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Empathy Impairments in Boys With Oppositional Defiant Disorder and Conduct Disorder

Examining Subtype Differences and The Role of Emotion Regulation

Empathie Stoornissen bij Jongens Met Een Oppositioneel-Opstandige Stoornis en Normoverschrijdend-Gedragsstoornis

Een Onderzoek Naar Verschillen Tussen Subtypen en De Rol van Emotieregulatie

(met een samenvatting in het Nederlands)

Proefschrift

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May your heart always be joyful

May your song always be sung

And may you stay

Forever young

"Forever Young" by Bob Dylan

Voor Noud

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Chapter I

General Introduction

Empathy, generally defined as the ability to understand and share another's emotional state (Eisenberg & Strayer, 1987), is an important social skill. It is thought to foster prosocial behaviour (Hoffman, 2008) and inhibit unwanted behaviour, like aggression (Austin, Bondü, & Elsner, 2017). Empathy problems are often associated with oppositional defiant disorder (ODD) and conduct disorder (CD) (De Wied, Gispen-De Wied, & Van Boxtel, 2010). Children and adolescents with ODD/CD form a heterogeneous group, however, and researchers suggest that there are individual differences in the mechanisms underlying their empathy deficits (e.g., Blair, 2013; De Wied et al., 2010). The literature often distinguishes between those with and without callous unemotional (CU) traits. CU traits are an extension of the interpersonal-affective dimension of adult psychopathy and are identified by a lack of empathy, a lack of guilt and shallow affect (Frick & Hare, 2001). Over the years, empathy in those with high levels of CU traits has received much research attention. Far less attention has been dedicated to empathic functioning of those without CU traits. We have therefore limited knowledge about empathy problems in children and adolescents with ODD/CD. A more thorough investigation of these problems in ODD/CD subtypes is crucial for the development of more targeted and effective treatment strategies to improve empathic functioning in children and adolescents with ODD/CD. In light of this, the current dissertation aims to elucidate the nature of empathy impairments in ODD/CD children and adolescents and to explore possible mechanisms involved.

Empathy: a Multidimensional Construct

According to Davis' (1996, 2006) *organizational model of empathy-related constructs*, empathy is a multidimensional construct encompassing traits (empathic tendencies), states (intrapersonal outcomes), and affective and cognitive components.

Affective empathy involves "psychological processes that make a person have feelings that are more congruent with another's situations than with his own situation" (Hoffman, 2000, p.30). In the literature, empathy is often distinguished from sympathy and personal distress (Eisenberg & Eggum, 2009). Empathy is an affect match between the observer and the target – feeling *with* another person. Above a certain threshold or with further cognitive processing, empathy is thought to evolve into sympathy, personal distress, or a combination of these constructs. Sympathy (or empathic concern) is an other-focused reaction involving feelings of concern or sorrow for the other – feeling *for* another person. By contrast, personal distress is a self-focused reaction involving feelings of anxiety and discomfort – feeling *by* another person (Batson, 2009). Empathy, sympathy and personal distress are strongly related constructs and often induced by the same emotional event (Eisenberg & Eggum, 2009; Lamm & Madjaniç, 2015).

Cognitive empathy involves the ability to understand another person's feelings without necessarily being in an affective condition oneself (Walter, 2012). Aspects like perspective taking (taking over the mental perspective of the observed other), Theory of Mind (ToM; the ability of an individual to infer what another person is feeling or thinking, and

what he or she may do based on those inferences), and empathic accuracy (the ability to accurately perceive other's thoughts, feelings and other inner mental states; Ickes & Hodges, 2013) may all be considered aspects of cognitive empathy.

Measuring Empathy

Over the years, different measures of empathy have been developed (Eisenberg & Fabes, 1990). There are several questionnaire measures of empathy to assess the dispositional tendency to engage in empathy-related processes (trait empathy). Frequently used questionnaires are, for instance, the Empathy Index for Children and Adolescents (IECA; Bryant, 1982; De Wied et al., 2007) and the Basic Empathy Scale (BES; Jolliffe & Farrington, 2006). The IECA taps into affective empathy, whereas the BES taps into both affective and cognitive empathy.

State empathy is generally assessed within laboratory settings. Empathic reactions are often evoked by empathy-inducing stimuli, such as film clips portraying individuals experiencing negative and positive emotions (e.g., De Wied, Van Boxtel, Matthys, & Meeus, 2012; Schwenck et al., 2012). Affective and cognitive outcomes of empathy can be measured at different levels of empathic functioning. Self-reports, facial and physiological indexes have all been used to examine empathy in children and adolescents with ODD/CD (e.g., Cohen & Strayer, 1996; De Wied et al., 2012; Marsh, Beauchaine, & Williams, 2008a). Moreover, event related potential (ERP) technique and functional Magnetic Resonance Imaging (fMRI) have been used to study brain reaction of ODD/CD adolescents while watching another person in pain (e.g., Cheng, Hung, & Decety, 2012; Marsh et al., 2013).

Each type of index has its advantages and disadvantages. For instance, self-reports are easy to administer, but reporting on one's own emotions can be difficult, especially for individuals with ODD/CD who are known for low verbal (e.g., Déry, Toupin, Pauzé, Mercier, & Fortin, 1999; Loney, Frick, Ellis, & McCoy, 1998) and self-referential abilities (Pardini, Barry, Barth, Lochman, & Wells, 2006). Using self-reports in this group of individuals may lead to less reliable reports of empathy. Autonomic indexes, such as heart rate (HR), may suffer less from such problems but may be difficult to interpret. For instance, some researchers consider HR acceleration to reflect empathy (e.g., Anastassiou-Hadjicharalambous & Warden, 2008b), whilst others suggest that HR deceleration reflects empathy/sympathy, and HR acceleration to reflect personal distress (Eisenberg & Eggum, 2009; Eisenberg & Fabes, 1990).

ODD/CD

Diagnostic Criteria for ODD and CD

When antisocial behaviour becomes pervasive, affecting various domains of children's daily functioning, clinicians can diagnose ODD or CD. The DSM-5 (APA, 2013) categorizes ODD and CD as disruptive, impulse-control and conduct disorders. ODD is defined as a pattern of angry/irritable mood, argumentative as well as vindictive behaviour. ODD may be a developmental precursor of CD, which is generally seen as a more severe disorder

characterized by a repetitive and persistent pattern of behaviour that violates the basic rights of others or major societal norms. A distinction is made between individuals who show at least one symptom of CD prior to 10 years of age (childhood-onset type), and those who show no symptoms of CD before 10 years of age (adolescent-onset type). Moreover, there is a specifier *limited prosocial emotions* that apply to those who meet criteria for CD and also show a callous and unemotional interpersonal style. The specifier refers to those showing a lack of guilt, lack of empathy, no concern about performance and shallow affect.

ODD/CD Subtypes

ODD and CD are the most prevalent psychiatric disorders in children and adolescents (e.g., Loeber, Burke, Lahey, Winters, & Zera, 2000; Ford, Goodman, & Meltzer, 2003). The presence of ODD/CD not only predicts antisocial behaviour, it also predicts a host of other negative outcomes, such as academic underachievement (Tremblay et al., 1992), delinquency (Bradshaw, Schaeffer, Petras, & Ialongo, 2010; Moffit et al., 2008) and incarceration at a young age – resulting in high costs to the society (Foster & Jones, 2005). Understandably, much research attention has been dedicated to children and adolescents with ODD/CD.

Children and adolescents with ODD/CD form a heterogeneous group. They show different developmental pathways and important differences in terms of etiology, prognosis and treatment success (Viding, Fontaine, & McCrory, 2012). To better understand these differences, researchers have proposed subtypes. Researchers have, for instance, subtyped on developmental onset of the disorder (childhood-onset versus adolescence-onset), type of aggression (reactive versus proactive), comorbidity with other disorders (e.g., anxiety or ADHD) and level of CU traits (Fanti, 2016). Over the past years, subtyping on CU traits has received considerable attention in the literature (e.g., Frick, 2012; Frick, Ray, Thornton, & Kahn, 2013). In their developmental model of antisocial behavior, Frick and Viding (2009) have outlined three pathways to conduct problems. Those with adolescent-onset conduct problems are proposed to show an exaggeration of normal adolescent rebellion, whereas those with childhood-onset conduct problems may show distinct pathways depending on the presence or absence of CU traits.

CU subtype. ODD/CD children and adolescents with CU traits form an important subgroup of children with conduct problems, exhibiting a severe behavioural disturbance that is persistent and stable throughout development (Frick & Viding, 2009; Viding et al., 2012). They show severe aggressive behaviour that is often proactive in its nature (e.g., Frick et al., 2013; Kerig & Stellwagen, 2010) and have a temperamental style associated with fearlessness, low emotional arousal and insensitivity to punishment cues, hampering socialization and interventions (Frick, 2012). They often engage in criminal activities (Frick & White, 2008) and are at increased risk for developing psychopathy in adulthood (Lynam, Caspi, Moffitt, Loeber, & Stouthamer-Loeber, 2007).

ODD/CD children and adolescents with CU traits are generally associated with a fearless temperamental style, indicating that they experience little anxiety (Raine, 1993). However, recent evidence suggests an atypical profile where CU traits may co-occur with

anxiety (e.g., Fanti, Demetriou, & Kimonis, 2013; Kahn, Frick, Golmary, & Marsee, 2017; Kimonis, Frick, Cauffman, Goldweber, & Skeem, 2012). It is thought that this "secondary variant" of CU traits is more likely to be associated with prior maltreatment experiences than the "primary variant" (those without anxiety), which has high genetic loadings (Viding & McCrory, 2012).

Non-CU subtype. Limited research attention has been devoted to empathy dysfunction in ODD/CD children and adolescents without CU traits. Those without CU traits are thought to have a fearful temperamental style with increased emotional arousal at rest and in response to emotional stimuli (Blair, 2013; Blair, Leibenluft, & Pine, 2014). Moreover, they may show cognitive deficits such as low verbal intelligence and poor emotion regulation and are more like to come from families with poor parenting strategies (Frick, 2012; Frick & Viding, 2009). It is suggested (Blair et al., 2014) that around 40% of them may also meet criteria for mood disorders, such as depression and anxiety.

Taken together, ODD/CD children and adolescents with and without CU traits seem to reflect etiologically distinct subgroups (Viding & McCrory, 2015). There is accumulating evidence for the robustness of these subgroups, as attested in several research reviews (e.g., Blair et al., 2014; Frick, 2012; Frick et al., 2013) and by adding the specifier *limited prosocial emotions* to the diagnosis of CD in the DSM-5 (APA, 2013).

Empathy Impairments in ODD/CD Subtypes

In order to better understand empathy impairments in ODD/CD children and adolescents, Blair's neuroscientific theory on CD (Blair et al., 2014) can provide a useful guiding framework. Blair and his colleagues (2014) suggest that deficient empathy selectively occurs in CD individuals with CU traits, whereas heightened threat sensitivity may selectively occur in CD individuals without CU traits. Impaired decision making, however, may occur in both CD individuals with and without CU traits (Blair et al., 2014). Thus, according to this theory a lack of empathy may differentiate those with and without CU traits.

