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Psychobiological adaptation to childhood adversity

The role of contextual and individual factors

Wesarg, C.

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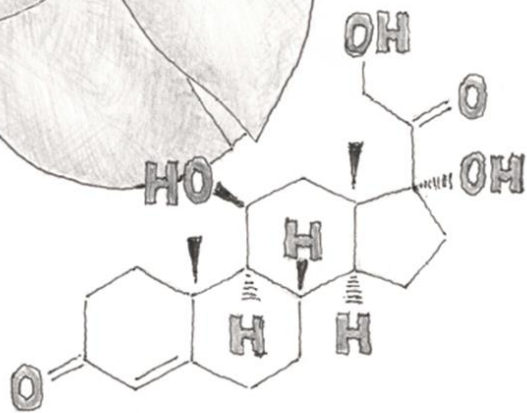
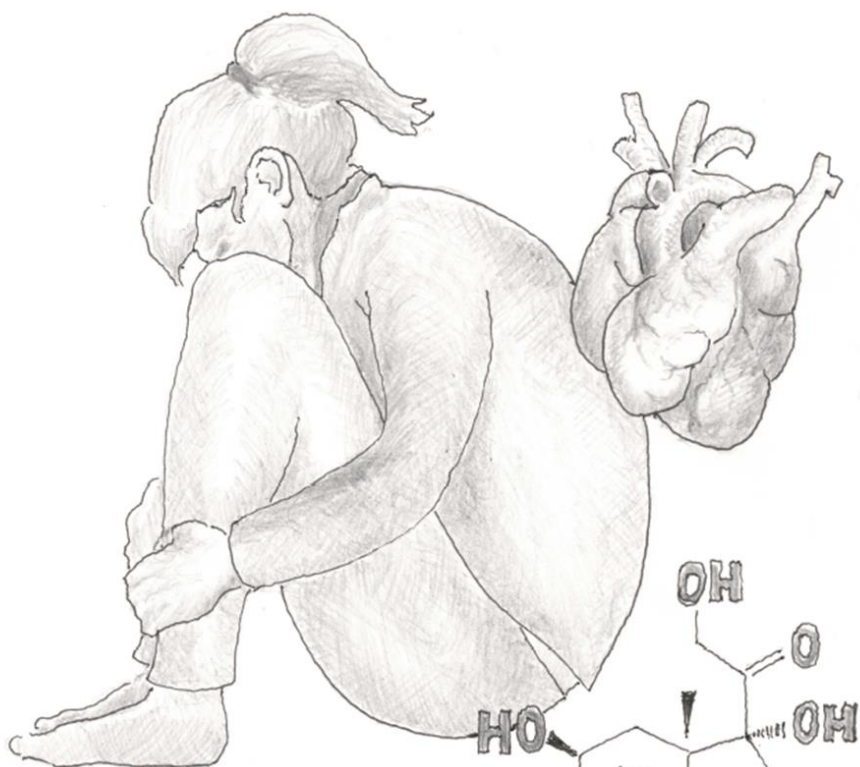
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General introduction

Chapter 1

Imagine two toddlers, Tom and Sarah. Tom grows up in a family with warm and caring parents. Since birth, he has had an ‘easy’ temperament and has delighted his parents. Given the lack of financial resources to afford housing in a safe district, the family lives in an urban area characterized by poverty and neighborhood violence. In a prosperous district on the other side of the city, Sarah grows up in a family in which the father is almost never present due to work, and the mother is feeling highly stressed due to the demands that come with parenting. As Sarah has a ‘difficult’ temperament, her mother feels overwhelmed and regularly reacts harshly to Sarah’s behavior. Ten years later, Tom enjoys going to school where he sees his friends, whereas Sarah regularly skips school as she feels excluded by her peers and fears going there. Twenty years later, Tom is in good mental health, whereas Sarah regularly experiences symptoms of anxiety and depression.

