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Self-regulation in boys with oppositional defiant disorder and conduct disorder

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CHAPTER 7

Summary and general discussion

The objective of this thesis was to study individual differences in self-regulation in a population of boys with oppositional defiant disorder (ODD) or conduct disorder (CD). Because of the high risk of negative outcomes in children showing high levels of aggressive and even antisocial behaviour, such as is shown in boys with ODD and CD, it is of great importance to understand the mechanisms driving their aggressive and antisocial behaviour. Classification categories such as ODD and CD are well described at a behavioural level (APA, 2013) and do not necessarily explain the mechanisms that may underlie these behavioural problems. Also, at a behavioural level children with aggressive and antisocial behaviour form a heterogeneous group, with individual differences in for example, type of aggression, and comorbid symptoms of anxiety, attention deficits and autism. If we want to learn more about the developmental mechanisms that result in these behaviours, and to be able to prevent and treat antisocial and aggressive behaviour, it is important to look at mechanisms underlying behaviour. Self-regulation difficulties may be an important mechanisms underlying antisocial and aggressive behaviour. Self-regulation can be captured with neurobiological, emotional and cognitive parameters. Self-regulation at a neurobiological level can be seen in the responsiveness of the two major human stress regulation systems, the autonomic nervous system (ANS) and the hypothalamic-pituiry-adrenal axis (HPA axis). We know from previous studies that low levels of activation (seen in ANS parameters like heart rate and skin conductance level) at rest as well as low responsiveness to stress are found to be associated with antisocial and aggressive behaviour (Lorber, 2004; Ortiz and Raine, 2004; Portnoy and Farrington, 2015). Furthermore, low levels of the stress hormone cortisol, the end product of the HPA axis, are associated with high levels of antisocial and aggressive behaviour (Alink et al., 2008; Van Goozen et al., 2007). Self-regulation at an emotional level can be measured in the ability to become aware of own and other's emotions, the ability to regulate one's emotions and the influence an emotional state can have on decision making. Self-regulation at a cognitive level can be measured by looking at the cognitive functions that are involved in regulation of emotion and behaviour, the so called executive functions. Knowledge about these dimensions of self-regulation (neurobiology, emotion and cognition) does not only help to understand different pathways to aggression, but might also help explain individual differences in responsivity to treatment and differences in developmental outcome. This knowledge may be used in identifying those children who are most likely to persist in engaging in severe antisocial and aggressive behaviour and may be used in selecting the best treatment option per individual. Treatment effectiveness might improve if interventions are tailor made, taking into account the individual profile, instead of a one-size fits all approach.

In five separate studies we answered the question if neurobiological, emotional and cognitive aspects of self-regulation are associated with aggression in

children with ODD/CD and if this relation is influenced by other symptomatology. In addition we explored the predictive value of these aspects of self-regulation for the course of aggression over one year.

MAIN FINDINGS

In **Chapter two**, we tested the hypothesis that within the population of children with ODD/CD various profiles of ANS dysfunction may exist. We found that boys with ODD/CD as a group, compared to typically developing boys, unexpectedly showed higher baseline heart rate and no differences in stress responsiveness on heart rate and heart rate variability or skin conductance level. However, focusing on the individual differences within the group of boys with ODD/CD, interesting differences were revealed in the relation between behavioural phenotype and ANS functioning. A pattern of high baseline heart rate and skin conductance level, but low stress heart rate variability, was related to more problems in reactive aggression and higher levels of anxiety symptoms. A pattern of the opposite neurobiological pattern (low heart rate, low stress skin conductance level and high stress heart rate variability) was associated with more problems in proactive aggression and attention regulation. These findings indicate heterogeneity within boys with ODD/CD in behavioural phenotype as well as in their biological profile and highlight the importance of using neurobiological parameters to differentiate boys with different ODD/CD subtypes.

