Aggressive behavior in early childhood : The role of prenatal risk and self-regulation

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CHAPTER 6

Summary and general discussion

Deficits in self-regulation across multiple domains of functioning, from the physiological to the cognitive, have been linked to the development of early aggressive behavior (Calkins & Keane, 2009). The studies described in this dissertation aimed to provide insight into mechanisms by which early self-regulation (measured at different levels of analysis, i.e. physiological, emotional and cognitive) and prenatal risk increase vulnerability for aggressive behavior, and into the effects of prenatal risk on early self-regulation (measured at a physiological level).

In short, summarizing our findings in light of the model described in Figure 1 (see General introduction), we found that at the emotional and cognitive level, higher levels of negative emotionality (NE) were associated with higher levels of aggressive behavior in preschool children, especially in preschoolers characterized by lower inhibitory control (IC) (**Chapter 2**). At the physiological level, we found that nonreciprocal patterns of parasympathetic (PNS) and sympathetic (SNS) activity in infancy, demonstrated by coinhibition and coactivation of the PNS and SNS, at baseline and/or in response to emotional challenge, increased vulnerability for physical aggression in toddlerhood, in the context of exposure to prenatal risk (**Chapter 4.1 and 4.2**). In turn, we found negative effects of prenatal risk on physiological self-regulation, indicated by increased PNS suppression and SNS activation in infants exposed to prenatal risk, specifically during recovery from emotional challenge (**Chapter 5**).

The main findings of the studies described in Chapter 2, 4.1, 4.2, and 5 are discussed in more detail below, followed by a discussion of the strengths and limitations of the research, and the presentation of some recommendations for future research and the concluding remarks.

Aggressive behavior in early childhood: The role of emotional and cognitive self-regulation

In **Chapter 2**, we examined how self-regulation at the emotional and cognitive level predicted aggressive behavior across the preschool years in a community sample of children aged 2-5 years. This study was based on Muris and Ollendick's interactive model (Muris & Ollendick, 2005), which states that the vulnerability for externalizing problems (and psychopathology in general) is determined by emotional and cognitive self-regulation, and that the highest levels of externalizing problems are present in children with both low emotional (i.e. NE) and cognitive (i.e. effortful control) self-regulation. We tested whether IC (a subcomponent of effortful control, specifically linked to aggressive behavior), moderated the effects of NE on aggressive behavior, and whether this effect would be consistent across the preschool years.

In addition to significant main effects of NE and IC on aggressive behavior, the results showed that aggressive behavior was indeed predicted by the interaction between NE and IC, such that the negative impact of higher levels of NE was reduced in the absence of IC deficits and enhanced by relatively poor IC. The highest levels of aggressive behavior (borderline to clinical levels) were reported in children characterized by high NE and low IC. These findings provide an extension of the research that has so far mainly been conducted in school-aged children and adolescents focusing on the broader construct of externalizing behavior or behavior problems, and using rather general assessments of effortful control (Eisenberg et al., 2001; Muris, Meesters, & Blijlevens, 2007; Valiente et al., 2003). Importantly, as opposed to some previous studies in early childhood (Belsky, Friedman, & Hsieh, 2001; Gartstein, Putnam, & Rothbart, 2012; Olson, Sameroff, Kerr, Lopez, & Wellman, 2005), we found that the interaction effect between NE and IC was consistent across the age range of 2-5 years. Although the behavioral representations of IC may develop across the preschool years, we conclude that cognitive self-regulation (IC), separately and in interaction with emotional self-regulation (NE), may already play a role in the development of aggressive behavior in children as young as two years old. It is important to note that the sample in this study was of relatively low-risk (with the children's parents having high educational levels and living in intact families), and it is therefore possible that our findings would be more pronounced in children with a higher-risk background.