Sarah and Tom are examples of an unacceptably high number of children growing up under conditions of adversity, experiencing abuse, neglect, separation from caregivers, chronic poverty, or neighborhood violence. It is estimated that about 12% of children in Western societies are exposed to physical abuse at some point during childhood (Moody et al., 2018), which rises to almost two thirds of children when other forms of adversity are considered (Merrick et al., 2018). Childhood adversities markedly increase the risk for psychopathology (R. C. Kessler et al., 2010), which has in part been attributed to alterations in stress physiology and brain function (McLaughlin, Weissman, et al., 2019; Raymond, Marin, et al., 2018). However, not all individuals exposed to adversity develop negative mental health outcomes (Koss & Gunnar, 2018; Oh et al., 2018). This raises two important questions: How do childhood adversities become biologically embedded to affect mental health outcomes? And what explains the individual variability in developmental trajectories after childhood adversity, in that Sarah develops psychopathology in the long run, whereas Tom stays in good mental health?

In this doctoral thesis, we address these open questions by reviewing evidence on adversity-related alterations in the functioning of the biological stress systems—including the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system (ANS)—which have been proposed as mechanisms through which childhood adversity becomes biologically embedded (Berens et al., 2017). We further examine whether different adversity types are linked to different types of alterations in the functioning of the stress systems. Finally, we investigate

whether individual factors such as genetic constitution and temperament influence psychobiological adaptation in the context of childhood adversity.

Although empirical and review work presented in this dissertation spans all developmental periods, a specific focus is placed on early childhood—the developmental period during which the biological embedding of childhood adversity likely occurs, and which provides a window of opportunity for early intervention (Cicchetti et al., 2011; Heim et al., 2019). A better understanding of contextual and individual factors that influence developmental trajectories after childhood adversity will help to identify those individuals who are most in need of support. We hope that knowledge on pathways leading from adversity to psychopathology gained in this doctoral work will inform prevention and treatment approaches, and thereby contribute to public health promotion.

Defining childhood adversity

Throughout this dissertation, childhood adversity is defined as “experiences that are likely to require significant adaptation by an average child and that represent a deviation from the expectable environment” (McLaughlin, 2016, p. 363). According to this definition, deviations from the expectable environment can consist of the presence of unexpected experiences which represent a significant threat to the child (e.g., violence exposure) or the absence of environmental input which would be necessary for the brain to develop normally (e.g., lack of a caregiver or sufficient nutrition; see also McLaughlin, Sheridan, & Lambert, 2014; Sheridan & McLaughlin, 2014). Further, adversities can either be chronic (e.g., poverty) or comprise single events that are severe enough to require significant adaptation by the child (e.g., sexual abuse; McLaughlin, 2016). The definition by McLaughlin (2016) was chosen as it is broad enough to span diverse types of adversity that have been linked to negative health outcomes, while being specific enough to exclude less stressful, rather normative experiences such as moving to a new home.

Allostatic load: A conceptual framework for studying the effects of childhood adversity on health

In this dissertation, we draw back on the allostatic load framework (McEwen & Stellar, 1993) to study the effects of stress. It describes the link between stress and the development of disease based on allostasis, referring to the organism’s ability to achieve homeostasis through change (McEwen & Stellar, 1993). A change is attained through the production of mediators of the stress response such as adrenaline, cortisol and other chemical messengers, which promote adaptation in the aftermath

of acute stress (McEwen, 2005). However, chronic activation of the stress systems leads to a “wear-and-tear” on the body, which can impair mental and physical health through maladaptive effects on brain plasticity and metabolic, immune, and cardiovascular pathophysiology, referred to as “allostatic load” (McEwen & Gianaros, 2011). When a challenge exceeds an individual’s coping resources, allostatic overload occurs, resulting in an extreme state in which the stress systems are constantly activated (Fava et al., 2019). Considerable evidence has associated childhood adversity with elevated allostatic load in adulthood, which in turn has been associated with poor health outcomes (Finlay et al., 2022; Guidi et al., 2021; Misiak et al., 2022).

