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

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# CHAPTER 1

## General introduction

Antisocial and aggressive behaviour are of great societal importance and termed top priority on political agendas in the Netherlands as well as abroad. Especially in children these behaviours are problematic because of the high risk of persistence and of all sorts of associated problems in adolescence and adulthood, e.g. school dropout, delinquency, unemployment, drug abuse, depression and other psychiatric problems (Bradshaw et al., 2010). Not only at the individual level these behaviours are problematic but also because of the risk of victimization and the great costs to society, which can be at least ten times as high as in typically developing children (Scott et al., 2001). Interventions targeting antisocial and aggressive behaviour in children have been found effective, but the individual differences in treatment outcome vary greatly (Moffit, 1993; Kazdin, 2000; Ogden et al., 2008; Stadler et al., 2008; Van de Wiel et al., 2004). In order to better understand why children show antisocial and aggressive behaviours and to be able to influence their developmental outcome effectively, we have to learn more about the underlying mechanisms of aggression. Knowledge about underlying mechanisms may be used to identify children with specific vulnerabilities and select the best preventive/protective intervention based on individual characteristics, thereby maximizing treatment effectiveness.

An important mechanism that might be relevant in the development and treatment of antisocial and aggressive behaviour is self-regulation, which refers to the ability to control emotion, thought and behaviour (Heatherton, 2011). Problems in self-regulation are known to be the core deficit in many forms of psychopathology (Cole and Deater-Deckard, 2009; Heatherton and Wagner, 2011). Aggression, i.e. any behaviour deliberately aimed at inflicting physical and/or psychological harm to an individual or property (Van Goozen et al., 2007), may be considered an extreme behavioural expression of self-regulation failure. In young children aggressive behaviour in response to frustration is quite common (Tremblay et al., 2005) due to lack or insufficient self-regulation at that developmental stage. When children grow older most of them develop effective regulation of this behaviour. But if they don't develop regulation of this behaviour and their aggressive and antisocial behaviour grows into a pervasive pattern, affecting diverse domains of children's functioning, this may lead to behavioural symptoms that are part of a diagnosis of oppositional defiant disorder (ODD) or conduct disorder (CD), belonging to the diagnostic class 'disruptive, impulse-control, and conduct disorders' of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association; APA, 2013). ODD is defined as a recurrent pattern of negativistic, defiant, disobedient and hostile behaviour towards authority figures lasting at least six months. ODD can be a precursor to CD, a classification referring to a more severe, repetitive and persistent pattern of behaviour in which the basic rights of others or societal norms or rules are violated. These problems are all defined on a behavioural level and

do not necessarily explain the mechanisms that may underlie these behavioural problems. Also, children with ODD/CD show great variability in type of co-occurring emotional/behavioural problems (Stadler, 2010; Loeber et al., 2000), in developmental course of aggressive behaviours, in responsiveness to treatment and in outcome (i.e. Moffit, 1993; Offord and Bennett, 1994; Ogden et al., 2008; Stadler et al., 2008; Van de Wiel et al., 2004).

So if we want to further understand the developmental mechanisms that result in antisocial and aggressive behaviour, and to be able to prevent and treat antisocial and aggressive behaviour, it is important to look at mechanisms that are part of self-regulation. Self-regulation can be captured with neurobiological, emotional and cognitive parameters that are sensitive in terms of identifying individual differences, and specific in terms of explaining individual behavioural problems (Van Goozen et al., 2007). Furthermore, knowledge about such mechanisms might also explain individual differences in responsivity to treatment and outcome. Examining neurobiological, emotional and cognitive functioning may help in identifying which children are most likely to persist in engaging in severe antisocial and aggressive behaviour. This knowledge may be used in the development of interventions.