In **Chapter three** differences in neurobiological profiles were further investigated by looking at the end product of the HPA axis, i.e. the stress hormone cortisol. Boys with ODD/CD were divided in an anxious (ODD/CD+ANX) and non-anxious (ODD/CD-ANX) group based on a comorbid diagnosis of anxiety disorder on a structured diagnostic interview. Boys with ODD/CD+ANX, ODD/CD-ANX and typically developing boys all reported similar levels of negative mood over the course of baseline, stress and recovery, but showed different cortisol patterns. Overall, i.e. irrespective of the phase, the ODD/CD-ANX group had lower cortisol levels than typically developing boys, while the high anxiety group could not be differentiated from the typical developing controls. When considering the three phases of cortisol separately, those with ODD/CD-ANX had lower baseline cortisol levels, whereas those with ODD/CD+ANX had an impaired cortisol recovery response. Within the group of children with ODD/CD high anxiety predicted high cortisol levels at baseline and recovery, whereas a high level of CD symptoms predicted reduced cortisol stress reactivity. Although boys with CD/ODD are generally characterized by an impaired cortisol stress response, we found that those with comorbid anxiety showed impaired cortisol recovery, whereas those without anxiety showed reduced baseline cortisol levels.

While Chapter two and three focused on the neurobiological parameters of self-regulation, **Chapter four** examined the emotional dimension of self-regulation. In this study we compared boys with ODD/CD and typically developing boys on their emotion regulation and emotional awareness. Previous studies on emotional awareness and emotion regulation primarily used (self-report) questionnaires. In our study we use an emotional decision making task (the Ultimatum Game) besides parent- and child reports. It was found that boys with ODD/CD showed impaired emotional decision making on the performance task and difficulty with emotion regulation in daily life according to their parents, but they have reduced awareness of this since they did not report impairments in emotional awareness or emotion regulation skills themselves. Within the group of boys with ODD/CD we did not find autism symptoms and attention deficit symptoms to be related to the quality of emotional decision making, indicating that emotion regulation difficulties exist in boys with ODD/CD independent of their comorbid autism symptoms and attention deficit symptoms.

Chapter five further investigated self-regulation by looking at the executive functions (EF), one of the cognitive domains that subserve self-regulation, and the role that stress plays in EF. The main finding of this study was that whereas performance in typically developing boys in specific subdomains of EF (sustained attention, inhibition, cognitive flexibility) improved as a result of increasing stress, performance of boys with ODD/CD was less influenced by stress in these domains. Although boys with ODD/CD did change performance in cognitive flexibility, other functions such as sustained attention and inhibition were not at all influenced by stress in boys with ODD/CD. This finding indicates that boys with ODD/CD may have difficulties in adapting their behaviour to an optimal level in emotional, demanding environments.

In **Chapter six** we predicted the course of aggression over one year from parental factors, i.e. parent training and parenting practices (monitoring, discipline, punishment), and neurobiological parameters of self-regulation, i.e. HR and cortisol, in boys with ODD/CD. The parent training was predictive of a reduction in aggression. Interestingly, on top of the effect of treatment, those with a lower cortisol reactivity and those with a weaker cortisol recovery response, had a worse prognosis in terms of development of aggression over time. Heart rate and parenting practices were not predictive of the course of aggression. These results indicate that individuals with a neurobiological risk profile, i.e. those who are less stress reactive and/or who recover less well from stress, are more persistent in aggressive behaviour compared to those who do not show this profile. These child neurobiological factors can predict persistence or reduction of aggression in boys with ODD/CD, and have unique prognostic value independent of parenting style or parent training effects.

General discussion

The main aim of this thesis was to study mechanisms that can explain individual differences in self-regulation in boys with ODD/CD by examining neurobiology, emotion, and cognition in relation to aggressive behaviour. We were interested in how self-regulation deficiencies in these domains are linked to specific emotional and behavioural problems.