CU subtype

Children and adolescents with high levels of CU traits are thougt to show a selective impairment in empathic distress, which may possibly result from underlying abnormalities in the amygdala (Blair, 2013; Blair et al., 2014). The amygdala plays a central role in aversive conditioning and the processing of distress cues, fear and sadness in particular (Olsson & Phelps, 2007). Indeed, brain-imaging studies have shown dysfunctions associated with the amygdala amongst individuals with psychopathic tendencies (for a review, see Alegria, Radua, & Rubia, 2016). For example, ODD/CD adolescents with CU traits have shown reduced amygdala reactivity while processing fearful facial expressions (Marsh et al., 2008) and ODD/CD boys with CU traits have shown dampened amygdala reactivity to pre-attentively presented fearful faces relative to those without CU traits (Viding et al., 2012). Moreover, abnormalities in the amygdala may also affect the attention network (White et al., 2012),

leading to a failure to attend to other people's eyes, and, in turn, problems with recognizing emotional expressions (Dadds, Cauchi, Wimalaweera, Hawes, & Brennan, 2012). Attention to other people's emotions is a necessary condition for empathy (Skuse, 2003) and not being able to attend to other people's emotions can therefore be expected to affect the ability to empathize. Indeed, less eye contact between high CU boys with antisocial behaviour and their parents was associated with lower levels of empathy (Dadds, Jambrak, Pasalich, Hawes, & Brennan, 2011). Consequently, children with lesions in the amygdala may not be able to attend to salient emotional cues in the environment and feel aversive arousal when observing someone else in distress. This can be expected to critically hamper affective empathy development that becomes apparent in dispositional traits (trait empathy) as well as in concrete empathic situations (state empathy). Although there is accumulating evidence that CU traits are associated with affective empathy deficits (Blair, 2008, 2013; Blair et al., 2014), studies have scarcely been done with clinical ODD/CD samples. Moreover, relatively few studies have directly compared ODD/CD individuals with and without CU traits on empathic responsiveness. It is therefore currently unclear as to whether a lack of empathy is different for those with high versus low CU traits. This research gap will be addressed in **Chapter II**.

Deficient empathy is not only a defining feature of CU traits, it is also a defining feature of autism spectrum disorder (ASD; Baron-Cohen, Leslie, & Frith, 1985). ASD is characterized by deficits in social interaction and communication alongside rigid and repetitive behavior (APA, 2013) and shows behavioural overlap with CU traits. That is, both ASD and CU traits are linked to disruptive behaviors (Frick et al., 2013; Kaat & Lecavalier, 2013) and show reduced empathic responsiveness (APA, 2013). There are conceptual and empirical reasons to suggest that the 'empathy disorders' can be differentiated on type of empathy impairment. The social deficits that characterize ASD are often explained by a core deficit in ToM (Baron-Cohen et al., 1985). Because ToM is closely related to cognitive empathy (Baron-Cohen & Wheelwright, 2004), researchers associate ASD with impairments in cognitive empathy rather than affective empathy. A body of research reveals deficits in aspects of cognitive empathy (for reviews, see Boucher, 2012; Hill & Frith, 2003) and intact affective empathy (e.g., Jones, Happé, Gilbert, Burnett, & Viding, 2010; Schwenck et al., 2012) amongst ASD individuals. According to Smith's empathy imbalance hypothesis (2008), people with ASD are even overly sensitive to other people's emotions, which places them, in combination with their weak cognitive empathy skills, at risk for empathic over-arousal. Given the behavioural overlap between CU traits and ASD symptoms, it seems important to account for both conditions while studying associated empathy deficits. Yet, this has scarcely been done and there is, therefore, limited evidence for the assumption that CU traits and ASD are associated with distinct empathy deficits. This research gap will be addressed in **Chapter III**.

Non-CU Subtype

Empathy deficits are common across the broader range of antisocial behaviour (e.g., De Wied et al., 2010; De Wied et al., 2012; Martin-Key, Brown, & Fairchild, 2017) and are thus not only tight to those with CU traits. Researchers suggest that the ability to empathize in

those without CU traits may be affected by other factors such as hostility, anxiety and/or poor emotion regulation (De Wied et al., 2010). Misjudging other's intentions as more threatening or hostile than is the case, is a symptom of CD in the DSM-5 (APA, 2013). Hostility may reduce empathic responding, as demonstrated in studies with students from community samples (e.g., Lanzetta & Englis, 1989; Singer, 2006). Alternatively, poor emotion regulation may play a role. Poor emotion regulation is common amongst ODD/CD individuals (e.g., Masi, Muratori, Manfredi, Pisano, & Milone, 2015; Northover, Thapar, Langley, & van Goozen, 2015) and studies into normative development suggest that people with poor regulatory skills may not be able to optimally control empathic arousal, rendering them at risk for personal distress (Eisenberg et al., 1994). This is thought to be particularly true for people who are highly sensitive to negative emotions. ODD/CD individuals without CU traits and patients with anxiety are thought to be highly sensitive to threat because of underlying impairments in the *basic treat circuit* (amygdala, hypothalamus, periquaductal grey; Blair et al., 2014). Indeed, a brain imaging study revealed that ODD/CD adolescents showed increased amygdala reactivity while observing someone in pain (Decety, Michalska, Akitsuki, & Lahey, 2009). Consequently, the interplay between increased sensitivity to distress cues and poor emotion regulation may render ODD/CD children with anxiety particularly susceptible for empathic over-arousal and are more likely to experience high levels of personal distress rather than empathy or sympathy for another person in need. There is currently no empirical evidence to support this hypothesis and therefore further study is warranted. This research gap will be addressed in Chapter IV and V by measuring emotion regulation at a cognitive (i.e., executive attention) and physiological level (i.e., resting respiratory sinus arrhythmia), respectively.

Emotion regulation is a broad concept that refers to a number of processes by which emotions can be regulated (Cole, Martin, & Dennis, 2004). Shifting attention away from distressing stimuli and refocusing on positive or non-threatening ideas can be helpful to regulate emotional reactivity. Intentional use of attention processes is known as *executive attention* (Eisenberg, Hofer, & Vaughan, 2007; Eisenberg, Smith, & Spinrad, 2011; Rothbart & Rueda, 2005) and can be considered a cognitive index of regulation. Because executive attention can help regulate emotional reactivity, it is thought to be particularly important to regulate empathic arousal (Eisenberg, Fabes, Nyman, Bernzweig, & Pinuelas, 1994; Eisenberg & Sulik, 2012). This assumption has received empirical support from studies conducted with children from community samples using behavioural measures of executive attention and indexes of state as well as trait empathy (Eisenberg et al., 1996, 1998; Gurthrie et al., 1997).

Resting respiratory sinus arrhythmia (RSA) is considered a physiological index of emotion regulation. It is thought to reflect tonic parasympathetic control of the heart (Berntson et al., 1997), and it involves the natural variation in heart rate during the breathing cycle, with HR acceleration during inhalation and HR deceleration during exhalation. Researchers suggest that RSA indicates emotion regulation because it has been linked to prefrontal cortex (PFC) functioning, a brain area that is implicated in the regulation of emotions (Beauchaine, 2015a; Thayer, Hansen, Saus-Rose, & Johnson, 2009). The link between RSA and PFC has been described in the neurovisceral integration model (Thayer et

al., 2009) and has received support from empirical studies demonstrating inhibitory efferent pathways from the medial PFC to the parasympathetic nervous system (Lane et al., 2009; Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012) and positive relationships between RSA and executive functioning (Cupuana et al., 2014).

Findings from community sample studies reveal that children with higher RSA (indicating more effective emotion regulation) are perceived as more empathic by their parents and teachers (Eisenberg et al., 1996; Taylor, Eisenberg, & Spinrad, 2015) and are more likely to show empathy/sympathy (Fabes et al., 1993) than personal distress (Fabes et al., 1994; Zahn-Waxler, Cole, Welsh, & Fox, 1995) when observing someone in pain.

Conclusion

Taken together, we may expect affective empathy impairments in ODD/CD children and adolescents that are associated with distinct underlying mechanisms. Some may show a lack of empathy because of *under* responsiveness to other's distress cues, whilst others may show a lack of empathy because of *over* responsiveness to other's distress cues, hostility and/or poor emotion regulation abilities (De Wied et al., 2010). The above-described taxonomy is central to this dissertation and provides a useful guidance for the four studies of this dissertation. The first two studies address empathy dysfunction related to the CU subtype, whereas the final two studies address empathy dysfunction related to the non-CU subtype. Table 1 provides an overview of our research aims and relevant concepts of all studies included in this dissertation.

The Current Dissertation

Chapter II. Empathy Problems in Youth with ODD/CD, With and Without CU Traits

The primary aim of this study was to investigate the assumption that ODD/CD individuals with CU traits have affective empathy impairments and whether a lack of empathy may be different for ODD/CD subtypes. To this end, we conducted a literature review primarily including children and adolescents clinically diagnosed with ODD/CD. We summarize studies conducted with undifferentiated samples (not accounting for CU traits) of ODD/CD children and adolescents, followed by studies examining empathy problems in ODD/CD children and adolescents with high versus low CU traits.

Chapter III. CU traits, ASD Symptoms and Empathy in Boys with ODD/CD

The primary aim of this study was to investigate the assumption that CU traits and ASD symptoms are associated with distinct empathy impairments. Specifically, we investigated the additive and interactive effects of CU traits and ASD symptoms in relation to affective and cognitive trait empathy in a clinical sample of ODD/CD boys.

Chapter IV. Executive Attention and Empathy in ODD/CD Boys, With and Without Comorbid Anxiety Disorder

The primary aim of this study was to investigate the assumption that emotion regulation is involved in empathy-related responding amongst ODD/CD individuals, especially for those with comorbid anxiety disorder. To this end, we investigated relationships between executive attention and self-reports of empathy and sympathy to sadness-inducing stimuli in a clinical sample of ODD/CD boys, with and without comorbid anxiety disorder.

Chapter V. Resting Respiratory Sinus Arrhythmia and HR Reactivity to sadness inducing stimuli in ODD/CD Boys, With and Without Comorbid Anxiety Disorder

The primary aim of the fourth study was to investigate at a physiological level whether emotion regulation is involved in empathy-related responding amongst ODD/CD individuals, especially amongst those with comorbid anxiety disorder. To this end, we investigated relationships between resting RSA and HR reactivity (as a state index of empathy-related responses) to sadness inducing stimuli amongst ODD/CD boys, with and without comorbid anxiety disorder.