Additional analyses with physical aggression (as opposed to aggressive behavior which includes also verbal and relational aggression) as outcome variable revealed a somewhat different pattern of results. Overall, there was a significant main effect of IC, but not of NE, on physical aggression. This indicates the importance of cognitive self-regulation in the development of physical aggression, whereas emotional self-regulation may be more predictive of other forms of aggressive behavior such as verbal or relational aggression. More detailed analyses revealed that the interaction between NE and IC in relation to physical aggression was present only in boys aged 4-5 years old, as opposed to 2-3 year old children and 4-5 year old girls, underlining the role of sex and age in the development of physical aggression, and indicating that cognitive self-regulation is especially important for older preschool boys with weaker emotional self-regulation. The absence of an interaction effect between IC and NE on physical aggression, as opposed to aggressive behavior measured in a broader form, for younger children and for girls may be explained in several ways. First, physical aggression is relatively normal in two-and three-year old boys and girls (Alink et al., 2006; NICHD Early Child Care Research Network, 2004). Individual differences in physical aggression and protective effects of IC may therefore become more apparent

in older children. Second, boys exhibit more physical aggression (Alink et al., 2006), whereas girls generally show more relational aggression (Ostrov & Keating, 2004), especially as they grow older (Hay, 2007). Third, girls generally have better effortful control skills (Kochanska, Murray, & Harlan, 2000). Because the CBCL Aggressive behavior scale (Achenbach & Rescorla, 2000) measures aggression in its broadest form, age and sex effects may not appear.

Aggressive behavior in early childhood: role of prenatal risk and physiological self-regulation

In **Chapter 4.1 and 4.2**, we examined how self-regulation at the physiological level (i.e., in terms of PNS and SNS functioning) in six-month-old infants, in interaction with prenatal risk, predicted aggressive behavior (specifically physical aggression) during toddlerhood. We were specifically interested in the interaction between the PNS and SNS as moderators of the effects of prenatal risk on physical aggression, as it is suggested that the effectiveness of physiological self-regulation depends on the coordination between these systems (Berntson, Cacioppo, & Quigley, 1991). PNS and SNS activity was measured at 6 months at baseline and in response to and during recovery from two well- established emotionally challenging tasks; the Still Face Paradigm (SFP) and the Car Seat (CS). Physical aggression was measured through maternal report at 20 months in Chapter 4.1. In Chapter 4.2, we extended the study in Chapter 4.1 by measuring physical aggression at 30 months (also through maternal report) and by investigating interactions between the PNS and SNS within dimensions (e.g. PNS baseline x SNS baseline etc.) and between dimensions (e.g. PNS baseline x SNS response, and PNS response x SNS recovery etc.). Further, in Chapter 4.2 we examined whether the interactive effects between prenatal risk and the ANS were specific for physical aggression as opposed to more broader forms of externalizing behavior problems (i.e. oppositional behavior problems) (Burt, 2012).

The findings described in Chapter 4.1 and 4.2, show significant main effects of prenatal risk on physical aggression in toddlerhood. However, as opposed to the significant associations between emotional and cognitive self-regulation and aggressive behavior in the preschool period (Chapter 2), infant physiological self-regulation was not robustly associated with physical aggression in toddlerhood. While studies in children and adolescents have consistently found main effects of autonomic nervous system (ANS) measures on aggressive and antisocial behavior (Van Goozen, Fairchild, Snoek, & Harold, 2007), our results align with theoretical frameworks suggesting that the complex association between physiology and behavior may be better understood as interactions with early adversity (Boyce & Ellis, 2005; El-Sheikh & Erath, 2011). It is possible that the association between individual difference factors, such as

physiological self-regulation, and aggressive behavior becomes stronger as children grow older, whereas the influence of the (early) environment behavioral development decreases.

The findings described in Chapter 4.1 and 4.2 were not unequivocal, but overall suggested that nonreciprocal activity of the PNS and SNS, specifically patterns of coactivation and coinhibition, in infancy were associated with higher levels of physical aggression in toddlerhood, but only in the context of higher levels of prenatal risk. On the other hand, coordinated activity of the PNS and SNS, specifically reciprocal PNS activation and reciprocal SNS activation, buffered the effects of prenatal risk on physical aggression.