**Self-regulation**

Self-regulation refers to *"the process by which people initiate, adjust, interrupt, stop or otherwise change thoughts, feelings or actions in order to effect realization of personal goals or plans or to maintain a current standard"* (Heatherton, 2011). This definition indicates that self-regulation can be a conscious process. However, even before one (un)consciously acts to control emotion, thought or behaviour, regulatory processes at a neurobiological level already take place. When perceiving a stressor, such as experiencing negative emotions, self-regulating processes start by automatically activating the two main human stress mechanisms: the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal axis (HPA axis) (Sapolsky, 1998). Negative emotions are among the most important triggers of self-regulation failure (Heatherton and Wagner, 2011). Therefore, another important dimension of examining self-regulation is the ability to be aware, process and regulate emotions. At a cognitive level we use executive functions to control emotions, thought and behaviour. These executive functions subserve emotion regulation and self-regulation. Finally, at the behavioural level self-regulation failure can be seen in behavioural problems such as aggression, anxiety, attention deficits and autisms symptoms. Fig. 1 shows these four dimensions of self-regulation and the parameters that will be used in this thesis.

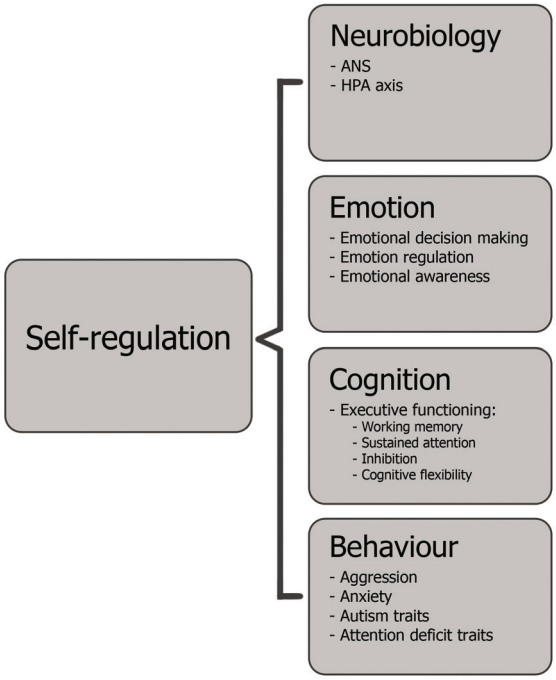


**Fig. 1.** Four dimensions of self-regulation.

**Neurobiology (ANS, HPA axis)**

Self-regulation at a neurobiological level can be studied by looking at the functioning of the two main stress regulation systems: the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal axis (HPA axis) (Sapolsky, 1998). The ANS is the fast acting pathway and consists of two systems: the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS). The PNS is involved in most daily activities promoting calm, vegetative activities, whereas the SNS becomes active when a stressor is perceived (Sapolsky, 1998). In times of stress, a nearly complete withdrawal of the vagus nerve, the main nerve of the PNS, occurs (Porges, 2001). Metabolic demands are suppressed, facilitating fight-flight reactions by accelerating heart rate and activating sweat glands, which increase skin conductance level (SCL). In times of rest, the vagus nerve decelerates heart rate, facilitating social engagement (Porges, 2007). Heart rate change is an indicator of both the PNS and SNS, whereas change in SCL reflects SNS. Activity of the vagus nerve can be measured by the heart rate variability (HRV), the fluctuation in intervals between heart beats. During stress HRV is thought to drop as a consequence of vagal withdrawal. High resting HRV enables an individual to select from a greater amount of actions to react to environmental demands if needed and is thought to be indicative of adequate self-

regulation skills (Porges, 1992). Malfunctioning of this ANS system might place children at risk for emotional dysregulation and thus aggression (Beauchaine, 2001).

Facing a stressor also activates the other (slower) stress regulation system, the HPA-axis. When a stressor is perceived the hypothalamus starts to release corticotrophin releasing hormone (CHR) from the paraventricular nucleus (Sapolsky, 1998). CHR subsequently stimulates to release adrenocorticotropic hormone (ACTH) from the pituitary, which in turn activates the adrenal glands, causing them to release the hormone cortisol. Especially this hormone at the end of the chain is often studied. The HPA axis is a self-regulating system through a negative feedback loop. The released cortisol crosses the blood-brain area and signals the paraventricular nucleus to decrease production of CHR and so on, turning to homeostasis again.

The functioning of these stress regulating mechanisms may contribute to individual differences in self-regulation and antisocial and aggressive behaviour, and therefore may explain the development and persistence of specific behavioural problems (Van Goozen, 2015). In the last two decades there is increasing evidence that these biological processes play an important role in the development of antisocial and aggressive behaviour in children, as evident in associated abnormal functioning of these two main human stress regulation systems (Lorber, 2004; Ortiz and Raine, 2004; Van Goozen et al., 2007).

