluded that the most likely mechanism is that ELA leads to a dysregulation of the ANS, evidenced by a low resting HRV (Sigrist et al., 2021a). In turn, low resting state HRV is associated with dysfunctional emotion regulation strategies, which increases the risk of developing mental disorders (Sigrist et al., 2021a). However, there is also evidence linking mental disorders with changes in the ANS, indicating that lower HRV could not only be a marker for vulnerability based on experiencing ELA but also a transdiagnosis marker for mental diseases (Beauchaine & Thayer, 2015). Since previous studies mainly focused on ANS activity at baseline, it is still unclear whether a blunted physiological and psychological relaxation response is associated with ELA, low baseline HRV, and mental disorders; see Figure 1 for a graphical representation of the current literature and open questions.

Figure 1. Schematic overview of previous findings examining the relationships between early life adversity, autonomic nervous system activity, and the development of mental disorders including the open questions investigated in this thesis.
PNS = parasympathetic nervous system.



1.5 Research questions of this thesis

This thesis aims to investigate the relaxation response and possible factors influencing the effectiveness of relaxation interventions to shed more light on the associations between ELA, PNS activity, and mental disorders. Since psychological and physiological mechanisms are postulated behind different relaxation interventions, my colleagues and I chose to employ two relaxation interventions (paced breathing and virtual nature exposure). The same interventions and study designs were employed in two intervention studies to enable comparison results within this thesis.

Since a standardized relaxation protocol is a prerequisite for investigating the relaxation response systematically, I focused on developing a successful and standardizable relaxation intervention as a first step. Since virtual interventions are easy to implement and standardize, the first study in this thesis employs a systematic literature review to explore which characteristics a virtual relaxation intervention should possess to induce psychophysiological relaxation successfully. In the second step, I focused on factors that possibly influence the relaxation response. Since ELA is a risk factor for mental diseases and is linked to reduced baseline PNS activity, the second study focused on the possible effects of ELA on the relaxation response in a healthy sample. Due to this link between the development of mental disorders and heightened exposure to ELA, we investigated the possible effects of mental diseases, namely borderline personality disorder (BPD), on the relaxation response in the third project.

In summary, this thesis aims to answer the following questions:

(1) Which characteristics should a virtual relaxation intervention possess to be successful?
A systematic review was employed to derive a virtual relaxation intervention based on the current literature.

(2) *Does ELA affect the relaxation response?*
While the link between ELA and blunted relaxation values at baseline seems robust, it is still unclear whether it also affects the relaxation response. Answering this question could add another link to the explanation of why ELA is a risk factor for mental diseases and possibly enable targeted therapeutic interventions.

(3) *Do mental disorders affect the relaxation response?*
Similarly to ELA, the association between mental disorders and lower resting state relaxation values appears robust, but possible effects on the relaxation response are still unclear.

2. Which characteristics should a virtual relaxation intervention possess to be successful?

The first project of this thesis delves into the investigation of the characteristics a virtual relaxation intervention should embody to effectively increase relaxation, employing a systematic literature review. The systematic review was published in the peer-reviewed *Journal of Environmental Psychology* in the special issue *Environmental Psychology and Health: Research in VR and Real Settings* in 2023 and was slightly edited for form to fit into this thesis.

Gaertner, R. J., Kossmann, K. E., Benz, A. B., Bentele, U. U., Meier, M., Denk, B. F., Klink, E. S. C., Dimitroff, S. J., & Pruessner, J. C. (2023). Relaxing effects of virtual environments on the autonomic nervous system indicated by heart rate variability: A systematic review. *Journal of Environmental Psychology*, 102035.

Contributions from all authors for this publication were as follows:
RJG: Conceptualization, Methodology, Data Curation, Investigation, Formal analysis, Visualization, Writing - Original Draft & Editing. KEK: Formal analysis, Writing - Review & Editing. ABEB, UUB, MM, BFD, SJD: Writing - Review & Editing. JCP: Formal analysis, Resources, Writing - Original Draft, Supervision, Conceptualization, Methodology. All authors approved the final version.

Link to access the publication: https://doi.org/10.1016/j.jenvp.2023.102035.

Link to access the protocol, which was preregistered at the Prospective Register of Systematic Reviews PROSPERO (ID CRD42021290162):
https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=290162

2.1 Abstract

Recently, a number of virtual relaxation interventions (e.g., watching nature videos using virtual reality glasses) have been developed. Their effectiveness and factors influencing their success in inducing physiological relaxation are unknown, however. This systematic review investigates first, whether virtual interventions can successfully induce changes in the autonomic nervous system associated with relaxation as measured by heart rate variability (HRV), and second, aims to determine whether specific intervention components exist that are necessary for their success. Online databases PubMed, Web of Science, and PsycInfo were included in the search. Out of 479 identified studies, 18 met the inclusion criteria, of which 17 found a significant physiological effect of a virtual relaxation intervention on HRV. Most used nature stimuli, either as pictures or videos, and assessed self-reported measurements in addition to HRV. Most studies also found an increase in HRV, with corresponding changes in various self-report measurements (e.g., decrease in anxiety). There was substantial heterogeneity between studies concerning the physiological outcome measures and details of the intervention. In summary, results from the included studies suggest that virtual relaxation interventions employing nature stimuli interventions are successful. Future studies should aim for a universal definition and operationalization of relaxation to allow easier comparison across different studies.

Keywords: relaxation, virtual, heart rate variability, systematic literature review

2.2 Introduction

2.2.1 Importance of relaxation

Relaxation is a necessary part of life. It contributes to psychological and physical regeneration, increases the quality of life and mental health (Smith et al., 2007), and serves as a protective factor against the negative effects of stress (e.g., on mental health; Bhasin et al., 2013). These positive effects of relaxation can be seen across the lifespan. In pediatric patients, relaxation leads to a decrease in frequency and intensity of headaches (Engel et al., 1992), and in older adults, it reduces depression and anxiety (Klainin-Yobas et al., 2015). Despite the importance of relaxation, there are still many open questions about the mechanisms by which relaxation has its effects, the associated affective changes, and moderating situational or personality factors. Since relaxation interventions differ greatly in the way they are implemented (e.g., yoga, Klainin-Yobas et al., 2015; massages, Meier et al., 2020; nature exposure, Farrow & Washburn, 2019; warm foot baths, Yamamoto & Nagata, 2011) but also in duration (from 90-second interventions e.g., Igarashi et al., 2014) to programs spanning several weeks (e.g., Solberg et al., 2000), it is at this point in time difficult to firm conclusions about overall success of the interventions, and possible moderating factors. A standardized relaxation protocol would enable an in-depth investigation of the mechanisms underlying the relaxation response and moderating factors, which would allow targeting bigger questions, for example, the possibility of a blunted relaxation capability being linked to psychological diseases. First efforts have been undertaken towards standardized relaxation protocols, for example by standardized massage interventions in a laboratory setting (Meier et al., 2020). We conducted this systematic review to specifically investigate existing virtual relaxation interventions and their effectiveness since virtual interventions possess some important advantages. While standardization presents a difficulty when using real-life interventions (e.g., exposure to nature outdoor settings) it is relatively easy to standardize interventions based on virtual environments. Additionally, the implementation of virtual interventions is possible almost anywhere (e.g., in a university laboratory as well as a hospital room) needing relatively little space, not only allowing it to be transferred easily across different research environments but also possibly becoming part of standardized treatment interventions. The usage of virtual interventions is easy to implement since no specific training is needed, depending on the exact intervention it is as easy as launching a computer program.

However, not only the variety of contents of virtual relaxation interventions is vast, ranging from virtual nature to games, but there is also a wide variety of other characteristics (e.g., duration, method of presentation) that could possibly modulate the effectiveness of an intervention. Therefore, a systematic review of the literature can potentially reveal which type of intervention is the most effective, enabling the development of a successful standardized relaxation protocol based on virtual environments. How relaxation is defined and measured should also be taken into account, since consistencies in used measurements would allow comparisons between different studies.

2.2.2 Definition of relaxation

Giving a conclusive definition of relaxation was not the focus and would thus be beyond the scope of this systematic review. Still, we suggest keeping physiological as well as psychological processes in mind when searching for a definition, as is done in recent research (Knaust et al., 2022). On the psychological level relaxation is experienced as a calm state of mind, with no worries or fear clouding the calmness (Steghaus & Poth, 2021). Pleasant emotions like happiness or contentment might be involved as well, though it is important to take the intensity of emotions into account. Even happiness experienced intensely is no expression of relaxation, since it can be associated with a high level of arousal (Knaust et al., 2022). Physiologically there is a relaxation of muscles (feeling warm and soft) as well as processes of the autonomic nervous system (increase in parasympathetic activity) that should be taken into account (Knaust et al., 2022). Another consideration, that to our knowledge has not been followed so far but could be examined closer, is a differentiation between state and trait relaxation, as it is with anxiety (Knowles & Olatunji, 2020) and mindfulness (Bravo et al., 2018). While relaxation as state could be induced in most of the participants with a successful intervention, looking at the baseline level could show interindividual differences in trait relaxation. How exactly high levels of trait relaxation would influence state relaxation remains speculative and thus is not further considered in this systematic review.

2.2.3 Measuring relaxation

A prerequisite for a standardized assessment of relaxation is a universal measurement of relaxation to make the results of different studies comparable. On the subjective experience level, there are many questionnaires used to measure affective states and changes, for example, the *Positive Affect Negative Affect*

Schedule (PANAS; Watson et al., 1988) or the *State-Trait Anxiety Inventory* (STAI; Spielberger et al., 1971). Those questionnaires can assess the psychological aspects of relaxation but are likely influenced by confounding factors, like social desirability. Not only self-report questionnaires in general (Fisher & Katz, 2000) but also questionnaires about well-being specifically (Brajša-Žganec et al., 2011) are at risk of being distorted by social desirability. It seems that a decreased negative affect aligns with socially desirable answers (Brajša-Žganec et al., 2011). Since the definition of relaxation used in studies sometimes includes the reduction of negative affect this could bias results derived from self-report measurements.

On a physiological level, relaxation is tightly linked with the activity of the autonomic nervous system, consisting of the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS; McCorry, 2007). Increased parasympathetic activity is associated with relaxation and positive emotions, while increased sympathetic activity is associated with stress, anxiety, and the fight-flight response (Shaffer & Ginsberg, 2017). Thus, the autonomic state of relaxation should be associated with high parasympathetic activity. Although SNS and PNS are not reciprocal (see the autonomic space model; Berntson et al., 1993a), relaxation has often been observed to include states of low SNS as well. Thus, the ratio of SNS and PNS is also often employed to measure relaxation. For example, low SNS and high PNS activity can be observed when people start getting sleepy and during the first phase of sleep (Miglis, 2017). Since relaxation is associated with a feeling of calm, even up to drowsiness, it makes sense to find autonomic activity patterns during relaxation comparable to those during the first phase of sleep (Miglis, 2017).

To measure PNS activity, an effective and valid method is the determination of heart rate variability (HRV). HRV describes the beat-to-beat fluctuation of heart rate and is dominantly influenced by PNS (Acharya et al., 2006). There are various ways to calculate HRV, grouped into linear algorithms (time and frequency domain measures), nonlinear algorithms (fractal measures, entropy measures, symbolic dynamics measures, and Poincaré plot representations), and detrended fluctuation analyses (Francesco et al., 2012; Voss et al., 2009). These different measurements typically correlate highly with each other and can be influenced by either parasympathetic activity, sympathetic activity, or both (Voss et al., 2009). However, different measures are influenced by different branches of the autonomic nervous system and therefore, HRV measurements are not necessarily exchangeable. When interpreting results it is important to keep in mind, which branch(es) of the autonomic nervous system influence the HRV measurement, and which conclusions about PNS or SNS activation can consequently be drawn.

The most commonly used HRV measures are time and frequency domain measures (Billman, 2011). High-frequency (HF) HRV is interpreted as a marker of PNS activity and low-frequency (LF) HRV was originally regarded as a marker for SNS (Acharya et al., 2006; Quintana & Heathers, 2014). The interpretation of LF as purely influenced by SNS has been criticized extensively, as has the use of LF/HF ratio as a marker for sympathovagal balance (Quintana & Heathers, 2014): first, LF does not increase in situations of increased sympathetic activity (e.g., exercise), second, it is influenced by the PNS as well as the SNS. Thus, it should not be used as a marker for sympathetic activation (Billman, 2011) but as a combination of SNS and PNS. HF is mostly considered to be solely influenced by the PNS (Acharya et al., 2006) and therefore often used as marker for the increase in parasympathetic activity associated with relaxation (Anderson et al., 2017; Kobayashi et al., 2018). Still, this interpretation of HF has also been criticized, arguing that sympathetic activity might influence HF after all (Billman, 2011). There is no final conclusion to this discussion and evidence is available for each claim. However, it seems safe to argue that there is a dominance of PNS in HF, and especially the contribution of PNS mediates respiration variation in HRV (respiratory sinus arrhythmia).

Together, the ongoing debate showcases the complexity of HRV parameters and their interpretation. In the end, HF is considered to be a valid marker for parasympathetic activity (Acharya et al., 2006; Shaffer & Ginsberg, 2017) but seems more strongly influenced by breathing depth and frequency (Quintana & Heathers, 2014). In contrast, time-domain markers are less susceptible to distortion due to changes in breathing and, for example, body posture. The root mean square of successive differences (RMSSD) is a time domain marker, strongly correlated with HF, but less influenced by breathing (Acharya et al., 2006; Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017).

Table 1 briefly summarizes all HRV markers used in the studies included in this review, as well as the autonomic branch(es) mostly influencing the marker, changes in association with relaxation, and positive correlations with other markers included in this table.

Table 1. HRV indices used in included studies and their interpretation in relation to parasympathetic activity.

Measurement (times used in included studies)	Description	Influence of SNS and PNS	Effect of relaxation	Additional information	Correlation
			Linear measurements		
			Time Domain		
RMSSD (n=4) (Bansal et al., 2009; Bertsch et al., 2012; Kleiger et al., 2005; Shaffer & Ginsberg, 2017)	Root mean square of the difference of successive RR intervals	Mostly influenced by PSN	Increase		HF, pNN50
SDNN (n=4) (Bansal et al., 2009; Kim et al., 2018; Shaffer & Ginsberg, 2017)	Standard deviation of all RR intervals	SNS and PNS,	Increase	more accurate in 24h recordings, indicator for cardiac risk, low values mean stress	VLF, LF
NN50 (n=1) (Bansal et al., 2009; Electrophysiolog y, 1996)	Adjacent RR intervals differing by more than 50 ms in entire ECG recording		Increase		HF
pNN50 (n=3) (Bansal et al., 2009; Bertsch et al., 2012; Kim et al., 2018; Kleiger et al., 2005; Shaffer & Ginsberg, 2017; Shaffer & Venner, 2013)	proportion of successive RR intervals that are larger than 50ms	Closely correlated to PNS activity	Increase	low values mean stress, more reliable than SDNN in short term recordings	RMSSD, HF, ApEN
RRI (n=1) (Byun et al., 2019; Choi et al., 2017)	time intervals between consecutive R-peaks	SNS and PNS	Increase	Decrease in response to stress (increase in SNS activity)	
SDSD (n=2) (Bansal et al., 2009; Electrophysiolog y, 1996)	Standard deviation of differences between adjacent RR intervals		Increase		HF
			Frequency domain		
VLF (n=4) (Bansal et al., 2009; Shaffer & Ginsberg, 2017; Shaffer & Venner, 2013)	Power in very low frequency range (.003 Hz – .04 Hz)	PNS and SNS (probably stronger PNS influence)	Increase		SDNN

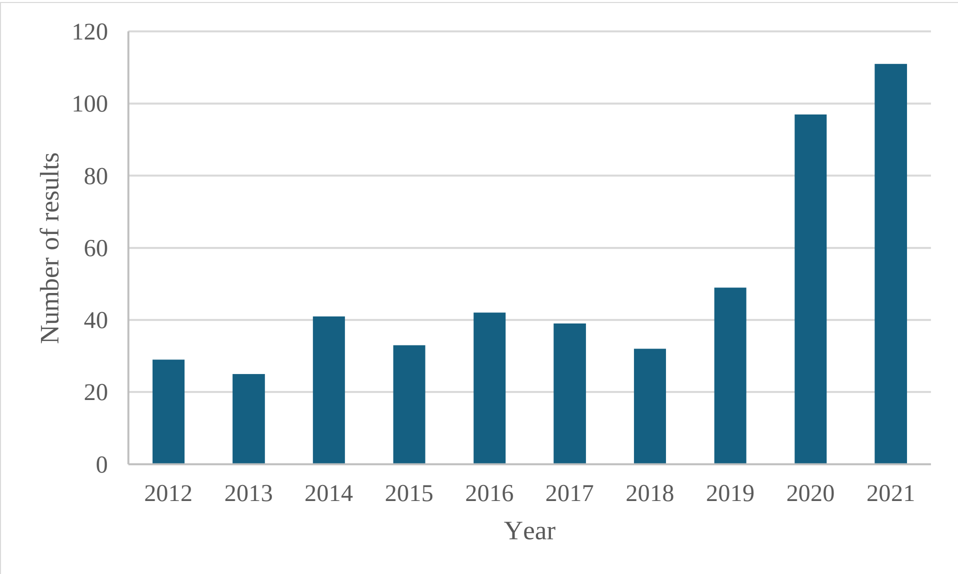
Measurement (times used in included studies)	Description	Influence of SNS and PNS	Effect of relaxation	Additional information	Correlation
LF (n=10) (Bansal et al., 2009; Kim et al., 2018; Shaffer & Ginsberg, 2017)	Power in low frequency range (.04 Hz – .15 Hz)	PNS and SNS	Decrease	high values interpreted as low PNS activity	
HF (n=10) (Bansal et al., 2009; Bertsch et al., 2012; Kim et al., 2018; Shaffer & Ginsberg, 2017)	Power in high frequency range (.15 Hz – .4 Hz)	PNS	Increase	low values associated with stress, panic anxiety worry; influenced by breathing	RMSSD, NN50, pNN50, SDSD, ApEN
LF/HF (n=10) (Bansal et al., 2009; Kim et al., 2018; Shaffer & Ginsberg, 2017; Shaffer & Venner, 2013)	Ratio of low and high frequency	SNS and PNS	Decrease	Low values mean PNS dominance (conserve energy); high values mean SNS dominance (stress) This interpretation has been heavily criticized (Billman, 2013)	
		Nonlinear measurements			
		Entropy			
ApEN (n=1) (Acharya et al., 2006; Voss et al., 2009)	Approximate entropy, index for the overall complexity and regularity of time series		Increase		RMSSD, pNN50, HF
SampEN (n=1) (Voss et al., 2009)	Sample entropy, conditional probability that two sequences of m consecutive data points that are similar to each other		Increase		negatively correlated with LF and LF/HF
FuzzEN (n=1) (Liu et al., 2013)	Fuzzy Entropy, Improvement of SampEN and ApEN, focus on the local characteristics of the sequence		Increase		
ShanEN (n=1) (Byun et al., 2019; Dua et al., 2012)	Shannon entropy, sum of entropy computed over the entire frequency range		Increase	Reduced in stress and increased in relaxation in healthy participants	

Notes: SNS = sympathetic nervous system, PNS = parasympathetic nervous system. For some markers no sources could be found describing which ANS branch(es) influence the marker. Those cells are left empty.

2.2.4 Virtual relaxation

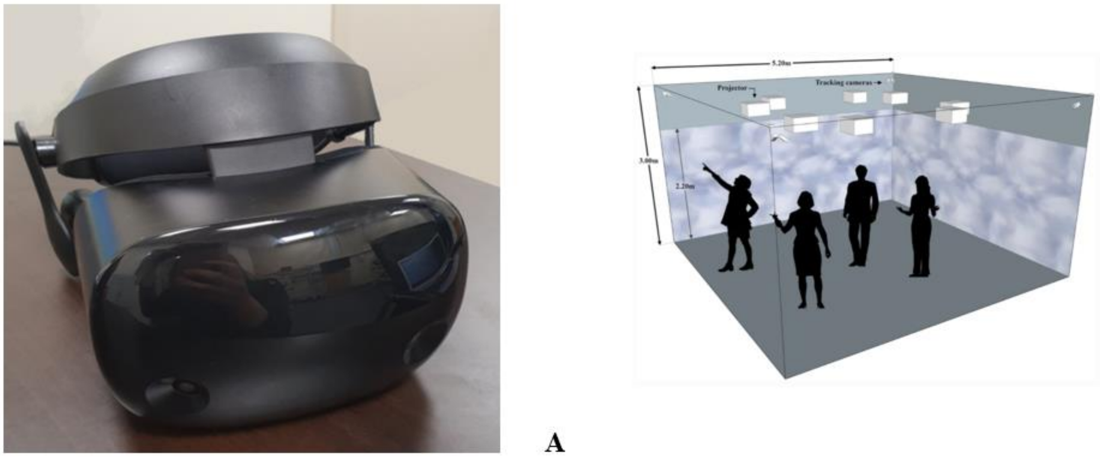
As described above (see 2.2.1), mechanisms and effectiveness of standardized relaxation protocols in virtual environments are largely unexplored. This is despite the fact that in recent years, an increased interest in virtual methods to induce relaxation could be observed. This can, for example, be seen in the increasing number of studies researching this topic. The online database PubMed lists 728 results for the search term “virtual relaxation”, with an increase in articles especially in recent years (see Figure 2), going up from 29 results in 2012 to 112 results in 2021 (PubMed, 29.12.2022).

Figure 2. Increase of results in the online database PubMed for the search term “virtual relaxation” from 2012 to 2021.



These studies include various employment methods of virtual relaxation, for example, computer screens, and head-mounted displays (HMD, see Figure 3a), which consist of either two small screens or one screen showing separate images for each eye. While applications are allowing a smartphone to be used as an HMD, it only shows one picture (Rebenitsch & Owen, 2016). Some studies use a cave system, projecting images onto walls and sometimes the floor, creating a virtual environment (e.g., de Back et al., 2020; see Figure 3b). While every method of presentation has advantages and disadvantages, they all can be used to induce relaxation in research settings (e.g., Annerstedt et al., 2013) and sometimes in therapeutic settings as well (e.g., Veling et al., 2021).

Figure 3. Exemplary pictures of a head-mounted display (A) and a cave system (B).



A B

(Kim et al., 2021) (de Back et al., 2020)

For example, using a computer screen and pictures of urban and natural environments, Gladwell and colleagues (2012) found an increase in HRV associated with an increase in subjective relaxation when participants viewed nature environments compared to urban environments. Using a cave system to expose participants to a virtual Trier Social Stress Test followed by a recovery phase in a virtual forest showed a faster recovery measured by an increase in HRV in a virtual forest with sounds compared to a virtual forest without sounds, or a normal room (Annerstedt et al., 2013). Besides the pure display of relaxation environments, some studies add biofeedback to the virtual environment (e.g., Rockstroh et al., 2019). Biofeedback uses physiological signals (e.g., heart rate, skin temperature) presented to the user in real-time to improve the understanding of physiological activities and positively influence health (Schwartz, 2010). Those physiological signals can be either presented as numbers (e.g., real-time heart rate) or can be integrated into the virtual environment. Integrated biofeedback has thereby, for example, been shown to help patients with generalized anxiety disorder to train relaxation techniques (Riva et al., 2010). In this particular study, there was a biofeedback component within the virtual environment, for example, a campfire changed in size according to the participant's heart rate.

2.2.5 Advantages of virtual nature exposure

It appears that on a subjective experience level, studies using virtual environments can successfully induce relaxation. It is at this point however unclear whether these findings extend to the physiological level. Exposure to nature environments in real-life settings appears to have these effects. For example, a walk in a forest is associated with increased HRV (HF), reduced blood pressure, and decreases in heart rate (Kobayashi et al., 2018; Payne & Delphinus, 2019). If these effects would extend to virtual environments, they would hold a number of important advantages for their use in therapeutic settings. Virtual environments allow a wide range of stimuli a patient can be safely exposed to, while physically remaining in secure surroundings. Virtual environments can further be used in almost all circumstances, as long as hard- and software requirements are met. Every aspect of the environment can be controlled, allowing standardization across participants (as opposed to, for example, a sudden change in weather when walking in a real forest). These advantages are especially important when aiming for standardized interventions in research settings.

2.2.6 Aim of the current systematic review

Riches and colleagues (2021) conducted a systematic review concerning the feasibility, acceptability, and effectiveness of relaxation interventions using a HMD. While they found a successful increase in relaxation in most studies, they did not distinguish between the different ways to measure relaxation, e.g., heart rate, HRV, and self-report measurements (e.g., PANAS, Brief Profile of Mood States). While these results show that virtual relaxation interventions are promising, they do not allow conclusions about the effects of virtual relaxation on the autonomic nervous system specifically.