ANS functioning

When looking at the group as a whole we found that boys with ODD/CD compared to typically developing boys had higher baseline heart rates, but there were no differences in heart rate reactivity under stress, in heart rate variability or skin conductance level in any condition (**Chapter two**). Although these findings are in contrast to the dominant view that children with ODD/CD have a low heart rate (Ortiz and Raine, 2004; Portnoy and Farrington, 2015), it is not uncommon to find a higher resting state heart rate (De Wied, et al. 2009; Zahn and Kruesi, 1993). Similar to our null finding on heart rate variability, heart rate variability has not always been found to be lower in children with ODD/CD at rest (i.e. Calkins, et al. 2007; Scott and Weems, 2014) or during stress (Beauchaine et al., 2007; Beauchaine et al., 2008). These conflicting results may be explained by different stress conditions between studies. Some used supine (rest) versus standing position (stress) (Dietrich et al., 2007; Mezzacappa et al., 1997), whereas others used watching a relaxing video clip (rest) versus a mental arithmetic task (stress) (Scott and Weems, 2014), or watching an emotional video of an argument (stress) (Beauchaine et al., 2007). Another explanation of different findings may be that at a neurobiological level boys with ODD/CD differ from each other and that different arousal profiles exist within the ODD/CD group. Our findings confirm this hypothesis. When individual profiles were not taken into account, there was no difference in responding to stress compared to typically developing boys. However, when we focussed on differences between boys with ODD/CD we found a specific relation between behavioural characteristics and ANS functioning. We found evidence of regulation difficulties in different subgroups of boys with ODD/CD. Some of the boys with ODD/CD showed a profile of high arousal, at rest as well as during stress, and this profile was associated with more reactive aggression and higher levels of anxiety. This profile fits the 'anger-frustration' theory, which states that reactive aggression is the consequence of sympathetic overarousal after perceiving threat or provocation (Xu et al., 2014). Although the anger-frustration theory specifically refers to situations eliciting anger (i.e. situations in which stress is perceived), one can argue that if the stress system is already primed to down regulate emotions and behaviour (at rest) it would get only worse adding stress. Even a minor stressor may cause a

reactively aggressive reaction because the stress system is already activated. The other profile we found was that of low arousal at rest and during stress, and this was associated with proactive aggression and higher levels of attention deficit problems. This profile fits the dominant view of boys with ODD/CD having low arousal (Van Goozen et al., 2007). It is stated that having a low level of arousal is aversive and therefore one seeks stimulating activities to increase arousal (*sensation seeking theory*; Zuckerman, 1979). Moreover, low levels of arousal are regarded as markers of low levels of fear and punishment sensitivity (*fearlessness theory*; Rain, 1993), conditions that are unfavourable for learning from the negative consequences of one's actions.

These findings implicate that 'high arousal' boys might benefit from interventions using consequence based strategies such as a 'time out'. This type of learning is crucial for children because if they associate their negative behaviour with negative consequences, they will refrain from it in the future because of anticipatory fear. Boys having a profile of 'low arousal' might not learn from consequence based strategies because they do not react physically to punishment cues and thus will not easily learn the association between their behaviour and related negative consequences.

HPA axis functioning (cortisol)

Looking at the levels of the stress hormone cortisol we again found evidence of different types of regulation difficulties within the group of ODD/CD children (**Chapter three**). We found a profile of low arousal and low stress reactivity within the boys with ODD/CD, consistent with the dominant view of the association between low cortisol response and the risk for high levels of aggression, which has been reported frequently (Fairchild et al., 2008; Feilhauer et al., 2013; Popma et al., 2006; Snoek et al., 2004; Van Goozen et al., 1998; Van Goozen et al., 2000). This profile was indeed associated with more symptoms of CD. So these boys with ODD/CD nicely fit the *sensation seeking theory* (aggression results from stimulation seeking behaviours due to low levels of arousal) (Zuckerman, 1979) and the fearlessness theory (there is no correction of behaviour due to low stress reactivity and therefore no anticipation of negative feeling) (Rain, 1993). This also implicates that pointing out the negative or positive consequences of their behaviour or punishing or rewarding (un)acceptable behaviour, will probably not have an effect in these children (Van Goozen and Fairchild, 2008). Interestingly, we also found evidence of another profile within the group of boys with ODD/CD. There was a subgroup of boys with ODD/CD who had higher baseline levels of cortisol and more cortisol reactivity towards the stressor compared to the boys fitting the other profile (although similar compared to typically developing boys). This profile was associated with more anxiety symptoms. The main finding was that these boys were not able to regulate their stress system once the stressor was withdrawn. Their