Childhood adversity and the stress systems

An extensive body of literature suggests that the functioning of the stress systems is shaped by exposure to childhood adversity (Koss & Gunnar, 2018; McCrory et al., 2010). Yet we have little understanding of the type of alterations in stress system functioning that are likely to be observed in the context of childhood adversity—particularly in early childhood. As one of the main aims of this dissertation was to review the effects of childhood adversity on cortisol as a measure of HPA axis functioning, and on heart rate variability (HRV) as a measure of autonomic functioning, the following section is dedicated to providing background information on both stress systems and their interplay in challenging situations.

Basal and reactive states of the stress systems

From the first days of life onwards, the perception of a stressor leads to the activation of two distinct but interrelated biological systems aimed at preparing an individual to cope with changing situational demands: the ANS providing a rapid response through its sympathetic and parasympathetic branches, and the HPA axis providing a slower, more protracted response. Both stress-response systems are activated, monitored and regulated by prefrontal and limbic structures, most prominently the medial prefrontal cortex, the hippocampus and the amygdala (Ulrich-Lai & Herman, 2009). They exert their effects on the organism via physiological ‘stress mediators’, including hormones such as cortisol, and catecholamines such as adrenaline and noradrenaline (McEwen, 1998a; McEwen & Seeman, 1999). Given interactions between various stress mediators and cross-communication between both stress systems, it is not surprising that the complex coordinated stress response has been described as a “neuro-symphony of stress” (Joëls & Baram, 2009). Next to their prominent role in mounting a stress response, the ANS and the HPA axis both hold important functions under non-stressed

(‘basal’) conditions, such as maintaining homeostasis of the internal environment and ensuring energy availability (Herman et al., 2016; R. W. Shields, 1993). Extensive research has related experiences of childhood adversity to alterations in both basal and reactive states of the stress systems (Brindle et al., 2022; Bunea et al., 2017)—which is why they are both considered in the framework of this dissertation.

The hypothalamic-pituitary-adrenal (HPA) axis

The first biological mediator of the adversity-psychopathology link that is of interest in this dissertation is cortisol, one of the ‘end products’ of the HPA axis (Elder et al., 2014). The HPA axis is a hormonal axis that connects the central nervous system to the endocrine system. Exposure to a stressor triggers activation of the HPA axis (see Fig. 1). Neurons located in the paraventricular nucleus of the hypothalamus release corticotropin-releasing hormone (CRH), which then binds to receptors at the anterior pituitary, inducing the secretion of adrenocorticotrophic hormone (ACTH) into the blood stream. ACTH then binds to the adrenal cortex, triggering the release of glucocorticoid hormones such as cortisol (Charmandari et al., 2005). Among the wide range of physiological effects that cortisol has in the body, it is critically involved in metabolism by mobilizing energy resources while suppressing digestion and reproduction (Kudielka & Kirschbaum, 2005).

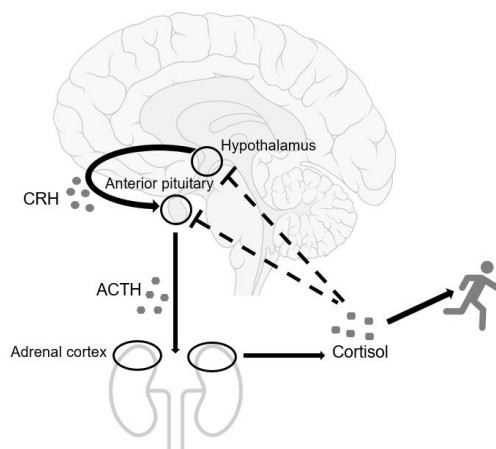


Figure 1. Schematic representation of the hypothalamic-pituitary-adrenal (HPA) axis

Note. CRH = corticotropin-releasing hormone; ACTH = adrenocorticotrophic hormone. Dashed arrows represent inhibition resulting in a negative feedback loop. Adapted from *Brain human sagittal section*, by P. J. Lynch and C. C. Jaffe, 2006, distributed under a Creative Commons Attribution 2.5 Generic license.