Research has shown that low activation of the ANS and the HPA axis might increase the risk for antisocial and aggressive behaviour because individuals might be unresponsive to environmental cues of potential danger and that individuals might even compensate for low responsiveness by seeking dangerous activities to increase arousal (Van Goozen and Fairchild, 2008). In general children showing antisocial behaviour have a low heart rate during rest as well as during stress (Ortiz and Raine, 2004; Portnoy and Farrington, 2015). SCL has been found to be lower in children with conduct problems, but not in all aggressive children (Lorber, 2004). Lower basal HRV has been found in children with conduct problems (Beauchaine et al., 2007; Beauchaine et al., 2008; Mezzacappa et al., 1997) as well as during (physical) stress in an aggressive community sample (Calkins et al., 2007; Scott and Weems, 2014). Studies in primary school-aged children with aggression problems have generally reported normal cortisol baselines but reduced cortisol reactivity to stress, compared to typically developing controls (Snoek et al., 2004; Van Goozen et al., 1998; Van Goozen et al., 2000). These findings support the low arousal theory (Van Goozen et al., 2007) stating that children with ODD/CD have a low basal arousal level (low heart rate and SCL) and therefore might seek stimulating activities (*sensation seeking theory;* Zuckerman, 1979) and do not fear the negative consequences of their dangerous/aggressive actions (*fearlessness theory;* Raine, 1993) as evident in low cortisol reactivity.

Although there is clear evidence pointing towards reduced arousal,

responsiveness and regulation in children with ODD/CD, some contradicting findings have been reported as well (Alink et al., 2008; Calkins et al., 2007; De Wied et al., 2009; De Wied et al., 2012; Dietrich et al., 2007; Garralda et al., 1991; Scott and Weems, 2014; Zahn and Kruesi, 1993). These inconsistencies in neurobiological studies might be explained by methodological differences, such as different populations or informants and type of stressors. Another explanation might be found in the notion that children with aggressive and antisocial behaviour form a heterogeneous group (Stadler, 2010), not only with respect to behavioural phenotype (individual differences in for example type of aggression, and comorbid symptoms of anxiety, attention deficits and autism), but also with respect to the underlying mechanisms that result in their behaviour. It is important to address these conflicting findings and examine the possibility that different arousal/responsiveness profiles may exist between children with ODD/CD. For example some children exhibit heightened SNS activity in rest (e.g., high SCL, low HRV) and are therefore over-aroused, instead of under-aroused, and may be especially vulnerable to stressful situations because their system is already 'primed' for reaction (Gatzke-Kopp et al., 2012), causing greater risk for displaying reactive aggression (Bubier and Drabick, 2009). Children showing under-arousal, on the other hand, might under react to stressful situations and are therefore unable to use environmental cues to adapt their behaviour accordingly. Thus within the group of children with ODD/CD individual differences in behavioural phenotype might be explained by differences at the level of neurobiology.

**Emotion**

Children with ODD/CD have been found to exhibit difficulties in the regulation of their own emotions (Roll et al., 2012), i.e. the processes by which *"individuals influence which emotions they have, when they have them, and how they experience and express these emotions"* (Gross, 1998). Studies have reported that children with aggressive and antisocial behaviour used less effective or more inappropriate regulatory strategies (Barrett et al., 1996; Blair et al., 2004; McLaughlin et al., 2011). Besides these problems in emotion regulation, children with ODD/CD have also been found to have specific problems in affect recognition. Often reduced emotional awareness is reported (Factor et al., 2013; McLaughlin et al., 2011; Zimmermann, 2006), which refers to insufficient awareness of one's own or other's emotions, or the difficulty in labelling them correctly. Furthermore, children with ODD/CD often show difficulties with the processing of affective information, such as facial and focal expressions (Marsh and Blair, 2008; Short et al., 2016). Especially negative emotions such as fear, distress and sadness are difficult to recognize. Difficulties in the processing of emotions may result in deficiencies in feeling fear, empathy and guilt. These emotions help a person to guide in social situations in a way that one can