Therefore, the present review focused on studies that measured HRV as a marker of the autonomic nervous system to investigate, whether physiological relaxation can be successfully induced using virtual relaxation interventions. To be able to derive the effect of virtual environments exclusively, studies using paced breathing were excluded. Paced breathing describes an exercise, where breathing patterns are synchronized to an external pacemaker (e.g., audio or visual), with varying (6 to 15) breathing cycles per minute (Szulczewski, 2019). Since there is a close relationship between breathing and especially frequency-domain measures of HRV (Shaffer & Ginsberg, 2017), paced breathing increases HRV, making it impossible to determine if the virtual environment alone affected HRV. Different presentation methods will be considered in this study since they vary in difficulty to use and financial costs. To find the most effective but at the same time, least cost-intensive method it is important to consider the implementation difficulty of a given relaxation intervention. In addition, the possibility to interact with individual virtual environments will be included as another focus of this review as well. Even though self-report measurements do not necessarily mirror changes in the autonomic nervous system associated with relaxation, they are frequently used to measure psychological relaxation, so this systematic review will consider and report on them as well.

In summary, this systematic review aims to answer the following questions:

1. Are HRV parameters reflective of PNS activity increased when participants are exposed to virtual relaxation environments? Are these changes dependent on (i) the possibility to interact with the environment, or (ii) on inclusion of biofeedback components in the virtual environment?
2. Is the effect of virtual relaxation interventions on HRV dependent on different applications of virtual presentation (e.g., head-mounted displays, computer screens)?
3. Do virtual environments successfully increase self-reported relaxation?

2.3 Methods

2.3.1 Protocol and search strategy

This systematic review was conducted following the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA; Moher et al., 2009). A protocol was written following the *PRISMA-P* guidelines (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols; Moher et al., 2015) and registered at the International Prospective Register of Systematic Reviews PROSPERO on 10.11.2021 and updated on 28.01.2022 (ID CRD42021290162; https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=290162).

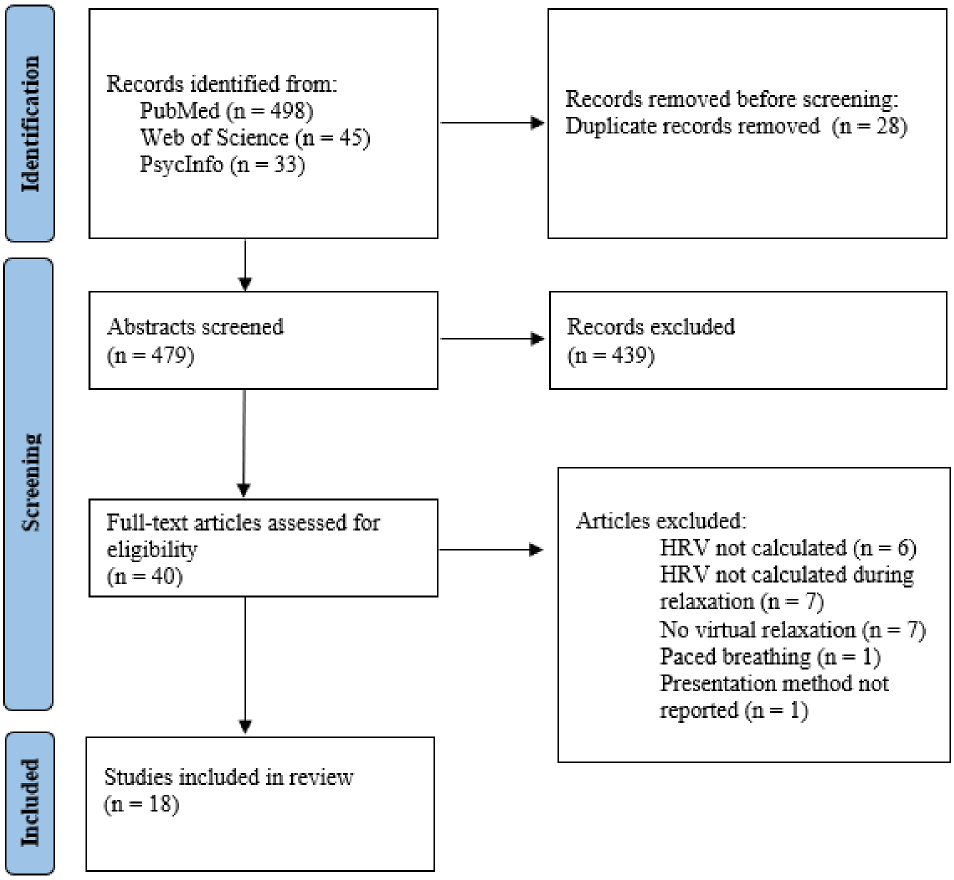
The online databases PubMed, Web of Science, and PsycInfo were searched for the last time on 28.01.2022. The following search terms were used for all three databases: (vr OR virtual reality OR virtual OR screen OR cave OR 360° OR video OR picture) AND (hrv OR heart rate variability) AND relaxation. No study design or language limits were imposed on the search. Results of the search were uploaded to the online tool for systematic reviews CADIMA (version 2.2.1; https://www.cadima.info/; Kohl et al., 2018). Using CADIMA duplicates were removed. Subsequently, title and abstract were screened for eligibility according to the predefined criteria, followed by a full-text screening (see Figure 4 for an overview of the procedure).

2.3.2 Inclusion and exclusion criteria

Articles were included in this review if they (i) reported original data, (ii) included human participants, (iii) used virtual interventions to promote relaxation, and (iv) measured at least one HRV marker in response to the relaxation intervention. All presentation methods for virtual environments (e.g., screen, HMD) were included. Articles in German or English were included. Studies using the virtual environment to promote a paced breathing intervention were excluded. Studies not giving information about the presentation method or the changes in HRV in response to the virtual relaxation intervention were excluded without contacting the authors beforehand.

Data were screened for the characteristics of the sample (number, age, sex) and details about the virtual intervention. This included presentation method, type of virtual environment (e.g., nature pictures, games), possibility to interact with the virtual environment (e.g., by using controllers), or biofeedback adaptions. The main outcome of interest was the changes in all HRV measures in response to the relaxation intervention. If no information about interaction with the virtual environment was provided, we assumed that neither biofeedback nor another kind of interaction was incorporated. As an additional outcome, the influences of virtual relaxation interventions on subjective self-report measurements (e.g., PANAS) are presented if such measurements were assessed in the included studies. 18 studies met the inclusion criteria (see Figure 4).

Figure 4. Flow diagram for the study selection process. Adapted after Page and colleagues (2021).



2.3.3 Quality assessment

To assess the risk of bias in individual studies the Cochrane risk of bias tool for randomized trials (sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting) was used (Chapter 8 in the Cochrane Handbook for Systematic Reviews of Interventions; Higgins et al., 2019). For each of the subscales, the risk of bias for each study is rated as low, unclear, or high. The assessment was done independently by two researchers (RJG and KEK) at study level. Afterward, the researchers came together to reach a consensus regarding the rating. In case of no success in reaching a consensus, a third researcher (JCP) would have been consulted.

2.3.4 Summary strategy

Data from the included studies were summarized. Effects of the virtual relaxation interventions on HRV were summarized, separately for each of the three subgroups: with interaction, with biofeedback, and without interaction. A special focus was put on whether changes in HRV can be interpreted as an increase in physiological relaxation. Effects on subjective self-report measurements were summarized within the subgroups.

In the systematic review protocol, it was stated that meta-biases will be addressed with a funnel plot, and the Grading of Recommendations Assessment Development and Evaluation (GRADE) will be used to assess the confidence in the found evidence. Since there is a huge heterogeneity between the included studies concerning outcome HRV measurements and interventions, we chose to omit these analyses. This paper thus presents a systematic review without additional meta-analyses.

2.4 Results

2.4.1 Included studies

A list of the included studies with authors and journal, sample description, presentation method, interaction possibility, details about the virtual relaxation intervention, HRV measurements, HRV results, and results of self-reported questionnaires are shown in Table 2. First, the studies that gave no possibility to interact with the virtual environment are included in the table, followed by those with interaction possibilities and those with biofeedback.

Table 2. Table of included studies.

Citation and Journal	Sample (N, age *M±SD*)	Presentation method	Interaction	Virtual relaxation intervention	HRV measurements	HRV results [a]	Self-report results [a]
Studies without interaction possibilities							
(Matsui et al., 2016) Journal of medical engineering & technology	MDD: 13 (7f), 41 ± 12; healthy: 28 (13f), 40 ± 12	Screen	No	10min; nature pictures (waterside) with relaxing sounds	LF, HF	HF: decrease after relaxation in MDD patients, increase after relaxation in healthy controls	n.a.
(Byun et al., 2019) Technology and Health Care	MDD: 33 (24f), 40.18 ± 16.10; healthy: 33 (24f), 40.21 ± 15.16	Screen	No	5min; nature pictures (stress before)	ApEN, SampEN, FuzzEN, ShanEN, RRI	No group effect: increase in RRI, FuzzEN, and ShanEN	n.a.

Citation and Journal	Sample (N, age *M*±*SD*)	Presentation method	Interaction	Virtual relaxation intervention	HRV measurements	HRV results [a]	Self-report results [a]
(Igarashi et al., 2014) Cognitive processing	19 (0f), 22.2 ± 0.6	Screen (dome)	No	90sec; a picture of water lily, 2D and 3D, within design	LF, ln(HF), ln(LF/HF)	ln(LF/HF) higher while viewing the 3D picture	n.a.
(Gaggioli et al., 2020) Annual Review of Cybertherapy and Telemedicine	47 (31f), 26.0 ± 7.9	HMD	No	Computer-generated garden with relaxation narrative and music or resting control (stress before)	RMSSD	RMSSD: increase in both groups	STAI: stronger reduction of anxiety after VR garden compared to control
(Liszio et al., 2018) Annual Review of Cybertherapy and Telemedicine	62 (36f), 22.6 ± 5.36	HMD and screen	No	9min; a computer-generated underwater world with sound, HMD, or screen or waiting (stress before)	SDSD	SDSD: increase in VR group, decrease in screen and waiting group	STAI: strongest decrease of anxiety in VR group; PANAS: increase in positive affect in VR group, a decrease of negative affect in VR and screen group; IPQ: highest scores in VR group
(Anderson et al., 2017) Aerospace medicine and human performance	18 (9f), 32 ± 12	HMD	No	15min; 360° videos, rural Ireland with sound, Australian beaches with sound and music and heat lamp, control indoor classroom (stress before), within design	LF, HF, LF/HF	*Beach*: HF higher during VR compared to stress and baseline, LF/HF lower during VR compared to stress and baseline; *Ireland*: LF lower at the beginning than during stress, HF higher during VR compared to stress; *Control*: LF lower during stress than at beginning of	MRJPQ: lower scores for control room

Citation and Journal	Sample (N, age *M±SD*)	Presentation method	Interaction	Virtual relaxation intervention	HRV measurements	HRV results [a]	Self-report results [a]
						VR, HF higher during VR compared to stress, LF/HF decreased during VR and lower compared to baseline	
(Tonacci et al., 2020) Processes	24 (19f), 27.4 ± 5.5	Screen	No	3min30sec; video about yoga with sound and color of chakra, then same video only sound or only video	SDNN, pNN50, LF, HF, LF/HF	SDNN decreased during only video compared to rest	Only video: reduction of anxiety in STAI and VAS; only audio: reduction of anxiety in VAS
(Huang et al., 2016) Research in gerontological nursing	30 (15f), 63.87 ± 7.56, with depressive symptoms	Screen	No	30min; sedative or stimulative music videos (Taiwanese folk songs), within design	LF/HF	LF/HF shows a treatment effect in both groups (decrease)	Reduction of depressive symptoms after both video conditions (GDS)
(Tsutsumi et al., 2017) Japan Journal of Nursing Science	12 (0f), 22.2 ± 1.7	Screen	No	15min; video of sea and forest, 15min full video then 15min only sound (eyes closed), within design	LF, ln(HF)	HF: average higher during sea than forest, higher for sea preference group in general, increase in forest preference group strongest	POMS: mood improvement (confusion, vigor) after both videos for the sea preference group
(Santarcangelo et al., 2012) International journal of psychophysiology	46 (25f), 19 – 30 years	Screen	No	30min; relaxation video (landscapes with music) or threatening (shining), within design	VLF, LF, HF, LF/HF	HF higher and LF/HF lower in females compared to males; during nature video: VLF and LF/HF decrease and HF increases	Increase in reported relaxation after nature video

Citation and Journal	Sample (N, age *M*±*SD*)	Presentation method	Interaction	Virtual relaxation intervention	HRV measurements	HRV results [a]	Self-report results [a]
			Studies with interaction possibilities				
(Liszio & Masuch, 2019) Annual Review of Cybertherapy and Telemedicine	57 (41f), 23.7 ± 5.67	HMD	Yes	9min; interactive VR (mini-games) and non-interactive VR (same environment) and control	SDSD	SDSD: increase during interactive VR, decrease during non-interactive VR	STAI: lower anxiety during interactive VR compared to control; IPQ: a higher feeling of presence in interactive VR compared to non-interactive VR)
(Russoniello et al., 2009a) Annual Review of Cybertherapy and Telemedicine; (Russoniello et al., 2009b) Journal of CyberTherapy & Rehabilitation [b]	134 (57f), mean age 24	Screen	Yes	20min; participants choose one mini-game or control (internet search), bejeweld2 (matching sequence, n=38), peggle (pinball game, n=36), bookworm (crossword, n=29)	VLF, LF, HF, LF/HF	Increase in relaxation in all markers after all games, compared to control bejeweld2 players show a decrease in VLF and increase in LF and LF/HF	POMS: decrease in tension, depression, fatigue, confusion, and anger after all games compared to control, increase in vigor after all conditions (bejeweld2 higher than control)
			Studies with biofeedback				
(Rockstroh et al., 2019) International Journal of Human-Computer Studies	69 (41f), 22.9 ± 4.0	HMD	BF	10min; 2D-BF with abstract graphical indicators or VR-BF with changes in the environment (e.g., clouds); no treatment control	RMSSD, SDNN, LF/HF	RMSSD: increased during the intervention in all groups; SDNN and LF/HF: during intervention both BF groups were higher than control	MDBF: more positive mood after intervention and both BF groups compared to control; motivation (VAS): highest for VR-BF; attention (VAS): highest in VR-BF group

Citation and Journal	Sample (N, age *M±SD*)	Presentation method	Interaction	Virtual relaxation intervention	HRV measurements	HRV results [a]	Self-report results [a]
(Kim et al., 2021) Frontiers in psychiatry; (Kim & Jeon, 2021) 15th International Conference on Ubiquitous Information Management and Communication (IMCOM) [b]	83 (43f), 38.53 ± 11.8 years	HMD	BF	10min30sec; virtual nature with soundtrack, with (VR) and without (BF) BF (stress before), within design	RMSSD, SDNN, pNN50, NN50; VLF, LF, HF, LF/HF	VLF: decrease in BF; LF and HF: increase in VR; NN50 and pNN50: decrease in VR and BF; SDNN and RMSSD: increase in BF	STAI and pain (NRS): lower after BF and VR
(Parnandi & Gutierrez-Osuna, 2015) IEEE Journal of biomedical and health informatics	25 (10f), 19 – 33 years	Screen (smart phone)	BF	8min; game (bubble shoot) with BF (games gets easier when more relaxed), BR or RMSSD or EDA for BF or no BF (stress before)	RMSSD	RMSSD increased during the game with BR-BF, decreased during the game with no BF	n.a.
(Parnandi & Gutierrez-Osuna, 2017) IEEE Transactions on Affective Computing	14 (9f), 19 – 31 years	Screen (smart phone)	BF	30min; game (bubble shoot) with BR-BF, BF as numerical representations or game changes or both or none (stress before)	SDNN, pNN50; LF, HF, LF/HF	n.s.	n.a.

Abbreviations: f = female, HMD = head mounted display, BF = biofeedback, MDBF = Mehrdimensionaler Befindlichkeitsfragebogen („*German Multidimensional Mood Questionnaire*"), VAS

= visual analogue scale, RMSSD = root mean square of successive differences, SDNN = standard deviation of all normal-to-normal intervals, LF = low frequency heart rate variability, HF = high frequency heart rate variability, VLF = very low frequency heart rate variability, pNN50 = proportion of successive RR intervals that are larger than 50ms, ApEN = Approximate entropy, FuzzEn = Fuzzy Entropy, ShanEn = Shannon entropy, NN50 = successive RR intervals differing by more than 50 ms, STAI = State trait anxiety scale, NRS = numeric rating scale, VR = virtual reality, MDD = major depression disorder, RRI = time interval between consecutive R-peaks, SampEN = Sample entropy, SDSD = standard deviation of successive differences, PANAS = Positive And Negative Affect Schedule, IPQ = Igroup Presence Questionnaire, MRJPQ = Modified Reality Judgment and Presence Questionnaire, BR = breathing rate, EDA = electrodermal activity, POMS = Profile of Mood States, ln() = natural logarithm, GDS = Geriatric Depression Scale, n.a. = not assessed.
[a] Only significant results will be presented in this table.
[b] Article and conference paper on the same sample, will be considered at as one study for this systematic review.

2.4.2 Risk of bias rating

The risk of bias was rated on study level independently by two researchers (RJG and KEK), using the Cochrane risk of bias tool (Chapter 8, Higgins et al., 2019). Following this tool, the criteria sequence generation, allocation concealment, blinding, incomplete data, and selective outcome reporting were used. Sequence generation describes the randomization of allocation sequence to avoid selection bias (e.g., assigning the participants to different intervention groups on the basis of a coin toss). Allocation concealment does not refer to the way the allocation is generated but if it was adequately concealed from participants and experimenters. If participants are aware of their allocation, they also are aware of the different parts of the experiment, and knowing what will happen next might influence their behavior in preceding parts of the experiment (e.g., knowing that a stressor is next could increase tension beforehand). Not only participants but also personnel should be blinded concerning outcome measures and interventions. Incomplete outcome data should be addressed, for example, reasons for participants dropping out. Selective reporting is given if, for example, only significant effects are reported even though additional measurements were assessed. For each criterion, the risk of bias was rated as high, low, or in case of insufficient information, as unclear (see Figure 5). The ratings for a high risk of bias stemmed from inadequate allocation concealment (e.g., participants knew that a stress test would be part of the experiment when they underwent the relaxation intervention) or unexplained dropout (e.g., why and how many participants of each group were not part of the final analyses). Since no study had more than one high risk of bias rating, we chose to include all in the data synthesis.

Figure 5. Risk of bias rating for individual studies. Created using robvis (McGuinness & Higgins, 2021; https://mcguinlu.shinyapps.io/robvis/).

2.4.3 Effects on HRV of interventions without interaction possibilities

Of the 18 included studies the majority of ten studies did not offer any kind of interaction possibilities for the participants Of those eight studies used nature pictures or videos (e.g., water lily, beach, forest, underwater; Anderson et al., 2017; Byun et al., 2019; Gaggioli et al., 2020; Igarashi et al., 2014; Liszio et al., 2018; Matsui et al., 2016; Santarcangelo et al., 2012; Tsutsumi et al., 2017), one study used music videos (Huang et al., 2016) and one study used a video about yoga and chakras (Tonacci et al., 2020). All ten studies found an effect of their respective virtual relaxation intervention on the measured HRV indices, indicating an increase in relaxation (e.g., an increase in HF or RMSSD). However, this seemed to be an unspecific effect on relaxation after a stressor in some studies. Gaggioli and colleagues (2020) found an increase in RMSSD after a stressor in the treatment group, viewing a computer-generated garden with a relaxation narrative and music, as well as in the control group, who relaxed in a chair without a virtual intervention. Anderson and colleagues (2017) found increased physiological relaxation (increase in HF) after a stressor when participants watched two sets of virtual nature environments (rural Ireland and Australian beach) and while watching the control environment, an indoor classroom. This hints at a general, unspecific relaxation effect of virtual environments. Other studies showed an increase in relaxation in response to watching a 30-minute nature video (increase in HF; Santarcangelo et al., 2012) or watching music videos for 30 minutes (decrease in LF/HF; Huang et al., 2016) without a preceding stressor.

Individual differences seem to influence the response to virtual relaxation interventions. Tsutsumi and colleagues (2017) found the preference for either forest or the sea to change their participants' response to a 15-minute-long video of those landscapes. While watching the forest video the sea preference group had higher HF values at baseline and during the video, but the increase in HF while watching the video was stronger in the forest preference group, even though the total HF values remained below those of the sea preference group during the whole video.

Furthermore, psychopathology also seems to play a role. In general, mental illnesses are associated with lower baseline HRV values (Acharya et al., 2006; Shaffer & Ginsberg, 2017). However, the lower baseline does not necessarily affect the magnitude of the response, yet results are inconclusive at this point. Matsui and colleagues (2016) found a decrease in HF in patients with major depressive disorder after watching nature pictures for 10 minutes but an increase in HF in healthy participants. In contrast, Byun and colleagues (2019) found no group differences between patients with a major depressive disorder and healthy participants in response to viewing nature pictures for five minutes after a stressor (ApEN, SampEN, FuzzEN, ShanEN, RRI). Methodological differences between those two studies make it difficult to compare their results (different HRV indices, different lengths of exposure to nature pictures, with and without preceding stressor). Accordingly, more research is needed to better understand the effects of psychopathology on the relaxation response.

2.4.4 Effects on HRV of interventions with interaction possibilities

Two studies gave their participants the possibility to interact with the virtual world without using biofeedback. Again, both studies found an effect on HRV indices in response to their respective interventions.

Russoniello et al., (2009a) and Russoniello et al (2009b) are two records referring to the same study whereas Russoniello and colleagues (2009a) report only partial results. In the context of this review, we will look at them together. The study compared 20 minutes of playing a mini-game (matching sequence, pinball game, or crossword) with an internet search activity (searching for articles about health and saving them in a folder). Participants in the game condition could choose one of three mini-games to play. They found a decrease in VLF and an increase in LF and LF/HF when playing the matching sequence game compared to an internet search. They interpreted those results as a stronger decrease of physical stress in response to the video game. However, those results cannot be interpreted as an increase in relaxation as defined by an increase in parasympathetic activity. LF is influenced by both SNS and PNS, thus an increase in LF might represent an increase in SNS activity.

Liszio and Masuch (2019) compared being exposed to nine minutes of a virtual beach, presented via HMD, with (interactive group) or without (non-interactive group) integrated mini-games (e.g., throwing coconuts into a box) with nine minutes of a waiting control condition. They found an increase in SDSD activity in the interactive group and a decrease in SDSD in the non-interactive group. This shows, that interacting actively with the virtual reality environment can enable physiological relaxation, in comparison to non-interactive alternatives, hinting at an influence of interaction possibilities on the effects a virtual relaxation intervention has on HRV.

2.4.5 Effects on HRV of interventions with biofeedback

Four studies used biofeedback in their virtual relaxation intervention. One study using smartphone screens as presentation method (Parnandi & Gutierrez-Osuna, 2017) failed to find significant effects of their intervention (mini-game on smartphone screen "Frozen Bubble" with breath rate biofeedback) on any of the assessed HRV indices (SDNN, pNN50, LF, HF, LF/HF). In contrast, the other study using a smartphone mini-game to transport biofeedback did observe effects on HRV parameters (Parnandi & Gutierrez-Osuna, 2015). Their participants played a bubble shoot mini-game ("Frozen

Bubble”, shooting colored bubbles into a line of colored bubbles, bubbles disappear when enough of the same color are next to each other) for eight minutes, either with or without biofeedback. Three physiological measures were used for the biofeedback: breathing rate, HRV (RMSSD), or electrodermal activity. When an increase in relaxation was detected (e.g., increase in RMSSD or slower breathing rate) the game got easier for the participants. RMSSD increased during the game in the breathing rate biofeedback group and decreased in the group without biofeedback. This indicates, that using breathing rate as a biofeedback marker might be more successful than other physiological markers, since breathing rate can be more easily controlled by participants than, for example, electrodermal activity. The decrease of RMSSD during the mini-game without biofeedback indicates, that a game alone might not lead to an increase in PNS activity and corresponds with the results by Russoniello and colleagues (2009a, 2009b).

Kim and colleagues (2018) and Kim and Jeon (2021) provided two publications based on the same experiment and sample, therefore we will consider them as one in the context of this systematic review. They used virtual nature with and without biofeedback after a stressor. In response to the biofeedback version, there was a decrease in VLF, nn50, and pNN50 and an increase in SDNN and RMSSD. In response to the no-biofeedback version, they found a decrease in NN50 and pNN50 and an increase in LF and HF. These results are puzzling, however, since RMSSD and pNN50 are usually positively correlated (Shaffer & Ginsberg, 2017). If anything, this emphasizes that there are different factors influencing the various HRV indices to different degrees, and even though some of the indices correlate with each other, they may still show significant interindividual variation. Nevertheless, the changes in HRV in response to both virtual environments can be interpreted as an, at least partly, increase in physical relaxation (as seen by the increase in RMSSD in response to the biofeedback version, and the increase in HF in response to the non-biofeedback version).

Rockstroh and colleagues (2019) used a 10-minute-long biofeedback session, either visualized by abstract graphical indicators (a circle changing colors) or by changes in the virtual environment (e.g., the density of clouds on the beach) compared to a waiting control group. RMSSD increased in all three groups, while SDNN and LF/HF only increased in the two biofeedback groups. This suggests that biofeedback influences HRV in general, regardless of how it is presented.