cortisol level did not drop like in typically developing children or boys with ODD/CD without anxiety. This pattern of hyperarousal after withdrawal of the stressor may be explained by an overly responsive 'basic threat circuit' (Blair, 2013) that continues to be active after the stress. This circuit runs from the amygdala to the hypothalamus to the periaqueductal gray and is known to be activated when a threat is experienced as impossible to escape. Blair (2013) suggested that this 'basic threat circuit' becomes overly responsive by prior priming or inadequate regulation. Our results indicate that some boys with ODD/CD may continue a longer reactive state in response to stressors and do not easily recover from stress. This subgroup of ODD/CD children might be characterized as having impaired recovery or regulation instead of low arousal. Self-regulation abilities are needed to manage stress levels and return to neutral/rest states. It is known that individuals with high levels of anxiety have reduced self-regulation and emotion regulation abilities. For example, individuals may have increased rumination, excessive worrying and decreased re-appraisal abilities (Meuwly et al., 2012; Stewart et al., 2013; Verstraeten et al., 2011), reflecting a lack of control over emotions and a continuation of emotional states even though the events that triggered these emotions have already subsided. Their system is still in a fight or flight mode and they might therefore react excessively to minor stressors. This might explain why some boys with ODD/CD overreact to minor events. Interestingly, at rest and in reaction to stress the system of boys with ODD/CD fitting this profile reacted. This indicates that this subgroup does respond physically to consequence based learning strategies. However, they find it difficult to deal with the evoked negative emotions and might keep ruminating over their unacceptable behaviour or the consequences. This group might benefit especially from psychological interventions that use positive teaching strategies to decrease stress levels and increase prosocial behaviour. Cognitive behaviour therapy is effective in treating children with anxiety disorders (Higa-McMillan et al., 2016) and may be beneficial for this subgroup of boys with ODD/CD, because it may help them to tackle their negative thoughts that may be of influence in their inability to regulate stress. Also, this subgroup of boys with ODD/CD might benefit from an intervention that will help them to learn how to regulate emotions and return to homeostasis again.

Emotion regulation and executive functioning

Self-regulation was further investigated by examining executive functions (EF), one of the cognitive domains that subserve self-regulation, and by looking into the interaction between stress and EF, also referred to as the comparison between 'cool' and 'hot ' EF (**Chapter five**). In neutral (no stress added) test conditions boys with ODD/CD showed impairments in working memory compared to typically developing boys. When stress was added to the cognitive challenge, boys with ODD/

CD not only showed EF impairments in the domain of working memory, they also showed impairments in sustained attention. Thus, under stress, boys with ODD/CD had more impaired EF functioning than typically developing boys. The main finding of this study was however that whereas performance in typical developing boys in specific domains of EF (sustained attention, inhibition, cognitive flexibility) improved as a result of increasing stress, boys with ODD/CD profited less in these domains. Although there was improvement in cognitive flexibility, other functions such as sustained attention and inhibition were not enhanced under influence of the stress condition in boys with ODD/CD. These findings indicate that boys with ODD/CD may have difficulties in adapting their behaviour to an optimal level in emotional, demanding environments. One might think that the EF problems in ODD/CD are a sign of comorbidity with ADHD symptoms or autism symptoms. However, the lack of responsivity to stress and the problem in enhancement of EF was not related to these symptom dimensions. The improvements of typically developing boys in EF can be explained by the broad accepted theory of Yerkes and Dodson (1908), who suggested that the inverted U shape model can explain the relation between optimal cognitive performance and arousal. An optimal level of arousal increases performance, whilst too much or too little impairs performance. The finding that boys with ODD/CD did not change their performance in different stress conditions in EF indicates that they may have different arousal levels or arousal responsivity than typically developing children, and as a result may not be able to benefit from increased arousal or from external stress factors to the same degree as typically developing children. Adequate functioning in daily life requires flexibly adapting to complex or changing environments. Their difficulty to adapt in complex or changing environments is an important finding. Problems in doing so may thus contribute to behavioural problems of children with ODD/CD. This idea is supported by the finding that boys with ODD/CD showed impaired emotional decision making: they were less able to make a cognitive and more rational decision compared to controls in ambiguous situations (**Chapter four**). This means that in emotionally charged situations boys with ODD/CD are less able to use their EF to flexibly adapt their behaviour and therefore act impulsively without thinking things through. So the impaired emotional decision making might indicate difficulties in self-regulation due to impaired EF. This finding was not related to comorbid symptoms of ADHD or autism symptoms, just like our previous finding that EF was not related to ADHD or autism symptoms. The inability to make a cognitive decision provides further information about how self-regulation difficulties may underlie behavioural problems in children with ODD/CD. The finding of difficulties in emotional decision making was supported by the parental reports that boys with ODD/CD had emotion regulation difficulties in daily life too, indicating problems in EF. Previous studies reported deficiencies in any of the steps that are part of emotion regulation, i.e.