respond in a socially acceptable way. Difficulties in the experiencing, processing and regulation of emotions may thus result in antisocial and aggressive behaviour. This is of interest because in everyday life we are regularly confronted with situations eliciting emotions and thus need proper emotion regulation skills. The studies on emotion regulation and emotional awareness, as reviewed above, have primarily used (self-report) questionnaires, with very few assessing the cognitive ability to process and regulate emotions. The effect emotions can have on decision making can reveal interesting information about the ability to regulate emotions. In this thesis we used a multi-method approach; we used parent- and child reports, as well as an emotional decision making task to get insight into emotional reactivity that results from automatic regulation processes that can take place without monitoring, insight or awareness (Gyurak et al., 2011).

**Cognition (EF)**

Executive functions (EF) are involved in controlling thought, emotions and behaviour, and subserve self-regulation and emotion regulation. Adequate social functioning requires being able to flexibly adapt to changing environments. This does not only require the ability to perceive and process emotions, but also the ability to adapt behaviour in situations that are new, complex, unpredictable, or have high load of information (Anderson, 2002). There are several key EF functions: working memory, attention, inhibition, cognitive flexibility, planning and monitoring (Anderson, 2002; Diamond, 2013). Emotions can influence EF and recently, studies have acknowledged this fact by distinguishing between EF in neutral situations and EF in the context of affect, incentives and motivation, i.e. 'cool' and 'hot' EF (Zelazo and Muller, 2002). In ODD/CD samples EF impairments in typical 'neutral' test environments, 'cool EF', have been found, but the cool EF impairments that are reported vary. Some studies observed difficulties in working memory, cognitive flexibility and planning impairments (Syngelaki et al., 2009), others reported impairments in sustained attention and inhibition (Hobson et al., 2011). Dolan and Lennox (2013), Fairchild et al., (2009), Van Goozen et al. (2004) and Woltering et al. (2015), on the other hand, did not find cool EF impairments in adolescents with CD and children with ODD or externalizing behaviour. Interestingly, studies on 'hot EF', EF tasks in which affect, incentives or motivation are incorporated in the task, all reported 'hot EF' impairments in ODD/CD samples (Dolan and Lennox, 2013; Fairchild et al., 2009; Hobson et al., 2011; Syngelaki et al., 2009; Van Goozen et al., 2004; Woltering et al., 2015). The literature on 'cool' and 'hot' EF reports different paradigms (tasks) to examine 'cool' and 'hot' EF. Because emotions or motivation probably influence EF (Welsh and Peterson, 2014), we examined 'cool' EFs under typical and stressful test conditions, thereby providing information about how control over thought and behaviour is modulated by stress in boys with ODD/CD.

**Behaviour**

If the mechanisms of self-regulation are deficient this will result in observable behavioural problems or symptoms. Deficient self-regulation leads to difficulties in adaptation to changing social environments. This may lead, for example, to the inability to inhibit first responses, the inability to resist interference from irrelevant stimuli and to difficulty with persistence on relevant tasks even if they are not enjoyable. These behavioural difficulties are captured in several other diagnostic categories besides ODD/CD, for example in attention-deficit/hyperactivity disorder (ADHD) or autism spectrum disorders (ASD). Indeed self-regulation failure might also explain problem behaviour seen in children with other types of psychopathology than ODD/CD (Anastopoulos et al., 2011; APA, 2013; Barkley, 2006; Geurts et al., 2004; Pennington and Ozonoff, 1996). According to Barkley (2006) children with ADHD have difficulty with inhibition, making it difficult for them to delay a response long enough to gather the information necessary to fully understand the situation. Aggression, as can be seen in anger tantrums or self-injury in children with ASD, is thought to be associated with difficulty to regulate emotion and behaviour (Mazefsky et al., 2013). On a behavioural level there is quite some overlap between symptoms of these childhood developmental disorders. Comorbidity rates of ODD or CD in children with ADHD is high (59% and 43% respectively) (Barkley, 2006; Pliszka, 2015) and aggression is displayed in over 50% of the children with ASD (Matson and Cervantes, 2014). According to a review containing seven studies, one in four children with ASD meets ODD or CD criteria (Kaat and Lecavalier, 2013) if this double diagnosis would have been allowed by the DSM-IV. A later study even reported that 41% of the children with ASD displayed clinical levels of symptoms of ODD/CD (Shawler and Sullivan, 2015). Because of this overlap in behavioural symptoms it is important to study self-regulation in children suffering from ODD/CD in relation to other comorbid symptoms such as attention deficits and autism symptoms. Taken together, the question addressed in this thesis is if there is evidence for self-regulation deficiencies in children with ODD/CD, and most important, if individual differences in self-regulation deficits help explain specific types of emotional and behavioural problems, including aggression symptoms, anxiety symptoms, autism symptoms and ADHD symptoms.