Sample of the Empirical Studies

Chapters III, IV and **V** make use of a clinical sample consisting of 53 ODD/CD boys between 7 and 12 years of age (M_{age}= 10.39, *SD* = 1.34; M_{IQ} = 95.29, *SD* = 13.41). The boys were recruited via clinical health centers and special education. Of the participants, 35 met criteria for ODD and 18 for CD. Comorbidity included ADHD (*n* = 38), anxiety (*n* = 34) and

depression (*n* = 9). All boys scored in the clinical range of externalizing as well as internalizing problem behavior (*T* > 60) on the Child Behavior Checklist *(*CBCL/6-18) and Teacher Report Form (TRF/6-18; Verhulst & Van der Ende, 2013). They scored in the moderate range (60 < T < 74) on ASD symptoms and in the slightly atypical range (56 < T < 60) on CU traits. Consistent with the literature (e.g., Blair, 2013; Frick, 2012), our sample represents a heterogeneous group of ODD/CD boys. Moreover, given the high comorbidity with anxiety, clinical scores on internalizing problems and mild levels of CU traits, our sample seems to represent a low rather than high CU subgroup of ODD/CD boys. Note, however, that the samples sizes in Chapters III, IV and V slightly differ because of differences in available data on main study variables.

Outline

This dissertation aimed to elucidate the nature of empathy impairments in ODD/CD children and adolescents and to explore possible mechanisms involved. We used a theoretical framework suggesting that some may show affective empathy impairments because of under-responsiveness to other's distress cues, whilst others may show affective empathy impairments because of over-responsiveness to other's distress cues, hostility and/or poor emotion regulation. **Chapter II** provides a comprehensive literature overview on empathy in ODD/CD individuals with and without CU traits. **Chapter III** examines the additive and interactive effects between CU traits and ASD symptoms in relation to affective and cognitive empathy in a clinical sample of ODD/CD boys. **Chapter IV** examines relationships between executive attention and self-reported empathic responses to sadness inducing film clips in boys with ODD/CD, with and without comorbid anxiety disorder and **Chapter V** examines relationships between RSA and HR reactivity to sadness inducing film clips in boys with ODD/CD, with and without comorbid anxiety disorder. **Chapter VI** is a general discussion of the theoretical and clinical implications of this research and provides potential directions for future research on empathy in children
and adolescents with ODD/CD.

Table 1. *Overview of Research Aims and Relevant Concepts of All Studies Included in This Dissertation*

Chapter	Research Aims	Study/Sample	Predictors	Measures	Outcomes	Measures	Trait/State Empathy
II	a) Examine the nature of empathy problems in clinical samples of ODD/CD children and adolescents with CU traits b) examine whether a lack of empathy contributes to a differentiation between ODD/CD subtypes.	Literature review	-	-	-	-	Trait and state
III	Examine additive and interactive effects of CU traits and ASD symptoms in relation to trait empathy in a clinical sample of ODD/CD boys.	Empirical study 49 ODD/CD boys	CU traits ASD symptoms	APSD CU scale (parent- and teacher-report) SRS total scale (parent-report)	Empathic sadness Affective empathy Cognitive empathy	IECA (child-report) BES (child-report) BES (child-report)	Trait
IV	Examine relationships between executive attention and self-reports of empathy and sympathy to sadness inducing stimuli in ODD/CD boys, with and without comorbid anxiety disorder.	Empirical study 49 ODD/CD boys	Executive attention Comorbid anxiety (yes/no)	ANT SSV (performance task) DISC Module A (parent interview)	Empathic sadness and sympathy	Self-reports to sadness-inducing film clips	State
V	Examine relationships between resting RSA and HR reactivity to sadness inducing film clips in ODD/CD boys, with and without comorbid anxiety disorder.	Empirical study 50 ODD/CD boys	RSA Comorbid anxiety (yes/no)	ECG (during aquatic video) DISC Module A (parent interview)	Empathic sadness	HR-reactivity to sadness-inducing film clips	State

Note. ODD = oppositional defiant disorder; CD = conduct disorder; CU = callous unemotional; ASD = autism spectrum disorder; RSA = respiratory sinus arrhythmia; HR = heart rate; APSD = Antisocial Personality Screening Device; SRS = Social Responsiveness Scale; ANT = Amsterdam Neuropsychological Tasks; SSVIS = Shifting attentional Set Visual; DISC = Diagnostic Interview Schedule for Children; ECG = electrocardiogram; IECA = Empathy Index for Children and Adolescents; BES = Basic Empathy Scale.

Chapter II

Empathy Problems in Youth with Disruptive Behavior Disorders, With and Without Callous Unemotional Traits

Pijper, J., De Wied, M., Van Goozen, S., & Meeus, W. (2017). Empathy problems in youth with disruptive behavior disorders, with and without callous unemotional traits. In L.C. Centifanti & D.M. Williams (Eds.), *The Wiley Handbook of Developmental Psychopathology* (pp.161-178). United Kingdom, UK: John Wiley and Sons Inc.

J.P. and M.d.W. conceptualized the study. J.P. wrote the manuscript. M.d.W., S.v.G. and W.M. provided feedback on the manuscript.

Abstract

The current literature review examined the assumption that ODD/CD children and adolescents with CU traits have affective empathy impairments, and whether a lack of empathy may be different for ODD/CD subtypes. We included studies that investigated a) clinical samples of ODD or CD youth (8-18 years) diagnosed according the DSM-IV (APA, 2000) criteria by clinicians, or with a well-validated and reliable diagnostic instrument, and b) state and/or trait empathy. We summarized studies conducted with undifferentiated samples (not accounting for CU traits) of ODD/CD children and adolescents, followed by studies examining empathy problems in those with high versus low CU traits. Findings reveal consistent evidence for affective empathy deficits in samples with ODD/CD children and adolescents differentiated and not differentiated on CU traits. The overall pattern of results was less consistent for cognitive empathy. Significant differences between ODD/CD subtypes emerged on autonomic indexes of affective state empathy. No differences were reported between ODD/CD subtypes on self-report and facial indexes of affective state empathy. Findings are discussed and the review concludes with clinical implications and suggestions for future research.

Empathy, generally defined as the ability to understand and share in another's emotional state, is important for moral understanding, motivating prosocial behavior (Eisenberg & Miller, 1987; Hoffman, 2008), and inhibiting unwanted behaviors such as delinquency and aggression (Miller & Eisenberg, 1988). Empathy problems are often associated with oppositional defiant disorder (ODD), and conduct disorder (CD), also referred to as disruptive behavior disorders (DBD) (American Psychiatric Association (APA), 2000). Children and adolescents with DBD may have empathy problems that are most striking in those with psychopathic tendencies or callous unemotional (CU) traits. CU traits are a precursor of the interpersonal-affective dimension of adult psychopathy, and central to the construct of psychopathic tendencies in youth (Frick & Hare, 2001; Lynam & Gudonis, 2005). In the fifth edition of the Diagnostic Statistical Manual of Mental Disorders (DSM-5) a specifier *with limited prosocial emotions* has been added to the classification of CD. This specifier applies to those who meet the criteria of CD, and also show a callous and unemotional interpersonal style, that is, lack of empathy, lack of guilt, and shallow affect (APA, 2013). Given the clinical importance of CU traits, it is important to examine whether lack of empathy can contribute to a differentiation between CD subtypes.

A growing body of research suggests that CU traits and psychopathic tendencies in children and adolescents are associated with significant impairments in empathy, especially emotional empathy (Blair, 2008, 2013; Blair, Leibenluft, & Pine, 2014). Yet, relatively few studies have directly compared youth with a CD diagnosis with and without CU traits on empathic responsiveness. In addition, although CU traits are tied to CD in the DSM-5 taxonomy of externalizing spectrum disorders, CU traits also co-occur with ODD and attention-deficit/hyperactivity disorder (ADHD) (e.g., Herpers, Rommelse, Bons, Buitelaar, & Scheepers, 2012). ODD and CD are frequently comorbid with ADHD (APA, 2013), and ADHD, in turn, has been linked to reduced empathy as well (e.g., Barkley, 2006; Braaten & Rosén, 2000; Marton, Wiener, Rogers, Moore, & Tannock, 2009), begging the question as to whether the empathy problems associated with CU traits are similar for those with pure DBD as for those with ADHD comorbidity.

Furthermore, empathy is a rather complex multidimensional construct (Davis, 2006), including affective and cognitive components, trait empathy (the tendency of an individual to respond empathically across different situations), state empathy (empathic reactions evoked within empathy-inducing situations), empathy-related processes and behavior. Previous reviews on empathy dysfunction in psychopathic youth (Blair, 2013; De Wied, Gispen-De Wied, & Van Boxtel, 2010; Frick, Ray, Thornton, & Kahn, 2013) have solely focused on aspects of affective versus cognitive empathy, but have made no distinction between trait and state empathy. This distinction is important, however, for at least two reasons: First, reviews on empathy in relation to pathological aggression (Lovett & Sheffield, 2007) and normative levels of externalizing behavior (Miller & Eisenberg, 1988) demonstrate stronger inverse relationships between empathy and antisocial behaviors for questionnaire measures of trait empathy than for indexes of state empathy. Second, and more important, based on the

hypothesis that CU traits may have a strong underlying genetic component (see Viding & McCrory, 2012 for a review), affecting neural circuits including the amygdala (Blair, 2013), there is reason to suggest that youth with CU traits will show particular deficits in both state and trait empathy. This chapter will take full account of the multidimensional construct of empathy, and discuss results obtained with measures of affective versus cognitive state and trait empathy separately.

A first aim of the current chapter is to examine the nature of empathy problems in clinically referred DBD youth with CU traits. A second aim is to examine whether a lack of empathy contributes to a differentiation between DBD subtypes. A third aim is to explore whether the empathy problems associated with CU traits are similar for those with pure DBD as for those with ADHD comorbidity. We start by considering the various components of empathy, using Davis' organizational model (1996, 2006), which emphasizes the connections between all components. Next, we reflect on the DSM-5 (APA, 2013) classifications of ODD and CD, summarize studies conducted with undifferentiated samples (not accounting for CU or psychopathic traits) of DBD youth, followed by studies examining empathy problems in DBD children and adolescents with high versus low CU traits. We close the chapter with clinical implications and suggestions for future research.

Empathy-Related Components

Davis' (1996, 2006) *organizational model of empathy-related constructs* treats empathy as a multidimensional phenomenon, involving traits (empathic tendencies), states (intrapersonal outcomes), affective and cognitive components. Affective empathy is a vicarious affective response more in line with another's situation than one's own (Hoffmann, 2000). A distinction is often made between empathy, sympathy and personal distress (Batson, 2009; Eisenberg, Shea, Carlo, & Knight, 1991). Empathy concerns an affect match between an observer and someone else's affective state, that is, feeling *with* another person. Sympathy, also labeled empathic concern, is an emotion oriented towards the other, that is, feeling *for* the other person. Personal distress is an aversive, self-focused, reaction which may consist of feelings of discomfort or anxiety when perceiving someone else's affective state, thus feeling *by* another person (Batson, 2009). Cognitive empathy is the ability to understand someone else's affective state without necessarily being in an affective condition oneself (Walter, 2012). Perspective taking, Theory of Mind (ToM; the ability of an individual to infer what another person is feeling or thinking, and what he or she may do based on those inferences), and empathic accuracy may all be considered aspects of cognitive empathy (see Table 1).