As described in Chapter 4.1, prenatal cumulative risk predicted physical aggression at 20 months, but only in infants who exhibited higher levels of coactivation of the PNS and SNS in response to emotional challenge (i.e. increased activity of both the PNS and SNS) at six months of age, whereas prenatal cumulative risk was not associated with physical aggression for infants who exhibited reciprocal PNS activation, reciprocal SNS activation or coinhibition. In Chapter 4.2, we found that the effects of cumulative risk on physical aggression were particularly evident in infants who exhibited low baseline PNS activity and/or higher levels of coinhibition (i.e. decreased activity of both the PNS and SNS) and coactivation (i.e. increased activity of both the PNS and SNS) at baseline and/or in response to emotional challenge at six months of age.

Our findings converge with a previous study in young children linking reciprocal ANS activity, specifically reciprocal SNS activity, to better emotion regulation (Stifter, Dollar, & Cipriano, 2011), and extend literature demonstrating adversity x ANS interactions that was so far only conducted in school-aged children with RSA and SCL measures (El-Sheikh et al., 2009; Gordis, Feres, Olezeski, Rabkin, & Trickett, 2010). Coinhibition and coactivation of the PNS and SNS may yield an ambivalent physiological response in which one branch increases arousal whereas the other branch dampens arousal (Berntson et al., 1991), resulting in physiological under- or over arousal that may limit a child's ability to generate an adaptive self-regulated behavioral response under challenging environmental conditions. Over time, these patterns of coinhibition and coactivation may consolidate and promote aggressive behavior, especially in environments that tend to elicit these behaviors more often.

Although levels of physical aggression for infants exhibiting coactivation at 20 months were well above one standard deviation of the averages reported in same-aged children from a large community sample (Alink et al., 2006), our findings show that at 30 months, ANS patterns of coinhibition conferred a higher risk of physical aggression than coactivation. The group mean for infants exhibiting coinhibition was

more than one standard deviation above the average aggression level reported by Alink et al. (2006), whereas the group mean of infants exhibiting coactivation lay within one standard deviation of the mean. Possibly, patterns of coinhibition over time confer greater risk for physical aggression than coactivation. In fact, it is suggested that while coinhibition, with reduced activity within the PNS and SNS, is linked to aggressive and antisocial behavior at a later age in children and adolescents, coactivation may promote anxiety or high-anxious externalizing problems (Beauchaine, 2001; Beauchaine, Gatzke-Kopp, & Mead, 2007; El-Sheikh & Erath, 2011). However, to date there is no empirical evidence to support this hypothesis (El-Sheikh et al., 2009).

All of the moderating effects reported in Chapter 4.2 were specific for physical aggression, and not for oppositional behavior problems. Other studies have demonstrated similar specific findings. For example, Baker et al. (2013) reported significant correlations between skin conductance levels at age 1 and aggressive behavior at age 3, but not for nonaggressive externalizing behavior problems (i.e. difficult or hard-to-manage behavior). Further, Raine et al (1997) reported that low resting heart rate at age 3 was specifically associated with aggressive behavior at age 11, as opposed to non-aggressive antisocial behavior. This suggests a stronger biological basis for physical aggression, whereas oppositional behavior problems may be more environmentally determined (Burt, 2012).

We found no main effects of PNS and SNS recovery, nor any interaction effects between (cumulative prenatal risk and) PNS and SNS recovery on physical aggression at 20 and 30 months. This point will be discussed further in the next paragraph.

Effects of prenatal risk on physiological self-regulation in infancy

The findings described in Chapter 4.1 and 4.2 highlight the role of physiological self-regulation in infancy in determining the impact of prenatal risk on physical aggression in toddlerhood. However, evidence suggests that physiological self-regulation itself is also influenced by exposure to risk factors during the prenatal period (Propper & Holochwost, 2013). We addressed this issue in **Chapter 5**, in which we examined the association between prenatal risk and the ANS. Previous literature in infancy has focused mainly on the effects of prenatal risk (factors) on the developing PNS, and much less is known about the effects of prenatal risk on the SNS (Propper & Holochwost, 2013). To address this gap and to more fully understand the effects of prenatal risk on the developing ANS, we examined measures of both PNS and SNS activity in response to and during recovery from an emotionally challenging task, the SFP, in six-month-old infants.