misinterpreted internal and external emotional cues (Manninen et al., 2011), limited range of strategies (Manninen et al., 2011; Barret et al., 1996) and lack of behavioural control (Blair et al., 2004), leading to handling unpleasant emotions with impulsive acting-out behaviour. Interestingly, the self-reports in our study indicated that boys with ODD/CD did not experience difficulties in emotional awareness or in the use of emotion regulation strategies, since we did not find any differences compared to the typically developing boys. This indicates that boys with ODD/CD are not aware of their difficulties with emotion regulation. Self-reflection, the knowledge about your own feelings, desires and impulses (Tyson, 2005), is an essential prerequisite for adequate self-regulation, and difficulty in self-reflection might therefore hamper adequate emotion regulation. Emotion regulation and executive functions are necessary for adequate functioning in daily life. Our findings make us conclude that problems in adaptability to stress/emotion, that might refer to a different stress level in ODD/CD or a different stress responsivity, result in insufficient flexibility in EF, and therefore less optimal adaptation if stress or emotions are present (hot EF). This might underlie inadequate social behaviour, like aggression.

Prognostic value of neurobiology

In **chapter six** we predicted the course of aggression over one year from parenting style (monitoring, discipline, punishment), parent training and neurobiological factors (heart rate and cortisol) in boys with ODD/CD. We found that boys whose parents received the parent training had reduced aggression levels one year later. Interestingly, boys with ODD/CD with relatively low cortisol reactivity and those with a weaker cortisol recovery response, had the worse prognosis in terms development of aggression over time. Heart rate and parenting practices were not predictive of the course of aggression. These results indicate that individuals with a neurobiological risk profile of 'stress non-responding' and/or 'stress non-recovery', were more persistent in aggressive behaviour compared to those who did not show this profile. These child neurobiological factors can predict persistence or reduction of aggression in boys with ODD/CD, and have unique prognostic value independent of parenting style or parent training effects. This might be important knowledge to determine what type of intervention fits the individual profile best. It is thought that children showing low reactivity towards a stressor have a worse prognosis than those who do react to stress (Van Goozen et al., 2007). This biological risk profile of 'non responding' is thought to be better treated with psychopharmacological interventions to alter the biological stress system than with psychotherapeutic interventions such as parent training programs (Van Goozen and Fairchild, 2008). Our results indicate that those boys who had difficulty in regulating their stress response once the stressor was withdrawn, also have a less well prognostic outcome in terms of future aggressive behaviour, compared to those children that showed a

better recovery. Although the parent training was effective in decreasing aggression levels in the group of boys with ODD/CD as a whole, the intervention may be even more effective if we could adjust the intervention based on their neurobiological profile. For example, those who find it difficult to regulate after a stressor might need extra help in regulation. This study thus illustrates that the functioning of the HPA axis of the child is an important predictor of the developmental course of aggression, independent of the impact of the parent training on aggression. Biological matching with specific interventions can be very important to enhance treatment effect in the future.