2.4.6 Influences of presentation method on intervention`s effects on HRV

Of the studies without interaction possibilities, eight used a computer or smartphone screen (Byun et al., 2019; Huang et al., 2016; Igarashi et al., 2014; Liszio et al., 2018; Matsui et al., 2016; Santarcangelo et al., 2012; Tonacci et al., 2020; Tsutsumi et al., 2017) and three used an HMD (Anderson et al., 2017; Gaggioli et al., 2020; Liszio et al., 2018) as the method of presentation. Looking at interventions with interaction possibilities, one study used computer games (matching sequence, pinball game, or crossword) played on a screen (Russoniello et al., 2009a, 2009b) and one study used an HMD with and without the possibility to interact with the environment (Liszio & Masuch, 2019). Of the studies with biofeedback interventions two used HMDs (Kim & Jeon, 2021; Kim et al., 2018; Rockstroh et al., 2019), and two used smartphone screens (Parnandi & Gutierrez-Osuna, 2015, 2017). In summary, the majority of 11 studies used screens (computer or smartphone) while six studies used an HMD. A possible explanation for the apparent preference for the usage of screens could be the lower costs and the advantage of more experience in using them compared to HMDs.

While different applications of virtual presentation were used in the included studies only Liszio and colleagues (2018) compared the effects of a virtual relaxation intervention using a computer screen or an HMD directly. Participants viewed a computer-generated underwater world for 9 minutes after a stressor. The control group waited for nine minutes in a chair. Relaxation increased only in the HMD group (increase in SDSD), while it decreased in the screen and waiting control groups. This finding indicates that a more realistic method of presentation (e.g., HMD is more realistic than PC screens, since the virtual environment is the only thing visible) is important for a successful increase in relaxation. Additionally, the only included study not finding a significant effect on HRV indices (SDNN, pNN50, LF, HF, LF/HF) used a smartphone screen (Parnandi & Gutierrez-Osuna, 2017) to present their intervention (mini-game on smartphone screen “Frozen Bubble” with breath rate biofeedback). Being the smallest screen used this could indicate that smartphone screens are allowing too many impressions besides the intervention to distract participants, highlighting the advantage of other applications like HMDs.

2.4.7 Effects on self-report measures of interventions without interaction possibility

Considering subjective ratings of the interventions without interaction possibilities, two assessed self-reported anxiety with the STAI (Gaggioli et al., 2020; Liszio et al., 2018) and one via a virtual analog scale (Tonacci et al., 2020), two assessed affect (PANAS; Liszio et al., 2018) or mood (*Profile of Mood States*, POMS; McNair et al., 1981 in Tsutsumi et al., 2017), two assessed presence in the virtual environment (*Igroup Presence Questionnaire*, IPQ; Schubert et al., 1999 in Liszio et al., 2018) or *Modified Reality Judgment and Presence Questionnaire*, MRJPQ; Witmer & Singer, 1998 in Anderson et al., 2017) and one each assessed depressive symptoms (*Geriatric Depression Scale*, GDS; Lee et al., 1993 in Huang et al., 2016) and self-reported relaxation (Santarcangelo et al., 2012). Three studies didn't assess any kind of self-reported measurement (Byun et al., 2019; Igarashi et al., 2014; Matsui et al., 2016). The subjective changes in self-report measurements were sometimes not associated with changes in HRV. For example, while RMSSD showed an increase in the virtual relaxation intervention group as well as the waiting control group, anxiety scores (STAI) were more strongly reduced in the intervention group (Gaggioli et al., 2020). Still, most studies showed changes in self-report measurements to be in line with changes in HRV. Watching the underwater world via the HMD increased SDSD, decreased anxiety (STAI) and negative affect, and increased positive affect (PANAS) (Liszio et al., 2018) Reported relaxation increased alongside HF after watching a video showing landscapes (Santarcangelo et al., 2012).

2.4.8 Effects on self-report measures of interventions with interaction possibility

Both studies reporting interventions with interaction possibilities (Liszio & Masuch, 2019; Russoniello et al., 2009a, 2009b) assessed additional self-reported measurements. Comparing the interactive version of the virtual beach with the waiting control group, lower anxiety scores (STAI) were found in the interactive group (Liszio & Masuch, 2019). This is consistent with the assessed increase in SDSD. Additionally, subjects in the interactive version group reported higher levels of presence (IPQ) than the non-interactive version. This is the second study included in this systematic review, although from the same group of authors, that found higher IPQ scores associated with an increase in physiological relaxation (increase in SDSD in both studies; (Liszio et al., 2018; Liszio & Masuch, 2019). The experiment using mini-games played on a screen (Russoniello et al., 2009a, 2009b), found positive changes in the POMS (e.g., decrease in tension and depression, increase in vigor) after all mini-games. Even though participants did not play complicated games, an increase in vigor was observed, which could be associated with the increase in SNS activity as measured by changes in HRV indices.

2.4.9 Effects on self-report measures of interventions with biofeedback

Both studies including biofeedback in a smartphone mini-game did not assess any additional self-reported questionnaires (Parnandi & Gutierrez-Osuna, 2015, 2017). Kim and colleagues (Kim & Jeon, 2021; Kim et al., 2018) found a decrease in both, anxiety (STAI) and pain (number rating scale) after their virtual intervention with and without biofeedback. Rockstroh and colleagues (2019) found an increase in positive mood assessed via the *German Multidimensional Mood Questionnaire* (MDBF, (Steyer et al., 1997) after both biofeedback versions. However, they found higher scores for motivation and attention (both visual analog scales) when biofeedback was presented as changes in the virtual environment compared to abstract graphical indicators. Even though both biofeedback versions were similar in their effect on HRV, this difference in motivation and attention can be of importance when considering using biofeedback as a treatment, since motivated patients are more likely to complete treatment.

2.5 Discussion

2.5.1 Summary of findings

The aim of this systematic review was to investigate the relaxing effects of virtual interventions using HRV as marker for PNS activity. 18 studies were included in this review. Overall, the studies found a positive effect of virtual relaxation interventions on HRV as shown by various HRV markers, indicating an increase in relaxation (specifically, an increase in HF, pNN50, and RMSSD), in all three subgroups (with and without interaction and with biofeedback). The only study not reporting an effect on HRV markers used a biofeedback mini-game presented on a smartphone screen. The only study to directly compare different interaction possibilities found a stronger increase in parasympathetic activity (increase in SDSD) in response to a virtual environment when interaction was possible compared to the same environment without. This difference can potentially be explained by the notion that interaction with virtual environments is more effortlessly capturing the attention of participants and therefore more easily enables relaxation. In contrast, without the option to interact, participants need to focus on one environment for nine minutes, which might require more voluntary attention to stop ruminating, therefore limiting the relaxing effects. On the other hand, interaction was shown to not always be superior to simply watching a virtual environment. Too complex interaction possibilities, like difficult mini-games, could thus have an arousing effect as well, demanding attention or even inducing tension.

The studies included in this review used either HMDs or screens to present the virtual environments. Of the 18 included studies the majority used a screen (computer or smartphone), probably because screens are less costly and used more frequently in daily life than HMDs. While there were significant effects of screen-based interventions on HRV, one study compared a screen directly with an HMD. This study found a significantly greater increase in parasympathetic activity (as indicated by an increase in SDSD) in response to the HMD based video, compared to the screen version. This was also associated with a greater sense of presence evoked by the HMD, indicating that being present in a virtual environment increases the positive effects the environment has on relaxation. HMDs are not as expensive or difficult to operate as they used to be when the technology first came out, thus making them a feasible relaxation intervention for many study groups nowadays.

Most studies included some form of self-report measurement, like PANAS or STAI. For most studies, results suggest that self-report measures changed in line with HRV measurements, for example, an increase in parasympathetic activity (HF) was associated with a decrease in reported anxiety (STAI). However, this relationship was not always seen, for example, one study (Parnandi & Gutierrez-Osuna, 2017) showed an increase in self-reported relaxation but no significant changes in HRV. This indicates, that there might be some differences between physiological and psychological relaxation, perhaps depending on the study design, or the population sample. This “dissociation” of subjective and objective measures has also been reported in stress research (Campbell & Ehlert, 2012; Dickerson & Kemeny, 2004) and thus seems to be generalizable across different psychophysiological states. It seems therefore good advice to always assess both when implementing a relaxation intervention.

Considering the different questionnaires used, the majority of studies did not assess relaxation directly (e.g., via a visual analog scale) but used other questionnaires, for example, asking subjects about anxiety or mood changes. Accordingly, a decrease in anxiety and negative affect and an increase in positive affect were interpreted as an increase in relaxation. Even though relaxation is associated with those changes in affect, it is unclear if they assess relaxation adequately and completely, since relaxation is likely more than a decrease in anxiety.

The virtual interventions implemented in the studies selected for this review used mostly nature stimuli (pictures, videos) to induce relaxation. Since all studies using nature stimuli reported a successful increase in parasympathetic activity, a successful transfer of the relaxing effects of real-life nature (for example, Kobayashi et al., 2018; Payne & Delphinus, 2019; Song et al., 2018) to virtual adaptions of nature appears likely.

Even though all except one of the included studies found an increase in physiological relaxation it is important to differentiate between studies using a stressor preceding the virtual relaxation intervention and studies without a stressor. Seven studies employed a stressor before the relaxation intervention (Anderson et al., 2017; Byun et al., 2019; Gaggioli et al., 2020; Kim et al., 2021; Kim & Jeon, 2021; Liszio et al., 2018; Parnandi & Gutierrez-Osuna, 2015, 2017), therefore it is possible that the measured increase in relaxation is influenced by the rebound effect after a stressor in addition to the relaxing effects of the according interventions. The rebound effect after a stressor describes an increase in HRV in a recovery phase above the baseline level, especially in the first minute after the stressor (Mezzacappa et al., 2001). Adding a stressor makes it impossible to differentiate those two effects and therefore to assess the success of an intervention. Even though more research is needed to differentiate an increase in relaxation due to a rebound effect from an effect of an intervention, first results suggest that virtual environments exceed the rebound effect and lead to a faster recovery after a stressor. After a virtual Trier Social Stress Test participants recovered either in a virtual forest with sound, in a virtual forest without sound, or in a room without a virtual environment. HRV (HF) significantly increased only in the group sitting in a virtual forest with sounds during recovery period, while there were no significant changes in HRV in the other two groups (Annerstedt et al., 2013). This hints at an effect of virtual environments beyond a rebound effect after a stressor. Still, the differences between an increased recovery after a stressor and an increase in relaxation due to an intervention starting from baseline need to be differentiated and studied further. It is possible that relaxation interventions as used in the included studies positively affect the recovery after a stressor and therefore lead to a significant increase in relaxation compared to the stressor and a recovery group without intervention. It is also possible that the same interventions show no effect when used without a stressor because of ceiling effects (Guyon et al., 2020) and the missing influence of a rebound effect after a stressor. However, future studies are needed to shed more light on this matter.

2.5.2 Strengths and limitations of included studies

All studies together assessed a total of n=816 (n=414 (50.74%) female) participants. Seven studies did not meet the criteria of at least 20 participants per cell, 11 did not use a within-subjects design and only three assessed an appropriate baseline, which are all methodological recommendations for the assessment of HRV as recommended by Quintana and Heathers (2014). Within-subjects experiments do however risk carry-over effects and fatigue. To minimize these risks, some studies assessed the different conditions on separate days, leading to greater expense for both, experimenter and participants, and increased the risk for dropout due to participants' attrition across study appointments. Despite the difficulties associated with within-subject designs, they have multiple advantages. Fewer participants are needed in total to meet the 20 participants per cell criterion, potentially facilitating recruitment. Since every subject is serving as their own control, unsystematic variation is reduced, This is especially an advantage when measuring HRV. HRV is influenced by multiple within-subject factors, for example, disease, age, sex (Acharya et al., 2006), body-mass-index, or menstrual cycle (Vallejo et al., 2005), to name just a few. Choosing an appropriate baseline is an important part of the experimental design since it is needed to allow drawing conclusions about the changes in HRV induced by an intervention. The baseline should be comparable to the intervention (e.g., if the intervention is done with eyes open so should the baseline) and instructions given should be described (Laborde et al., 2017; Quintana et al., 2016; Quintana & Heathers, 2014). Of the included studies only three followed those recommendations (Anderson et al., 2017; Byun et al., 2019; Tonacci et al., 2020), eight assessed a baseline not following these recommendations (e.g., using a questionnaire assessment as a baseline, e.g., Liszio & Masuch, 2019) and five did not assess a baseline at all. Most studies used a sample of young adults (approx. 20

to 30 years), with only one study using older participants (60 to 70 years), and no study assessed children. This limits the generalizability of results, as the very young, middle-aged, and older subjects are so far missing from or underrepresented in this type of investigation.

Across studies, a great diversity of the types of implemented HRV markers could be observed. Only one study used entropy measurements, all others used time and/or frequency domain measurements. This makes it difficult to compare results across the different studies adequately since different measurements are influenced by different factors. When looking at the physiological component of relaxation an increase in parasympathetic activity is expected, therefore studies should focus on the markers that are associated with PNS activity. Most prominently is high-frequency HRV, which is only influenced by the PNS (Berntson et al., 1993b). Since breathing has a huge impact on HF it is useful to assess other markers as well, for example, RMSSD or pNN50. Even though there is a small sympathetic influence in both of those markers they correlate highly with HF, indicating a dominant parasympathetic influence, and are not as strongly affected by breathing as HF (Laborde et al., 2017).

Special care is also needed when interpreting the HRV indices more strongly associated with sympathetic activity or a mix between parasympathetic and sympathetic activity (LF and LF/HF). Often a decrease of those markers and therefore sympathetic activity is interpreted as an increase in relaxation. This leads to the misconception that a decrease in sympathetic activity is always associated with an increase in parasympathetic activity and the other way around. The interactions between the two branches of the autonomic nervous system are complex and not that easy to interpret, since an increase in one can also lead to an increase in the other. They can exert opposing or synergetic effects and can vary in activity reciprocally, independently, or coactively (see *Autonomic Space Model*, Berntson et al., 1993b). Therefore, it is recommended to assess parasympathetic activity, using multiple markers (e.g., HF as frequency domain measurement and RMSSD as time domain measurement), since there are different factors influencing them, and not infer PNS activity from sympathetic activity, as this leads to wrong conclusions. When assessing HRV it is important to follow guidelines for the report of HRV measures (e.g., Quintana et al., 2016) and their interpretation. To enable the comparison of different studies it is strongly recommended that future studies follow those guidelines and report multiple markers strongly influenced by the PNS when physical relaxation is among the outcomes of interest.

An additional difficulty when using HRV as an outcome measurement are the various confounding factors influencing HRV. It is impossible to assess all of them, still, researchers should aim to give a comprehensive sample description including possible influencing factors, for example, age, sex, physical and psychological health (Acharya et al., 2006; Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017), menstrual cycle (Vallejo et al., 2005) but also nicotine and caffeine intake before the experiment (Quintana & Heathers, 2014). Looking at the studies included in this systematic review shows a considerable lack of information about and consideration of possible influencing factors. Some studies reported assessing only healthy participants (e.g., Tonacci et al., 2020), or matching groups in age and sex (e.g., Rockstroh et al., 2019) but most studies did not take any influencing factors into account. This is another factor that complicates the interpretation of results.

2.5.3 Strengths and limitations of this review

A protocol for this systematic review was preregistered to make retracing the review process possible. The risk of bias rating for individual studies was done by two researchers independently, to reduce the possibility of bias.

The main limitation of this systematic review is the heterogeneity between included studies. This heterogeneity most clearly reveals itself when looking at the employed HRV indices, where studies used varying HRV markers as measurement for parasympathetic activity. The heterogeneity can also be seen when looking at the different interventions used to induce relaxation. Most studies used nature pictures, but some studies used mini-games, and therefore differ substantially from each other. The duration of exposure to virtual relaxation environments differed significantly, ranging from 90 seconds to 30 minutes across studies. It is not clear whether a longer exposure will always lead to stronger effects, as boredom and limited attention span will likely mean that there is an upper limit for the PNS stimulating effects. However, we are not aware of studies that have systematically investigated the effects of different time intervals on HRV markers in the context of relaxation. Additionally, the concepts of relaxation itself differed between studies, for example, not all studies defined a decrease in anxiety as an increase in relaxation. Finding a universally valid definition of relaxation is not an easy task. At a minimum, relaxation can be defined as a decrease of arousal on a physiological level (Smith et al., 2007), but this definition fails to include changes on an affective level, which are likely also an integral part of relaxation, to allow differentiating it, for example, from fatigue. Other studies include physiological as well as psychological measurements for relaxation (e.g., Knaust et al., 2022). Even though they do not always correlate (e.g., (Hernandez-Ruiz et al., 2020) both are needed to assess the relaxation on various levels. Since studies rarely define their concept of relaxation explicitly, this is an important point in which the studies differ from one another.

Since all except one study found a significant effect of their respective relaxation interventions on HRV indices this raises the question whether a publication bias played a role here. Since we did not deploy meta-analytic statistics we cannot answer this question based on statistical results. Nevertheless, it seems unlikely that about 94% of all studies investigating the relaxation response using virtual interventions and measuring HRV found a significant effect, especially since HRV values are easily biased by external (e.g., room temperature) or internal (e.g., menstrual cycle) factors and ceiling effects are a known problem when assessing relaxation. It appears more likely that other similar studies not finding a significant effect simply were not published. This is a common problem, especially in psychology (Ferguson & Heene, 2012) adversely affecting the ability to reject theories. Thus, as a note of caution, readers should keep in mind that likely there are unpublished studies without a significant effect of virtual relaxation interventions on HRV. Publishing those in the future would be a considerable contribution in search for a successful standardized relaxation protocol. Nevertheless, we can only base future research on studies that were published, deriving characteristics of a successful relaxation intervention from the results of this systematic review.

2.5.4 Considerations of previous research

To our knowledge, there is no review article describing different relaxation interventions and their effects on mental and physical health dependent on specifics of the intervention. Instead, there are many different articles, focusing for example on a certain type of intervention (as we did with this systematic review) or on a certain type of participants (e.g., patients with depression). Nevertheless, a previous systematic review (Jo et al., 2019) found positive effects on physiological parameters when viewing pictures of nature and additionally suggests an increased positive effect associated with a more realistic presentation of virtual nature environments, aligning with our findings. The article also mentions influences of interindividual differences like personality traits on the relaxation response, alongside considerations of other potentially influencing factors like mental diseases and the need for future research into this question. Since various physiological parameters including HRV were taken into account this hints that an increase in physiological relaxation in response to nature stimuli is not specific to HRV but instead a general physiological relaxation response. The success of virtual interventions to induce mental and physical relaxation was found to vary with the details of the experimental intervention (Diniz Bernardo et al., 2021). Even though the authors did not specify this finding, it highlights the importance of taking a closer look at the details of an intervention. Additionally, this review found that most studies assessed college students, emphasizing the need for studies with more diverse samples. Virtual nature stimuli are not only used in research settings but also in treatments for patients with mental disorders. First results are promising, showing increased mental and physical relaxation and even a greater effect of virtual reality based nature interventions compared to non-virtual interventions (e.g., guided meditation, Riches, et al., 2023a). Similar results were found for healthy participants (Riches et al., 2021). Additionally, a positive effect of 360° nature videos on depressive and anxiety symptoms was found (Ionescu et al., 2021). While these reviews emphasize the success of virtual nature environments as relaxation interventions for healthy participants and clinical samples, they all considered different physiological measures as well as self-report measures without distinguishing between mental and physical relaxation as separate aspects of the relaxation process, as we did in this systematic review. They also did not try to determine how the details of a successful relaxation intervention should look like. This might be due to the wide variety of measurements used in the included study. As in our review, others also described a significant heterogeneity in the characteristics of virtual relaxation intervention as well as little diversity regarding age and ethnicity of the study samples. Heterogeneity in measurements and interventions seems to be a general problem in the field of relaxation interventions, making it excessively difficult for this field of research to generalize findings across different studies and come to firm conclusions. This emphasizes the need for a standardized relaxation protocol, which would allow an in-depth investigation of the mechanisms behind the relaxation response as well as researching possible factors influencing relaxation and options to incorporate relaxation interventions into treatment plans.

2.5.5 Implications for future work

Despite the fundamental differences across the reported studies, all expect one found a significant increase in physiological relaxation as measured by HRV in response to the virtual interventions. These results suggest that virtual relaxation interventions could become an integral part of a standardized relaxation protocol to investigate the specifics of the relaxation response and its contribution to health and disease. Relaxation is a central aspect of a healthy lifestyle and part of many treatments in the context of psychopathology, thus making an in-depth understanding of the relaxation response and its effects crucial. First studies already show the influence of depression (Matsui et al., 2016) and interindividual differences on physiological relaxation (Benz et al., 2022), indicating that more research is needed to explore the various influences on the relaxation response. One aim of this study was to investigate whether virtual interventions could be part of a standardized relaxation protocol and which characteristics should be included in a successful relaxation intervention based on virtual environments. Since the main difficulty of this systematic review was the huge variety in relaxation interventions and measurements we summarized what a successful relaxation intervention should look like based on the findings. The majority of studies we included used virtual nature stimuli and found them to be effective in inducing relaxation, therefore this seems a promising start to developing a standardized relaxation intervention. Apparently, the greatest effects on physiological relaxation were observed in studies that achieved a high feeling of presence induced by the virtual intervention. This can be implemented, for example, by using HMD as presentation method or by adding means to interact with the virtual environment. Concerning the length of the intervention we found no hint of a systematic effect in the included studies, even though the interventions ranged from 90 seconds to 30 minutes. Here, more research is needed to determine what the optimal length for a relaxation intervention is. Of importance for a standardized relaxation protocol are not only the specifics of the intervention but also how relaxation is measured. All protocols interested in studying the parasympathetic branch of the autonomic nervous system should be aware of the different HRV indices and report both time and frequency domain measures. When using HRV as many different influencing factors as feasible should be assessed and reported, as well as adherence to the guidelines for HRV measurements (at least 20 participants per cell, within-subject design, adequate baseline, keep influence of SNS and PNS in mind when interpreting markers). Studies investigating specifically the relaxation response should make sure to include their definition of relaxation, to make comparison across studies easier. To assess the psychological aspects of relaxation in addition to the physiological ones, self-report questionnaires should always be used as well. Future projects should consider these aspects regardless of whether the aim is to develop a new protocol or implement a virtual relaxation method in the context of a clinical intervention.

2.5.6 Conclusion

This systematic review investigated whether virtual relaxation interventions can successfully increase relaxation measured by HRV. Despite significant heterogeneity across studies, results showed, that virtual interventions are promising relaxation interventions, especially when using nature stimuli and increasing the sense of presence. Future studies should aim to implement a standardized relaxation protocol using virtual interventions, to be able to investigate open questions concerning the relaxation response and its impact on health and disease. To accomplish this task a universal definition of relaxation and guidelines for its measurement are crucial to enable comparison and synthesis of different studies. Guidelines for relaxation measurement should include measuring psychological as well as physiological markers. When using HRV the guidelines for its measurement should be followed. If we work on this together, we are sure this will push the field of relaxation research considerably ahead, so that future research can work with a standardized virtual intervention, and insights thus gained can improve not only therapeutic interventions but also everyday life.

3. Does Early Life Adversity affect the relaxation response?

This chapter presents the article “Early Life Adversity Blunts The Subjective And Physiological Relaxation Response In Healthy Adults" submitted to the peer-reviewed Journal *Scientific Reports* on April 17, 2024. The manuscript was under review by the time of thesis submission (submission ID: 472e891e-0037-45d0-96a0-78c157f0dbf6; see supplemented Email confirmation of manuscript submission to *Scientific Reports*). The article investigates the psychophysiological relaxation response in healthy adults induced by paced breathing and a virtual nature relaxation intervention while focusing on the effects of ELA.

Gaertner, R. J., Burkart, M., Richter, L., Schnell, P., Finkhäuser, M., Klink, E.S.C., Denk, B.F., Meier, M., Bentele, U.U., Wienholdt, S., Kossmann, K.E., & Pruessner, J. C. (under review). Early Life Adversity Blunts The Subjective And Physiological Relaxation Response In Healthy Adults. *Scientific Reports.*

Contributions from all authors for this publication were as follows:
RJG: Project administration, Conceptualization, Methodology, Data Curation, Investigation, Formal analysis, Visualization, Writing - Original Draft & Editing. MB, LR, PS, MF: Methodology, Investigation, Writing – Review & Editing. ESCK, MM, BFD, UUB, SW, KEK: Writing - Review & Editing. JCP: Formal analysis, Resources, Writing - Review & Editing, Supervision, Conceptualization, Methodology. All authors approved the final version.

Link to access the preregistration of the study at the Open Science Framework: https://osf.io/jsrze.

3.1 Abstract

While Early Live Adversity (ELA) is a known risk factor for mental and physical diseases, the investigation into the mechanisms behind this connection is ongoing. In the present study, we investigated whether ELA blunts the relaxation response in healthy adults. Using a within-subjects design, we employed a paced breathing exercise (four seconds inhale, six seconds exhale) and a 360° nature video as relaxation interventions while measuring physiological relaxation using heart rate variability and subjective relaxation using the Relaxation State Questionnaire. A total of 103 participants (63.11% female; age_{mean} = 22.73±3.43 years) completed the Parental Bonding Instrument and the Childhood Trauma Questionnaire to assess ELA retrospectively. For subjective relaxation, a blunted relaxation reaction was associated with lower scores of paternal care and higher scores of paternal overprotection, physical abuse, physical neglect, and emotional abuse. For heart rate variability, emotional abuse in interaction with nicotine consumption was related to a blunted relaxation response. This indicates that experiencing ELA negatively affects the relaxation capability in a healthy sample and emphasizes the importance of assessing relaxation at a physiological and subjective level.