A cortisol response to stress can be observed in infants (e.g., Beijers et al., 2017) just as in adults (Kudielka et al., 2004). From a temporal perspective, cortisol levels increase within minutes, reaching their peak level between 20-40 min after stressor onset, and recover within 60 min after stressor cessation (Dickerson & Kemeny, 2004). As prolonged and excessive cortisol release can exert detrimental effects on the brain, body, and health, various feedback loops at different levels of the HPA axis ensure that the system returns to homeostasis (Nicolaidis et al., 2014). The self-inhibiting function of the HPA axis is primarily mediated by glucocorticoid receptors to which cortisol binds at the level of the hippocampus, hypothalamus or pituitary, thereby suppressing further HPA axis activation and allowing cortisol to return to baseline levels (see Fig. 1; de Kloet, 1991; Reul & de Kloet, 1985; Tsigos & Chrousos, 2002).

The cortisol stress response is superimposed on a diurnal cortisol rhythm, which is characterized in adults by cortisol levels that peak about 30 min after awakening, sharply decline over the next hour or two, and more gradually decline during the rest of the day (Fries et al., 2009; Pruessner et al., 1997). While a diurnal cortisol rhythm is established during the second half-year of life (de Weerth et al., 2003), it becomes more like that of adults throughout early childhood (Baeumler et al., 2013; Saridjan et al., 2010; Tribble et al., 2015; Watamura et al., 2004). Given differences in basal cortisol concentrations throughout the day, it is recommended to register and—if possible—standardize time of day in the measurement of basal cortisol and cortisol reactivity (Hansen et al., 2008). A widely used approach yielding a short-term measure of HPA axis functioning is to assess the amount of circulating cortisol in saliva once or multiple times throughout the day (Kirschbaum & Hellhammer, 1994). In the present dissertation, we draw back on various parameters of diurnal cortisol, including mean concentrations at different collection time points, total daily cortisol production, and dynamic parameters such as the diurnal slope (see also Hulett et al., 2019).

To inform researchers in deciding on a cortisol sampling protocol, a range of methodological studies have revealed recommendations that pertain to school-aged children and adolescents (Michels et al., 2012; Rotenberg et al., 2012), and adults (Hruschka et al., 2005; Kraemer et al., 2006; Segerstrom et al., 2014). Yet recommendations on reliable cortisol sampling times for early childhood studies are lacking. In this light, it is not surprising that early childhood studies have adopted very different cortisol sampling protocols, ranging from one salivary sample on one day (e.g., Cicchetti et al., 2011) to multiple samples over multiple days (e.g., Scher et al., 2010). Given that we aimed to investigate HPA axis functioning in toddlerhood

in the framework of this thesis (see Chapter 6), a secondary aim was to examine what times of day would be most reliable in revealing between-individual differences in toddlers' cortisol levels (see Chapter 5).

Effects of childhood adversity on HPA axis functioning

While studies over the past three decades have provided evidence that childhood adversity shapes the functioning of the HPA axis (Engel & Gunnar, 2020), both heightened (Gonzalez et al., 2009; Nicolson, 2004; Saridjan et al., 2010) and lowered (Bernard, Zwerling, & Dozier, 2015; Koss et al., 2016; Kuras et al., 2017; E. Robson et al., 2021) levels of diurnal cortisol have been observed in children and adults with a history of childhood adversity. To reconcile these inconsistent findings, various hypotheses have been brought forward to explain under which circumstances the HPA axis up- or downregulates. A prominent hypothesis is the “attenuation hypothesis” (Fries et al., 2005; Susman, 2006), stating that *hypo*activity of the HPA axis emerges following a state of *hyper*activity in response to chronic stress in order to protect the organism from the toxic effects of stress hormones (Fries et al., 2005). At the same time, it has been suggested that the type of adversity (Cicchetti & Rogosch, 2001; C. L. Kessler et al., 2021; Sullivan et al., 2013) and developmental timing may affect HPA axis functioning differently (Bosch et al., 2012; Raymond et al., 2021).