The tendency to share affective responses (affective trait empathy), and to engage in empathy-related cognitive processes such as role taking (cognitive trait empathy) may affect both empathy-related processes and intrapersonal outcomes (i.e., affective and/or cognitive state empathy). Empathy-related processes, in turn, may differ in terms of cognitive control, ranging from primitive processes such as motor mimicry to the most advanced cognitive

processes such as perspective taking. Motor mimicry, sometimes referred to as motor empathy (Blair, 2007), is thought to be an early component in the process of empathy. Motor mimicry may lead to the automatic transmission of emotions, and contribute to emotional contagion (Hatfield, Rapson, & Le, 2009). Evidence suggests that both humans (Molenberghs, Cunnington, & Mattingley, 2012) and other primate species (Iacoboni, 2005; Rizzolatti, 2005) possess a mirror neuron system underlying automatic mimicry, suggesting an evolutionary history for the capacity of empathy. Motor mimicry plays an important role in the development of empathy, especially in the preverbal years (Hoffman, 2000). As the cognitive system develops, higher order cognitive processes come to play a more important role, producing more sophisticated affective and cognitive empathic responses. Table 1 provides an overview of the key terms discussed in this chapter.

Brain-imaging studies suggest that distinct but interacting brain structures are involved in affective and cognitive empathy (see Shamay-Tsoory, 2009; Singer, 2006; Völlm et al., 2006). The insula and limbic structures are involved in affective empathy, while prefrontal brain areas are involved in perspective taking processes and ToM. The cognitive and affective empathy networks may also include the mirror neuron system in premotor areas (Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003). As such, it is possible that motor, affective and cognitive components of empathy become selectively, or jointly impaired with consequential differences in conduct problems and treatment options.

Table 1. *Key Terms in This Chapter*

Trait empathy	The tendency of an individual to respond empathically across different situations.
State empathy	Empathic reactions evoked during empathy-inducing situations.
Motor empathy	Spontaneous and automatic mimicry processes, which may lead to the automatic transmission of emotions.
Affective empathy	A vicarious affective response more in line with another person's situation than one's own. Affect matches, sympathy and/or personal distress are all considered aspects of affective empathy.
Cognitive empathy	The ability to understand and represent another person's emotional state, thoughts and beliefs. Perspective taking, ToM, and empathic accuracy may all be considered aspects of cognitive empathy.

Note. ToM = Theory of Mind.

Measuring Empathy

Different empathy indexes have been developed to assess motor mimicry and aspects of either the affective or cognitive components (or both) of state and trait empathy (e.g., Eisenberg & Fabes, 1990; Zhou, Valiente, & Eisenberg, 2003). Motor mimicry is usually studied within a laboratory setting where individuals are exposed to static or dynamic emotional facial expressions. Facial mimicry can be assessed using visual coding techniques (e.g., Marsh, Beauchaine, & Williams, 2008a), or facial electromyographic (EMG) procedures (e.g., De Wied, Van Boxtel, Zaalberg, Goudena, & Matthys, 2006). Facial EMG is a more sensitive measure, which may capture both automatic facial mimicry and facial expressions of vicarious emotional experiences (e.g., Dimberg, 1990; Dimberg, Thunberg, & Elmehed, 2000).

State empathy is routinely assessed within laboratory or field settings. Empathic responses are often elicited by more complex, empathy inducing stimuli, such as video-vignettes portraying other persons experiencing negative or positive emotions (e.g., Cohen & Strayer, 1996; De Wied, Van Boxtel, Matthys, & Meeus, 2012). Affective and cognitive outcomes can be measured at different levels of empathic functioning. Self-report, facial and autonomic indexes of empathy have all been used to assess empathy-related responses in children and adolescents with DBD (e.g., Cohen & Strayer, 1996; De Wied et al., 2012; Marsh et al., 2008a). In addition, brain event-related potential (ERP) technique (e.g., Cheng, Hung, & Decety, 2012) and functional Magnetic Resonance Imaging (fMRI) (e.g., Decety, Michalska, Akitsuki, & Lahey, 2009) have been employed to assess brain activity while respondents witness another person experiencing pain.

There are advantages and disadvantages associated with each type of index (e.g., Zhou et al., 2003). Self-report indexes are easy to administer, but appear to be affected by demand characteristics, such as the sex of the experimenter, and social desirability. Social desirability bias may influence facial indexes of empathy, although facial EMG responses suffer less from such biases than observational measures since it captures – in part – automatic mimicry processes (Dimberg, Thunberg, & Grunedal, 2002). Autonomic indexes of empathy, such as heart rate (HR), are relatively free from social desirability bias, but may be difficult to interpret. Some researchers consider HR acceleration to reflect empathy (e.g., Anastassiou-Hadjicharalambous & Warden, 2008b), others suggest that HR acceleration reflects self-focused personal distress reactions, and HR deceleration empathic concern (e.g., Eisenberg et al., 1988a, 1988b).

Over the years, various questionnaire measures have been developed to assess the dispositional tendency to engage in empathy-related processes (trait empathy) such as perspective taking or vicarious affective responding. Frequently used self-report questionnaire measures of empathy are the Empathy Index for Children and Adolescents (IECA, Bryant, 1982) and the Interpersonal Reactivity Index (IRI, Davis, 1983). The IECA is a 22-item self-report questionnaire, developed to assess affective empathy in children from the age of six years and older. The IRI is a 28-item self-report questionnaire, developed to assess both affective and cognitive empathy in adolescents and adults.

DBD: a Heterogeneous Disorder

Diagnostic Criteria for ODD and CD

In the DSM-5 (APA, 2013) ODD and CD are categorized as the disruptive, impulsive-control, and conduct disorders. ODD is characterized by a frequent and persistent pattern of angry/irritable mood, argumentative/defiant behavior or vindictiveness. ODD may be a developmental precursor of CD, especially for those with the childhood-onset type. The essential feature of CD is a repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated. The behaviors fall into four main groupings: aggression towards people and animals, destruction of property, deceitfulness or theft, and serious violations of rules. A distinction is made between individuals who show at least one symptom of CD prior to 10 years of age (childhood-onset type), and those who show no symptom characteristics before 10 years of age (adolescent-onset type). Moreover, a specifier *with limited prosocial emotions* has been added to the DSM-5 classification of CD, which applies to those who meet the criteria for CD, and also show a callous and unemotional interpersonal style. Characteristics of the specifier are lack of guilt, lack of empathy, no concern about performance and shallow affect. Those who qualify for the specifier are most likely to have the childhood-onset type of CD, and to have conduct disorder that persists into adulthood.

Multiple Pathways to Conduct Disorder

The subtyping of CD is based on research suggesting that antisocial individuals with CU traits not only differ in the severity and stability of antisocial behavior (Lynam & Gudonis, 2005), but also exhibit distinct emotional and cognitive characteristics (Frick et al., 2013), discrete pathophysiology (Blair, 2013; Blair et al., 2014), and different responses to treatment (Waller, Gardner, & Hyde, 2013), suggesting an etiologically distinct subgroup of antisocial youth. In their developmental model of antisocial behavior, Frick and Viding (2009) have outlined three pathways to conduct problems: one adolescent-onset pathway and two childhood-onset pathways. Youth with adolescent-onset conduct problems are proposed to show an exaggeration of normal adolescent rebellion. Youth with childhood-onset conduct problems may show distinct pathways depending on the presence or absence of CU traits. Youth with CU traits show a temperamental style characterized by low emotional arousal and insensitivity to punishment cues that interferes with the normal development of empathy, guilt and other aspects of conscience. Youth without CU traits may show high levels of emotional arousal, cognitive deficits, such as low verbal intelligence, and problems related to ineffective parenting, which may lead to emotion regulation problems (Frick & Viding, 2009, see also Frick et al., 2013 for a comprehensive review).

Empathy Problems in DBD Subtypes

Blair (2007, 2013) suggests that DBD youth with CU traits are likely to encounter *affective* empathy problems because of a genetic predisposition to show reduced amygdala responsiveness to distress cues. The amygdala contributes to aversive conditioning and the processing of distress cues, especially fear-related information (Olsson & Phelps, 2007). Abnormalities in this circuit may critically hamper socialization, and structurally affect empathy development. Indeed, brain imaging studies show reduced amygdala activation while processing fearful facial expressions in DBD youth with CU traits (Marsh et al., 2008b) and in boys with conduct problems and CU traits (Jones, Laurens, Herba, Barker, & Viding, 2009), relative to controls. Significant differences between DBD subtypes have more recently been demonstrated by Viding and colleagues (2012): DBD boys with high CU traits show less amygdala reactivity to preattentively presented fearful faces than those with low CU traits. Amygdala dysfunction in individuals with psychopathic traits may also affect the attention network (White et al., 2012), possibly leading to fear recognition deficits (e.g., Dadds, El Masry, Wimalaweera, & Guestella, 2008a). Reduced amygdala responsiveness to distress cues can structurally affect empathy development in youth with high CU traits. This may become apparent in dispositional characteristics (trait empathy), but also in primitive processes (such as mimicry) and more sophisticated empathic responses (state empathy).

DBD youth without CU traits may also show empathy problems (e.g., De Wied et al., 2012). However, their ability to empathize with others may be affected by different sources, such as negative sentiments, hostile attributions, or poor regulatory skills. The tendency to misperceive others intentions as more threatening or hostile than is the case, is listed as an associated feature of CD in the DSM-5 (APA, 2013). Negative sentiments and hostility may reduce empathic responding, as demonstrated in studies with healthy students (e.g., Lanzetta & Englis, 1989; Singer, 2006). Alternatively, it is possible that poor regulatory skills are related to empathy problems in DBD youth without CU traits. Eisenberg and colleagues (1994) argue that people who are sensitive to others' distress, but poor in emotion regulation, may be prone to personal distress. This could be true for DBD individuals without CU traits because they may have a highly sensitive *basic threat circuit* (amygdala, hypothalamus, periquaductal grey (PAG)) due to early trauma, violence or neglect (Blair, 2013), and poor regulatory skills (e.g., Beauchaine, Gatzke-Kopp, & Mead, 2007). To summarize, both DBD subtypes are likely to have empathy problems. However, youth with DBD and high CU traits may have empathy problems because of under-responsiveness to distress cues, whereas those without CU traits may have empathy problems because of over-responsiveness to distress cues, poor regulatory skills, and/or hostility bias (De Wied et al., 2010).

Empirical Evidence for Empathy Problems in DBD Youth

An increasing number of studies suggest that antisocial youth with CU or psychopathic traits are poor empathizers (e.g., Blair, 2013; Blair et al., 2014; Frick et al., 2013). Still, only a

minority of studies has investigated empathy dysfunction in *clinical* samples of youth with DBD. This chapter focuses on empathy dysfunction in clinical samples of children and adolescents with DBD. We will start reviewing studies conducted with undifferentiated samples of DBD youth, followed by studies that accounted for CU or psychopathic traits. We included studies that investigated a) clinical samples of ODD or CD youth (8-18 years) diagnosed according the DSM-IV (APA, 2000) criteria by clinicians, or with a well-validated and reliable diagnostic instrument, and b) state and/or trait empathy. Accordingly, we did not include studies conducted with community samples using screening instruments to assess conduct problems (ODD/CD) (e.g., Lockwood et al., 2013; Sebastian et al., 2012), or studies with children from special schools without clinical assessments of ODD/CD (Blair, 1999). However, we did include one study with children attending special schools scoring in the clinical range of CD problems as assessed with a screening instrument following DSM-IV criteria (Jones, Happé, Gilbert, Burnett, & Viding, 2010).