Keywords: early life adversity, relaxation, paced breathing, virtual nature, heart rate variability

3.2 Introduction

3.2.1 Effects of early life adversity on health

While there is no universal definition for early life adversity (ELA), the term describes stressful events, such as poverty, abuse, bullying, or absent parents, that endanger a child's mental and physical well-being and often require adaption of behavioral and neurophysiological systems (Berman et al., 2022; Sigrist et al., 2021a). These experiences have been shown to impact not only in childhood but also throughout the lifespan, increasing the risk of developing psychological and physiological disorders (Berman et al., 2022; Smith & Pollak, 2021). However, despite numerous explanatory approaches (Jin et al., 2018; Sigrist et al., 2021a), the underlying mechanisms behind ELA as a risk factor for diseases are unclear. The variety of theories and mechanisms is also reflected in the vast number of ELA questionnaires, with considerable heterogeneity in the way ELA is assessed (Koppold et al., 2023). Most questionnaires assess ELA retrospectively by asking adults about their experiences during their childhood and youth.

3.2.2 Effects of relaxation on health

Relaxation has been linked to increased well-being and health, contributing to a healthy life (Bhasin et al., 2013). There are vast interindividual differences when looking at the effectiveness of relaxation interventions (Jo et al., 2019), indicating that multiple factors influence a person's ability to relax. While this field of research is growing, initial studies report a negative effect of depression (Matsui et al., 2016) and a positive effect of trait mindfulness (Benz et al., 2022) on the relaxation response. Further studies are needed to investigate possible influencing factors using different relaxation methods.

3.2.3 Relaxation interventions

There are many different relaxation interventions, such as massages (Meier et al., 2020), breathing exercises (Szulczewski, 2019), and forest bathing (Farrow & Washburn, 2019). In the current study, we chose a 360° virtual nature video and a breathing exercise because of their easy implementation and the different mechanisms behind these interventions. Nature stimuli have been shown to increase subjective and physical relaxation (Farrow & Washburn, 2019; Payne & Delphinus, 2019), either as real-life stimuli (Song et al., 2018) or as virtual stimuli (Gladwell et al., 2012). The *Psychoevolutionary Theory* (Ulrich, 1983) postulates that humans have an evolutionary advantage linked to their capability to recover quickly in a safe and non-threatening natural environment, linking nature to a positive emotional reaction (Payne & Delphinus, 2019). Complementary, breathing exercises are also effective in inducing subjective relaxation (Szulczewski, 2019), for example, breathing steadily with a slow rhythm (six breaths per minute; Russo et al., 2017). Breathing rhythm and heart activity are closely linked via the vagus nerve. Therefore, a slow breathing rhythm can trigger the physiological relaxation response (Kromenacker et al., 2018).

3.2.4 Measuring relaxation

Relaxation can be measured at both subjective and physiological levels. While definitions of relaxation vary, subjective relaxation commonly includes a calm state of mind, specific affective states (e.g., calmness and joy), and a perceived reduction in mental and physiological arousal (Benson, 1975; Steghaus & Poth, 2021). At the physiological level, reduced arousal is associated with a change in autonomic nervous system (ANS) activity, usually an increase in parasympathetic nervous system (PNS) activity and a simultaneous decrease in sympathetic nervous system (SNS) activity. It should be noted that an increase in PNS activity does not necessarily lead to a decrease in SNS activity (Berntson et al., 1993a). A noninvasive and valid way to measure PNS activity is the assessment of vagally mediated heart rate variability (HRV), describing the beat-to-beat fluctuation of heart rate (Acharya et al., 2006; Quintana & Heathers, 2014). There are many factors affecting HRV (e.g., age, sex, health, and breathing rhythm; Acharya et al., 2006; Shaffer & Ginsberg, 2017) which should be taken into account.

3.2.5 Effects of ELA on the relaxation reaction

While numerous studies have found a distortion of the affective and physiological reaction to stress related to ELA (Engert et al., 2010; Ion et al., 2023; Pruessner et al., 2010), there is a considerable lack of studies focusing on the effect on relaxation. Previous studies have found a decrease in resting state HRV associated with ELA (Jankovic et al., 2021; Sigrist et al., 2021a; Thurston et al., 2020). This implies a distortion of the PNS, which can also influence the relaxation response. Additionally, as HRV generally serves as a marker for adaptability (Acharya et al., 2006; Thayer et al., 2012), a reduced baseline HRV can indicate a blunting in the relaxation response since relaxation can be seen as an adaptation to safe situations. No study has investigated possible changes in relaxation reactivity related to ELA at the time of writing. We conducted the present study as a first step to fill this gap in the literature.

3.2.6 Present study

The present study aimed to investigate a possible distortion of the subjective and physiological relaxation responses in healthy participants linked to ELA using two relaxation interventions. The study was preregistered at the Open Science Framework before data analysis (https://osf.io/jsrze). We defined physiological relaxation as an increase in parasympathetic activity, as measured by HRV. We chose the root mean square of successive differences (RMSSD) as a marker of HRV since it adequately represents the increase in PNS activity associated with relaxation independent of breathing cycle (Quintana & Heathers, 2014). We also assessed high-frequency HRV; however, as it only adequately represents vagal tone within breathing rates of nine to 24 cycles per minute (Zaccaro et al., 2018), we focused on RMSSD. We also assessed subjective relaxation through the *Relaxation State Questionnaire* (RSQ; Steghaus & Poth, 2021) since subjective and physiological markers often diverge (Campbell et al., 2016; Gaertner et al., 2023). From the vast range of available ELA measures (Koppold et al., 2023), we chose to assess two retrospective questionnaires, the German translation of the *Parental Bonding Inventory* (PBI; Benz et al., 2021) and the German translation of the *Childhood Trauma Questionnaire* (CTQ; Wingenfeld et al., 2010).

We hypothesized increased physiological (HRV) and subjective (RSQ) relaxation markers in reaction to both relaxation interventions. We hypothesized that the breathing exercise would solely increase HRV during the intervention. In contrast, we expected the nature video to induce relaxation and continue to have a relaxing effect after the VR intervention. For the influence of ELA, we hypothesize that a blunted relaxation response in both relaxation interventions would be associated with higher scores in both forms of ELA.

3.3 Methods

3.3.1 Participants

We recruited participants at the University of Konstanz between December 2022 and May 2023 for a total of 117 participants. Of those, five were excluded as they only attended one experimental session, two were excluded due to technical difficulties, and seven were excluded as they indicated suffering from a mental disorder. Thus, the final sample consists of 103 participants (see Table 3). Inclusion criteria were as follows: fluency in German, being mentally and physically healthy (especially no diabetes, epilepsy, heart diseases, or cardiac pacemakers), having a body mass index (BMI) between 18.5 and 29.9, and currently not working night shifts. Participants were asked to refrain from consuming caffeine, alcohol, and nicotine for four hours before the experiment and intensive sports 12 hours before the experiment. Those criteria were implemented to minimize confounding effects on HRV (Acharya et al., 2006; Quintana et al., 2016; Quintana & Heathers, 2014; Sammito & Böckelmann, 2016; Shaffer & Ginsberg, 2017) and to minimize the risk for participants since virtual reality glasses can trigger epileptic seizures (Bureau et al., 2004). Participants received 20 € or course credit for their participation. The study procedure was approved by the Ethics Committee of the University of Konstanz and followed the guidelines of the Declaration of Helsinki.

Table 3. Sample characteristics.

	Total Sample N=103 *M* ± *SD*
Sex	
Female	n=65 (63.11%)
Male	n=38 (36.89%)
Age	22.73 ± 3.43
BMI	22.20 ± 2.67
Alcohol consumption	5.55 ± 03.15
Nicotine use	.52 ± 1.91
Depressive Symptoms (BDI)	7.07 ± 5.26
Parental Bonding (PBI)	
Without father figure	n=6
Father overprotection[1]	8.03 ± 6.74
Father care[1]	25.16 ± 6.72
Without mother figure	n=2
Mother overprotection[2]	11.35 ± 8.26
Mother care[2]	28.93 ± 6.56

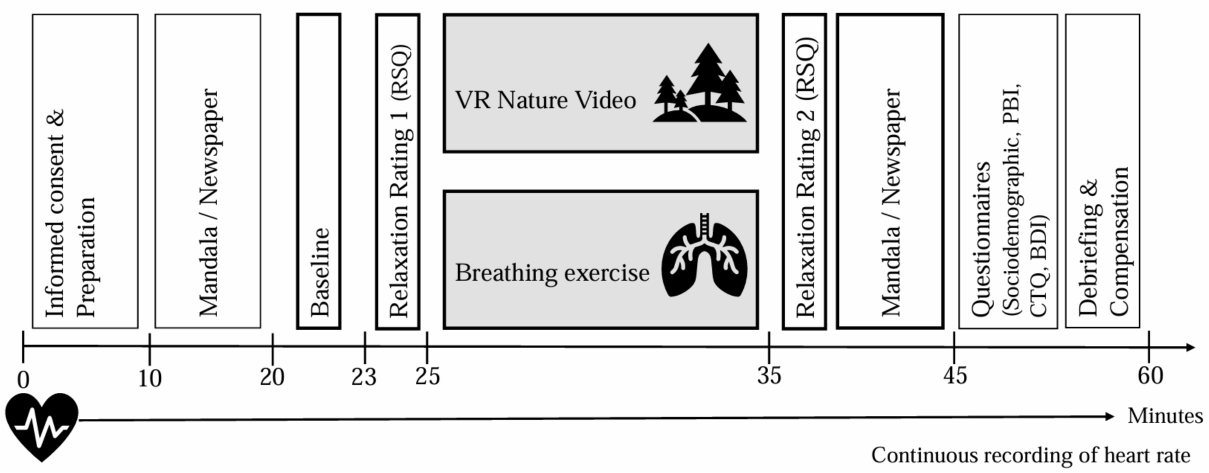
	Total Sample N=103 *M* ± *SD*
Childhood trauma (CTQ)	
Emotional abuse	8.20 ± 3.90
Physical abuse	5.85 ± 2.60
Sexual abuse	5.78 ± 2.53
Emotional neglect	8.57 ± 3.63
Physical neglect	6.60 ± 2.08

Note. Female and male describe the biological sex assigned at birth; BMI = Body Mass Index; Alcohol = glasses of alcoholic beverage consumed per week; Nicotine = cigarettes consumed per day; BDI = Beck Depression Inventory, range: 0-63; PBI overprotection range: 0-39; PBI care range: 0-36; CTQ range per subscale: 5-25.
[1] data collected from n=97 participants.
[2] data collected from n=101 participants.

3.3.2 Study procedure

Both sessions of the within-design took place five to nine days apart to minimize carry-over effects, with the order of experimental conditions randomized. At the first session, participants were informed of the experimental procedure and provided their written informed consent. Subsequently, both sessions followed the same procedure; see Figure 6 for a graphical representation of the study procedure. For the first ten minutes, participants could choose between a newspaper or mandala to let their heart rate reach a resting baseline. During the baseline period, participants viewed a fixation cross for three minutes. After that, participants rated their subjective relaxation using the RSQ. The seven-minute relaxation intervention followed, wherein participants either watched a nature video or completed a paced breathing exercise. Subsequently, they completed the RSQ for the second time. This was followed by a ten-minute interval in which participants were again given the choice between a newspaper and a mandala. Finally, various questionnaires were completed (sociodemographic and ELA questionnaires). With this design, we followed the recommendations for HRV assessment (Quintana & Heathers, 2014).

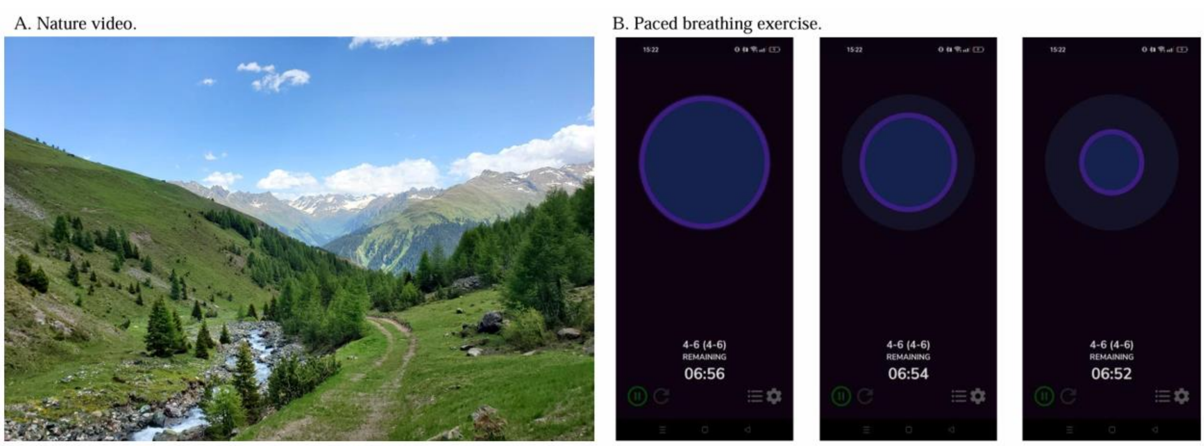
Figure 6. Graphical representation of the within-study design. The bold frames indicate which phases of the experiment were included in the HRV analyses.



3.3.3 Relaxation interventions

Two relaxation interventions were conducted since the mechanisms behind their relaxing effects are postulated to differ. The nature relaxation intervention ("nature") was a 360° video depicting mountains, a flowing river, green meadows, and trees with the associated sounds. The video was recorded in the Swiss Alps near Davos using an Insta360 Pro 2 video camera (Insta360, California, USA). Participants watched the video using virtual reality glasses (Meta Quest 2; Meta Platforms Inc., California, USA), allowing them to experience the view by turning their heads. For the breathing intervention ("breath"), participants followed a pacer, which guided them to breathe six breaths per minute (four seconds inhale, six seconds exhale). The pacer was presented as an increasing and decreasing circle on an iPad using the app "Awesome Breathing: Pacer Timer" (Gollehon & Troia, 2022); see Figure 7.

Figure 7. Depictions of both relaxation interventions.



3.3.4 Measurements

Physiological Relaxation Measurement. To measure relaxation on a physiological level, participants applied the Polar H 10 sensor (Polar Electro GmbH Deutschland, Germany) to their chest, which was connected via Bluetooth to the “HRV Logger” app (Altini, 2022) running on iPads.

Subjective Relaxation Measurement. The RSQ (Steghaus & Poth, 2021) was used to measure subjective relaxation at the current moment directly before and after the intervention. To calculate the total RSQ score, all items are added with higher values, indicating a higher level of relaxation. The RSQ allows to derive changes induced by a short-term relaxation intervention with reliability rated as high (ω = .83; Steghaus & Poth, 2021).

Early Life Adversity. We employed two questionnaires assessing ELA retrospectively. The PBI (original: Parker et al., 1979; German translation: Benz et al., 2021) assesses the parenting style of mother and father. For each parent, the items are cumulated in the subscales “care” and “overprotection”. A low care score and/or a high overprotection score are considered forms of ELA. For the German translation, reliability is considered high (Cronbach‘s α = .86 to .95; Benz et al., 2021). The CTQ (original: Bernstein et al., 2003; German translation: Wingenfeld et al., 2010) assesses five different forms of abuse and neglect: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. For each subscale, the items are added up, with higher values indicating a higher level of abuse or neglect. It is a widely used questionnaire to assess ELA retrospectively (Koppold et al., 2023), with high reliability for the total questionnaire (Cronbach‘s α = .94; Wingenfeld et al., 2010).

Covariates. Various covariates influence HRV (Acharya et al., 2006; Quintana & Heathers, 2014). We chose to assess and include BMI, age, sex, alcohol consumption (glasses of alcoholic beverages per week), nicotine consumption (cigarettes per day), and depressive symptoms measured with *Becks Depression Inventory* (BDI-II; original: Beck et al., 1996; German translation: Pietsch et al., 2012) as covariates.

3.3.5 Data preprocessing

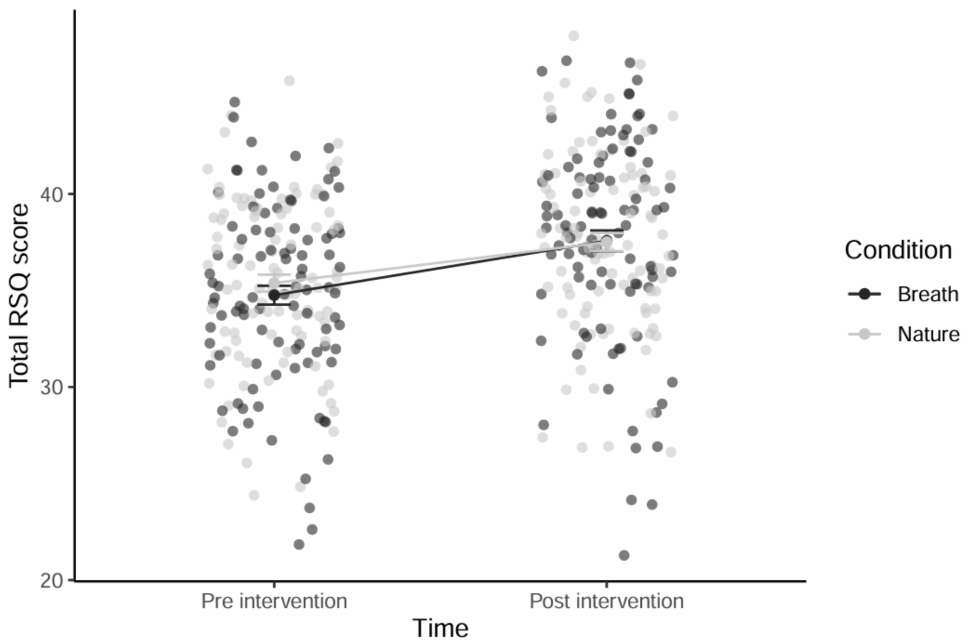
R (R Core Team, 2022) with the R Studio interface (Posit team, 2022) was used to preprocess the heart rate data to minimize the influence of artifacts, outliers, and missing entries. In the case of outliers, no more than 3% of data was changed, missing entries were interpolated as long as no more than ten seconds of consecutive entries were missing, and artifacts were removed. Using the package RHRV (Rodriguez-Linares et al., 2022), the HRV marker RMSSD was calculated for three-minute intervals (one at baseline, two during the relaxation intervention, and three intervals subsequently). To minimize the effects of statistical outliers for all dependent variables, we employed winsorizing (±3*SD*). Graphs were created using the package ggpubr (Kassambara, 2022), for calculating ANOVAs and ANCOVAs we used the package ez (Lawrence, 2016), and for multilevel models the package multilevel (Bliese, 2022).

3.4 Results

3.4.1 Subjective Relaxation (RSQ)

We conducted a mixed ANOVA to analyze the effects of both relaxation interventions on changes in total RSQ scores from pre to post-intervention. We found only a significant main effect of time ($F(1,190) = 40.26$, $p < .001$; $\eta^2 = .06$), indicating a significant increase in RSQ in reaction to both relaxation interventions (see Figure 8). The main effect of time remained significant after controlling for all covariates by conducting ANCOVAs.

Figure 8. Changes in total RMSSD scores for both experimental interventions (nature and breath) with individual data points. Error bars indicate the standard error.



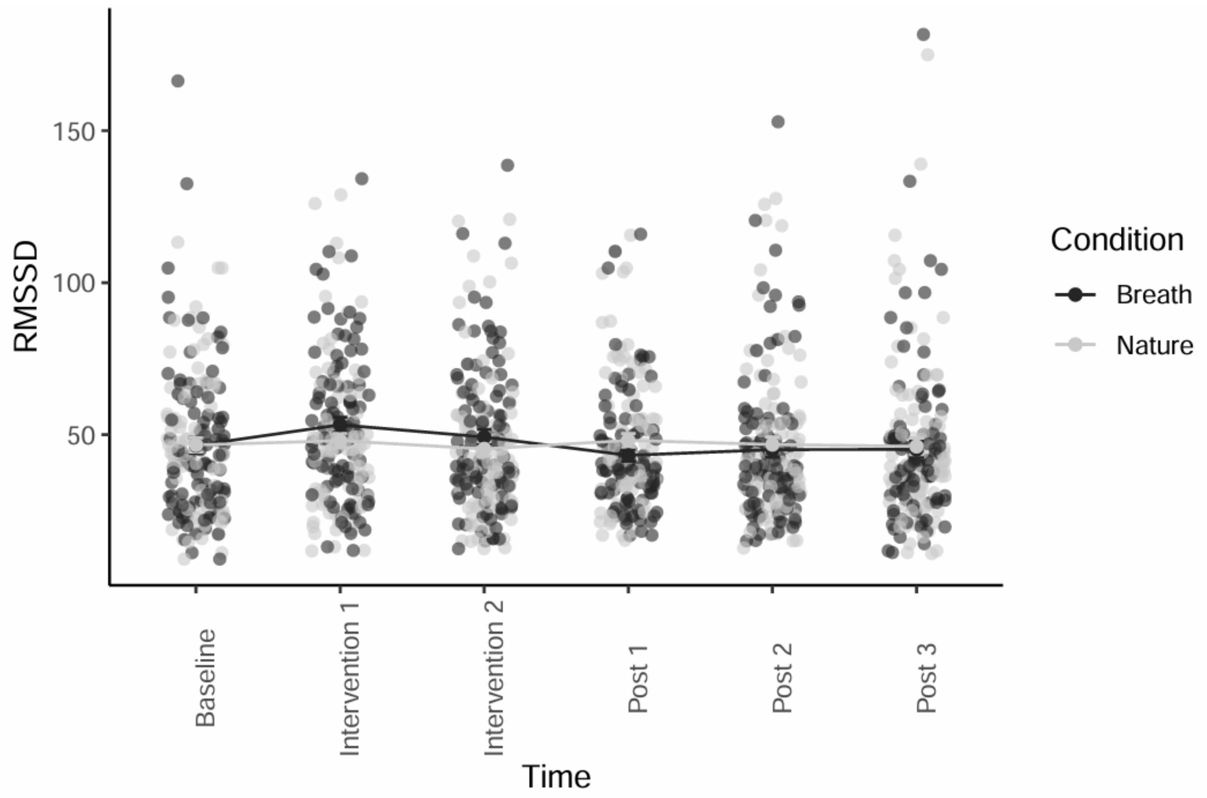
We conducted a mixed ANOVA for each PBI subscale. Maternal care and overprotection had no significant effect. The main effects of paternal care (F(1,188) = 9.67, p < .01; η^2 = .03) and paternal overprotection (F(1,188) = 6.68, p = .01; η^2 = .02) each reached statistical significance in addition to the main effect of time. Post-hoc tests revealed that, overall, lower subjective relaxation was associated with lower paternal care (r = -.24) and higher paternal overprotection (r = .21) independent of time.

In line with the analyses of the influence of PBI, we conducted mixed ANOVAs for each CTQ subscale. Sexual abuse and emotional neglect had no significant effect. In addition to the main effect of time, we found a significant main effect of emotional abuse (F(1,188) = 5.63, p < .05; η^2 = .02), with post hoc tests showing that higher scores of emotional abuse were associated with lower overall RSQ scores independent of time (r = -.14). Physical abuse (F(1,188) = 8.66, p < .01; η^2 = .01) and physical neglect (F(1,188) = 5.52, p < .05; η^2 = .009) both showed a significant interaction with time in addition to the main effect of time. As a post-hoc test, we calculated the area under the curve with respect to increase (AUCi; Pruessner et al., 2003) as a measure of change in RSQ scores over time. We found smaller changes in RSQ to be associated with higher scores in physical abuse and physical neglect.

3.4.2 Physiological Relaxation (HRV)

Figure 9 depicts a graphical representation of the change in RMSSD over time. We employed multilevel models (MLM) since the data are nested (repeated HRV measures nested within participants nested within conditions), and the differences between participants (random effects) are greater for physiological measures than for questionnaire data. There were no missing data. Maximum likelihood was used to estimate the model. The basic model included a random intercept and a random cubic slope. The Intraclass Correlation Coefficient was 70.95%. Adding a main effect of condition significantly improved the model fit, as did the interaction between changes in RMSSD and condition. This indicates that only the breath condition significantly increased RMSSD.

Figure 9. Changes in total RMSSD scores for both experimental interventions (nature and breath) with individual data points. Error bars indicate the standard error.