In fact, our understanding of whether and when alterations in HPA axis functioning emerge after adversity, and the direction of change that is likely to be observed, is far from complete. Given evidence on normative developmental changes in cortisol mean concentrations throughout life (Schreiber et al., 2006; Shenk et al., 2022), and evidence on differential effects of adversity on HPA axis activity dependent on developmental timing, a better understanding of the emergence of cortisol alterations may be achieved through studying early childhood. Will we observe a consistent pattern of HPA axis alterations in children's first years of life when they were exposed to adversity? And if no consistent pattern emerges, may different types of adversity explain the presence of HPA axis hyper- or hypoactivity? In this dissertation, we aimed to address these questions in a systematic review focusing on diurnal HPA axis functioning in children below the age of five who were exposed to different types of adversity including maltreatment, adverse parenting or poverty (see Chapter 2).

The autonomic nervous system (ANS)

The second biological mediator of the adversity-psychopathology link that is of interest in this dissertation is vagal regulation, a specific aspect of ANS functioning (Thayer & Sternberg, 2006). The ANS is a component of the peripheral nervous system that regulates involuntary physiologic processes such as heart rate, blood pressure, respiration, and digestion (Waxenbaum & Varacallo, 2019). It consists of the sympathetic nervous system (SNS) which is responsible for the “fight-or-flight” response by rapidly increasing physiological arousal, and the parasympathetic nervous system (PNS) which modulates the SNS to restore homeostasis (Beauchaine, 2015; Porges, 2007). At rest, the parasympathetic branch exerts constant inhibitory control over the heart via the tenth cranial nerve, the vagus nerve. Under challenging conditions, parasympathetic (vagal) withdrawal enables sympathetic activation, leading to an increase in circulating adrenaline and noradrenaline which stimulates heart rate, vasoconstriction and energy mobilisation. In order to stop prolonged sympathetic activation, the parasympathetic branch reflexively reinstates the ‘vagal brake’, leading to a reduction in heart rate and arousal in a timely manner (Porges, 1995, 2007). The interplay of sympathetic and parasympathetic inputs to the cardiac sinoatrial node (the ‘pacemaker’ of the heart) produces HRV, defined as the variability in length of time between consecutive heartbeats (Acharya et al., 2006; Thayer & Ruiz-Padial, 2006). Although the SNS and PNS act largely in a reciprocal manner, both systems can also show coupled responses either in form of coactivation or coinhibition, or uncoupled responses (Berntson et al., 1991).

Effects of childhood adversity on vagal regulation

In parallel to the vast literature focusing on the HPA axis, there has also been considerable interest in the effects of adversity on vagal functioning during rest and in response to challenges. Higher levels of resting vagally-mediated HRV (vmHRV)—an index of vagal activity that is of interest in the present dissertation—have been associated with greater self-regulatory capacities and adaptive social behavior (Holzman & Bridgett, 2017; Isgett et al., 2017; Lischke et al., 2018; D. P. Williams, Tracy, et al., 2019). In response to challenge, moderate vagal withdrawal, reflected in a concurrent rise in vmHRV, is thought to reflect effective regulatory processes (Gentzler et al., 2009; Graziano & Derefinko, 2013; Marcovitch et al., 2010). Given evidence from two lines of research, it has been hypothesized that individuals with a history of childhood adversity demonstrate alterations in vagal functioning at rest and in response to challenge: First, studies have revealed self-regulatory difficulties in individuals exposed to childhood adversity (Gruhn &

Compas, 2020; Kim et al., 2021), and meta-analytic evidence has demonstrated that impairments in emotion regulation mediate the adversity-psychopathology link (Miu et al., 2022). Second, childhood adversity has been related to alterations in the structure and functioning of brain regions involved in vagal regulation (Teicher & Samson, 2016). Hence, if alterations in vmHRV are present in individuals exposed to adversity, they may represent a downstream marker of alterations in central functioning and self-regulatory difficulties.