Studies With Undifferentiated Groups of DBD Youth

Motor empathy. De Wied and colleagues (2006) investigated facial EMG responses to dynamic facial expressions in DBD boys and controls. DBD boys showed subnormal facial EMG reactivity to angry faces, but not to happy faces. Using the same sample, De Wied and colleagues also examined facial EMG responses to more complex empathy-inducing film clips (De Wied, Van Boxtel, Posthumus, Goudena, & Matthys, 2009). Because EMG responses to empathy-inducing film clips may reflect facial expressions of empathic experiences in addition to spontaneous mimicry responses, findings from this study will be discussed below with other studies on *affective state empathy*.

Affective state empathy. A total of five studies investigated affective empathy, three with DBD boys (De Wied, Goudena, & Matthys, 2005; De Wied et al., 2009; Marsh et al., 2008a) and two with CD adolescents (Cohen & Strayer, 1996; Decety et al., 2009). De Wied and colleagues examined verbal, facial and autonomic responses to empathy-inducing film clips portraying negative (sadness and anger) and positive (happiness) emotions. Relative to controls, DBD boys reported less empathy (De Wied et al., 2005), and showed less facial EMG and HR reactivity in response to negative (not positive) emotions (De Wied et al., 2009). Consistent with the one study on motor empathy (discussed above), the results of De Wied and colleagues (2005, 2009) suggest that DBD boys are selectively impaired in dysphoric (not euphoric) empathy. Marsh and colleagues (2008a), however, found no indications of affective empathy impairments in DBD boys on various autonomic measures and an observational measure of facial mimicry to a sadness-inducing film clip. As for studies with adolescents, Cohen and Strayer (1996) were the first to show that CD adolescents reported less affective empathy in relation to various empathy-inducing film clips than controls. Decety and colleagues (2009) demonstrated that DBD boys, relative to controls, show increased brain reactivity in parts of the limbic system (involved in affective empathy) to pictures of others in pain accidentally inflicted by someone else. In sum, these studies support that DBD boys have

impaired affective empathy, especially when witnessing other persons in distress.

Cognitive state empathy. To our knowledge, three studies have investigated cognitive empathy in DBD youth, two with children (Downs & Smith, 2004; Happé & Frith, 1996) and one with adolescents (Cohen & Strayer, 1996). Downs and Smith (2004) demonstrated that ODD boys obtained lower scores than controls on emotion recognition and false belief tasks. Similarly, Cohen and Strayer (1996) demonstrated that CD adolescents showed impaired cognitive attributions to empathy-inducing film clips. In contrast, Happé and Frith (1996), found no differences between CD children and controls on a false belief task. However, the CD children scored lower than controls on items that required ToM according to the Vineland Adaptive Behavior Scales (VABS; Sparrow, Balla, & Cicchetti, 1984) interview (Happé & Frith, 1996). Given the distinct methods, samples, and the limited number of studies, it is still too soon to draw conclusions about possible cognitive empathy impairments in DBD youth.

Affective and cognitive trait empathy. One study with DBD boys (De Wied et al., 2005) and two with CD adolescents (Cohen & Strayer, 1996; Sterzer, Stadler, Poustka, & Kleinschmidt, 2007), showed that both DBD boys and CD adolescents obtained lower scores on questionnaire measures of affective empathy. Cohen and Strayer (1996) also demonstrated that CD adolescents are impaired in their perspective taking abilities, assessed with Davis' IRI (1983).

In sum, most studies with undifferentiated samples of DBD youth suggest a systematic impairment in affective trait and state empathy. Impairments in cognitive empathy have also been demonstrated, though studies are few, and results are inconsistent. Initial evidence suggests that DBD boys may have impaired motor empathy, but these findings need replication before we can draw conclusions.

Empirical Studies With DBD Subtypes

Affective state empathy. In total six studies examined affective state empathy, two with children (Anastassiou-Hadjicharalambous & Warden, 2008b; Schwenck et al., 2012) and four with adolescents (Cheng et al., 2012; De Wied et al., 2012; Marsh et al., 2011; Marsh et al., 2013). The majority of these studies reveal affective empathy problems in both DBD subtypes. Anastassiou-Hadjicharalambous and Warden (2008b) assessed self-report and autonomic responses of CD children (24% had comorbid ADHD) and controls to an empathy-inducing film clip portraying fear. Both CD children with and without CU traits reported less empathy than controls; no significant differences were found between subtypes. Interestingly, CD children with high CU traits showed lower HR activity and lower HR change from baseline than CD children with low CU traits and controls, suggesting less empathic concern. Those with low CU traits did not differ from controls on HR indexes of empathy. Schwenck and colleagues (2012) used self-report indexes to examine empathy in CD children (34% comorbid ADHD) and controls to empathy-inducing film clips (specific emotions were not reported). CD children with high CU traits reported less affective empathy than controls.

No differences occurred between the CD subtypes, nor did the low CU children report less affective empathy than controls. Findings remained the same after excluding children with ADHD.

As for studies with adolescents, Marsh and colleagues (2011) asked DBD adolescents (62% had ADHD comorbidity) with psychopathic traits and controls to recall emotional events, and to report their experienced physiological arousal during those events. Relative to controls, DBD adolescents with psychopathic traits reported less physiological arousal during fearful experiences. De Wied and colleagues (2012) examined empathy in DBD male adolescents (68% had ADHD comorbidity) with high and low CU traits and controls, using facial EMG, self-report and autonomic indexes of empathy. All respondents were exposed to film clips involving negative (sadness, anger) and positive (happiness) emotions. Compared to controls, both subtypes showed less facial responsiveness (less frowning muscle activity) to sadness, and reported less empathic happiness. Moreover, high CU adolescents reported less empathic sadness, and showed less HR deceleration to sadness than controls. Importantly, significant differences in HR change from baseline were found between DBD subtypes: DBD adolescents with high CU traits showed less HR change from baseline during sadness than those with low CU traits, indicating less empathic concern. Low CU adolescents did not differ from controls in HR change from baseline during sadness. Because the majority of the adolescents also had ADHD, the authors were unable to determine whether the results were exemplary for pure DBD or DBD with ADHD comorbidity (De Wied et al., 2012).

In an ERP study, Cheng and colleagues (2012) studied the cortical reactivity of CD adolescent offenders with high or low psychopathic traits (ADHD comorbidity not reported) and controls. Researchers measured cortical reactivity from brain regions associated with early affective arousal and late cognitive processing, during exposure to pictures of individuals in painful or nonpainful situations. In response to painful situations (relative to nonpainful situations), CD adolescents with high psychopathic traits showed early affective arousal and late cognitive processing deficits, whereas those with low psychopathic traits only showed late cognitive processing deficits. The psychopathic subtype, however, demonstrated intact late cognitive processing reactivity in response to pictures in which someone was intentionally harmed. In other words, findings suggest an impaired early affective arousal to empathy-eliciting stimuli for CD adolescents with high (not low) psychopathic traits, but an intact capacity to understand social situations in which someone is intentionally harmed.

In one fMRI study, Marsh and colleagues (2013) compared DBD adolescents (57% had ADHD comorbidity) and psychopathic traits with a control group. All adolescents were exposed to pictures of hands and feet in a painful or nonpainful situation, and asked to imagine that the situation was either happening to themselves or to someone else. Relative to controls, DBD adolescents with psychopathic traits showed reduced reactivity in the anterior cingulate cortex (ACC) and ventral striatum, cortical areas associated with pain. In response to pictures of others in pain, they also showed reduced reactivity in the left amygdala/uncus, left superior frontal gyrus, and insula than controls. Results remained

unchanged when those with ADHD were excluded from the analyses, suggesting that ADHD did not affect the results. In short, studies with DBD children and adolescents quite consistently reveal that both DBD subtypes are impaired in affective empathy as assessed by self-report, facial and autonomic measures of empathy. Differences between DBD subtypes have only been found on autonomic indexes of affective empathy.

Cognitive state empathy. Three studies examined ToM in children with CD (Anastassiou-Hadjicharalambous & Warden, 2008a; Schwenck et al., 2012) and children with clinical levels of CD problems (Jones et al., 2010), with inconsistent results. Anastassiou-Hadjicharalambous and Warden (2008a) examined affective and cognitive perspective taking (aspects of cognitive empathy) in CD children (31% had ADHD comorbidity) with high versus low CU traits and controls. Relative to controls, the CD children with low CU traits showed impaired affective and cognitive perspective taking. The CD children with high CU traits only showed impaired affective perspective taking compared to controls. Interestingly, the high CU children still outperformed the low CU children on affective perspective taking. The authors suggested that the weak cognitive perspective taking skills of those with low CU traits may negatively affect their affective perspective taking skills. A second study conducted by Jones and colleagues (2010) revealed no differences in ToM abilities between children with CD problems and high or low CU traits (ADHD comorbidity not reported), both subtypes also did not differ relative to controls. Likewise, clinically diagnosed CD children (34% had ADHD comorbidity) with high and low CU traits showed no differences in ToM, and both groups also showed no differences relative to controls. Omitting children with ADHD from the analyses did not change the results (Schwenck et al., 2012).

Affective and cognitive trait empathy. Three studies with children (Anastassiou-Hadjicharalambous & Warden, 2008b; Jones et al., 2010; Pasalich, Dadds, & Hawes, 2014), and one with adolescent offenders (Cheng et al., 2012) reveal inconsistent results. Using an affective empathy self-report questionnaire (IECA, Bryant, 1982), Anastassiou-Hadjicharalambous and Warden (2008b) demonstrated that CD children with both high and low CU traits report less affective empathy than controls, with no significant differences between CD subtypes. Jones and colleagues (2010) demonstrated that boys with CD problems (comorbid symptoms not reported) and high CU traits care less about being punished for their actions, care less about their victim's feelings, and place greater value on being the boss than controls. No significant differences emerged between those with high and low CU traits, nor between those with low CU traits and controls (Jones et al., 2010). A more recent correlational study (Pasalich et al., 2014), revealed an inverse relationship between CU traits and parent-reported affective and cognitive empathy in DBD children (24% ADHD), as assessed by the Griffith Empathy Measure (GEM; Dadds et al., 2008b). Researchers also found some evidence for an interaction effect between CU traits and ASD symptoms in relation to affective empathy. That is, higher CU traits were associated with lower affective empathy for moderate to high ASD symptoms. In addition, ASD symptoms were negatively related to cognitive empathy. Results did not change when researchers accounted for ADHD

comorbidity. In the Cheng and colleagues (2012) study, CD adolescent offenders (ADHD comorbidity not reported) with high or low psychopathic traits and controls completed a self-report questionnaire measuring both affective and cognitive trait empathy (IRI; Davis, 1996). Surprisingly, both subtypes reported less cognitive rather than affective trait empathy compared with controls. No differences emerged between CD subtypes. In sum, results suggest that CD children with high CU traits have impaired affective trait empathy, but CD subtypes do not seem to differ in this respect. Interestingly, preliminary evidence suggests that CU traits might also be related to impaired cognitive trait empathy.