We added each subscale of PBI and CTQ separately to the model to test if they significantly increased the model fit, which was only the case for the main effect of emotional abuse. Higher emotional abuse scores were associated with blunted physiological relaxation. Of the covariates, only nicotine consumption significantly improved the model fit. Interestingly, adding the effect of nicotine consumption to the model affected the main effect of emotional abuse, attenuating its influence so that it did not reach significance. Therefore, we added the interaction of emotional abuse and nicotine consumption, which increased the overall model fit. In this new model, only the interaction of emotional abuse and nicotine consumption reached statistical significance, while both main effects were not statistically significant. This indicates that nicotine consumption seems to mediate the effect of emotional abuse on the physiological relaxation reaction. For detailed parameters of the final model, see Table 4.

Table 4. Parameters of the final model for RMSSD.

	Value		
Predictors	*Estimates*	*CI* (95%)	*p*
(Intercept)	43.76	35.10 – 52.42	**<.001**
time	-1.09	-1.75 – -.43	**.001**
condition [nature]	-2.95	-5.29 – -.60	**.014**
Emotional abuse	.63	-.35 – 1.61	.204
Nicotine	-5.23	-13.31 – 2.85	.203
Time: condition [nature]	1.00	.23 – 1.78	**.011**
Emotional abuse: nicotine	.67	.04 – 1.30	**.039**
N code	103		
Observations	1236		

Note. Emotional abuse is the sum score of the CTQ subscale “emotional abuse”; nicotine consumption was assessed as cigarettes consumed per day.

3.5 Discussion

This research aimed to investigate whether experiencing ELA leads to a distortion of the subjective and physiological relaxation response in reaction to a paced breathing exercise and a nature video in healthy participants. We found that both interventions successfully increased subjective relaxation. Concerning the influence of ELA, we found the subjective relaxation reaction to be blunted in association with lower paternal care, higher paternal overprotection, and higher scores on emotional abuse, physical abuse, and physical neglect. On a physiological level, we found an increase in RMSSD evoked only by the paced breathing intervention. Higher emotional abuse scores in interaction with nicotine consumption were associated with a blunted physiological relaxation response.

Both interventions being similarly effective in increasing subjective relaxation fits with previous studies reporting changes in affect associated with relaxation in response to nature stimuli (Payne & Delphinus, 2019) and paced breathing interventions

(Szulczewski, 2019). Only the breathing exercise leading to increased physiological relaxation partly supports our hypotheses since we expected an increase in subjective and physiological relaxation in response to both interventions. The increase in RMSSD induced by a breathing rhythm of six breaths per minute replicates findings from previous research (Laborde et al., 2022; Noble & Hochman, 2019; Ring et al., 1999; Russo et al., 2017; Tavares et al., 2017). The nature video being not effective in increasing HRV fits with the ambiguous picture in the current literature (Gaertner et al., 2023), with some studies finding an effect (Santarcangelo et al., 2012) while others did not (Snell et al., 2019). Several factors may explain why our intervention did not significantly increase RMSSD. Since the quality of the nature video was 4K and lacked tactile or olfactory impressions, the evoked experience may not felt real enough to elicit a physiological relaxation response. In this sample, the vast majority had rarely or never used VR. Therefore, using VR could have been stressful or exciting, with the possibility of masking the potential relaxing effects of nature videos. Furthermore, ceiling effects are an issue when inducing relaxation (Gomes et al., 2020), possibly masking the relaxing effects of the nature video in our study since we did not stress participants prior to the relaxation interventions.

While for subjective relaxation, various forms of ELA were found to be influential, only the influence of emotional abuse in interaction with smoking reached statistical significance for physiological relaxation. Both, the PBI and CTQ questionnaires were used to evaluate self-reported ELA, which may elucidate the greater impact on subjective relaxation compared to physiological relaxation. Perhaps the subjective feeling of relaxation is subconsciously linked to the overall subjective evaluation of life experiences. Similar to the negativity bias (Watters & Williams, 2011) this could associate perceiving events as more negative with a general focus on negative experiences. Difficulties in experiencing subjective relaxation might, in turn, reduce the subjective relaxation capability.

While there was no main effect of any of the ELA scores, the interaction of emotional abuse and nicotine consumption blunted the physiological relaxation reaction. This finding is consistent with previous studies that have found ELA to be associated with an increase in health risk behaviors such as nicotine consumption (Duffy et al., 2018), as well as an association between reduced resting state HRV, smoking (Dinas et al., 2013) and ELA (Sigrist et al., 2021a). In addition to these effects on baseline HRV, the current findings indicate that there seems to be a reduced reactivity to relaxation interventions associated with smoking and ELA, even in a healthy sample. HRV is discussed to be a marker of ANS adaptability, which is an integral part of physical and mental health (Acharya et al., 2006; Laborde et al., 2018; Thayer et al., 2012). Decreased resting-state HRV is related to various mental and physiological diseases (Acharya et al., 2006; Pham et al., 2021; Sammito & Böckelmann, 2016). While so far, changes in HRV reactivity in relation to diseases have been studied less, the first studies show blunted HRV reactivity to nature videos associated with psychopathology, such as major depression disorder (Matsui et al., 2016). The link between ELA, lower HRV, and psychopathology is still unclear, with multiple pathways forming plausible theoretical explanations for associations. First, ELA could lead to maladaptive emotion regulation strategies, increasing the risk of psychopathology, which in turn leads to a lower HRV (Jin et al., 2018). Second, ELA could directly lead to dysregulation in the ANS – indicated by lower HRV – which then affects emotion regulation and leads to psychopathology. Third, ELA could affect brain development which then affects emotion regulation and HRV independently (Sigrist et al., 2021a). In turn, higher HRV is associated with higher emotion regulation capabilities and adequately rating safe environments as such (Thayer et al., 2012). While the mechanisms behind the association between ELA, lower HRV, and psychopathology are still unclear, there is considerable evidence linking ELA to physical and mental diseases (Campbell et al., 2016; Duffy et al., 2018; Kessler et al., 2010; Wegman & Stetler, 2009). A distortion of the relaxation response, in addition to the distorted baseline HRV, could add another factor to the model. For example, on a physiological level, ELA leads to a distortion of the ANS not only during baseline but also in reaction to safe stimuli driven by a blunted PNS activity. This limits the ability to recover from stressful situations, potentially increasing allostatic load and thus increasing the risk of psychopathology (Thayer et al., 2012). This maladaptation leads to an increase in uncomfortable emotions, which require emotion regulation strategies to be adequately handled. However, ELA has already been linked to poorer emotion regulation skills (Duffy et al., 2018). This may also be reflected in the link between ELA and an increase in health-risk behaviors such as smoking, as these behaviors can be used as maladaptive emotion regulation strategies (Duffy et al., 2018). This may explain why we found especially emotional abuse to affect the subjective and physiological relaxation response, even in a healthy sample.

While the included sample size was adequate to find a small effect, our sample consisted of relatively young individuals. A previous meta-analysis found the effect of ELA on HRV to be more profound in older samples (Sigrist et al., 2021a), highlighting the importance of taking age into account. Additionally, the sample reported overall low ELA scores, which also likely limited the effect of ELA on HRV (Sigrist et al., 2021a).

Looking at the employed relaxation interventions, the nature video did not significantly increase physiological relaxation. Possible factors limiting the video's effectiveness are missing olfactory and tactile inputs, slightly blurred video, missing possibility to interact with the environment, and VR glasses as unfamiliar devices inducing stress or arousal. However, these limitations always have to be considered when using VR glasses.

Future studies should assess different forms of ELA since they seem to have specific influences on HRV and the relaxation reaction. When using the PBI, the subscales for both mother and father should be taken into account, as in the present sample, only paternal behavior significantly impacted subjective relaxation. Additionally, a broader sample should be assessed, including a wider age range and psychopathology as factors that affect the influence of ELA on HRV. The effectiveness of both relaxation interventions could be improved. For the nature video, the sense of presence could be amplified by increasing the video quality and the possibility of interacting with the virtual environment. Preferences for different nature scenes (e.g., forest or beach) could also be considered. For the breathing exercise, breathing rhythm should be measured to check that participants follow the pacer accurately since, in a previous study, participants could not follow a pacer with six breaths per minute (Steffen et al., 2021).

In the present study, we found the subjective and physiological relaxation reaction of healthy participants to be blunted in association with ELA, especially emotional abuse. This adds another link to the relationship between ELA and psychopathology, indicating that not only resting state HRV is reduced, but also the physiological and subjective relaxation capabilities are blunted, even in a healthy sample. Many effective therapeutic approaches include relaxation techniques (e.g., *Progressive Muscle Relaxation*; Vancampfort et al., 2013), hinting that increasing relaxation capabilities is an essential aspect of the treatment of psychopathology. Whether it is possible to reduce the risk for mental and physiological diseases arising from experiencing ELA by regularly performing relaxation exercises is still unclear. Nevertheless, it constitutes a promising interventional approach, as it could be an important aspect in the prevention and treatment of disease, increasing health and well-being in the population.

4. Do mental disorders affect the relaxation response?

This chapter focuses on the possible effects of BPD on the psychophysiological relaxation response. We compare the relaxation response induced with paced breathing and a virtual nature relaxation intervention of BPD patients and healthy controls. The chapter compromises the manuscript “Patients With Borderline Personality Disorder Show Initially Reduced Psychophysiological Relaxation Levels But Intact Relaxation Response”, which is currently being prepared for submission to a peer-reviewed journal. The submission will follow the publication of the article related to the ELA Relax project (see Chapter 3). Since both projects used the same study design and a subset of the ELA Relax project's sample served as the healthy controls for the BPD Relax project, we have chosen to delay submission in order to properly cite the ELA Relax project.

Gaertner, R. J., Klink, E.S.C., Benz, A.B.E., Denk, B.F., Meier, M., Wienholdt, S., Volkmer, N., Kossmann, K.E., & Pruessner, J. C. (in preparation). Participants With Borderline Personality Disorder Show Initially Reduced Psychophysiological Relaxation Levels But Intact Relaxation Response.

Contributions from all authors for this publication were as follows:
RJG: Project administration, Conceptualization, Methodology, Data Curation, Investigation, Formal analysis, Visualization, Writing - Original Draft & Editing. ESCK, ABEB, BFD, MM, SW, NV, KEK: Writing - Review & Editing. JCP: Formal analysis, Resources, Writing - Review & Editing, Supervision, Conceptualization, Methodology.

Since the study design is identical to the ELA Relax study, both studies were preregistered together at the Open Science Framework: https://osf.io/jsrze.

4.1 Abstract

Introduction. Borderline Personality Disorder (BPD) is associated with psychological as well as physiological dysregulation in patients, including reduced parasympathetic activity at baseline and difficulties returning to baseline after a stressor. Whether this impacts the relaxation response independent of a stressor has yet to be investigated. **Methods.** In a within-subject design, we compared two relaxation interventions, a virtual reality nature video and a paced breathing intervention. We assessed a female-only sample, with 20 BPD patients (age_{mean}=23.75±4.39) during their inpatient treatment and 22 matched healthy controls (HC; age_{mean}=22.68±2.68). Psychological relaxation was assessed using the Relaxation State Questionnaire (RSQ), and physiological relaxation was assessed using vagally mediated heart rate variability (HRV). **Results.** We employed multilevel models to test whether BPD significantly influenced the psychophysiological relaxation response. For psychological relaxation, we found an increase in RSQ scores in both groups in response to both interventions. The HC showed overall higher RSQ scores. We found overall higher HRV values in the HC group for physiological relaxation but no differences in the relaxation response. **Conclusion.** BPD patients exhibit overall lower psychophysiological relaxation levels, while the reactivity to relaxation interventions was similar to that of HC. Future studies should focus on interventions targeting baseline psychophysiological relaxation in BPD patients.

Keywords: borderline personality disorder, relaxation, heart rate variability, paced breathing, virtual nature

4.2 Introduction

4.2.1 Borderline Personality Disorder

Borderline personality disorder (BPD) is characterized by intense emotions that often change rapidly within a short period of time. Patients also experience an almost constant inner tension with difficulties in regulating both emotions and tension, frequently falling back on dysfunctional regulation strategies such as suicidal behavior, self-harm, or impulsive behavior in potentially self-damaging areas (e.g., risky driving, consumption of drugs, or alcohol). Interpersonal relationships and identity are also affected and often subject to sudden shifts. BPD affects approximately .7% to 2.7% of the general population and is associated with considerable costs for the person affected, their families and friends, and the health care system (DGPPN e. V., 2022; Leichsenring et al., 2023; World Health Organization, 1992). The vast majority suffer from comorbid diseases (85% affective disorders, 78% substance use disorders, 30% posttraumatic stress disorder), making BPD challenging to treat (Leichsenring et al., 2023).

The etiology of BPD comprises a complex interplay of genetic, physiological, psychological, and social factors, summarized as the Biopsychosocial Model of BPD as first introduced by Linehan (1993) and expanded in the following years (Carpenter & Trull, 2013; Crowell et al., 2009). One of the physiological factors, the autonomic nervous system (ANS), which is prominently implicated in healthy physiological and psychological functioning (e.g., emotion regulation; Brown et al., 2022), shows significant regulation differences between BPD patients and healthy controls. These differences suggest a reduced activity of the parasympathetic nervous system (PNS), indicated by lower vagally mediated heart rate variability (HRV) in BPD patients (Koenig et al., 2016). Previous studies also found a negative impact of the severity of BPD symptoms on resting state HRV, indicating an increased dominance of the sympathetic nervous system (SNS) linked with a blunted PNS activity (Geiss et al., 2021; Koenig et al., 2017). Regarding social and developmental factors, BPD patients often report extremely adverse childhood experiences with various forms of abuse and/or neglect (Crowell et al., 2009; Leichsenring et al., 2023). BPD patients were even found to be 3.15 times more likely to have experienced adverse childhoods than patients with other mental disorders (Porter et al., 2020). Early life adversity (ELA) was found to be a general risk factor for various mental and physiological diseases (Berman et al., 2022; Smith & Pollak, 2021) and is related to dysfunctional emotion regulation strategies (Duffy et al., 2018). In summary, the interplay between physiological changes associated with impulsivity and emotion regulation (e.g., changes in ANS activity), adverse childhood experiences, and a lack of adaptive and adequate emotion regulation strategies may contribute to the development of BPD (Carpenter & Trull, 2013; Crowell et al., 2009; Leichsenring et al., 2023; Linehan, 1993).

So far, there is no effective pharmacotherapeutic treatment for BPD. However, antidepressants, mood stabilizers, or benzodiazepines are used to manage some symptoms short-term. Psychotherapy was found to be effective in decreasing BPD-related symptoms, especially self-harm and suicidal behavior, while increasing psychosocial functioning up to 21 months post-treatment (Bloom et al., 2012; Leichsenring et al., 2023). Dialectic Behavioral Therapy (DBT) was developed specifically to treat BPD, and its effectiveness is supported empirically (Bloom et al., 2012; Linehan, 1993; Linehan & Dexter-Mazza, 2008). DBT's main components include mindfulness, emotion regulation, and distress tolerance, and it can be used in inpatient as well as outpatient settings (Bloom et al., 2012; Linehan & Dexter-Mazza, 2008).

4.2.2 Relaxation

While relaxation is not a core component of DBT, it is often added as a separate group intervention or in the course of mindfulness exercises (e.g., breathing exercises). While there are different forms of relaxation interventions (e.g., massages, Meier et al., 2020; guided imagery, Bigham et al., 2014), breathing interventions are easy to implement and have proven to be effective in inducing relaxation (Zaccaro et al., 2018). Physiologically, changes in the ANS are associated with relaxation, namely an increase in PNS activity (Del Giudice et al., 2011). Vagally mediated HRV is frequently used to track such changes in PNS activity, even though it can be influenced by other factors (e.g., age, sex, mental or physiological diseases; Acharya et al., 2006; Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017). Since breathing rhythm and PNS activity are linked via the vagus nerve, breathing with a rhythm of six breaths per minute increases physiological relaxation while also leading to psychological changes associated with relaxation (Kromenacker et al., 2018; Szulczewski, 2019). On a psychological level, those changes include increased pleasant emotions and reduced arousal (Benson, 1975; Steghaus & Poth, 2021).

Exposure to nature stimuli is another effective relaxation intervention. Nature stimuli in both real-life settings and virtual interventions were shown to increase not only HRV but also positive affect (Farrow & Washburn, 2019; Gladwell et al., 2012; Jo et al., 2019; Payne & Delphinus, 2019; Song et al., 2018). While the mechanisms behind breathing exercises function on a physiological level via direct vagal stimulation (baroreceptor reflex), the mechanisms behind the effects of nature exposure are likely psychological. Nature environments that convey security induce relaxation and, therefore, enable the restoration of resources. A proposed mechanism for these effects is based on the idea that these environments are considered evolutionary advantageous to humans (*Psychoevolutionary Theory*; Ulrich, 1983). While the effects of virtual nature interventions on PNS activation are inconsistent, an increased sense of presence in the virtual environment seems beneficial for inducing relaxation (Gaertner et al., 2023; Liszio et al., 2018). Overall, the effectiveness of short-term relaxation interventions on the relaxation response is mixed, with a wide variety of interventions, durations, and measurements used. While our group previously reported on interpersonal factors, like trait mindfulness (Benz et al., 2022) or a history of ELA (Gaertner et al., under review), to affect the relaxation response, many questions remain, for example, about the effects of psychopathology (Jo et al., 2019). So far, one previous study found that patients suffering from major depressive disorder did not show an increase in HRV while viewing a nature video, in contrast to healthy controls (Matsui et al., 2016). Whether BPD patients are affected similarly is unclear. Another previous study has shown that BPD is associated with changes in the ANS when exposed to and recovering from stress, as well as a reduced baseline vagally mediated HRV (Geiss et al., 2021; Koenig et al., 2016, 2017). It is unknown whether BPD affects the relaxation response as well.

4.2.3 Present study

To fill this gap in the literature, we used two short-term relaxation interventions (nature video and paced breathing). We tested their effect on psychological and physiological relaxation in BPD patients and healthy controls (HC). We employed the same study design we implemented previously to investigate the effects of ELA on the psychophysiological relaxation response in a healthy sample (Gaertner et al., under review). The design and hypotheses were registered at the Open Science Framework before data analyses (https://osf.io/jsrze). As an index for physiological relaxation, we chose the vagally-mediated HRV parameter root mean square of successive differences (RMSSD), which represents PNS activity independent of the breathing cycle (Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017). The psychological relaxation response was assessed using the *Relaxation State Questionnaire* (Steghaus & Poth, 2021), which successfully detects short-term changes in subjective relaxation. Both the BPD patients and the HC group underwent a paced breathing exercise and viewed a 360° nature video as relaxation interventions in two separate sessions. We chose to assess two interventions to be able to reveal different mechanisms behind their effectiveness, if present. Since we found ELA to blunt the relaxation response in healthy participants in a previous study (Gaertner et al., under review), we assessed ELA in this sample as well, using the *Childhood Trauma Questionnaire* (Bernstein et al., 2003) and the *Parental Bonding Instrument* (Parker et al., 1979).

We hypothesized an increase in psychological and physiological relaxation in response to the breathing exercise for BPD patients and HC, with an overall lower HRV in the BPD group compared to the HC group. For the nature video, we expected an increase in both relaxation markers only in the HC group, expecting a blunted relaxation response in BPD patients to a virtual nature stimulus, similar to the effect of depression (Matsui et al., 2016).

4.3 Methods

4.3.1 Participants

We invited BPD patients at the local psychiatric clinic (Centre for Psychiatry Reichenau, Germany) undergoing inpatient DBT treatment. We chose to assess only female patients for feasibility reasons since the majority of BPD patients are female (Widiger et al., 2013), and sex affects HRV (Shaffer & Ginsberg, 2017). Patients were only invited if the treating psychotherapist deemed the patient fit enough for participation in the study. Patients were informed that participating in the study was voluntary and not part of the inpatient treatment, and refusal would have no consequences on their stay at the ward. Both sessions of the within-subjects design took place between November 2022 and August 2023. A total of 24 patients participated in the study. Four patients were excluded (only taking part in one session, getting dizzy when using VR glasses, technical difficulties, having a cardiac pacemaker), leaving a sample of 20 BPD patients (age_{mean} = 23.75±4.39). The HC sample was a subset from a more significant sample of 103 subjects (65 women and

38 men), which we had previously tested to investigate the effects of ELA on the relaxation response in healthy participants (Gaertner et al., under review), where we had used the same study design as in the present study. As healthy controls, we selected 22 female participants (age_{mean} = 22.68±2.68) according to age and Body Mass Index (BMI) to be similar to the BPD patients; see Table 5 for a detailed description of sample characteristics. For both samples, the inclusion criteria were: being fluent in German, being physically healthy (especially no diabetes, epilepsy, or heart diseases), and having a BMI between 18.5 and 29.9. While there were stricter rules in place for the healthy sample (no caffeine, alcohol, and nicotine four hours before the experiment, no intensive sports 12 hours before the experiment), we chose not to implement the same restrictions on the BPD sample, since exercise is part of the treatment plan and asking patients to refrain from smoking probably would have led to significant difficulties in recruitment. However, none of the patients consumed alcohol during their stay at the ward, as this is a prerequisite for the inpatient DBT treatment. Inclusion criteria were implemented to limit modulating effects on HRV (Quintana et al., 2016; Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017) and to minimize the potential risks of using VR glasses since the use can trigger epileptic seizures (Bureau et al., 2004). All patients who were prescribed antidepressants were taking selective serotonin reuptake inhibitors, which have a weak association with lower baseline HRV that is postulated to be caused by factors other than the medication (Noordam et al., 2016). Similarly, neuroleptics were not associated with HRV changes (Malaspina et al., 2002). The study procedure was approved by the Ethics Committee of the University of Konstanz and followed the guidelines of the Declaration of Helsinki.

Table 5. Sample characteristics.

	Total (N=42)		
	BPD n=20 (47.62%) *M±SD*	HC n=22 (52.38%) *M±SD*	*p* value
Age (in years)	23.75±4.39	22.68±2.68	.18
BMI (in kg/m2)	22.28±2.63	24.51±2.54	<.001
Nicotine	6.15±6.10	1.14±3.90	<.001
Alcohol	3.95±4.21	5.41±2.87	.05
Education			
Secondary School	n=2 (10.00%)	n=0	
Middle School	n=3 (15.00%)	n=0	
High School Diploma	n=8 (40.00%)	n=18 (81.80%)	
Apprenticeship	n=5 (25.00%)	n=1 (4.50%)	
Bachelor	n=2 (10.00%)	n=3 (13.60%)	
Medication			
Antidepressant	n=3	n=0	
Neuroleptic	n=2	n=0	
Oral contraceptive	n=0	n=1	
Depressive Symptoms (BDI)	27.00±8.14	6.55±4.74	<.001
Parental Bonding (PBI)			
No father figure	n=5	n=1	<.001
Paternal care	15.13±10.971	24.10±7.762	<.001
Paternal overprotection	16.33±10.521	8.81±7.012	<.001
No mother figure	n=0	n=0	<.001
Maternal care	16.15±9.02	28.77±7.49	<.001
Maternal overprotection	18.10±10.36	11.68±7.81	.002
Childhood Trauma (CTQ)			
Emotional abuse	16.73±6.11	9.09±4.36	<.001
Physical abuse	9.25±6.14	5.77±1.88	<.001
Sexual abuse	9.95±5.54	5.41±1.39	<.001
Emotional neglect	16.17±6.78	8.68±3.30	<.001
Physical neglect	9.68±4.03	6.81±1.99	<.001

Notes. BPD = patients with borderline personality disorder, HC = healthy controls, BMI = Body Mass Index; Nicotine = cigarettes smoked per day; Alcohol = alcoholic beverages consumed per week, patients referred to consumption behavior outside of inpatient treatment; BDI = Beck Depression Inventory; scores for father and mother care and overprotection were collected with the Parental Bonding Instrument; scores for emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect were collected with the Childhood Trauma Questionnaire.

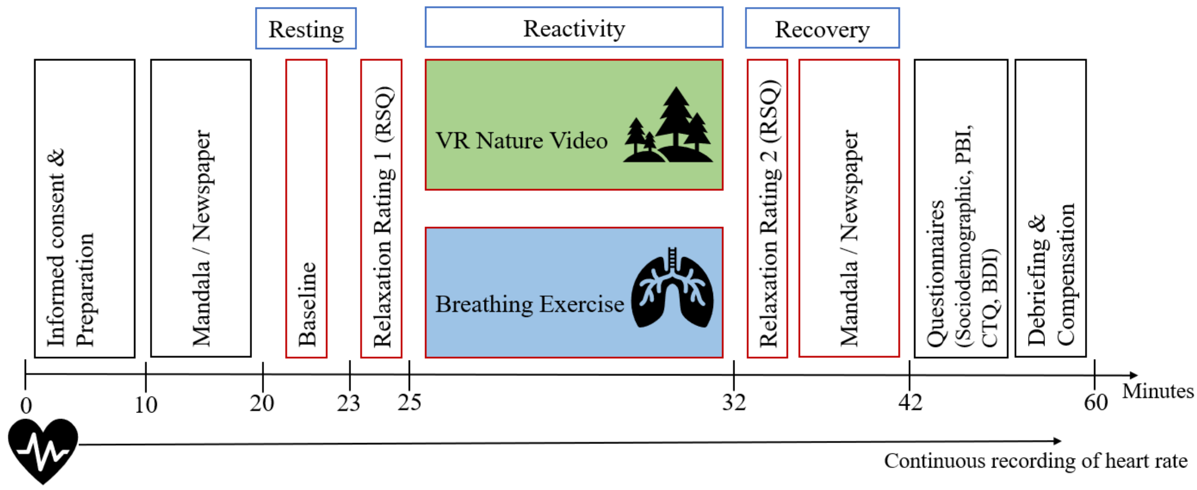
[1] data collected from n=15 participants.