Limitations and directions for future research

With respect to the aim of this thesis that we would like to be able to explain individual differences in self-regulation in boys with ODD/CD by examining neurobiology, emotion, and cognition in relation to aggression and other emotional/behavioural problems, our study was limited in that we had a follow up design of one year only, for practical reasons. We know from previous studies that interventions, such as the parent management training (PMTO) the parents received in our study, are effective for a percentage of the population. Accordingly, we found that six months after the intervention ended (that is one year after our first measurement) the parents of the boys receiving the intervention reported significant reductions in aggression in their children. However, based on our study, we do not know if these reductions in aggression will hold for longer periods of time. The long term effectiveness of interventions is especially important in finding parameters that can predict outcome. Interestingly, we found that neurobiological parameters were as important as receiving the parent training in predicting aggression one year later. It is important to find out if neurobiology can help predict long term reductions in aggression following treatment over longer periods of time. Also, it would be interesting if we could study specific subgroups within the ODD/CD group with different neurobiological profiles and interventions matched to their profile to find out if that increases treatment success. So longitudinal studies are warranted, especially with a longer follow up time.

Our sample of boys in the intervention group was too small to investigate if different neurobiological profiles could predict treatment outcome. Van de Wiel et al. (2004) found that boys who did not respond to stress with their cortisol levels pre-treatment had higher levels of aggression than boys who did respond to stress after treatment. It would have been interesting if we could have predicted treatment outcome in terms of aggression within the intervention group using our (neurobiological) self-regulation measures.

Another limitation of this study is that we included only boys. Problems with aggressive and antisocial behaviour are not unique to boys, they have been

found in girls as well (e.g. Beauchaine et al., 2008). To what extent the results of our study can be generalized to girls needs to be investigated first.

In this study we have examined self-regulation using a neurobiological, emotional and cognitive dimension. Examining the neurobiological dimension revealed that within the group of boys with ODD/CD differences in ANS and HPA axis functioning existed and were related to specific behavioural and emotional problems. Emotional and cognitive functioning was impaired in boys with ODD/CD, indicating that self-regulation is difficult for them. The difficulties we found in emotional decision making, emotion regulation and behavioural adaptation (in EF) were not associated with more problems in attention deficit symptoms or autism symptoms. Because of the overlap in behavioural symptoms within these disorders and ODD/CD we had expected that such profiles, for example linking emotional dysfunction to autism symptoms, might exist. Our study indicates that neurobiology is especially informative when it comes to distinguishing individual profiles linked to emotional/behavioural problems.

Finally, boys with ODD/CD and typically developing boys did not differ from each other in self-reports with respect to emotional awareness, emotion regulation strategies or mood reports, while we did find differences in their cortisol levels, emotional decision making and parent reported emotion regulation. This indicates that boys with ODD/CD might not be able to reflect upon themselves properly. Studies using self-reports in ODD/CD populations must be aware of their limited ability to self-reflect. Based on the findings of our study we strongly recommend to use other measures besides self-reports in this population in future studies.

Our study indicates that neurobiological measures are especially informative when it comes to detecting differences between boys with ODD/CD and the prediction of future aggressive behaviour. However, cognitive measures, such as EF, provide information about the ability to regulate emotions, thoughts and behaviour. This information may help explain individual differences from another perspective and may be of great importance in shaping interventions for subtypes of children with ODD/CD. In our study we were not able to detect different profiles of EF and emotion regulation within the ODD/CD group. However, we do think that these measures are important indicators of self-regulation and should be included in future research.

Clinical implications

Although the dominant view is that boys displaying antisocial and aggressive behaviour, such as is shown by children suffering from ODD and CD, are under-aroused, this thesis provides evidence that not all boys with ODD/CD show low levels of arousal. In fact, some are better described as having regulation difficulties,