**Predictive value of self-regulation for the developmental course of aggression**

Finally, further knowledge about the mechanisms underlying antisocial and aggressive behaviour in children may help to identify the factors that may influence the developmental course of aggression. Individual differences in self-regulation in neurobiological, emotional and cognitive functioning may enhance our understanding of childhood aggression at different ages, which may ultimately provide knowledge that is relevant for the design of interventions aiming at

improving outcome of developmental course. Neurobiological, emotional and cognitive functioning can also be used to identify the children that are most likely to persist in engaging in severe antisocial and aggressive behaviour and to identify those that might benefit from psychological treatment, such as parent management training. Interventions targeting parenting practices have been found effective in reducing antisocial and aggressive behaviour (Kazdin, 1997; Lundahl et al., 2006; Ogden and Hagen, 2008). Poor parenting is associated with higher levels of aggression in children (Griffin et al., 2000; Patterson and Stouthamer-Loeber, 1984), and by improving parenting practices aggression in children can be reduced (Furlong et al., 2012; Gardner et al., 2015; Kazdin, 1997; Lundahl et al., 2006; Michelson et al., 2012; Ogden and Hagen, 2008). However, success rates show that not all children with antisocial and aggressive behaviour respond positively to parent training programs and there is great variability in the amount of change achieved (Ogden and Hagen, 2008). Individual neurobiological characteristics might be able to explain why some children persist in their aggressive behaviour (Van Goozen and Fairchild, 2008) and why others are sensitive to for example parenting style. For example, low heart rate has been related to future aggression in community samples (Ortiz and Raine, 2004; Portnoy and Farrington, 2015). In clinical populations evidence is mixed. Some found that children with disruptive behaviour disorders with low resting heart rate showed less reductions in ODD/CD symptoms after intervention than those with higher resting heart rate (Stadler et al., 2008), whereas others did not find resting heart rate to be predictive of changes in externalizing problems in children with ODD/CD who received treatment (Van Bokhoven et al., 2005). Conflicting findings are also reported for cortisol. Low cortisol reactivity to stress was found to be predictive of higher levels of aggressive behaviour in school-aged boys after treatment for ODD/CD, indicating that cortisol non-responders are more persistent in aggressive behaviour than cortisol stress responders (Van de Wiel et al., 2004). In another study with an ODD/CD sample cortisol reactivity was not predictive of persistence in externalizing problems after treatment, although low skin conductance level was predictive of more externalizing problems after treatment (Van Bokhoven et al., 2005). Thus further research is needed to investigate the value of neurobiology in predicting aggression outcome. Therefore, this thesis will also focus on the additive value of individual differences in neurobiological factors beyond parental factors in predicting the course of aggression.

**Aims and outline of this thesis**

Children showing antisocial and aggressive behaviour are at risk for numerous negative developmental outcomes. To be able to prevent an adverse outcome we need to know more about the mechanisms underlying their aggressive and antisocial behaviour, in particular about self-regulation. In this thesis individual differences

in self-regulation in neurobiological, emotional and cognitive functioning in boys with ODD/CD were investigated in relation to behavioural symptoms. The aim was to identify emotional, cognitive and neurobiological factors that are differentially related to the degree and type of aggression and other emotional and behavioural problems in boys with ODD/CD. In identifying 'risk profiles' of deficient self-regulation, such as those showing low or high neurobiological responsivity to stress, it was also evaluated whether the impact of impaired self-regulation was not only linked to aggression in boys with ODD/CD, but also to comorbid symptoms of anxiety, ADHD and autism symptoms in this population. In addition, it was investigated if neurobiological, emotional and cognitive measures of self-regulation could predict the course of aggression over time, thereby determining the prognostic value of these measures.