[2] data collected from n=21 participants.

4.3.2 Study procedure

This study was a within-subjects design, with all participants undergoing both conditions five to nine days apart. The order of the conditions was randomized using a coin toss. With this study design, we aimed to follow the *Vagal Thank Theory* (Laborde et al., 2018), which postulates that it is important to measure physiological markers at baseline (*Resting*), during the intervention (*Reactivity*), and afterward (*Recovery*), to assess the complete response dynamic induced by the interventions (see Figure 10 for a graphical representation of the study procedure). At the first session, participants provided written informed consent. Subsequently, both appointments followed the same procedure, starting with participants applying the sensor to measure their cardiac activity. Participants were given ten minutes of either drawing a mandala or reading a non-arousing local newspaper to allow their heart activity to arrive at baseline level before a three-minute baseline was recorded (Resting). During the baseline, participants watched a fixation cross, sitting with feet on the floor to make baseline and interventions as comparable as possible, as recommended when assessing HRV (Quintana & Heathers, 2014). Directly after that, they rated their psychological relaxation for the first time (Relaxation Rating 1), followed by the intervention of either watching a 360° nature video with virtual reality (VR) glasses or doing a paced breathing exercise for seven minutes (Reactivity). After the intervention, they rated their psychological relaxation a second time (Relaxation Rating 2) before being given ten minutes to read or draw (Recovery). The sessions ended with different questionnaires being assessed (e.g., sociodemographic questionnaire, ELA questionnaires).

Figure 10. Graphical representation of the study procedure. Red frames indicate which experimental phases were included in the HRV analyses, and blue frames indicate the phases according to the Vagal Tank Theory (Laborde et al., 2018).

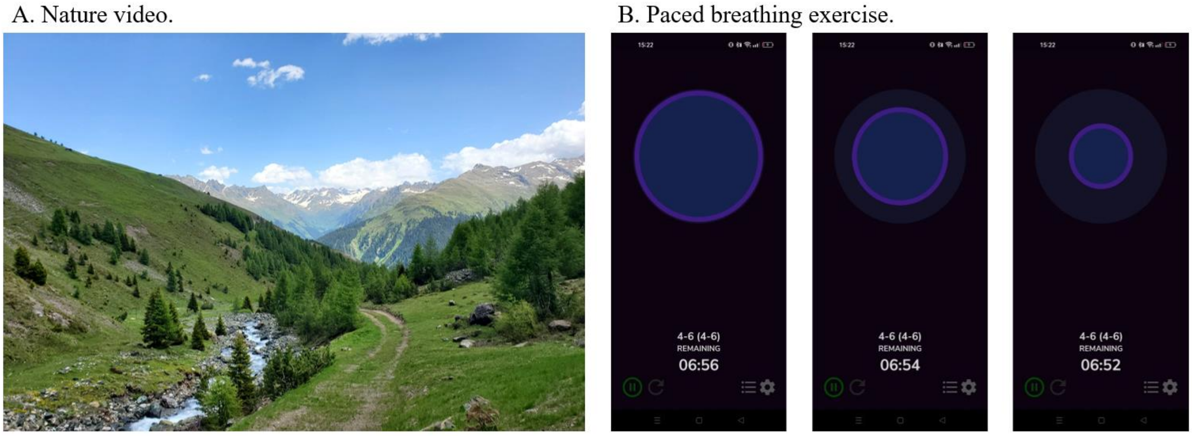


Notes: RSQ = Relaxation State Questionnaire; VR = virtual reality; PBI = Parental Bonding Instrument; CTQ = Childhood Trauma Questionnaire; BDI = Becks Depression Inventory.

4.3.3 Relaxation interventions

Both interventions were already implemented in a previous study to investigate the effects of ELA on the relaxation response in a healthy sample (Gaertner et al., under review); see Figure 11 for a depiction of both interventions. During the VR nature video intervention (“nature”), participants watched a 360° video recorded by us in the Swiss Alps near Davos (camera: Insta360 Pro 2, Insta360, California, USA). We used VR glasses (Meta Quest 2; Meta Platforms Inc., California, USA) to present the video to increase the sense of presence in the virtual environment to promote the relaxing effect of the video (Gaertner et al., 2023; Liszio et al., 2018). The video included the recorded sounds of a running river, wind, and birds. With sounds and showing predominantly green mountains and a flowing river this video meets the criteria for a nature environment that can be perceived as relaxing (Annerstedt et al., 2013; Snell et al., 2019). During the breathing exercise (“breath”), we employed the app “Awesome Breathing: Pacer Timer“ (Gollehon & Troia, 2022) to guide participants to breathe six breaths per minute (four seconds inhale, six seconds exhale), a rhythm that was found to induce psychological and physiological relaxation successfully (Russo et al., 2017; Szulczewski, 2019).

Figure 11. Depictions of both relaxation interventions.



4.3.4 Measurements

4.3.4.1 Physiological relaxation

We chose to assess RMSSD as an index of vagally-mediated HRV since it adequately represents PNS activity independent of the breathing cycle (Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017). All HRV markers are based on the beat-to-beat variance of R-R intervals, RMSSD is allocated to the time-domain markers and calculated based on the time between two peaks of a heart rhythm (Acharya et al., 2006; Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017). Initially, we planned to calculate the frequency-domain marker high-frequency HRV as well. However, since it is strongly influenced by breathing depth and rhythm (Shaffer & Ginsberg, 2017; Zaccaro et al., 2018), we chose to focus solely on RMSSD. While intervals of five minutes are considered to be the gold standard when calculating RMSSD, shorter intervals have been shown to yield valid results as well (Laborde et al., 2017). We calculated three-minute intervals to keep the experiment as short as possible. To record heart activity, participants applied a Polar H10 Sensor (Polar Electro GmbH Deutschland, Germany) with a chest strap. To record the data from the sensor, we used the app “HRV Logger” (Altini, 2022) running on an iPad that connected to the sensor via Bluetooth, where the data was stored until preprocessing.

4.3.4.2 Psychological relaxation

We assessed psychological relaxation using the *Relaxation State Questionnaire* (RSQ; Steghaus & Poth, 2021) directly before and after the interventions to measure changes in psychological relaxation. The RSQ was shown to have good reliability (ω = .83; Steghaus & Poth, 2021) and consists of 10 statements about physical (e.g., "my muscles feel loose") and mental ("right now, I am completely calm") relaxation. Agreement to each statement can be given on a five-point Likert scale. Those values are summed up to the RSQ score (min = 5, max = 50), with higher values indicating higher levels of psychological relaxation.

4.3.4.3 Early Life Adversity

Since there is no universally accepted definition of ELA, there is significant variability in its assessment (Koppold et al., 2023). Here, we chose to implement measurement via two questionnaires to cover different concepts of ELA. The *Childhood Trauma Questionnaire* (CTQ; original: Bernstein et al., 2003; German translation: Wingenfeld et al., 2010¸ Cronbach's α = .94) assesses different types of childhood trauma on the subscales of emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse with five items each for the first sixteen years of life. Higher scores indicate higher levels of abuse or neglect, therefore indicating greater exposure to ELA (min = 5, max = 25). The *Parental Bonding Instrument* (PBI; original: Parker et al., 1979; German translation: Benz et al., 2021; Cronbach's α = .86 to .95) focuses on parental caregiving behavior, separated for maternal and paternal behavior. For each parent, participants answer items on the two subscales "care" (e.g., "spoke to me in a warm and friendly voice"; min. 0, max. 36) and "overprotection"(e.g., "tried to control everything"; min. 0, max. 39), with lower levels of care and higher levels of overprotection indicating ELA. In addition to the scores for each subscale, we combined them to an overall parenting style for each parent according to thresholds reported previously (*affectionless constraint*: low care and high overprotection; *affectionate control*: high care and high overprotection; *neglectful parenting*: low care and low overprotection; *optimal parenting*: high care and low overprotection; Parker et al., 1979).

4.3.4.4 Covariates related to BPD

All BPD participants were assessed during their inpatient treatment at the Center for Psychiatry Reichenau, Germany, while being enrolled in the DBT program for eight to ten weeks. We included the number of weeks that they had already spent on the DBT ward as a possible covariate during data analysis. Part of the inpatient treatment included filling out the short version of the *Borderline Symptom List* (BSL-23; Wolf et al., 2009; Cronbach's α = .94 to .97) every week to assess the severity of BPD-related symptoms (e.g., "In the course of the last week I experienced stressful inner tension") and self-harm behavior (e.g., "During the last week I hurt myself by cutting, burning, strangling, headbanging, etc.”). For each of the 23 statements concerning symptoms, patients could rate their agreement on a five-point Likert scale, which was summed up to a total BSL score (min. 0, max. 92), with higher values indicating greater severity of symptoms. Since the severity of BPD symptomatology was found to influence HRV (Geiss et al., 2021; Koenig et al., 2017), we collected the questionnaires filled out during the week in which data collection took place. We assessed if additional psychological diagnoses were reported via self-report answers and based on the official patient file (yes or no). Sixteen of the 20 included patients reported comorbidities, while the clinical patient files indicated comorbidities for 11 patients. Due to the discrepancy between self-report and patient files, we included both in the data analyses. Depression was the most common comorbidity in both datasets.

4.3.4.5 Covariates

Since age, BMI, sleep (hours slept in the previous night), smoking (cigarettes per day), and alcohol consumption (glasses of alcoholic beverages per week) influence HRV (Acharya et al., 2006; Quintana & Heathers, 2014), we assessed them via self-report questionnaires. Further, depressive symptoms were assessed via the *Beck Depression Inventory* (BDI-II; original: Beck et al., 1996; German translation: Pietsch et al., 2012), as they have been shown to affect HRV as well (Kemp et al., 2010; Wang et al., 2013).

4.3.5 Data analysis plan

All data preprocessing and analysis steps were executed with R (R Core Team, 2022) using the interface R Studio (Posit team, 2022). After preprocessing the raw signal, RMSSD was calculated using the package “RHRV” (Rodriguez-Linares et al., 2022). We calculated six three-minute intervals of interest: one during the baseline, two during the intervention, and three following the intervention. Before psychological and physiological relaxation data was entered into data analysis, we employed winsorizing to minimize the influence of extreme outliers (defined as ±3*SD* from the mean of the sample).

We calculated multilevel models using the package “multilevel” (Bliese, 2022) since data was nested (changes over time nested in participants, nested in groups [HC or BPD], nested in conditions [nature or breath]). We calculated the basic model for RMSSD and RSQ scores as outcome variables, investigating which intercept and time trend fitted the data best before adding group and condition as predictors. As the last step, the potential covariates (sleep duration in the previous night, age, BDI, BMI, alcoholic beverages consumed per week, cigarettes consumed per day) were added to each model. For the models including the BPD patients only, the additional covariates BSL score, time spent at the ward, comorbidity based on self-report, and comorbidity based on patient file were included. Only covariates reaching significance are reported. Model fit was calculated using the maximum likelihood method, and model fits of nested models were compared using the Chi-squared test. Since higher scores of ELA are strongly correlated with psychopathology and our group tested the link between ELA and the relaxation response in a healthy sample in another study (Gaertner et al., under review), we investigated the effects of ELA on the psychophysiological relaxation response only in the BPD subsample. As markers of ELA, we used the scores of the CTQ subscales emotional abuse, physical abuse, sexual abuse, physical neglect, and emotional neglect, as well as maternal and paternal care and overprotection in addition to maternal and paternal parenting style as derived from the PBI. Graphs were created using “ggpubr” (Kassambara, 2022).

4.4 Results

4.4.1 Psychological relaxation (RSQ)

4.4.1.1 Main Analyses

The basic model with the best fit for RSQ scores as outcome included a random intercept and a fixed linear slope per participant, with the Intraclass Correlation Coefficient (ICC) indicating that 66.46% of the variability within the dataset can be attributed to interindividual differences. Adding a main effect of group (BPD or HC) and a main effect of condition (nature or breath) significantly improved the model fit, none of the interactions reached significance. Of the added covariates, only the main effect of BDI significantly improved the model fit. The final model included a random intercept and a fixed linear slope, indicating the main effect of time and the main effects of group, condition, and BDI. Belonging to the HC group, as well as the nature condition, were associated with higher RSQ values. Higher BDI scores were linked to lower RSQ values (see Table 6 for the parameters of the final model). Figure 12 depicts changes in RSQ scores over time.

Figure 12. Graphical representation of changes in total RSQ scores for both conditions (nature and breath) in both groups (BPD and HC) with individual data points. Error bars depict the standard error.

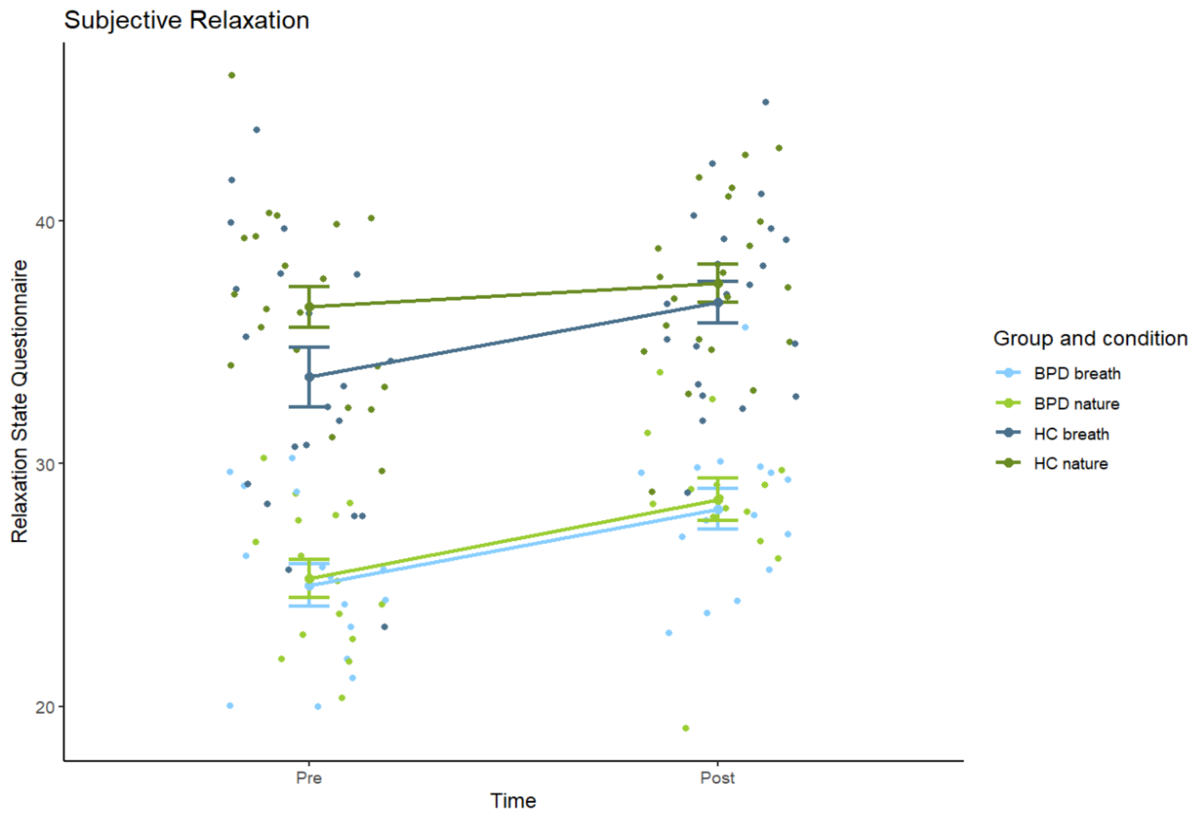


Table 6. Parameters of the final model for RSQ in the total sample.

Predictors	*Estimates*	*CI* (95%)	*p*
(Intercept)	28.70	25.11 – 32.28	**<.001**
time	2.61	1.59 – 3.62	**<.001**
group	6.58	3.54 – 9.62	**<.001**
condition	1.04	.02 – 2.05	**.049**
BDI	-.15	-.27 – -.02	**.027**
Random Effects			
σ2	11.03		
τ00	4.08		
N	42		
Observations	168		
Marginal R^2	.70		

4.4.1.2 Additional analyses: Effect of ELA on BPD patients

The basic model, which included only the BPD patients, included a random intercept (β = 52.55, p < .001, 95% *CI* [30.38, 74.72]) and a fixed linear slope (β = 3.40, p < .001, 95% *CI* [2.15, 4.65]), ICC: 28.10%). Adding the PBI and CTQ scores to the basic model revealed a significant main effect of sexual abuse (β = -2.50, p = .008, 95% *CI* [-4.26, -.74]), a main effect of self-reported comorbidity (yes or no; β = -25.33, p = .04, 95% *CI* [-48.65, -2.01]) and a significant interaction of sexual abuse and self-reported comorbidity (β = 2.30, p = .014, 95% *CI* [.53, 4.07]) with marginal R^2 = .427, conditional R^2 = .521 and ICC = .16 for the final model. Higher scores of sexual abuse and having self-reported comorbidity were associated with lower RSQ scores. For the interaction effect, post-hoc tests revealed higher sexual abuse scores in the group without self-reported comorbidity. Within the subgroup with self-reported comorbidity, higher sexual abuse scores were associated with lower RSQ scores. However, these results should be interpreted cautiously since only four patients did not indicate self-reported comorbidities.

4.4.2 Physiological relaxation (RMSSD)

4.4.2.1 Main analyses

The basic model with RMSSD as a criterion variable included a random intercept per participant (ICC of 72.57%) and a fixed linear slope, indicating a significant main effect of time. The main effect of the group and the main effect of the condition significantly improved the model fit, and no interaction reached statistical significance. The HC group was associated with higher RMSSD values, as was the nature condition. Concerning the covariates, only the main effect of hours slept in the previous night reached significance, indicating lower values of RMSSD were unexpectedly associated with more hours slept in the previous night (see Table 7). Changes in RMMSD over time are depicted in Figure 13.

Figure 13. Graphical representation of changes in RMSSD for both conditions (nature and breath) in both groups (BPD and HC) with individual data points. Error bars depict the standard error. Dark blue frames indicate the phases according to the Vagal Tank Theory (Laborde et al., 2018).

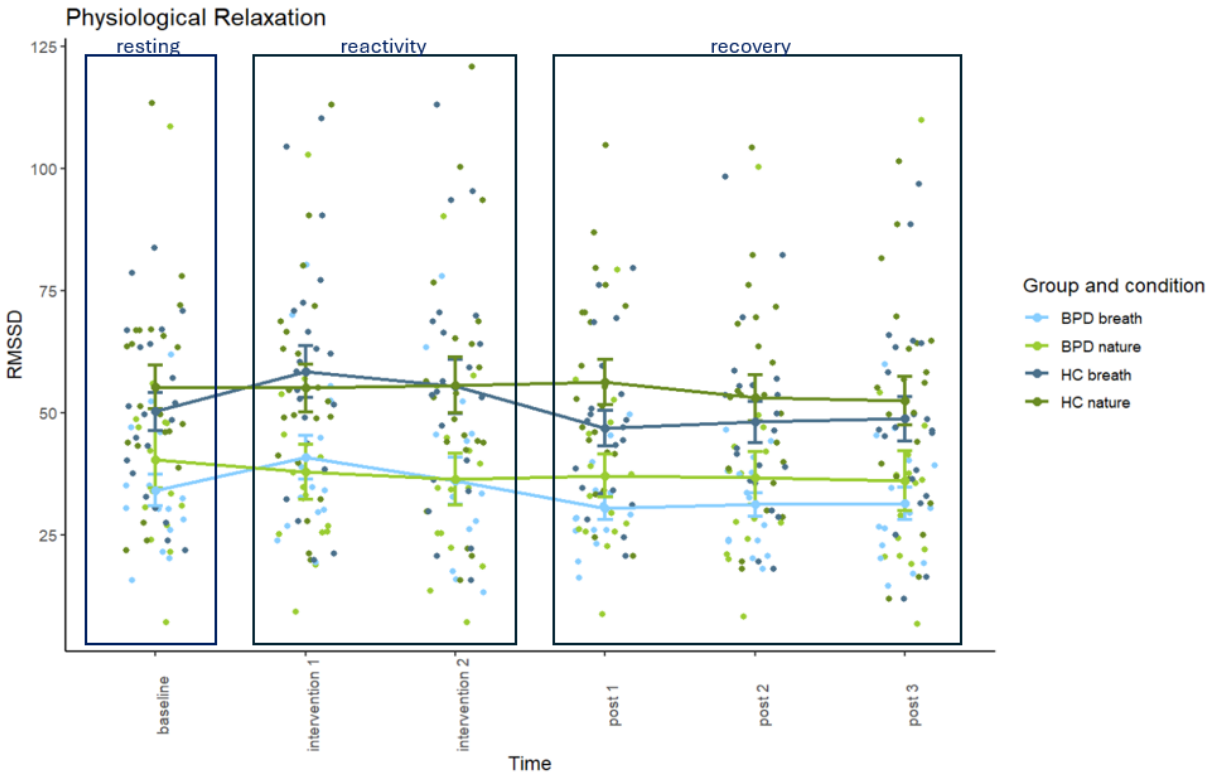


Table 7. Parameters of the final model for RMSSD in the total sample.

Predictors	*Estimates*	*CI* (95%)	*p*
(Intercept)	46.69	34.88 – 58.50	**<.001**
time	-.78	-1.35 – -.21	**.008**
group [HC]	15.04	4.02 – 26.07	**.009**
condition [nature]	5.13	3.19 – 7.08	**<.001**
sleep hours current	-1.31	-2.58 – -.05	**.043**
Random Effects			
σ2	123.03		
τ00	300.22		
N	42		
Observations	504		
Marginal R^2	.34		

4.4.2.2 Additional analyses: Effect of ELA on BPD patients

Investigating the influence of the CTQ subscales on RMSSD in the BPD subsample, we found no significant improvement of the model fit by adding a random or fixed time effect, leaving the basic model with the random intercept (β = 21.63, p = .088, 95% *CI* [-2.99, 46.25]) and an ICC of 60.85%. Of the CTQ subscales, only the main effect of physical neglect significantly improved the model fit (β = 3.37, p < .001, 95% *CI* [1.74, 5.01]), indicating higher scores of physical neglect to be associated with higher RMSSD scores, in contrast to our expectations. Of the covariates, adding self-reported comorbidity (β = 14.15, p = .076, 95% *CI* [-1.48, 29.77]) and hours slept in the previous night (β = -3.96, p < .001, 95% *CI* [-5.89, -2.03]) significantly improved the model fit, even if the main effect of self-reported comorbidity did not reach significance in the final model. More hours of sleep were unexpectedly associated with lower RMSSD values. The marginal R^2 for the final model was .659.

For the PBI subscales, we found only the main effect of maternal care to significantly improve the model fit (β = -.70, p = .046, 95% *CI* [-1.38, -.02]), indicating lower RMSSD scores to be associated with higher maternal care, contrary to our expectations. Of the covariates, the main effects of BDI (β = -1.15, p = .006, 95% *CI* [-1.91, -.39]) and hours slept in the previous night (β = -4.07, p < .001, 95% *CI* [-6.04, -2.09]) both increased the model fit significantly, with marginal R^2 = .513 for the final model. Higher scores of BDI and a greater number of hours slept in the previous night were associated with lower RMSSD scores.

4.5 Discussion

We assessed the psychophysiological relaxation response induced by a paced breathing intervention and a virtual reality nature video in patients with borderline personality disorder and healthy controls to investigate a possible distortion of the relaxation response associated with BPD. We found an increase in psychological relaxation induced by both interventions, with higher psychological relaxation values in the HC group before and after both interventions. Depressive symptoms were associated with lower psychological relaxation. For physiological relaxation, we found a successful increase in vagally mediated HRV induced by the interventions in both groups. Additionally, we found higher HRV scores in the HC group during the whole experiment and a negative effect of hours slept during the previous night on overall HRV level. These findings only partly support our hypotheses. While we found lower

HRV scores in the BPD patients at all time points, we did not find differences in the relaxation response induced by the interventions.

Especially the link between more hours slept during the previous night and overall lower HRV level is noteworthy since it is counterintuitive, with previous studies finding lower vagally mediated HRV associated with fewer hours slept during the last night (Castro-Diehl et al., 2016; Dettoni et al., 2012; Schlagintweit et al., 2023). However, those studies manipulated sleep duration (Dettoni et al., 2012; Schlagintweit et al., 2023), measured HRV after multiple nights of partial sleep deprivation (Dettoni et al., 2012), or measured the sleep duration with actigraphy (Castro-Diehl et al., 2016; Dettoni et al., 2012), or polysomnography (Schlagintweit et al., 2023). Since we did not manipulate sleep duration, the effects observed in previous studies might be specific to situations where sleep duration is intentionally altered. Furthermore, we assessed sleep duration through self-reporting, so participants may not have accurately indicated their sleep duration. Additionally, since we did not screen for sleep duration, the great variability of baseline RMSSD values was linked to the middle range of sleep duration, distorting the association between RMSSD and sleep duration. Besides, there are many other factors despite sleep influencing baseline HRV (Acharya et al., 2006; Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017).