both seen in their neurobiology, i.e. over-aroused, impaired cortisol recovery, as well as in their cognitive abilities, i.e. difficulties in behaviour adaptation and their emotion regulation abilities, i.e. more influenced by emotions in decision making, and their behaviour, i.e. higher levels of anxiety and reactive aggression. This finding is important because it may help determine what intervention fits the individual profile best. It is thought that children showing underarousel during stress have worse prognosis than those who do react to the stressor. Children showing difficulties in responding to a stressor will not learn from the consequence of their behaviour because they do not react physically to punishment or reward cues and therefore, might not learn the association between their (inappropriate) behaviour and the negative or positive consequences of their behaviour. In future situations they might not behave differently because they might not have learned to feel anticipatory fear of the negative consequences of their behaviour. This biological risk profile of 'non responding' is thought to be better treated with psychopharmacological interventions to alter the biological stress system than psychotherapeutic interventions such as parent training programs (Van Goozen and Fairchild, 2008). However, there is some evidence in preschool children at risk for developing antisocial behaviour (Brotman et al., 2007; O'Neal et al., 2010) and school aged children with ODD/CD (Dorn et al., 2011) that cortisol response to a social challenge can be positively affected by psychological treatment which in turn may have an effect on aggressive behaviour (O'Neal et al., 2010). Nevertheless, this study illustrates that we need to beware of the underlying mechanisms of the problem behaviour and adjust the treatment accordingly, instead of providing the same intervention to all children showing aggressive behaviour.

Our results indicated that another risk profile exists in boys with ODD/CD, those who have difficulty in recovering from stress. Boys with ODD/CD who were less able to recover after the stressor had ended, showing difficulties in regulating, had higher levels of aggression one year later. Although aggression levels reduced after the parent training, we found that the reduction in aggression levels was less in those who showed less recovery in cortisol levels. What intervention is best for children with this risk profile has to be investigated. These children might need help in learning self-regulation strategies so that they become able to deal with stressors and will not react for example with (reactive) aggression. They might benefit from interventions such as 'mindfulness' (Bogels et al., 2008). Mindfulness is a particular way of paying attention (Kabat-Zinn, 2003) and may help to focus on other things when they become aroused. Also, they might benefit from learning new adequate coping strategies. Cognitive-behaviour therapy might help them to cope with frustrations. Furthermore, parents of children fitting this profile might help them by validating positive behaviours so that these behaviours will be shown more often. These two risk profiles show us that we need to carefully consider what mechanisms

explain the problem behaviour. So we need to differentiate within the group of children showing ODD/CD symptoms and consider treatment options based on their individual profile.

Screening for such profiles, boys that 'have difficulty in responding to stress' and boys that 'have difficulty in regulating after stress', means that we have to know how their stress systems functions at rest, in reaction to a stressor and once the stressor is withdrawn. Although cortisol levels can be obtained easily via a mouth swab, to establish the level of cortisol we would need a laboratory and normative values to determine if cortisol levels are altered. So for now we unfortunately cannot easily incorporate cortisol measures as an additional tool in clinical practice. Other neurobiological measures such as heart rate or skin conductance can be obtained more easily and provide information about the relation between the mechanism underlying behaviour and the behaviour itself. However, these measures also need normative values for comparisons. Information about the regulation of cognition, emotion and thought are also important for determining individual characteristics and provide additional information about self-regulation. Finally, questionnaires will still be valuable because they can provide information from a different perspective, for example how the behaviour is expressed at home or at the child's school. Combining all these measures would ultimately result in a complete picture of the functioning of the child that can be used to select the best intervention per child.

Our studies provide evidence for the important role neurobiology, emotion and cognition can play in predicting and managing the development of aggressive behaviour. Cortisol stress reactivity levels as well as cortisol recovery levels were predictive of aggression one year later. Thus neurobiology is at least as important as parental factors in terms of predicting the developmental course of boys with ODD/CD.

Finally, our results do imply that we need to carefully consider what underlying mechanisms cause the antisocial and aggressive behaviour and tailor the intervention per individual. The idea of tailored interventions have very recently been urged by Ng and Weisz (2016), who recommend starting to work with 'personalized interventions' in youth mental health. If therapies can be fitted more closely to individual characteristics, they might be more effective. The use of neurobiology, emotion and cognition in assessment can play an important role in determining individual characteristics. This information could be used in selecting the best intervention, based on their individual profile of weak and strong abilities. Hopefully this will help improve treatment effectiveness and result in positive outcomes for these children.