To this end five studies were conducted in 65 boys with ODD/CD and 38 typically developing boys for comparison. The ODD/CD group had a mean age of 10.3 (*SD*=1.28) and an age range of 7.8-12.9. The typically developing boys had a mean age of 10.1 (*SD*=1.27) and an age range of 8.0-12.7. Both groups had an estimated IQ>70. Boys with ODD/CD were recruited at clinical health centres, special education schools and regular elementary schools. They all met the criteria for ODD classification according to the DSM IV and 22 (34%) boys also met the criteria for CD. Comorbid classifications were: ADHD (*n*=45, 69%), anxiety disorder (*n*=38, 58%), depression (*n*=9, 14%) and other disorders such as eating and tic disorder (*n*=18, 27%) as based on the Diagnostic Interview Schedule for Children (DISC-IV) (Shaffer et al., 2000). Typically developing boys were all recruited at regular elementary schools and showed no aggression, expressed as a diagnosis of ODD or CD according to the DISC-IV interview or a score in the borderline or clinical range (T>60) on the externalizing scale of the Child Behavior Checklist (CBCL/6–18) or Teacher Report Form (TRF/6–18) (Achenbach and Rescorla, 2001).

Self-regulation was measured at four dimensions: (1) neurobiology (ANS and HPA axis functioning), (2) emotion, (3) cognition (EF) and (4) behaviour. Self-regulation was examined by comparing baseline or typical 'neutral' test conditions versus stressful test conditions. The stressful condition was carried out in a laboratory at the Department of Clinical Child and Adolescent Studies at the Faculty of Social and Behavioural Sciences at Leiden University, using an established and ecologically valid psychosocial stressor that involved provocation, frustration and competition to increase emotional arousal (this paradigm was used in other studies as well, see Fairchild et al., 2009; Van Goozen et al., 2000 and explained in more detail in chapter 2 and 5). In **Chapter 2** the hypothesis was tested that different profiles of arousal dysfunction (ANS) may exist between children with ODD/CD. This knowledge could explain variability within children with ODD/CD, both in terms of specific types of aggression (reactive/proactive) as well as comorbid symptoms

(e.g. other emotional/behavioural problems). In **Chapter 3** the other main human stress regulation system, the HPA axis, was examined in relation to comorbid anxiety. It was hypothesized that specific profiles of HPA axis functioning are associated with anxiety. Cortisol was examined under baseline, stress and recovery conditions. All three parameters were supposed to provide unique important information; baseline levels tell us something about the level of arousal during rest. Cortisol levels during stress tell us about the reactivity of the stress system. Cortisol recovery has hardly been studied separately from stress reactivity before, and provides information about regulation after a stressor is removed (instead of during exposure to a stressor) and might be an important mechanism in behavioural adaption. **Chapter 4** concerns emotion regulation. Emotion regulation has often been studied using (self-report) questionnaires. In this study however, three perspectives of emotion regulation were studied: an emotional decision making task, a parent report of emotion regulation and self-reports of emotional awareness and emotion regulation strategies. Impairments in these measures of emotion regulation within the ODD/CD group were related to autism and attention deficits symptoms. It was investigated if emotion regulation difficulties are characteristic of ODD/CD or if emotion regulation difficulties underlie other behavioural problems displayed by boys with ODD/CD, such as attention deficit symptoms and autism symptoms. In **Chapter 5** EFs, the cognitive processes underlying self-regulation, were studied. We measured EF under typical test conditions, 'cool EF', and under stressful test conditions, 'hot EF', to find out how stress modulates EF in boys with ODD/CD. In order to assess whether EF deficits are not limited to those boys with ODD/CD with high levels of ADHD symptoms or autism symptoms, we also examined within the ODD/CD group the relation between EF, under typical and stressful conditions, and ADHD symptoms and autism symptoms. In **Chapter 6** the predictive value of neurobiological parameters (heart rate and cortisol) next to parental variables (style of parenting) and the influence of a parent training on the developmental course of aggression across one year were examined within the ODD/CD group. Finally, in **Chapter 7** the main findings of this thesis are discussed.