Our findings showed increased heart rate and PNS withdrawal among high-risk infants, compared to low-risk infants. In line with previous studies (Conradt & Ablow, 2010; Haley & Stansbury, 2003), this difference became only apparent during the recovery phase of the SFP. Further, we found increased SNS activation during the recovery phase in high-risk infants compared to low-risk infants. Also, as the number of prenatal risk factors increased, infants in the high-risk group exhibited greater SNS activation. In additional analyses we tested for the potential differential effects of different types of risk factors on ANS activity during recovery. Our findings showed that the presence of maternal psychiatric problems during pregnancy, as opposed to prenatal exposure to maternal substance use or social adversity, was the strongest predictor of increased SNS activation in the high-risk group during recovery. This converges with previous literature linking maternal psychopathology during pregnancy to offspring aggression over and above the effects of other prenatal risk factors such as maternal smoking and sociodemographic factors (Hay et al., 2011; Hay, Pawlby, Waters, Perra, & Sharp, 2010).

Infants in the low-risk group exhibited a typical pattern of ANS reactivity when confronted with emotional challenge (see Mesman, Van IJzendoorn, & Bakermans-Kranenburg, 2009), with decreases in PNS activity and mild increases in SNS activity in response to challenge, and increases in PNS activity and decreases in SNS activity during recovery. However, infants in the high-risk group, on the other hand, showed increasing levels of physiological arousal as the SFP progressed. In other words, infants in the high-risk group continued to suppress PNS activity and mobilized sympathetic resources, even during the recovery phase. Moreover, increased heart rate during the recovery phase in high-risk infants was mediated both by PNS and SNS activity, indicating PNS withdrawal and mobilization of sympathetic resources when confronted with socio-emotional challenge.

Although activation of the SNS when confronted with environmental challenge may reflect an adaptive physiological response in the short term, frequent and chronic activation of the SNS taxes physiological systems in the form of bodily wear and tear resulting in greater risk for psychopathology (McEwen & Gianaros, 2010). Children born in high-risk families, suffering from early adversity both prenatally and postnatally, are likely to be exposed to risk factors frequently and continuously. Eventually, chronic activation of the SNS may alter the integrity of physiological regulatory systems and may eventually lead to attenuated ANS functioning as observed in other studies (Alkon et al., 2014).

How is it possible that we only found differences between low-risk and high-risk infants in the recovery phase given that we expected differences between these groups in response to stress? Perhaps the SFP is more challenging as it progresses for

infants who are less self-regulated than for infants who are better regulated. Well-regulated infants showed better PNS- and SNS regulation during recovery enabling them to use their environment (the mother) to recover from emotional challenge. This is supported by the findings from additional analyses in which we found that low-risk infants looked more often to their mother and cried less, an effect that was mediated by increases in PNS activity and decreases in SNS activity during recovery. Physiological arousal increased across the SFP in high-risk infants as evident by increased PNS withdrawal and SNS activity during recovery which in turn were associated with less attentional engagement with the mother and more distress during the recovery phase, indicating that these infants were less able to use their mother to decrease their physiological arousal.

Contrary to our expectations, we did not find any main or interaction effects for physiological self-regulation during recovery from emotional challenge on the development of physical aggression (as described in Chapter 4.1 and 4.2). This was even more unexpected given the effects of prenatal risk on ANS functioning that were present mainly during recovery from emotional challenge (Chapter 5). Baseline ANS levels and ANS reactivity to emotional challenge have been examined in numerous studies. However, although recognized as an important parameter of ANS functioning (Porges, 2007), ANS recovery following emotional challenge is surprisingly understudied (El-Sheikh & Erath, 2011). One study in adolescents linked blunted SNS recovery to more antisocial behavior (Sijtsema, Van Roon, Groot, & Riese, 2015). Another study in 4-7 year old children showed that lower vagal recovery was associated with maladaptive emotional regulation strategies to frustration (i.e. a negative focus on delay) (Santucci et al., 2008). To our knowledge, no other studies have examined the association between ANS activity during recovery and outcome in infancy or childhood. It is possible that methodological issues explain the absence of effects for physiological recovery on the development of physical aggression. First, in Chapter 4.1 and 4.2, we examined average ANS recovery from challenge across two different tasks, the SFP and the CS task, while in Chapter 5, we examined ANS recovery from challenge only during the SFP. Second, although there were significant correlations between ANS recovery on the SFP and the CS, the level of SNS recovery for the CS was different than for the SFP. Whereas on average, infants showed decreases in SNS activity from challenge to recovery on the CS, they showed hardly any difference in SNS activity from challenge to recovery on the SFP, indicating that on average infants did not recover from the SFP challenge.