Discussion

This chapter reviewed empirical studies on empathy problems in clinically referred DBD youth with and without CU traits. A first aim was to examine the nature of empathy dysfunction in those with CU traits. The relatively few studies show consistent evidence for impaired affective empathy in DBD children and adolescents with CU traits on indexes of both state (Anastassiou-Hadjicharalambous & Warden, 2008b; Cheng et al., 2012; De Wied et al., 2012; Marsh et al., 2011; Marsh et al., 2013; Schwenck et al., 2012) and trait empathy (Anastassiou-Hadjicharalambous & Warden, 2008b; Jones et al., 2010; Pasalich et al., 2014). Studies with undifferentiated groups of DBD youth also show consistent evidence for affective empathy impairment on indexes of both state and trait empathy (e.g., Cohen & Strayer, 1996; Decetey et al., 2009; De Wied et al., 2005, 2006, 2009; Sterzer et al., 2007), suggesting that impaired affective empathy is common across the broader range of disruptive behavior disorders.

As for cognitive empathy, the overall pattern of results is less consistent in samples of both undifferentiated and differentiated DBD youth. At least three studies suggest that CU traits may be associated with impaired cognitive empathy (Anastassiou-Hadjicharalambous & Warden, 2008a; Cheng et al., 2012; Pasalich et al., 2014). Interestingly, two studies used measures of cognitive empathy that might also involve affective components, that is, affective perspective taking (Anastassiou-Hadjicharalambous & Warden, 2008a), and cognitive trait empathy assessed with questionnaire items that might tap into affective components (Pasalich et al., 2014). Accordingly, the above-mentioned impairments in cognitive empathy could be due to the involvement of affective components in the assessment tools. Negative associations between CU traits and aspects of cognitive empathy have previously been found when affective components were involved. For example, adult offenders with significant levels of psychopathic traits showed impaired affective (not cognitive) ToM abilities, relative to controls (Shamay-Tsoory, Harari, Aharon-Peretz, & Levkovitz, 2010). High CU individuals may have an affective-specific impairment, which becomes apparent in their weak affective empathy, but also in their cognitive empathy abilities when it taps into emotional components.

A second aim was to investigate whether a lack of empathy contributes to a differentiation between DBD subtypes. As of yet, no between-group differences have been reported with indexes of cognitive state empathy, or with self-report and facial indexes of affective state empathy. However, significant differences have been demonstrated with autonomic indexes of affective state empathy. DBD subtypes differ in HR reactivity while observing others in distress, that is, high CU individuals show less HR change from baseline than low CU individuals. Interestingly, this pattern is seen in children with CD (Anastassiou-Hadjicharalambous & Warden, 2008b) and adolescents with DBD (De Wied et al., 2012). Similar results have also been found in an earlier study with emotionally disturbed children (DSM classifications of ODD and/or CD were not reported) conducted by Blair (1999). Blair obtained children's skin conductance responses to distressing (e.g., crying face), threatening (e.g., angry face), and neutral pictures (e.g., hairdryer). Children with high levels of psychopathic traits showed less skin conductance responses to distressed pictures than those with low levels of psychopathic traits and controls. Thus, high and low CU individuals from different samples, show distinct patterns of autonomic reactivity to distress cues, which possibly stem from genetically influenced abnormalities in the limbic system including the amygdala (Blair, 2013).

Abnormalities in the amygdala are proposed to affect the processing of distress cues (Olsson & Phelps, 2007), which may hamper socialization. Distortions in the amygdala are also thought to affect aversive stimulus-reinforcement associations. Accordingly, children with lesions in this area may learn to use (instrumental) aggression to achieve their goals because they do not acquire an uncomfortable feeling (i.e., aversive arousal) of others' distress. In others words, they do not feel aversely aroused or "punished" for their aggressive acts (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006).

So far, no studies have demonstrated significant differences between the DBD subtypes on self-report indexes of affective (or cognitive) trait empathy. Based on the assumption that CU traits delineate a distinct causal pathway to conduct problems (Frick et al., 2013), we may expect particular deficits in both state and trait empathy for high CU individuals. It is quite possible that self-report questionnaires of empathy are not sensitive enough to capture differences in trait empathy between the DBD subtypes. Even so, amygdala dysfunction, early trauma, and/or neglect may all hamper empathy development, leading to reduced empathic experiences across different situations for both DBD subtypes.

It is suggested that the mechanisms underlying empathy problems may be different for DBD subtypes. High CU individuals may show little empathy due to reduced sensitivity to distress cues (Blair, 2013), or impaired attention to the eyes (Dadds et al., 2006; Dadds et al., 2008a; Dadds, Jambrak, Pasalich, Hawes, & Brennan, 2011) because of a hyposensitive amygdala. Low CU individuals may show little empathy for a variety of reasons (De Wied et al., 2012), such as hostility bias (Dodge, Price, Bachorowski, & Newman, 1990; Orobio de Castro, Veerman, Koops, Bosch, & Monshouwer, 2002), and/or enhanced sensitivity to distress cues combined with poor regulatory skills (Eisenberg et al., 1994). It is thought that

individuals with low CU traits may have a hypersensitive basic threat circuit (Blair, 2013), as seen in their increased amygdala reactivity to fearful faces (Viding et al., 2012). To date, empirical studies on empathy dysfunction in DBD subtypes are scarce, and most studies demonstrate deficits without providing evidence for the mechanisms involved. Understanding the underlying mechanisms is essential, however, to improve prevention and intervention programs.

A third aim of the chapter was to explore whether the empathy problems associated with CU traits are similar for those with pure DBD as for those with comorbid ADHD. Upon examination of the samples, we can observe that five studies were conducted with CD youth and four with DBD youth. Seven out of nine studies reported on ADHD comorbidity, but only three tested whether the results remained the same after controlling for ADHD (Marsh et al., 2013; Pasalich et al., 2014; Schwenck et al., 2012). Although strong conclusions cannot be drawn, initial evidence seems to suggest that empathy problems in youth with DBD are not related to ADHD comorbidity. Because ADHD has also been related to empathy problems (Barkley, 2006) accounting for ADHD is important to gain more insight into the nature of empathy problems in DBD. Future studies should aim to control for ADHD or recruit samples with pure DBD individuals, and compare empathy-related responding to samples with pure ADHD individuals.

Clinical Implications

A clear understanding of the nature and cause of empathy problems associated with DBD and DBD subtypes is crucial to improve differential diagnostic procedures and treatment options. Currently, limited empirical evidence suggests that self-report measures of affective empathy (state and trait) are not able to make a distinction between the DBD subtypes. This stresses the need to develop new empathy indexes for diagnostic purposes in clinical practice.

The hypothesis that empathy inhibits aggression implies that enhancing empathic skills may reduce aggressive behavior. It is therefore not surprising that empathy training is generally included in broader interventions to reduce aggressive behavior in antisocial youth. Yet, it seems that these interventions mainly focus on enhancing aspects of cognitive empathy, that is, perspective taking skills. For example, the EQUIP program – an intervention to reduce antisocial behavior in juvenile delinquents – focuses on improving moral development by enhancing perspective taking skills (Gibbs, Potter, & Goldstein, 1995). Strengthening perspective taking skills is perhaps the best option so far, given the current lack of programs to improve affective empathy. However, based on the assumption that the two empathy components interact (see Shamay-Tsoory, 2009; Singer, 2006; Völlm et al., 2006), it could be possible that promoting aspects of cognitive empathy may also enhance affective empathy.

In addition, it is suggested that the empathy problems in DBD subtypes are related to impairments in distinct underlying mechanisms. This may call for different treatment

approaches to improve empathy-related responding in both subtypes. For those with CU traits, for example, improving emotion recognition (because of the possibility of impaired attention to the eyes) may enhance empathy-related responding. Indeed, initial findings suggest that emotion recognition training significantly improves affective trait empathy and conduct problems in children with significant levels of CU traits (Dadds, Cauchi, Wimalaweera, Hawes, & Brennan, 2012). For those without CU traits, however, one could speculate that improving self-regulation skills might be more effective to stimulate empathy.

Conclusion

It is proposed that distinct underlying mechanisms may be involved in the empathy problems associated with DBD subtypes. Relatively few studies have investigated empathy in clinically referred DBD youth, and those that have reveal deficits without providing evidence for the mechanisms involved. Both DBD subtypes show more consistent impairments in aspects of affective than cognitive empathy. Evidence for significant differences between subtypes is scarce, and is only demonstrated in studies that used autonomic measures of affective state empathy. Given the limited number of studies, considerably more research with multi-measure approaches is needed to examine the nature and causes of not only state but also trait empathy in DBD youth with and without CU traits.

Chapter III

Callous Unemotional Traits, Autism Spectrum Disorder Symptoms and Empathy in Boys with Oppositional Defiant Disorder or Conduct Disorder

Pijper, J., De Wied, M., Van Rijn, S., Van Goozen, S., Swaab, H., & Meeus, W. (2016). Callous unemotional traits, autism spectrum disorder symptoms, and empathy in boys with oppositional defiant disorder or conduct disorder. *Psychiatry Research, 245,* 340-345.

J.P. and M.d.W. conceptualized the study. J.P. analyzed the data and wrote the manuscript. M.d.W., S.v.R., H.S., S.v.G. and W.M. provided feedback on the analyses and manuscript.

Abstract

This study examined additive and interactive effects of callous unemotional (CU) traits and autism spectrum disorder (ASD) symptoms in relation to trait empathy, in boys with oppositional defiant disorder (ODD) or conduct disorder (CD). Participants were 49 boys with ODD/CD, aged between 7 – 12 years. Boys completed a questionnaire measure of empathic sadness and a broader questionnaire measure of affective and cognitive empathy. Parents and teachers reported on CU traits, and parents reported on ASD symptoms. In agreement with predictions, results reveal a negative association between CU traits and empathic sadness, particularly strong for ODD/CD boys with low levels of ASD symptoms. Results also reveal a negative association between ASD symptoms and cognitive empathy. Findings suggest that CU traits and ASD symptoms are associated with distinct empathy deficits with poor empathic sadness being more typical of CU traits than ASD symptoms.

Lack of empathy is a core feature of callous unemotional (CU) traits. CU traits are closely related to the interpersonal-affective dimension of adult psychopathy, and identify a particular severe and violent subgroup of individuals with oppositional defiant disorder (ODD) and conduct disorder (CD; for a review see Frick, Ray, Thornton, & Kahn, 2013). Research suggests that ODD/CD individuals with CU traits are impaired in affective empathy (sharing others' emotions) rather than cognitive empathy (understanding others' emotions; Blair, 2013; Blair, Leibenluft, & Pine, 2014). This impairment has been linked to amygdala dysfunction, potentially reducing emotional responsiveness (Blair, 2013) and/or attention (White et al., 2012) to another person's distress.