These results suggest overall lower levels of psychophysiological relaxation parameters in BPD patients, while the relaxation response appears comparable across groups. For psychological relaxation markers, previous studies found greater self-reported tension, negative affect, and less positive affect in BPD patients at baseline compared to HC (Ebner-Priemer et al., 2007; Willis et al., 2018). This aligns with our finding of lower baseline subjective relaxation levels. The results for physiological relaxation show overall higher scores in the HC group but no significant differences in the relaxation response induced by the relaxation interventions. These results align with previous studies that found lower baseline HRV in BPD patients than HC (Koenig et al., 2016; Maiß et al., 2021). This not only fortifies reduced baseline PNS activity as part of the biopsychosocial model of BPD but also expands the disorder-specific knowledge, showing that the relaxation response seems to be comparable to HC. This is noteworthy, as baseline PNS activity has been discussed as a marker of adaptability and emotional and cognitive flexibility and is associated with executive functions and emotion regulation, which are impaired in BPD patients (Pham et al., 2021; Thayer et al., 2012). An intact relaxation response is a vital resource and could allow interventions to be based upon. For example, future interventions could specifically target the relaxation response with relaxation training employing paced breathing to increase PNS activity. However, whether this would affect PNS activity during the intervention and at baseline has yet to be investigated.

The driving factor of the differences in psychophysiological relaxation between BPD patients and HC seemed to be the overall differences in RMSSD levels, putting patients 15 to 20 points below healthy controls across the entire experiment. This raises the question of where those baseline differences come from and allows future interventions to focus on improving baseline RMSSD levels of BPD patients. Group interventions like a psychoeducational group and metacognitive training were found to successfully reduce baseline levels of self-reported tension, which can be interpreted as a psychological marker associated with relaxation (Ridolfi et al., 2019; Schilling et al., 2018). To our knowledge, no study has investigated interventions to increase baseline HRV in BPD patients. However, strategies based on acceptance of emotions were found to increase HRV in BPD patients during social rejection, emphasizing that developing adaptive emotion regulation strategies should be an integral part of BPD treatment (Dixon-Gordon et al., 2017), which could increase baseline HRV over time. Looking at other psychopathologies, biofeedback was found to increase vagally-mediated HRV in patients with depression, either as training over four weeks without additional psychotherapy (Park & Jung, 2020) or in addition to psychotherapy (Caldwell & Steffen, 2018). Similar effects were found for psychotherapy combined with breathing exercises (Chien et al., 2015). While psychotherapy alone did not increase HRV in patients with major depressive disorder (Caldwell & Steffen, 2018; Neyer et al., 2021), psychotherapy was found to increase HRV in panic disorder patients (Garakani et al., 2009). These heterogeneous findings indicate disorder-specific effects of interventions, limiting the generalizability across different psychopathologies. A first study investigating the effects of a DBT intervention in adolescents with BPD found no overall changes in HRV associated with treatment. However, an increase in HRV was associated with a decrease in BPD symptomatology (Weise et al., 2021).

For healthy participants, various interventions have been shown to improve baseline HRV, for example, mindfulness training (Kirk & Axelsen, 2020) and high-intensity interval training (Navarro-Lomas et al., 2022). Whether these interventions are similarly effective in BPD patients has not been investigated so far. Successfully increasing baseline HRV could be beneficial for BPD patients since previous studies found baseline vagally-mediated HRV to be a predictor for clinical outcomes in BPD patients (Sigrist et al., 2021b; Weise et al., 2021).

4.5.1 Associations between BPD, HRV, and ELA

In a previous study, we found that the presence of ELA is associated with a blunted relaxation response in healthy participants (Gaertner et al., under review). Therefore, we further investigated the possible effect of ELA on the psychophysiological relaxation response of BPD patients using the CTQ and PBI. Of the CTQ subscales, only physical neglect significantly influenced RMSSD. Contrary to previous studies (Sigrist et al., 2021a; Thurston et al., 2020), we found higher physical neglect scores associated with higher RMSSD values. Additionally, having self-reported comorbidities was associated with higher RMSSD. However, only four participants did not report comorbidities, which prevented us from drawing firm conclusions from this result. Of the PBI subscales, only maternal care significantly influenced RMSSD, associated with lower RMSSD values. Again, this contradicts previous results where higher care was associated with higher HRV (Benz et al., 2022).

While several possible explanations exist for these unexpected associations between ELA and HRV, the following explanatory approaches are speculative and warrant a thorough investigation. A closer look at the individual data points revealed noticeable outliers with RMSSD values above the mean. Such values after winsorizing could indicate undiscovered artifacts or other distortions during data collection. Additionally, there are several other factors, aside from ELA, that influence baseline HRV values (Acharya et al., 2006; Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017). According to the *Polyvagal Theory* (Porges, 2003), high values of vagally mediated HRV and an active PNS might also signal a shift toward a *freeze* response triggered by a threat rather than accurately indicating relaxation (Del Giudice et al., 2011; Porges, 2003). Additionally, ELA was assessed retrospectively using self-report questionnaires, which may be distorted by memory effects or the negativity bias often associated with BPD (Domes et al., 2009).

To date, few studies investigated the effects of ELA on HRV in BPD patients. For example, it was found that the severity of ELA is associated with lower vagally-mediated HRV and longer response times during an emotional working memory task (Krause-Utz et al., 2022). However, in adolescent BPD patients, ELA did not significantly affect HRV while still being significantly associated with clinical improvement over time (Sigrist et al., 2021b; Weise et al., 2021). While these findings are inconsistent and warrant a closer investigation in the future, a close relationship between ELA and BPD has been shown consistently, with BPD patients being 13.91 times more likely to have experienced ELA than healthy participants and 3.15 times more likely than patients with other mental disorders (Cattane et al., 2017). This accords with the Biopsychosocial Model of BPD, attributing ELA an important role in the development of BPD. The biological factors associated with BPD indicated heightened impulsivity and intensity of emotions (e.g., neurological conspicuous characteristics in the prefrontal cortex and amygdala; Crowell et al., 2009; Leichsenring et al., 2023). This biological vulnerability might explain why the association between ELA and BPD seems to be even stronger than the association between ELA and other mental diseases (Cattane et al., 2017). Experiencing ELA and especially an invalidating environment neglects to teach children how to detect and regulate their emotions. In turn, this might lead to social difficulties and a lack of adequate emotion regulation strategies not only during childhood but also later in life (Crowell et al., 2009; Linehan, 1993). Additionally, BPD patients show an increased focus on unpleasant emotions such as fear or anger, not only in themselves but also in others. Therefore, the detection of emotions in their counterparts shifts towards negative emotions (negativity bias; Domes et al., 2009). This might contribute to an increase in arousal and inner tension (Kramer et al., 2019) with increased reactivity to stress and negative emotions and difficulties in returning to baseline afterward (Crowell et al., 2009; Glaser et al., 2008; Linehan, 1993). These findings overall indicate that the stress response seems to be altered in BPD patients. Expanding these findings, the results from the current study show that the response to relaxation interventions appears similar to those of healthy participants. Therefore, BPD seems to be associated with differences in ANS activity at baseline and during the stress response but not with altered relaxation responses. Whether the detected changes in the ANS, namely the reduced PNS activity at baseline, are a consequence of BPD or if it is a risk factor present before the development of BPD is still unclear. Future longitudinal studies are needed to further investigate this question.

4.5.2 Strengths and limitations

The generalizability of our results is limited since we assessed only female participants. Nevertheless, we chose to accept this limitation since we also limited the confounding effects of sex on HRV. The sample consisted of young adults (23.75±4.39 years for BPD patients and 22.68±2.68 years for HC) since, at this age, most patients start their treatment for BPD. However, a previous study found the influence of ELA on HRV to increase with age (Sigrist et al., 2021b), emphasizing that age is an essential factor affecting HRV and should therefore be considered. While we imposed additional prerequisites in the HC group (no caffeine, alcohol, and nicotine four hours before the experiment, and no intensive sports 12 hours before the experiment), we refrained from implementing them in the BPD group to achieve a higher number of volunteers for the study and to avoid conflicts with the individual treatment plans. During the paced breathing intervention, we did not assess the actual breathing rhythm which would have granted us additional insight, especially concerning the ability of participants to follow the rhythm given during the paced breathing intervention. Therefore it is possible that not all participants successfully followed the breathing rhythm for the duration of the intervention. Despite these limitations, we are convinced these results are noteworthy since this study also has considerable strengths. Our sample size enabled us to detect a small effect (effect size f=.2) with a power of .9. Looking at the study design, we conducted a well-controlled study that followed the recommendations for HRV assessment to collect data of at least 20 participants per cell (Quintana & Heathers, 2014). In addition, our study design conformed with the Vagal Tank Theory (Laborde et al., 2018), enabling us to assess the HRV at rest in response to the relaxation intervention and during recovery. We also followed the recommendations by Quintana and Heathers (2014), employing a counterbalanced within-subjects design, including an adequate baseline and limiting possible confounding factors, while still employing a naturalistic setting. We recruited a realistic sample of BPD patients, avoiding a high selectivity by including patients with comorbid mental disorders. Therefore the results showing an intact psychophysiological relaxation response in realistic DBT patients are especially impactful for developing future interventions.

4.5.3 Future research

Since we found reduced overall psychophysiological relaxation markers in BPD patients but no differences in the relaxation response compared to healthy controls future studies should focus on interventions to improve baseline levels of psychophysiological relaxation. As mentioned above, possible interventions include biofeedback training, mindfulness training, breathing exercises, high-intensity interval training, and psychotherapy focusing on emotion regulation strategies. While there seems to be an association between ELA, BPD, and HRV the exact mechanisms not only in the development of BPD but also in the effect those factors have on the relaxation response are still unclear. Future studies are needed to add additional insights into this complex relationship. Since we tested the relaxation response without a previous stressor future studies should also investigate possible benefits for BPD patients to apply relaxation techniques like breathing exercises to return to baseline level after stressful situations, especially in light of findings indicating that effective recovery from stressors is impaired in BPD. Successful implementation of relaxation interventions could be critical for BPD patients to reduce inner tension without resorting to dysfunctional strategies like suicidal behavior, non-suicidal self-harm, or impulsive behavior.

4.5.4 Conclusion

To our knowledge, this is the first study to investigate a possible distortion of the relaxation response associated with BPD. While we found no differences in the psychophysiological relaxation response between BPD patients and HC, we found significant differences in overall psychophysiological relaxation levels, confirming previous results. This indicates that BPD patients may not lose their ability to relax when exposed to a relaxation intervention, but instead exhibit overall lower relaxation levels. Future studies and treatment interventions should thus focus on increasing the baseline levels of psychophysiological relaxation in BPD patients. This would help to deepen our understanding of possible psychophysiological mechanisms contributing to the development of BPD. A better understanding of these mechanisms would allow for steadily improving the treatment to minimize the suffering of persons affected and their social environment, thereby increasing health and well-being.

5. General Discussion

The objective of this thesis was to gain insight into the characteristics of an effective and standardizable relaxation intervention and to explore the potential involvement of the relaxation response in resilience and the onset of mental disorders. The three projects of this thesis answered the initial research questions as follows:

(1) *Which characteristics should a virtual relaxation intervention possess to be successful?*
Virtual nature interventions can successfully trigger the relaxation response. An increased sense of presence seems to be beneficial.

(2) *Does Early life adversity affect the relaxation response?*
ELA blunts the psychophysiological relaxation response in healthy adults. Various forms of neglect and abuse blunt the psychological relaxation response, while for the physiological relaxation response only emotional abuse in combination with nicotine consumption was found to be significantly associated with a blunted relaxation response.

(3) *Do mental disorders affect the relaxation response?*
The psychophysiological relaxation response of patients with borderline personality disorder appears intact. While baseline levels of the relaxation parameters were lower in BPD patients, the psychophysiological relaxation response did not differ compared to healthy controls.

5.1 Summary of main findings

5.1.1 Virtual nature interventions can successfully trigger the relaxation response

The first study, a systematic literature review, was employed to derive the properties of a successful virtual relaxation intervention from the current literature. Searching the online databases PubMed, Web of Science, and PsycInfo yielded 479 results, of which 18 studies fit the inclusion criteria. While 17 out of 18 included studies found an increase in HRV as a marker for physiological relaxation, there was great heterogeneity in the operationalization of relaxation. The virtual interventions differed, ranging from nature pictures and videos to music videos and mini-games. Still, nature stimuli were the most common intervention (Gaertner et al., 2023). This fits with previous research, identifying nature scenes showing predominantly green scenes with running water to induce relaxation effectively (Snell et al., 2019).

The properties of the virtual interventions also differed greatly, some were presented on a screen (PC or smartphone) and some via head-mounted displays. Some interventions included biofeedback or the option to interact with the virtual environment, while others did not. They also differed in study design, some employing a preceding stressor while others focused solely on the relaxation response. While we planned to include a meta-analysis in this study, those mentioned differences did not allow us to combine the studies statistically. However, a meta-analysis would be needed to investigate which virtual relaxation interventions are most effective, regardless of the frequency with which they are used. Looking at the included subjective questionnaires, we found that most studies indirectly assessed changes associated with relaxation (e.g., via a decrease in anxiety). Only one study assessed subjective relaxation directly, and four focused on the increase in positive affect associated with relaxation. These discrepancies between the operationalizations of relaxation emphasize the importance of a standardized relaxation protocol (Gaertner et al., 2023).

The properties of the interventions that increased physiological relaxation, especially nature stimuli, were found to be successful, either as pictures or videos. In general, results indicate immersion's importance in increasing the effect of virtual nature relaxation interventions on physiological and subjective markers (Gaertner et al., 2023; Knaust et al., 2022). High levels of immersion can be achieved by using videos with sounds instead of pictures (Annerstedt et al., 2013), presenting the video via head-mounted displays instead of PC screens (Liszio et al., 2018), and incorporating the possibility of interacting with the virtual environment (Knaust et al., 2022; Liszio & Masuch, 2019).

Drawing upon the systematic literature review findings, we derived the key properties of an effective virtual relaxation intervention. Those include nature scenes (predominantly green, running water) presented to increase immersion (with sounds, HMD, and interaction possibilities).

5.1.2 Early life adversity blunts the psychophysiological relaxation response in healthy adults

We developed a virtual relaxation intervention following the results of the systematic review. Namely, I recorded a 360° nature video showing mountains, green meadows, trees, and a running river. The video also included the recorded audio. The following studies presented this video with an HMD to increase immersion as a virtual nature relaxation intervention.

Employing a within-subjects design the second project included the assessment of 103 healthy young adults. Two relaxation interventions were tested: the virtual nature intervention developed based on the systematic review and a paced breathing exercise (six breaths per minute; Gaertner et al., under review). As described in the general introduction the mechanisms behind the relaxing effects of nature stimuli and paced breathing are postulated to differ, with nature stimuli relying on psychological mechanisms and paced breathing on physiological mechanisms. Physiological relaxation was assessed with the HRV marker RMSSD, and subjective relaxation was assessed with the RSQ. For ELA we used the Childhood Trauma Questionnaire and the Parental Bonding Instrument.

First, looking at the effectiveness of the relaxation interventions, we found the nature video and paced breathing exercises to successfully increase subjective relaxation. However, only the paced breathing intervention increased physiological relaxation. It is possible that the nature video did not successfully trigger the physiological relaxation response since important properties were missing compared to real-life nature (e.g., tactile and olfactory stimuli). Additionally, since the majority of the sample had no or minimal prior experience with HMDs, they could have been excited by using a new technological instrument, therefore masking the induced physiological relaxation response. Also, there was no possibility of interacting with the environment, which could be added in future studies to increase the sense of presence in the virtual environment.

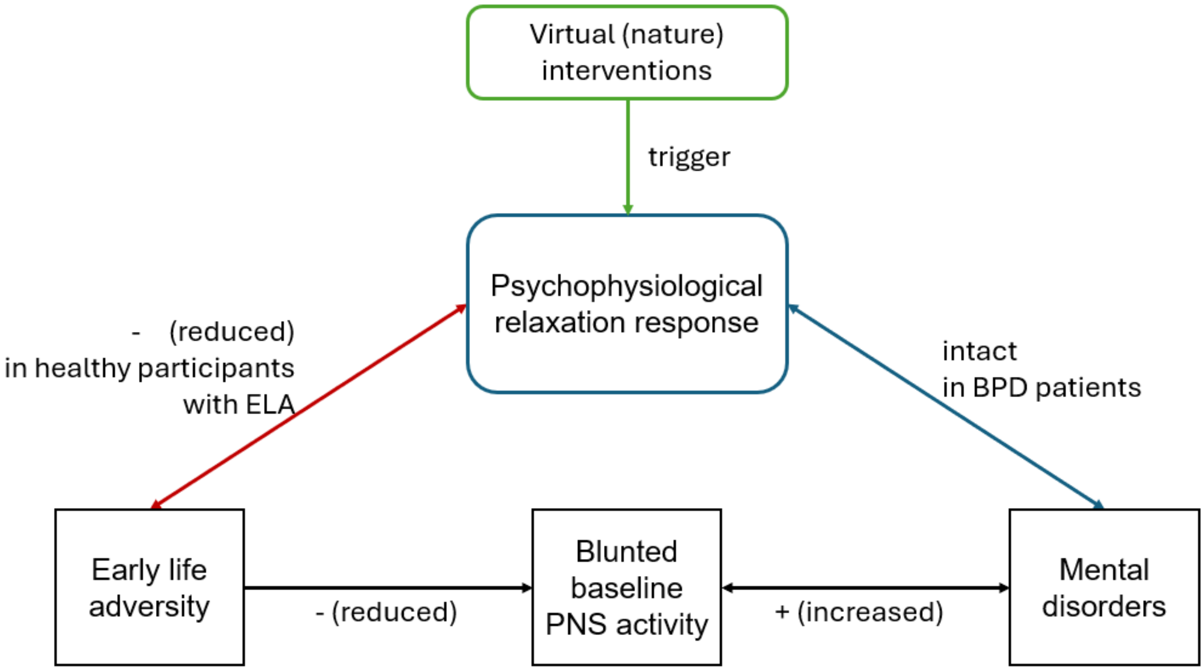
Second, looking at the effect of ELA on the relaxation response, we found subjective relaxation to be blunted in association with lower paternal care, higher paternal overprotection, and higher scores on emotional abuse, physical abuse, and physical neglect. For physiological relaxation, higher emotional abuse scores in combination with nicotine consumption led to a blunted relaxation response. This hints at the possible role of a blunted relaxation response in the association between ELA and the development of mental disorders.

5.1.3 The psychophysiological relaxation response of patients with borderline personality disorder appears intact

For the third project, we collaborated with Ward 61 of the Center for Psychiatry Reichenau, enabling us to assess 20 female BPD patients. Since we employed the same study design as in the second project, we selected a female subset of the sample assessed in the second project as an HC group. While the subjective and physiological relaxation parameters were lower in the BPD patients throughout the experiment, the relaxation response induced by both relaxation interventions did not differ from controls (Gaertner et al., in preparation). These results align with previous studies finding lower values of relaxation parameters in BPD patients at baseline (Ebner-Priemer et al., 2007; Koenig et al., 2016; Maiß et al., 2021; Willis et al., 2018). Additionally, they indicate that the psychophysiological relaxation response is still intact in BPD patients.

In summary, the included studies demonstrated the effectiveness of a virtual nature-based relaxation intervention and a paced breathing intervention in eliciting the psychological relaxation response. However, since only the paced breathing intervention reliably increased physiological relaxation, further investigations are needed to understand the specifics of successfully implementing virtual interventions for triggering the physiological relaxation response. The relaxation response appears blunted in healthy participants with higher levels of ELA but not in patients with BPD (see Figure 14). The subsequent sections will delve deeper into the implications of the projects associated with this thesis.

Figure 14. Overview of the key findings included in this thesis based on the previously defined open questions.
ELA = early life adversity, PNS = parasympathetic nervous system, BPD = borderline personality disorder.



5.2 Operationalization of relaxation

The significant heterogeneity between studies investigating the relaxation response limits the comparability and general conclusions that can be drawn from the existing literature. Therefore, in the following sections, I will summarize the insights about a successful operationalization of relaxation that can be concluded from this thesis.

5.2.1 Measurements

To our knowledge, our projects are among the first to include the Relaxation State Questionnaire (RSQ; Steghaus & Poth, 2021) to assess changes in self-reported relaxation induced by short-term interventions. Both interventions, the nature video and the paced breathing exercise, successfully led to a significant increase in RSQ scores, indicating that the RSQ is a valid instrument to assess short-term changes in subjective relaxation. However, since it is a relatively new questionnaire, further studies are needed to investigate its reliability and validity more closely. Assessing subjective relaxation directly should be part of every future study aiming to measure the relaxation response.

For physiological relaxation, we chose to assess the HRV marker RMSSD. While we initially calculated HF as well, we decided not to use it in the analysis since HF does not adequately present PNS activity with a breathing rhythm of six breaths per minute (Zaccaro et al., 2018). This is just one example of the various factors that need to be considered when assessing HRV. Not only the breathing rate but also individual characteristics (e.g., sex) and behavior before the experiment (e.g., caffeine or nicotine consumption) can influence HRV parameters (Quintana et al., 2016; Quintana & Heathers, 2014; Shaffer & Ginsberg, 2017). While it is impossible to control for every one of those parameters, a concise assessment of as many variables as feasible is highly recommended (Quintana et al., 2016). Despite those challenges in the assessment of HRV, we found an increase in RMSSD induced by the breathing exercise, indicating that HRV is a valid marker for physiological changes linked to the relaxation response.

Discrepancies were observed in the impact of relaxation interventions on subjective and physiological relaxation parameters. Although the nature video increased psychological relaxation, it did not induce significant changes in physiological relaxation. Conversely, the breathing exercise prompted significant increases in both subjective and physiological relaxation levels (Gaertner et al., under review). This discordance between subjective and physiological markers aligns with findings in stress research. (Campbell et al., 2016; Dickerson & Kemeny, 2004; Hernandez-Ruiz et al., 2020). In stress research, only 25% of studies employing a Trier Social Stress Test found significant correlations between physiological (salivary cortisol) and subjective (e.g., anxiety, positive and negative affect) markers (Campbell et al., 2016). This review also highlighted the significance of the timing of subjective marker collection. While pre-intervention ratings of subjective stress were not associated with the physiological parameters, ratings collected during the stressor were significantly correlated with salivary cortisol and HRV (Campbell et al., 2016). Although considering that the endocrine stress response may temporally lag, it can be concluded that subjective states tend to change more rapidly. The correlation between subjective stress levels and HRV suggests that even the swift ANS response may be more closely associated with subjective states during an intervention than evaluating subjective states before and after the intervention. While it certainly poses a methodological challenge to assess subjective relaxation parameters during an intervention, future studies could face this challenge to understand the interaction between physiological and subjective markers involved in the relaxation response more comprehensively. Nevertheless, assessing both subjective and physiological levels of relaxation is essential to a valid operationalization of the relaxation response.

5.2.2 Interventions

When designing the nature video intervention, we followed the results from the systematic review, using a 360° video presented via an HMD with recorded audio to increase the sense of presence in the virtual environment, aiming to bolster the effect the video had on the relaxation parameters (Gaertner et al., 2023). Still, the nature video only increased subjective relaxation in the healthy sample. In contrast, the changes in physiological relaxation did not reach statistical significance (Gaertner et al., under review). However, in the third project, we found changes in both subjective and physiological relaxation induced by the nature video (Gaertner et al., in preparation). These discrepancies in effectiveness indicate that the intervention could not reliably trigger a physiological relaxation response. Factors negatively impacting the nature videos' effectiveness include missing sensory input in addition to audio and visual stimuli, the 4K quality of the video, and missing options to interact with the virtual environment. Improving the video quality or adding interaction possibilities could increase the sense of presence in the virtual environment and, therefore, likely increase the impact on physiological relaxation. To investigate the importance of interaction possibilities on the relaxation response, a future study could compare a recorded 360° video and a computer-generated version of the same environment that enables interaction (e.g., allowing users to pick up rocks and throw them into a river). Adding sensory input could also increase the sense of presence and, therefore, the effectiveness of a virtual intervention. This could be achieved by physically building surroundings that match the texture of the components of the virtual environment, adding heat lamps if it is a sunny scene or fans for the impression of wind. Recent advancements towards lighter, more affordable, and user-friendly VR hardware and software have expanded recreational use and the potential for scientific and therapeutic interventions. The rapid progress in artificial intelligence has also simplified the programming required for computer-generated virtual environments and interactive features, making these tools more accessible to a broader range of researchers. This, in turn, supports the continued expansion of virtual interventions across various fields.

The paced breathing exercise successfully increased subjective and physiological relaxation in healthy participants and BPD patients (Gaertner et al., in preparation, under review). The effects align with previous studies that found not only an increase in PNS activity but also positive subjective changes associated with a breathing rhythm of six breaths per minute (Kromenacker et al., 2018; Russo et al., 2017; Zaccaro et al., 2018). Even though the significant effects indicate that participants completed the breathing exercise, we cannot conclude that with certainty since we did not assess the breathing cycle. A previous study found that some participants could not hold a rhythm of six breaths per minute (Steffen et al., 2021). This might hint at an individual optimal breathing rhythm to maximize PNS activity, which should be investigated further to optimize interventions based on paced breathing.