In previous studies, childhood adversity has been positively, negatively or not significantly associated with baseline vagal activity (e.g., Dale et al., 2018; De Witte et al., 2016; Giuliano et al., 2018) and vagal reactivity to challenges (e.g., Goulter et al., 2019; Lafko et al., 2015; Hagan et al., 2020). To provide a quantitative summary of findings, we addressed the question of whether alterations in vagal regulation are present in individuals with a history of adversity in a meta-analysis (see Chapter 3). Given that different dimensions of adversity (i.e., deprivation and threat) may influence vagal functioning in distinct ways (Busso et al., 2017), we further tested the moderating influence of the dimension of adversity next to several other adversity characteristics.

Not everyone adapts in the same way: Individual factors moderating the association between childhood adversity and psychobiological functioning

A broad literature suggests that individual factors such as executive functions (Traub & Boynton-Jarrett, 2017) and mindfulness (Beshai & Parmar, 2019) may protect the individual from developing mental health problems after childhood adversity. Yet less is known about factors that render an individual more or less vulnerable to develop psychobiological alterations in the face of adversity. The following section will provide background information on two potential moderating factors studied in this thesis: the *FKBP5* gene and the temperamental dimension of effortful control.

Genetic factors as moderators: The role of FKBP5

Accumulating evidence suggests that the effects of childhood adversity may be conditional on an individual's genotype. Researchers have commonly focused on genes that influence the functioning of brain and hormonal circuits involved in the stress response, including variations in genes coding for the serotonin transporter (*5-HTT*), glucocorticoid receptor (*GR*, also known as *NR3C1*), and FK506-binding protein 5 (*FKBP5*; Jabbi et al., 2007; Mahon et al., 2013; Velders et al., 2012).

Several studies have demonstrated that the interaction of genetic predisposition and childhood adversity can explain additional variance in the prediction of psychiatric disorders as compared to models including main effects only (Assary et al., 2018; Byrd & Manuck, 2014; Moffitt et al., 2006; Wang et al., 2018; M. Zhao et al., 2018). In line with the diathesis-stress framework, this implies that some individuals are at heightened risk to develop psychopathology after adversity because of their genetic background, whereas others who lack the genetic vulnerability maintain normative functioning even when exposed to the same adversity (Rende & Plomin, 1992).

A promising candidate gene in the study of the diathesis-stress model is the FKBP5 gene. Attention has been drawn to rs1360780, a common single nucleotide polymorphism within the FKBP5 gene that has been shown to influence the stress response (Binder, 2009). Former studies have revealed that individuals who were exposed to childhood adversity and who carried the TT ('risk') allele of rs1360780 had reduced grey matter volumes in brain regions of the salience network and responded with increased amygdala reactivity to threat as compared to adversity-exposed individuals who were not carriers of that risk allele (Grabe et al., 2016; Holz et al., 2015; M. G. White et al., 2012). However, it remains unclear whether FKBP5 rs1360780 also modulates the effects of child abuse on the communication between brain regions during rest. This is important because alterations in resting-state functional connectivity have been observed in individuals diagnosed with major depression (Mulders et al., 2015) and post-traumatic stress disorder (S. B. J. Koch et al., 2016), and testing for a moderating role of genotype may help to identify those individuals who are most vulnerable to develop negative mental health outcomes after adversity. Hence, we addressed this question in a study testing the interaction between child abuse and FKBP5 rs1360780 on resting-state functional connectivity between the amygdala and other areas of the salience network, including the insula and the anterior cingulate cortex (Chapter 4).