Strengths and limitations

Although the studies described in this dissertation have important strengths, including the use of a longitudinal design, the comprehensive assessments of ANS functioning (i.e. baseline, response and recovery, as well as PNS and SNS measures and their interaction), the focus on infancy, and two different emotional challenge tasks, there are also limitations that should be discussed.

First, we measured infant ANS functioning at one time point, at six months of age, but we know relatively little about the stability of PNS and SNS measures (i.e. RSA and PEP) across the first years of life. There is some evidence for moderate stability of RSA and PEP during resting and challenging conditions from 6 to 60 months (Alkon, Boyce, Davis, & Eskenazi, 2011; Alkon et al., 2006), however these studies have reported low stability for reactivity measures (representing the difference between resting and challenging conditions; Alkon et al., 2011; Alkon et al., 2006). Importantly, repeated and chronic exposure to higher levels of stress during postnatal development may have consequences for the stability of ANS measures (Alkon et al., 2014; Conradt et al., 2016). Further, as opposed to available research on the stability of individual RSA and PEP measures, there have been no studies that have investigated the stability of profiles of different ANS measures (i.e. reciprocal SNS activation, reciprocal PNS activation, coinhibition, coactivation) across (early) childhood. Data from two cross-sectional studies demonstrated developmental differences in ANS patterns in early childhood compared to late childhood and adolescence, with patterns of coinhibition being more prevalent in younger children (3-8-year-olds; Alkon et al., 2003) and reciprocal SNS activation more prevalent in older children and adolescents (8-10- and 15-17-year-olds; Salomon, Matthews, & Allen, 2000). This indicates that during the first few years of life the ANS is not yet fully developed and that developmental shifts are possible. Does this mean that measures of early ANS functioning are only predictive of behavioral problems in toddlerhood? Not necessarily. For example, there is evidence that ANS functioning measured early in development is predictive of later behavioral outcome even if there is no relation between that later behavioral outcome and concurrent ANS functioning. One study found that children with lower decreases in RSA during challenge (reflecting less PNS suppression) at age 2 continued to show more aggressive behavior during the preschool years, even if they were able to suppress RSA during challenge as preschoolers, indicating that deficiencies in early physiological regulation may have far reaching effects on development (Calkins, 2009). Future longitudinal investigations should examine the stability of PNS and SNS measures, and specifically the patterns of coinhibition and coactivation, across development in relation to behavioral

outcomes, and as moderators of the effects of early adversity on behavioral outcome in childhood and adolescence.

Second, our measure of toddler aggressive behavior involved maternal report. Parental reports of child functioning include a subjective component potentially reflecting biases associated with differences in parental personality, emotional status, relationship with the child, knowledge of child behavior and inconsistent interpretation of items (Kagan, 1994). Further, since prenatal risk was positively associated with maternal ratings of aggressive behavior, it is possible that mothers with higher levels of cumulative risk rated their child's behavior as more negative. Therefore, future studies should incorporate behavioral ratings and multiple informants to measure aggressive behavior.

Third, the level of cumulative prenatal risk in our sample was low, having on average 1.6 risk factors, and most mothers in the high-risk group had only one or two risk factors, which is not high compared to some high-risk and clinical samples used in other studies (e.g. Lester et al., 2002). Although nearly all mothers in the high-risk group had a psychiatric diagnosis or used substances during pregnancy, it is important to emphasize that the relatively low level of cumulative risk within the high-risk group may limit the generalizability of our results to high-risk or clinical populations. As noted by Beauchaine (2009) and Raine (2002), it is possible that different mechanisms of environmental and physiological risk and resilience operate in clinical populations. Nevertheless, our sample represents a realistic reflection of the general population and the effect sizes in this study are therefore more representative of the relations between prenatal risk, self-regulation and aggressive behavior in the general population.