Lack of empathy is also a defining feature of autism spectrum disorder (ASD; Baron-cohen, Leslie, & Frith, 1985). Individuals with ASD show persistent deficits in social interactions and communication together with rigid and repetitive behavior (American Psychiatric Association (APA), 2013). Empathy problems in ASD seem to be related to aspects of cognitive empathy rather than affective empathy (Blair, 2005). The social deficits that characterize ASD have been explained by deficits in Theory of Mind (ToM; Baron-Cohen et al., 1985). ToM is conceptually linked to cognitive empathy (Baron-Cohen & Wheelwright, 2004), and involves the ability to understand that people have mental states, such as thoughts, believes and desires that are different to one's own (Baron-Cohen et al., 1985). Multiple studies have demonstrated that individuals with ASD indeed have deficits in aspects of cognitive empathy (for reviews see Boucher, 2012; Hill & Frith, 2003).

Some behavioral overlap exists between CU traits and ASD, as both are linked to disruptive behaviors (Frick et al., 2013; Kaat & Lecavalier, 2013) and reduced empathic responsiveness (APA, 2013). Accordingly, it seems important to account for both conditions while studying associated empathy deficits. Until now, only four studies have done this in clinical samples. Two studies have compared empathic profiles in boys with severe conduct problems and CU traits, ASD, and controls, revealing distinct profiles: boys with CU traits showed less affective empathy, whereas boys with ASD showed less cognitive empathy (Jones, Happé, Gilbert, Burnett, & Viding, 2010; Schwenck et al., 2012). One study compared profiles of aggressive ASD male adolescents with high or low CU traits (Rogers, Viding, Blair, Frith, & Happé, 2006). Both groups showed impaired cognitive empathy, those with CU traits also showed impairments in aspects of affective empathy. The fourth study examined additive and interactive effects of CU traits and ASD symptoms in relation to empathy in ODD/CD boys and girls between 3 and 9 years of age (Pasalich, Dadds, & Hawes, 2014). Findings revealed negative associations between CU traits and affective empathy and negative associations between ASD symptoms and cognitive empathy. Rather unexpected, higher CU traits were also related to lower levels of cognitive empathy, and a 'double hit' of high CU traits and high ASD symptoms tended to predict the lowest levels of affective empathy. Starting from the work of Rogers and colleagues (2006), Pasalich and colleagues (2014) took these results to suggest that high levels of both CU traits and ASD symptoms may be associated with serious conduct problems and therefore also with low levels of affective empathy. Yet, based on

studies suggesting that ASD individuals are actually quite sensitive (Schwenck et al., 2012), perhaps even overly sensitive to another person's distress (Smith, 2008), ASD symptoms might as well be expected to confound the "true" relationship between CU traits and affective empathy. If so, antisocial individuals with high levels of CU traits may show particularly low levels of affective empathy at low rather than high levels of ASD symptoms. By lack of empirical evidence we can only speculate about the role of ASD symptoms in the relationship between CU traits and affective empathy.

The aim of this study is to investigate additive and interactive effects of CU traits and ASD symptoms in relation to trait empathy in a clinical sample of ODD/CD boys. To the best of our knowledge this study tests the effects for the first time in boys with ODD/CD between 7 and 12 years of age. To examine the unique relationship between CU traits and empathic sadness, the current study includes a measure of empathic sadness in addition to broader measures of affective and cognitive empathy. Starting from the hypothesis that children with CU traits are selectively less emotionally responsive to distress cues (fear and sadness; Blair, 2013), we expect to find inverse relationships between CU traits and affective empathy, in particular with empathic sadness. Based on the hypothesis that children with ASD are poor in ToM (Baron-Cohen et al., 1985), we expect to find an inverse association between ASD symptoms and cognitive empathy. By lack of evidence we cannot formulate strong hypotheses about interaction effects. The work of Pasalich and colleagues (2014) suggests that the lowest levels of affective empathy could be expected in boys who have high levels of CU traits and ASD symptoms. By contrast, there is reason to expect lowest levels of affective empathy in ODD/CD boys high on CU traits but particularly *low* on ASD symptoms because ASD symptoms may confound the "true" association between CU traits and affective empathy.

Method

This study was approved by the Medical Ethical Committee of Leiden University Medical Centre (LUMC), and parents gave written consent prior to participation according to the declaration of Helsinki.

Participants

An initial group of 56 ODD/CD boys aged between 7 – 12 years were recruited via clinical health centers (n = 21) and special education schools (n = 35) in the Netherlands. The presence of ODD or CD, as set out by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR, APA, 2000), was determined by the parent-version of the Diagnostic Interview Schedule for Children (DISC-IV; Dutch version; Ferdinand & Van der Ende, 2002). A researcher in clinical child psychopathology carried out the interview. Exclusion criteria for the sample included estimated intelligence quotient (IQ) below 70 (n = 2), or no data on IQ (n = 3). Estimated IQ was assessed by Dutch versions (Kort et al., 2005) of the subtests Block Design and Vocabulary of the Wechsler Intelligence Scale for Children (WISC-III; Wechsler,

1991) administered by trained students. The subtests have a correlation of 0.90 with the full-scale intelligence quotient (Sattler, 1992). Two boys were additionally excluded from the sample because of no data on CU traits (*n* =1) or ASD symptoms (*n* =1).

Our sample obtained 49 boys with ODD (*n* = 32) or CD (*n* = 17) with a mean age of 10.28 (*SD* = 1.31). All boys had an estimated IQ in the normal range (*M* = 96.51, *SD* = 13.01; range 74-129). Comorbidity included attention deficit hyperactivity disorder (ADHD; *n* = 36), anxiety (*n* = 32) and depression (*n* = 8). Mean raw ASD symptoms, measured with the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005), are listed in Table 1. In total, 18 boys scored in the clinical range, 18 in the subclinical range, and 13 in the normal range of ASD symptoms. To verify ODD/CD diagnoses, we checked aggressive and externalizing problem behavior using the Dutch versions of the Child Behavior Checklist (CBCL/6-18) and Teacher Report Form (TRF/6-18; Verhulst & Van der Ende, 2013) completed by parents and teachers, respectively. All boys scored in the clinical range of aggressive (*T* > 65) and externalizing problem behavior (*T* > 60) on the CBCL and TRF. Twenty-three boys used psycho-pharmalogical treatment: 21 used psycho-stimulants, one used anti-psychotics, and one used both. There were no differences between boys with or without psycho-pharmalogical treatment on main study variables. Table 1 includes descriptive characteristics of the sample.

Measures

Dispositional empathy. All boys completed the Empathy Index for Children and Adolescents (IECA; Bryant, 1982) and the Basic Empathy Scale (BES; Jolliffe & Farrington, 2006). Affective empathy was assessed using the 7-item empathic sadness scale of the IECA (De Wied et al., 2007), which reflects emotional responsiveness to another person's sadness (e.g., 'Seeing a (girl/boy) cry makes me feel like crying') and the 11-item affective empathy scale of the BES, which reflects emotional responsiveness to a broader range of emotions (e.g., 'Other people's feelings do not affect me'). Cognitive empathy was assessed using the 9-item cognitive empathy scale of the BES (e.g., 'I can often understand how people are feeling even before they tell me'). The original binary (yes/no) response format was employed for the IECA and a 5-point Likert scale for the BES. Consequently, a sum-score was calculated for the IECA scale (range 0-7) and mean scores for the BES scales (range 1-5). Higher scores on all scales represented higher levels of dispositional empathy. Correlations between empathic sadness and affective empathy and both scales of the BES were significantly positive. Correlation between empathic sadness and cognitive empathy (BES) was marginally significant (Table 2). Sufficient psychometric properties have been found in previous studies for the empathic sadness scale of the IECA (De Wied et al., 2007) and both scales of the BES (Jolliffe & Farrington, 2006). In the current study internal consistency was good for the empathic sadness scale (α = .80) and acceptable for the affective (α = .77) and cognitive (α = .72) subscales of the BES.

CU traits and Impulsivity/Conduct Problems. Parents and teachers completed the Dutch version (De Wied, Van der Baan, Raaijmakers, De Ruiter, & Meeus, 2014) of the Antisocial Process Screening Device (APSD; Frick & Hare, 2001) designed to measure psychopathic tendencies in children and adolescents. The scale includes three subscales: CU, narcissism and impulsivity. A 3-point Likert scale was used. Following manual instructions, we combined parent and teacher ratings by taking the highest rated score on each item (Frick & Hare, 2001). We calculated a sum-score for the 6-item CU scale (range 0-12). Because the 7-item narcissism and 5-item impulsivity scales were highly correlated (r = .53, p < .001), we combined the scales to create an impulsivity/conduct problems (I/CP) scale (range 0-24) (Frick and Hare, 2001). Higher scores represented higher levels of CU traits and I/CP. Correlation between the CU and I/CP scale was significantly positive (Table 2). Sufficient psychometric properties have previously been found for the Dutch version of the APSD (De Wied et al., 2014). In the current study, internal consistency was acceptable for I/CP (α = .73) but poor for CU (α = .58). Poor internal consistency has more often been found for the CU scale (Pardini, Lochman, & Frick, 2003), and in this study the scale revealed good concurrent validity by showing a strong positive association with the externalizing scale of the TRF (r = .52, p < .001).

ASD symptoms. Parents completed the Dutch version (Roeyers, Thys, Druart, De Schryver, & Schittekatte, 2011) of the SRS (Constantino & Gruber, 2005). The SRS has 65 items and a 3-point response format measuring ASD symptoms. We used the total-score of all 65 items (range 0 -195), with higher scores representing higher levels of ASD symptoms. The SRS has shown good psychometric properties in both community (Constantino & Todd, 2003) and clinical samples (Constantino et al., 2003). In the current study internal consistency was good for the total scale (α = .93).

Statistical analyses

Separate hierarchical multiple regression analyses were conducted with empathic sadness (IECA), affective empathy (BES), and cognitive empathy (BES) as outcome variables. In step 1, we entered I/CP as a control variable because we were specifically interested in the association between CU traits and ASD symptoms with empathic tendencies. Because affective and cognitive empathy are related constructs (Hoffman, 2000), as supported by their positive correlations (see Table 2), we controlled for cognitive empathy when empathic sadness and affective empathy were the outcome variables. We also controlled for affective empathy (BES) when cognitive empathy was the outcome variable. In step 2, we entered CU traits and ASD symptoms as main effects. In step 3, we entered the product term CU traits X ASD symptoms to examine interactive effects. Because of potential lack of power due to our small sample size, we re-analyzed our data with bootstrap analyses by drawing 1000 resamples from our original sample using Statistical Package Software for the Social Sciences (SPSS) 22. For a 95% confidence interval 1000 resamples are recommended (Davison & Hinkley, 1997). Prior to analyses variables were standardized (M = 0; SD = 1). We dismantled significant interactions by testing whether slopes differed significantly from zero at low (-1

SD), mean (*M*) and high (+1 *SD*) levels of ASD symptoms (Hayes & Matthes, 2009). Analyses were repeated while controlling for ADHD and anxiety as assessed with the DISC-IV. Probabilities of all tests were two-tailed, except in regressions testing for main effects of CU traits and ASD symptoms, as earlier research consistently found negative links between CU traits and ASD symptoms and affective and cognitive empathy, respectively. Significance level .05 was used in all tests.