Temperament as a moderator: The role of effortful control

Extensive evidence suggests that several other individual factors moderate the effects of childhood adversity on mental health outcomes (J. Fritz et al., 2018; Racine et al., 2020; Y. Zhao et al., 2022). To exemplify, mindfulness was found to buffer the effect of childhood adversity on depression (Beshai & Parmar, 2019; Marks et al., 2010), whereas low self-esteem was found to strengthen the effect (Hoppen & Chalder, 2018). While trait mindfulness and self-esteem have been outlined as protective factors which benefit children regardless of whether they have experienced adversity or not, these factors do not yet play a role in the first years of life. However, as some children are born into adversity, it is important to identify

risk and protective factors which are of relevance early in development to identify those children who are most in need of support.

A protective factor in the face of adversity that already seems relevant to young children is effortful control (M. J. Thompson et al., 2020), a regulatory dimension of temperament which enables children to shift their attention away from threatening stimuli toward soothing stimuli (Derryberry & Rothbart, 1997). Slowly emerging at the end of the first year, effortful control continues to develop more rapidly in the toddler and preschool years (Rothbart, 1989). Higher levels of effortful control may enable children to better regulate their attention, cognition and emotions in order to cope more effectively with stressors (Eisenberg et al., 2004, Obradović, 2016; Taylor & Ruiz, 2019). Several studies have shown that inconsistent parental discipline and interparental conflict predicted higher externalizing problems in children who were low in effortful control, but not in those who were high in effortful control (Lengua et al., 2008; M. J. Thompson et al., 2020). Yet it remains unclear whether such a moderation effect also pertains to psychobiological adaptation after adversity. If that would be the case, prevention approaches could specifically target young children with low levels of effortful control to reduce their likelihood of developing negative mental health outcomes. Hence, we investigated whether effortful control would moderate the association between parenting stress and diurnal cortisol levels in toddlers (Chapter 6).

While effortful control appears to be an indicator of self-regulation skills in early childhood (Eisenberg, 2012), later-emerging self-regulation skills such as cognitive reappraisal have also been shown protective against the development of psychopathology after adversity (X. Chen et al., 2022). However, it is difficult to compare and integrate former findings on the contributions of self-regulation to adaptive and adverse outcomes throughout development, as self-regulation has been defined and operationalized in various ways (Bridgett et al., 2013; Nigg, 2017). Hence, a secondary aim of this thesis was to review the development of self-regulation by placing emphasis on the various concepts studied across the developmental science disciplines. Given that the development of self-regulation is an inherently social process (Bandura, 1991; Piaget, 1950), we further reviewed how parents, teachers and peers are involved in shaping self-regulation development (see Chapter 7).

Aims of the present thesis

This dissertation is divided into four sections, each with a separate aim (see Figure 2). The first section aimed to review evidence on whether and how biological stress systems adapt after childhood adversity, focusing on the HPA axis (Chapter 2) and vagal functioning (Chapter 3). In the second section, we examined whether characteristics of childhood adversity explain different patterns of psychobiological adaptation (Chapters 2 and 3). In the third section, we investigated whether individual characteristics, including genetic constitution and effortful control (Chapters 4 and 6), but also demographic and health characteristics (Chapter 3), influence psychobiological adaptation. The fourth section contains two secondary aims of this dissertation, which were to broaden recommendations on cortisol sampling protocols to early childhood studies (Chapter 5), and to synthesize knowledge on the development and socialization of self-regulatory capacities, goals and motivation from infancy to adolescence (Chapter 7).