Recommendations for future research

The results described in Chapter 4.1 and 4.2 underline the importance of studying patterns of stress reactivity across systems in infancy, using specific measures of PNS and SNS functioning, and their interplay with prenatal risk. However, it should be noted that only a small portion of variance in physical aggression in toddlerhood was explained by ANS functioning. Even in combination with prenatal risk, approximately 80% of the variance in physical aggression was left unexplained. It is therefore imperative for future research to include more factors to fully capture the development of aggressive behavior. Interestingly studies that investigate the ANS in conjunction with the other major stress regulation system, hypothalamic-pituitary-adrenal (HPA) axis, show that the interaction of the ANS and HPA axis predict behavioral problems better than measures of ANS or HPA axis alone (Blair, Berry, Mills-Koonce, Granger, & Invest, 2013; Chen, Raine, Soyfer, & Granger, 2015; Nederhof, Marceau, Shirtcliff, Hastings, & Oldehinkel, 2015). Moreover, future

studies should address the relations and the interactions between the different levels of self-regulation described in this dissertation across (early) childhood in the development of aggressive behavior, as it is proposed that more intentional and self-conscious (emotional and cognitive) self-regulation, which emerges during the early preschool years, depends on and may be constrained by physiological regulation of arousal earlier in life (Calkins & Keane, 2009).

We had a clear rationale for examining prenatal risk as a cumulative (Chapter 4.1, 4.2, and 5) or dichotomous (Chapter 5) variable. First of all, risk factors often co-occur, which makes it difficult to separate the effect of one adverse experience from another on ANS development and behavioral outcome. And second, because cumulative risk models are considered to be more powerful than single risk models in predicting problem behavior (Appleyard, Egeland, van Dulmen, & Sroufe, 2005). However, although we examined differential relations between different types of maternal risk factors (e.g. psychiatric diagnosis, differential substance use, social adversity) on the ANS in additional analyses (see Chapter 5), we did not address the potential differential effects of timing (prenatal versus postnatal) of maternal risk factors on the ANS, as well as potential interactive effects between different types of maternal risk factors and the ANS on later behavioral outcome. Support for our approach was found in a recent review (Propper & Holochwost, 2013) that showed that a broad range of specific prenatal and postnatal risk factors were associated with an altered pattern of ANS (re)activity. However, a recent longitudinal study (Alkon et al., 2014) reported significant differential effects of different maternal risk factors during the prenatal period and ANS trajectories from 6 to 60 months of age. Specifically, whereas prenatal exposure to limited social support was found to be associated with attenuated heart rate trajectories, prenatal exposure to socioeconomic adversity was associated with dampened PEP trajectories. Further, in another study (Waters, Boyce, Eskenazi, & Alkon, 2016) maternal chronic depression and overcrowded housing were examined as moderators of the relation between infant ANS functioning and externalizing behavior at age 10. Significant moderating effects of maternal chronic depression were found, but not for overcrowded housing. While prenatal and postnatal environments are often correlated, there is evidence that prenatal and postnatal exposure to risk may involve distinct causal pathways (Hickey, Suess, Newlin, Spurgeon, & Porges, 1995). For example, the comparison of PNS reactivity patterns for children exposed to drugs in utero to those of children whose mothers began using drugs after they were born, shows that prenatal use of drugs is associated with distinctive, adverse patterns of PNS reactivity that suggest that risk exposure during fetal development goes above and beyond risk exposure during infant development (Hickey et al., 1995). In sum, future studies adopting a different

analytical approach investigating the potential independent effects of different types and timing of maternal risk factors on ANS development and its interactive effects with ANS functioning in infancy on behavioral outcome could contribute to a better understanding of the individual differences in biological sensitivity to maternal risk factors and the mechanisms by which this biological sensitivity influences behavioral development. This type of research could also have important implications for future studies on the effect of early adversity on the developing ANS and subsequent (early childhood) aggressive behavior as well as inform intervention (research).