By applying a nature video and paced breathing exercises in the second and third projects (Gaertner et al., in preparation, under review), we employed one intervention whose mechanisms are postulated to be psychological (nature video) and one whose effectiveness is based on physiological mechanisms (breathing exercise). This distinction between physiological and psychological interventions is also done in stress research. Some stressors are considered to be physiological (e.g., sport, electric shock), while others are psychological stressors (arithmetic tasks, public speaking, uncontrollable situations, including social evaluation; Dickerson & Kemeny, 2004). Depending on individual characteristics, differences were found in the response to certain types of stressors. For example, the stress response of patients with social phobia induced by a physiological stressor did not differ from HC. However, a more substantial increase in salivary cortisol when facing a psychological stressor was linked to social phobia (Furlan et al., 2001). While we did not find differences between HC and BPD patients depending on the type of relaxation intervention (Gaertner et al., in preparation), the results from different types of stressors still indicate that future studies investigating the relaxation response should also consider employing a psychological and a physiological relaxation intervention.

5.2.3 Study design

One major strength of the study design of the second and third projects (Gaertner et al., in preparation, under review) is assessing the relaxation response without a preceding stressor. Relaxation interventions have demonstrated their capacity to positively influence recovery following an acute stressor (Annerstedt et al., 2013). However, integrating stressors with relaxation interventions renders it impossible to distinguish between the recovery following a stressor and the distinct impacts of relaxation interventions. Moreover, assessing PNS activity at baseline, during the intervention, and post-intervention allows comprehensive insights into the entirety of the relaxation response (Laborde et al., 2018).

Even following these insights, there are still open questions about the design of an optimal relaxation intervention, for example, concerning the length of an intervention or the effects of a relaxation training program. Descriptively, our results indicated the most significant effects on physiological relaxation within the first half of the interventions, hinting that interventions lasting five minutes could already be effective and interventions lasting too long might induce boredom or other aversive states that impact the relaxation parameters (Gaertner et al., in preparation, under review). Therefore, future studies should compare various intervention durations to find the most efficient length that is both concise and feasible yet effective. Similarly, it is unclear how long the recording after an intervention must be to assess the recovery period adequately. Again, the descriptive results of the studies included in this thesis hint that ten minutes might be longer than necessary for the PNS to return to baseline levels after relaxation interventions (Gaertner et al., in preparation, under review). Nevertheless, these directives stem from descriptive rather than statistically significant findings, warranting further investigation.

5.3 Role of the relaxation response in resilience and development of mental disorders

The role of the relaxation response in the development of mental disorders has scarcely been investigated so far. However, HRV as a marker for physiological relaxation at baseline shows a robust link with health and resilience (Carnevali et al., 2018; Heiss et al., 2021). Characteristics associated with high levels of resilience, like optimism, active coping, and prosocial behavior, are linked with higher baseline HRV (Carnevali et al., 2018). While a low baseline HRV is discussed to be a transdiagnostic marker for mental disorders (Beauchaine & Thayer, 2015), there still seem to be disorder-specific effects on baseline HRV. Though most mental disorders are associated with a lower HRV at baseline (e.g., anxiety disorders, autism, depression, panic disorder, schizophrenia, posttraumatic stress disorder, BPD; Beauchaine & Thayer, 2015; Pham et al., 2021; Shaffer & Ginsberg, 2017), eating disorders, especially anorexia nervosa, are linked to heightened baseline HRV. A possible explanation for this link is an increase in PNS activity when the body is threatened with starvation. PNS activity increases to preserve energy and resources, leading to an increase in baseline HRV (Heiss et al., 2021). Therefore, while, in general, a high baseline HRV seems to be linked with health and resilience, there appears to be an ideal range for HRV at rest, with values too high or too low being associated with mental disorders (Heiss et al., 2021).

To investigate the possible role of the relaxation response in resilience and the development of mental disorders, the included studies focused on the relaxation response in healthy adults who experienced ELA and patients with BPD. While various forms of abuse, neglect, and parental bonding were found to blunt the subjective relaxation response, only emotional abuse blunted the physiological relaxation response in a healthy sample (Gaertner et al., under review). Looking at physiological relaxation, if the effect of smoking as a potential covariate was added, only the interaction between emotional abuse and smoking remained significant (Gaertner et al., under review). While emotional abuse blunted the physiological relaxation response in itself, the significant interaction with nicotine consumption hints at a link between ELA and smoking, namely an increased nicotine consumption associated with increased exposure to ELA. Previously, it had already been shown that ELA increases the risk for negative health-related behaviors, like nicotine consumption (Duffy et al., 2018). Nicotine consumption, in turn, is associated with lower HRV values (Dinas et al., 2013). Therefore, it is possible that the effect of emotional abuse on HRV values was found due to its close link with nicotine consumption. In that case, it would indicate that nicotine consumption is the driving factor linking ELA exposure to a blunted physiological relaxation response and that healthy adults show an intact physiological relaxation response. In contrast, their subjective relaxation response is blunted. This intact physiological relaxation response could be a sign of resilience in a healthy sample, while the distorted subjective relaxation response could be linked to an increased negativity bias associated with ELA (Watters & Williams, 2011).

Looking at the BPD patients, we found high scores on all subscales of the Childhood Trauma Questionnaire, especially emotional abuse according to previously reported thresholds (Bernstein et al., 2003; Gaertner et al., in preparation), which fits with previous research that found BPD patients to be 13.91 more likely to have experienced ELA compared to healthy adults and 3.15 times more likely to have experienced ELA compared to patients with other mental disorders (Porter et al., 2020). We expected a blunted relaxation response in BPD patients, similar to healthy adults who have experienced ELA. However, we found an intact psychophysiological relaxation response in BPD patients instead (Gaertner et al., in preparation).

While one potential rationale for this unexpected result includes inadequate measurement of the outcome variable, this is highly unlikely. As described in the measurements section of the discussion (see section 5.2.1), we followed the guidelines for recording HRV data (Quintana & Heathers, 2014) and employed valid measurements for psychological and physiological relaxation.

Another possible explanation focuses on the employed interventions. While we assessed two relaxation interventions, both were assessed in artificial settings, differing from situations that induce relaxation in everyday life. Although patients with BPD exhibit an intact relaxation response during acute relaxation interventions, it is possible they do not experience the same response in everyday situations that typically induce relaxation in healthy individuals, leading to lower baseline levels of subjective and physiological relaxation. Situations that induce relaxation in everyday life are often interpersonal situations in which safety signals can be detected (Brosschot et al., 2017). Learning to detect those safety signals happens mostly during early childhood, which is most likely impaired when experiencing ELA (Brosschot et al., 2016; Porges, 2015). Not detecting those signals is associated with the development of different mental disorders, an increased negativity bias, and a reduced HRV at baseline (Brosschot et al., 2016; Porges, 2022; Thayer et al., 2012). This, in turn, limits prosocial behavior and the forming of long-lasting interpersonal relationships, which can also be observed in BPD patients (Porges, 2022; World Health Organization, 1992). This potential lack of activation of the relaxation response in everyday life is likely linked to increased inner tension and decreased relaxation parameters at baseline, which are associated with BPD (Koenig et al., 2016; Maiß et al., 2021; Ridolfi et al., 2019; Schilling et al., 2018). To conclude, while the psychophysiological relaxation response in BPD patients appears intact, they possibly lack the detection of safety signals in everyday situations, leading to unfavorable consequences, like a decrease in prosocial behavior. However, further investigation is needed to examine the relaxation response induced by everyday situations (e.g., interpersonal situations) in BPD patients. At this point, it is assumed that the relaxation response in BPD patients differs between specific relaxation interventions like paced breathing and everyday (interpersonal) situations, which should be investigated in future studies.

A third potential rationale for the unexpected findings could be that the sample we gathered still exhibits resilience while reporting highly adverse childhoods. Although they all had a diagnosis of BPD, they were deemed healthy enough to participate in a DBT treatment program, were not exhibiting acute suicidal behavior or consuming drugs, and generally maintained a focus on future perspectives. Additionally, their respective therapists deemed the patients fit for the study, likely further aiding in selecting a relatively resilient sample of BPD patients. Following the adaptive calibration model, changes in ANS activity associated with ELA can also be interpreted as adaption to adverse experiences during childhood. Physiologically, leaning towards a reduced PNS activity and, therefore, a disinhibited SNS might have been vital for survival, even though it negatively impacts well-being and prosocial behavior in the long run (Del Giudice et al., 2011). On a behavioral level, symptoms associated with BPD also show adaptive qualities. For example, dissociation can be interpreted as adaptive when faced with traumatic events, unbearable thoughts, or emotions. Therefore, developing BPD in association with a highly adverse childhood can be interpreted as an adaptive response to the environment, therefore exhibiting some form of resilience. Consequently, an intact psychophysiological relaxation response in BPD patients might indicate a form of resilience.

To summarize, we found patterns in the psychophysiological relaxation response in healthy adults who experienced ELA and BPD patients to differ from each other, even though BPD patients experienced high levels of ELA. Therefore, when assessing ELA, mental disorders should always be considered as additional factors influencing the impacts of ELA on outcome variables. This further strengthens previous studies that found the effect of ELA on HRV depending on the presence of mental disorders (Sigrist et al., 2021a; Stone et al., 2018).

5.4 Limitations and future questions

The studies included in this thesis employed a well-controlled experimental design to assess HRV, including controlling for or reporting important sample characteristics (Quintana et al., 2016; Quintana & Heathers, 2014). While the measurement of PNS activity via HRV is considered valid, only PNS activity was measured as a marker for the physiological relaxation response (Gaertner et al., in preparation, under review).

This leaves the question regarding the involvement of the SNS or the endocrine system in the relaxation response unanswered. Examining the stress response reveals its reliance on the interaction among the SNS, PNS, and the hypothalamic-pituitary-adrenal axis (HPA; Andrews et al., 2013; Del Giudice et al., 2011; Ulrich-Lai & Herman, 2009). The PNS initiates the quickest response to an acute stressor by disinhibiting the SNS, and the HPA takes the longest to activate. Nonetheless, all three systems remain crucial components of the acute stress response during the subsequent recovery phase (Del Giudice et al., 2011; Engert et al., 2010; Wadsworth et al., 2019). These systems are postulated to affect each other, with a dysregulation in one system possibly influencing the other systems (Andrews et al., 2013). This interplay of the systems is a central aspect of the adaptive calibration model (Del Giudice et al., 2011). The model suggests various activation patterns influenced by early life experiences, impacting responses to threat and safety signals throughout the lifespan (Del Giudice et al., 2011). The activity of the three stress systems in relaxation shows an increase in PNS and a decrease in SNS activity. So far, very little research has investigated the changes in the HPA associated with relaxation. However, the first studies found reduced salivary cortisol and, therefore, HPA activity associated with short-term relaxation interventions like guided imagery (Jones et al., 2014) or progressive muscle relaxation (Pawlow & Jones, 2002). While these results hint at an interplay of PNS, SNS, and HPA in the acute relaxation response, future studies are needed to investigate this complex relationship in detail.

While the assessment of a representative sample of BPD patients certainly is a strength of the third project (Gaertner et al., in preparation), it leaves the question of possible distortion of the relaxation response associated with other mental disorders open. A previous study also investigated the changes in PNS activity induced by watching a nature video in patients with major depression and HC. This study found a blunted relaxation response in patients compared to HC (Matsui et al., 2016), while our study found an intact relaxation response in BPD patients (Gaertner et al., in preparation). This difference suggests that there are disorder-specific effects on the relaxation response, emphasizing the need for future research to explore the relationships between the relaxation response and mental disorders.

Another aspect to consider in future research is the potential differentiation between relaxation as a trait and state. For anxiety and mindfulness, the distinction between state and trait is typically made when assessing those parameters, indicating that there are fundamental differences between state and trait (Bravo et al., 2018; Endler et al., 1991). The projects included in this thesis seem to support a similar relaxation distinction. For example, differences between BPD patients and HC were found when looking at the baseline values of relaxation parameters (trait) but not in the relaxation response (state; Gaertner et al., in preparation). This distinction would also fit with the Vagal Tank Theory (Laborde et al., 2018), which emphasizes a fundamental difference between assessing physiological markers during rest and responding to an intervention. Future studies should clearly state whether they investigate relaxation as a trait (baseline parameters) or a state (relaxation response).

When investigating the influence of ELA on the relaxation response in a healthy sample, we collected a sample with relatively low scores on the ELA questionnaires (Gaertner et al., under review). For example, all CTQ subscales indicated a weak exposure to ELA according to previously reported thresholds (Bernstein et al., 2003). Future studies should aim to assess a sample with a broader range in ELA to investigate further a possible distortion of the relaxation response associated with ELA. Since this thesis concluded that the effects of ELA seem to differ depending on the development of mental disorders, future studies should aim to investigate the relaxation response by comparing a healthy sample with low exposure to ELA, a healthy sample with high exposure to ELA, and a sample with mental disorders to shed more light into the complex relationship between ELA, resilience and the development of mental disorders. Alternatively, ELA and mental disorders could both be assessed dichotomously (yes/no), allowing a four-cell design to disentangle them (e.g., following the design by Heim et al., 2008). For HRV as a baseline relaxation marker, a previous study found no differences between a healthy sample and depressive patients with low exposure to ELA. However, patients suffering from depression and high levels of ELA showed lower baseline HRV values compared to the other groups (Stone et al., 2018). Here, ELA and not the development of a mental disorder seems to be the differentiating factor leading to lower baseline HRV levels. Whether these effects can be transferred to other mental disorders and the relaxation response is unclear and warrants further investigation.

While the second and third projects included a paced breathing intervention and a nature video to consider the possible differences between psychological and physiological relaxation interventions, both were short-term interventions (Gaertner et al., in preparation, under review). This leaves the question regarding the effects of long-term relaxation interventions unanswered. Results for breathing exercises and mindfulness interventions indicate favorable physiological effects associated with long-term interventions in healthy participants. For example, one study found an increase in HRV associated with a ten-day mindfulness intervention (Kirk & Axelsen, 2020). Looking at breathing exercises, an intervention lasting four weeks and including 15 minutes per day of alternate nostril breathing found a significant decrease in pulse rate, respiratory rate, and diastolic blood pressure after the intervention (Dhungel et al., 2008). However, a study investigating the effect of a four-week intervention of daily slow, deep breathing on patients with irritable bowel syndrome found no changes in physiological markers like HRV (Jurek et al., 2021). Similarly, a six-week program using the same intervention in patients with lower extremity joint pain found no significant effects on pain and physiological parameters like HRV (Larsen et al., 2019). The variation in the efficacy of long-term interventions depending on the prevalence of health and diseases in the sample underscores the need to study their effects on samples with mental disorders directly. Results observed in healthy participants seem not necessarily translatable to samples with mental disorders.

A possible successful relaxation training that positively impacts the relaxation parameters long-term could be essential for persons who have experienced ELA or another form of highly adverse event, like accidents or sudden deaths of close relatives. It could be possible for such an intervention to increase baseline relaxation parameters like HRV, which in turn are associated with resilience (Carnevali et al., 2018) and more favorable outcomes of psychotherapy (Sigrist et al., 2021b; Weise et al., 2021). For patients suffering from mental disorders, psychotherapy alone (Garakani et al., 2009) or in combination with biofeedback (Caldwell & Steffen, 2018) or breathing exercises (Chien et al., 2015) was found to increase baseline HRV. However, the effect seems to be disorder-specific since an increase in HRV associated with psychotherapy was found in patients with panic disorder (Garakani et al., 2009) but not in patients with major depression (Neyer et al., 2021).

The results of the third project, showing reduced relaxation parameters at baseline but an intact relaxation response in BPD patients (Gaertner et al., in preparation), could indicate that BPD patients are unable to detect safety signals in everyday life, leading to chronic disinhibition of the SNS. While the diminished ability to detect safety signals is associated with mental disorders in general (e.g., anxiety disorders, depression, posttraumatic stress disorder, schizophrenia), it is also linked to an increased negativity bias (Thayer et al., 2012). An increased negativity bias was also found in BPD patients, who exhibited an increased focus on unpleasant emotions such as fear or anger in themselves and others (Domes et al., 2009). Interventions to reduce the negativity bias have found promising results for mindfulness-based stress reduction training, which was found to reduce the negativity bias up to eight weeks past intervention (Harp et al., 2022). Trait mindfulness, in general, is associated with a decreased negativity bias (Ho et al., 2015). Part of mindfulness is awareness and acceptance of experiences like emotions, not rating them as positive or negative (Kabat-Zinn, 1994). Similarly to mindfulness, a core aspect of acceptance and commitment therapy (ACT) is active acceptance of unpleasant thoughts or emotions. This therapeutic approach was found to be effective for various mental disorders (e.g., depression and psychosis; Coyne et al., 2011; Morris et al., 2024). An intervention based on ACT was also found effective in the treatment of BPD patients, reaching similar results to a DBT-based intervention, significantly decreasing symptom severity and increasing mindfulness (Reyes-Ortega et al., 2020). Looking at the effect on physiological markers in BPD patients, an intervention based on acceptance of emotions was found to be successful in increasing HRV during a social rejection task (Dixon-Gordon et al., 2017). In summary, strategies based on mindfulness and acceptance were found to positively affect subjective and physiological parameters linked to relaxation in patients with mental disorders. The conclusion that such interventions positively affect the detection of safety signals seems close at hand. Still, future studies are required to explore interventions and their specific impact on detecting safety signals and baseline relaxation parameters in patients with mental disorders.

While employing virtual relaxation interventions for research purposes was a central part of the three projects included in this thesis, diagnosis and treatment of mental illnesses is another field in which the use of VR has grown in recent years and continues to be an expanding area (Schröder et al., 2023; Wiebe et al., 2022). For instance, psychotherapists in Germany have been able to prescribe digital health applications since 2019 (*digitale Gesundheitsanwendungen*), which are designed either to help patients manage the waiting period until a therapy spot becomes available or to complement ongoing psychotherapy (Bundesministerium für Gesundheit, 2024). They offer exposure therapy, psychoeducation, daily assessments, and other interventions, traditionally done using pen and paper in a digital format. While the most common application of VR in therapy so far is exposure therapy (Baghaei et al., 2021; Schröder et al., 2023; Wiebe et al., 2022), there are also first implementations that aim for an increase in relaxation. For instance, patients with various mental health conditions (anxiety, depression, bipolar disorder, and psychosis) experienced a significant decrease in negative affect after regularly watching nature-themed videos over ten days (Veling et al., 2021). Another study found similar effects on affect in patients who viewed VR nature videos for at least three weeks in addition to outpatient therapy (Humbert et al., 2023). These results indicate that interventions similar to the nature relaxation intervention implemented in two projects of this thesis (Gaertner et al., in preparation, under review) can also be successfully included in psychotherapy. The first results show that virtual relaxation interventions can successfully be implemented in acute psychiatric wards, increasing positive and decreasing adverse effects in patients. Additionally, violent incidents and restrictive practices were significantly reduced during the weeks in which the VR relaxation intervention was available (Riches et al., 2023b). Since those interventions are not only reported to be effective but also user-friendly (Humbert et al., 2023), they represent a promising addition to classical psychotherapy.

However, there are notable shortcomings in the current implementation of VR-based interventions in psychotherapy. The effective integration of VR-based interventions requires further training for psychotherapists, a component largely absent from most training programs to date. Furthermore, most existing VR videos and environments are based on Western cultural contexts, which may limit their applicability and relevance for people from other cultural backgrounds (Emmelkamp & Meyerbröker, 2021). Additionally, many of the current studies suffer from methodological weaknesses (e.g., no randomized controlled trial) and involve homogenous samples limited mainly to patients with anxiety disorders and young to middle-aged adults, which impacts the reliability and generalizability of the findings (Baghaei et al., 2021; Schröder et al., 2023; Wiebe et al., 2022). Future research needs to address these issues to improve the robustness of results.

While virtual environments show promise as a foundation for both scientific and therapeutic relaxation interventions, they also offer broader applications. Guided imagery (Bigham et al., 2014) is a well-established technique to promote relaxation in research and therapy. However, its effectiveness can vary based on a person's level of suggestibility (Milling et al., 2010). For individuals who are less responsive to guided imagery, the ability to create their own virtual environment tailored to their preferences and needs could be especially beneficial. Another common intervention involves guiding participants to imagine a "safe place" and explore its sensory details, an exercise shown to increase feelings of safety, help patients cope with complex medical procedures, and reduce subjective stress in response to an acute stressor (Schmidt et al., 2024). Allowing individuals to design their own personalized "safe place" in a virtual environment could further amplify the positive effects of this exercise. Additionally, users could incorporate interactive features if desired, creating a highly individualized and immersive experience that enhances the therapeutic benefits of the safe place exercise.

Such a virtual environment could not only be used in experiments or as a relaxation intervention in psychotherapy but also aid in pursuing other therapeutic goals. For instance, patients with mental health disorders, particularly those diagnosed with dissociative disorders and panic attacks, exhibit impaired interoceptive accuracy, which describes their difficulties in sensing and interpreting their internal bodily signals (Schäflein et al., 2018). Technological devices like smartwatches, designed to track physiological signals in daily life, can alert users when physiological parameters like HRV indicate increased stress, prompting them to engage in relaxation activities. Upon receiving such stress alerts, patients could first focus on their thoughts, emotions, and physiological sensations to better understand how stress feels for them. Second, they would immerse themselves in their personalized virtual environment to effectively reduce stress and enhance relaxation. Once their physiological signals indicate a sufficient reduction in stress, as tracked by the device, patients could refocus on their physiological sensations to observe the calming effects induced by the virtual safe place. Over time, this approach could provide a personalized and effective relaxation tool but also help improve interoceptive accuracy.

The relaxing effects of a personalized virtual environment could be further improved by integrating physiological data from, for example, a smartwatch. In addition to alerting users to stress or relaxation levels, incorporating biofeedback into the virtual environment would allow patients to see real-time changes in their physiological signals, such as heart rate. This feedback could help them learn to actively influence these signals, thereby improving interoceptive accuracy and teaching them effective self-relaxation techniques.

These ideas offer a glimpse into the potential future of experimental and therapeutic interventions using VR. As VR devices become more widespread in recreational settings, they are likely to evolve into standard tools for a broad audience, making their integration into psychotherapy more practical. Additionally, advancements in artificial intelligence are expected to lower the technical barriers associated with developing specific interventions (e.g., computer-generated environments), thereby expanding access to a broader range of researchers and psychotherapists.

5.5 Concluding remarks

With this thesis, I aimed to shed light on the relaxation response and its possible role in resilience and the development of mental disorders. Adequate operationalization of relaxation is a prerequisite to investigating the relaxation response systematically. To summarize, relaxation should be assessed on subjective and physiological levels for the entirety of the relaxation response (at baseline, during the intervention, and while recovering from the intervention). Recognizing potential differences between psychological and physiological interventions is crucial when examining the relaxation response. These findings regarding the operationalization of relaxation are intended to serve as a foundation for future research.

In the first step, the systematic literature review indicated virtual nature interventions as promising options for standardized and effective relaxation interventions (Gaertner et al., 2023). Nevertheless, the findings from the intervention studies, which involved a relaxation intervention utilizing a virtual natural setting, did not consistently reveal a significant increase in physiological relaxation induced by the intervention (Gaertner et al., in preparation, under review). This emphasizes the need for future studies to find the ideal way to present a virtual nature relaxation intervention, maximizing its effect on the relaxation response. As a second step, we investigated ELA and BPD as possible factors influencing the relaxation response. In a healthy sample, ELA was associated with a blunted psychophysiological relaxation response (Gaertner et al., under review). Comparing BPD patients with HC showed an intact relaxation response but lower baseline relaxation parameters in BPD patients (Gaertner et al., in preparation). Based on the findings of this thesis, it becomes apparent that assessing the combination of mental disorders and ELA is crucial. The impact of ELA on the relaxation response appears to vary depending on the presence of mental disorders.

A potential area of focus for future studies involves investigating interventions based on mindfulness, acceptance, and relaxation and their long-term impact on relaxation parameters in healthy populations and populations with mental diseases. Such interventions could target enhancing baseline relaxation parameters in individuals with mental disorders or bolstering resilience in vulnerable populations. In the long run, those interventions could be included in the treatment of mental disorders, leading to the extension or development of effective, evidence-based psychotherapeutic interventions. Improving evidence-based interventions is crucial, as they, along with the flexibility of the treating psychotherapist, form the cornerstone of treatment for all mental disorders (Luyten, 2015). By further improving our understanding of the development of mental disorders, we can optimize treatments and strengthen resilience, decreasing the number of patients affected by mental disorders.

6. Supplementary materials

6.1 Email confirmation of submission to *Scientific Reports*

Email confirming the submission of the manuscript “Early Life Adversity Blunts The Subjective And Physiological Relaxation Response In Healthy Adults” to *Scientific Reports*. According to the submission portal, the manuscript is in peer review since Juli 02, 2024.

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