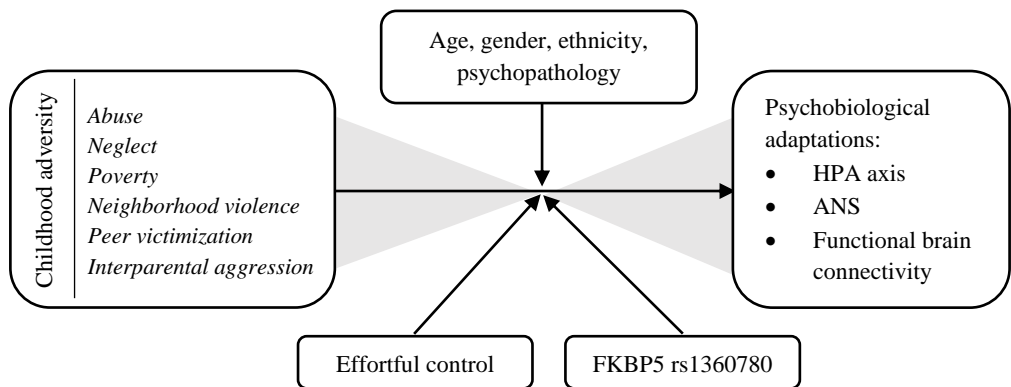


Figure 2. Framework of associations studied in this dissertation

Overview of chapters

Chapter 2 provides a qualitative summary of HPA axis alterations in children up to 5 years of age who were exposed to different types of adversity. We reviewed the literature separately for adversities affecting the child directly (e.g., maladaptive parenting, maltreatment) and contextual adversities rather affecting the child indirectly (e.g., poverty, neighborhood violence). Possible explanations are brought forward to reconcile inconsistent study findings, attempting to provide an answer to the question under what circumstances heightened or lowered levels of diurnal cortisol are observed in the context of adversity. Going one step further, we outline

a possible pathway which relates adversity-related HPA axis alterations to impairments in self-regulation that may further explain the increased risk for psychopathology after adversity. Finally, implications for interventions are shortly described in this review.

Chapter 3 proceeds with a quantitative review addressing the question whether individuals with a history of childhood adversity demonstrate alterations in vagal regulation. To this end, two meta-analyses are presented; one focusing on baseline vagal functioning and one on vagal reactivity to challenges. For both meta-analyses, we further investigated the role of potential moderators relating to characteristics of the study (e.g., publication year, country), participants (e.g., age, gender, ethnicity), adversity (e.g., type, recency, severity), and the measurement of constructs (e.g., HRV index, task setting). Moreover, we examined whether publication bias was present in the data sets included in both meta-analyses.

Chapter 4 describes a study in which we examined if the interaction between a genetic variation of the FKBP5 gene and child abuse would predict resting-state functional connectivity (rsFC) between the amygdala and other areas of the salience network, including the ACC and the insula. We focused on rs1360780, a common single nucleotide polymorphism within the FKBP5 gene which has been shown to influence HPA axis functioning in the context of stress recovery (Ising et al., 2008). Data stemmed from 774 young European adults from the general population who took part in the IMAGEN study (Schumann et al., 2010).

Chapter 5 describes a methodological study that determined which times of day would be most reliable to reveal between-individual differences in toddler's cortisol levels. This study aimed to inform the cortisol sampling protocol of a larger longitudinal study testing the effects of a parenting intervention on children's self-regulation and stress system functioning.

Chapter 6 addresses the role of effortful control, a self-regulatory dimension of child temperament, in moderating the association between parenting stress and toddlers' cortisol levels. We expected to find stronger associations between parenting stress and toddlers' cortisol levels in toddlers with lower levels of effortful control, as they may be less able to engage in self-distracting strategies during stressful interactions with parents. Data stemmed from 31 families who took part in the baseline wave of an intervention study for which the cortisol sampling protocol was determined in a methodological study (described in Chapter 5).

Chapter 1

Chapter 7 presents a review of reviews on the development of self-regulation which was conducted in an interdisciplinary collaboration. Including systematic and non-systematic reviews as well as meta-analyses, we addressed the question of how self-regulatory capacities, goals and motivation develop throughout different developmental periods from infancy to adolescence. Further, we synthesized knowledge on the role of parents, teachers, and peers in self-regulation development via two pathways: by affecting capacities on the one hand, and goals and motivation on the other hand. In addition, we highlight currently underrepresented topics in the self-regulation literature and discuss implications for research and practice.

Finally, Chapter 8 includes a discussion on the present thesis' contribution to the research on childhood adversity along with its implications for future studies and clinical practice.