Conclusion

The studies described in this dissertation focused on the role of prenatal risk and self-regulation in infancy and the preschool period in the development of aggressive behavior, and the influence of prenatal risk on self-regulation in infancy. Three main conclusions can be drawn. First, aggressive behavior in the preschool period can be predicted from the interplay between self-regulation at the emotional and cognitive level (Chapter 2). Children who experience difficulties in regulating negative emotions such as anger, sadness and fear, are more prone to aggressive behavior if they have reduced inhibitory control. However, this effect is reduced if they exhibit better inhibitory control. Interestingly, we found moderating effects of age and sex for physical aggression that provide more insight into the specificity of the interaction effects of emotional and cognitive self-regulation for aggressive behavior in preschoolers. Practical implications of these findings suggest that interventions aimed at reducing aggressive behavior in toddlers and preschool children should focus on improving inhibitory control, especially in children with high levels of negative emotionality and boys with high negative emotionality who exhibit physical aggression.

Second, physiological self-regulation in infancy, as reflected by the coordination between the PNS and SNS, determines the impact of prenatal risk on the development of physical aggression in toddlerhood (Chapter 4.1 and 4.2). Infants characterized by low (re)activity of both the PNS and SNS (coinhibition) or high (re)activity of both the PNS and SNS (coactivation), are more vulnerable to the negative effects of prenatal risk (i.e. show higher levels of physical aggression), compared to infants characterized by reciprocal (re)activity of the PNS and SNS. Notably, in the context of higher prenatal risk, children characterized by reciprocal (re)activity of the PNS and SNS exhibit levels of physical aggression similar to those of children who were not exposed to prenatal risk. It should be noted, however, that our measures of physiological self-regulation were only predictive of physical aggression in combination with prenatal risk. It is therefore important to recognize

that vulnerability to aggressive behavior relies on the combination of the specific ANS profile and (prenatal) risk factors (Moore, 2009), and that these physiological measures should be examined together with the developmental context in which children grow up.

Our study is the first to examine the coordination between the PNS and SNS in infancy in relation to later behavioral outcome. The results highlight the need to consider measures of both PNS and SNS functioning and their interaction with the environmental context in order to elucidate its role in developmental processes leading to early aggression. However, caution is warranted in suggesting practical implications of our findings and future research is necessary to replicate our findings. Nevertheless, our findings show that we may be able to identify children who run the highest risk of developing aggressive behavior in toddlerhood based on assessment of their prenatal risk and their ANS profile in infancy. Maturation of the ANS during infancy lays the foundation for adaptive emotional and cognitive self-regulation later in development (Porges & Furman, 2011). Further, the ANS is rapidly developing during the first year (Porges, 2003), which is associated with increased susceptibility to environmental influences, and therefore also entails increased opportunities for early intervention programs focusing on mitigation of early environmental adverse effects (Beauchaine, Neuhaus, Brenner, & Gatzke-Kopp, 2008). A number of studies have shown that the ANS is sensitive to the early postnatal rearing environment. For example, sensitive parenting has been associated with more effective PNS regulation (Conradt & Ablow, 2010; Moore et al., 2009). Infants with less effective physiological self-regulation may therefore benefit from early prevention or intervention programs aimed at promoting maternal sensitivity.

Third, physiological self-regulation in infancy was found to be associated with prenatal risk (Chapter 5). Infants exposed to risk factors, such as maternal psychiatric problems, substance (ab)use, and social adversity during the prenatal period, showed increased PNS withdrawal and SNS activation during recovery from emotional challenge, which is indicative of impaired physiological self-regulation and might contribute to less effective emotional self-regulation. These findings underscore the importance of identifying women with a high-risk profile during pregnancy in order to offer prevention and intervention programs aimed at improving prenatal and postnatal circumstances. Intensive home-visiting programs have been found to positively influence maternal and child development (Avellar & Supplee, 2013; Mejdoubi et al., 2015; Olds, Sadler, & Kitzman, 2007; Ordway et al., 2014; Peacock, Konrad, Watson, Nickel, & Muhajarine, 2013; Sweet & Appelbaum, 2004). However, it is currently unknown whether these programs also affect infant physiological self-regulation. Examination of the infant ANS functioning as part of early intervention research may

indicate not only whether the intervention has an effect on this most basic self-regulatory mechanism, but also consequently affect the later development of emotional and cognitive self-regulation.