Results

Table 1 includes the means and standard deviations for all variables. Table 2 includes the bivariate correlations between the main study variables.

Table 1. *Sample characteristics*

	ODD/CD boys (*n* = 49)	
	M	*SD*
APSD		
CU	6.86	2.29
I/CP	14.47	3.97
SRS		
Total ASD	74.08	29.28
Low ASD	38.46	8.85
Moderate ASD	69.11	8.88
Severe ASD	104.78	17.10
CBCL		
Externalizing	67.61	8.88
Aggressive behavior	71.20	10.63
TRF[a]		
Externalizing	64.69	9.68
Aggressive behavior	67.67	12.87
IECA		
Empathic sadness	2.84	2.05
BES		
Affective empathy	3.00	.77
Cognitive empathy	3.54	.74

Note. APSD = Antisocial Personality Screening Device; CU = callous unemotional traits; I/CP = impulsivity/conduct problems; SRS = Social Responsiveness Scale; ASD = autism spectrum disorder; CBCL = Child Behavior Checklist; TRF = Teacher Report Form; IECA = Empathy Index for Children and Adolescents; BES = Basic Empathy Scale.
[a] $n = 45$.

Table 2. *Bivariate correlations between main study variables*

	1	2	3	4	5
1. CU					
2. ASD	.21				
3. I/CP	.53**	-.15			
4. Empathic sadness	-.23	.03	-.00		
5. Affective empathy	-.08	.05	-.06	.47**	
6. Cognitive empathy	.02	-.28[†]	.29*	.26	.45**

Note. CU = callous unemotional traits; ASD = autism spectrum disorder; I/CP = impulsivity/conduct problems.
*$p < .05$. **$p < .01$, two-tailed.
[†] $p < .05$, one-tailed.

Empathic sadness. Table 3 shows that after controlling for I/CP and cognitive empathy, the association between CU traits and empathic sadness was significantly negative. ASD symptoms were not significantly associated with empathic sadness. Interestingly, the interaction between CU traits and ASD symptoms was significant, R^2 = .26, F(5, 43) = 2.95, p = .022. At mean (B = -.34, p = .047) to low (B = -.70, p = .003) levels of ASD symptoms the association between CU traits and empathic sadness was significantly negative. The association was not significant at high levels of ASD symptoms (B = .03, p = .901). Model's adjusted R^2 was .17 representing a medium effect size. Bootstrap analyses supported significant main effect of CU traits (B = -.34, SE = .15, bootstrapped SE = .17 and lower limit of 90% CI = -.63 because of one-sided test) and interaction effect between CU traits and ASD symptoms (B = .37, SE = .15, bootstrapped SE = .18 and 95% CI = .01 – .75) demonstrating limited biases between estimates. The interaction effect remained significant after controlling for ADHD (β = -.16, n.s.) and anxiety (β = .16, n.s.), R^2 = .29, F(7,41) = 2.37, p = .040, adjusted R^2 = .17. Figure 1 visualizes the interactive effect by plotting simple slopes at low (-1 *SD*), mean (*M*) and high (+1 *SD*) levels of ASD symptoms.

Table 3. *CU traits and ASD symptoms in relation to empathic sadness (IECA)*

	Step 1		Step 2		Step 3	
	β	$R^2\Delta$	β	$R^2\Delta$	β	$R^2\Delta$
I/CP	-.08	.07	.13	.08	.08	.10*
Cognitive empathy	.28		.28		.29	
CU			-.34†		-.34*	
ASD			.20		.15	
CU X ASD					.32*	

Note. I/CP = impulsivity/conduct problems; CU = callous unemotional; ASD = autism spectrum disorder.
*p < .05, two-tailed.
†p < .05, one-tailed.

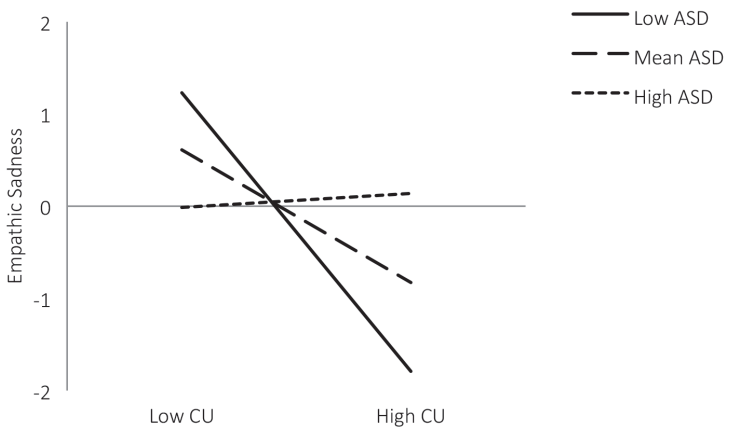

Figure 1. Interaction between callous unemotional (CU) traits and autism spectrum disorder (ASD) symptoms predicting empathic sadness.

Affective empathy. Table 4 shows that after controlling for I/CP and cognitive empathy, CU traits and ASD symptoms were not associated with affective empathy. The interaction between CU traits and ASD symptoms was marginally significant, R^2 = .33, F(5, 43) = 4.15, p = .004 (total model). However, further analyses revealed no significant slopes at low (B = -.29, p = .187), mean (B = -.03, p = .856) or high (B = .23, p = .292) levels of ASD symptoms. Bootstrap analyses also revealed neither significant main effects nor a significant interaction. The results remained the same after controlling for ADHD (β = -.09, n.s.) and anxiety (β = .36, p = .016), R^2 = .42, F(7, 41) = 4.17, p = .002.

Table 4. *CU traits and ASD symptoms in relation to affective empathy (BES)*

	Step 1		Step 2		Step 3	
	β	$R^2\Delta$	β	$R^2\Delta$	β	$R^2\Delta$
I/CP	-.21	.25**	-.18	.03	-.21	.05
Cognitive empathy	.52***		.56***		.56***	
CU			-.03		-.03	
ASD			.19		.15	
CUXASD					.23	

Note. I/CP = impulsivity/conduct problems; CU = callous unemotional traits; ASD = autism spectrum disorder.
**p < .01. ***p < .001, two-tailed.

Cognitive empathy. Table 5 shows that after controlling for I/CP and affective empathy, there was no association between CU traits and cognitive empathy. The association between ASD symptoms and cognitive empathy was significantly negative, R^2 = .38, F(4, 44) = 6.60, p < .001. Model's adjusted R^2 was .32 representing a medium to large effect size. Interaction between CU traits and ASD symptoms was not significant. Bootstrap analyses supported significant main effect of ASD symptoms demonstrating limited bias between

estimates (B = -.24, SE = .13, bootstrapped SE = .14 and lower limit of 90% CI = -.45 because of one-sided test). Main effect of ASD symptoms remained after controlling for ADHD (β = -.03, n.s.) and anxiety (β = -.01, n.s.), R^2 = .38, $F(6, 42) = 4.21$, p = .002, adjusted R^2 = .29.

Table 5. *CU traits and ASD Symptoms in Relation to Cognitive Empathy (BES)*

	Step 1		Step 2		Step 3	
	β	$R^2\Delta$	β	$R^2\Delta$	β	$R^2\Delta$
I/CP	.32*	.31***	.32*	.07	.33*	.01
Affective empathy	.47***		.48***		.51***	
CU			-.06		-.06	
ASD			-.24†		-.22†	
CUXASD					-.12	

Note. I/CP = impulsivity/conduct problems; CU = callous unemotional traits; ASD = autism spectrum disorder.
*p < .05. ***p < .001, two-tailed.
†p < .05, one-tailed.

Discussion

This study investigated additive and interactive effects of CU traits and ASD symptoms in relation to trait empathy in ODD/CD boys between 7 and 12 years of age. In line with predictions, we found an inverse association between CU traits and empathic sadness. The negative association between CU traits and the broader measure of affective empathy was not significant, however. The finding is consistent with theory and research (Blair, 2013; Blair et al., 2014) demonstrating that ODD/CD children with CU traits are particularly less responsive to another person's distress.

As predicted, we also found an inverse association between ASD symptoms and cognitive empathy, though the association was weak. The inverse association is consistent with studies revealing impaired cognitive trait empathy in ASD adolescents (e.g., Mazza et al., 2014; Pouw, Rieffe, Oosterveld, Huskens, & Stockmann, 2013) and studies showing ToM deficits in ASD (Boucher, 2012), as literature suggests that ToM and cognitive empathy are closely linked constructs (Baron-Cohen & Wheelwright, 2004).

Interestingly, ASD symptoms moderated the relationship between CU traits and aspects of affective empathy, significantly for empathic sadness (IECA) and marginally significant for affective empathy (BES). Hence, in contrast to findings obtained by Pasalich and colleagues (2014), our findings suggest that CU traits are inversely related to empathic sadness at *low* levels of ASD symptoms (not high). We offer four explanations to account for these differential findings. First, the interaction reported by Pasalich and colleagues (2014) was found for affective empathy, whereas our interaction was found for empathic sadness. However, given the considerable overlap between affective empathy and empathic sadness, we believe that other methodological differences between the studies offer more substantial explanations. Second, this study has a multi-informant design with parent and teacher reports of CU traits, parent reports of ASD symptoms and self-reports of empathy. This implies that our findings cannot be attributed to single reporter bias. This bias cannot be ruled out for the

findings of Pasalich and colleagues (2014), as acknowledged by the authors in the discussion of their study's limitations. Third, as previously mentioned, we used self-reports of empathy, whereas Pasalich and colleagues (2014) used parent-reports. There is evidence for low parent-child agreement regarding empathic behavior of the child (Sánchez-Pérez, Fuentes, Jolliffe, González-Salinas, 2014), potentially leading to differential findings. Low parent-child agreement may not be surprising as both may judge empathic behavior in different contexts. Furthermore, parents have to infer inner states from apparent behavior, while the children have to reflect on their own behavior. Last, but not least, different from the sample of Pasalich and colleagues (2014), our sample included boys meeting DSM-IV criteria for ASD (*n* = 11). It has been suggested that ASD individuals are *hyper* responsive to other's feelings (Smith, 2008), as evidenced by their self-reported overstrung reactions (Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007) and increased autonomic arousal to another's distress (Järvinen et al., 2015). Potential false positives for CU traits at high levels of ASD could thus confound the inverse relationship between CU traits and affective empathy. Accordingly, it is quite understandable to find lowest levels of empathic sadness in ODD/CD boys high on CU traits but low on ASD symptoms and to find no association in ODD/CD boys high on CU traits and ASD symptoms. In sum, these four differences can explain differential findings between the research of Pasalich and colleagues (2014) and our study.

Our study has some limitations. First, the CU subscale had low reliability. Low reliability, however, has a downward bias on parameter estimates (Furr & Bacharach, 2008). The effects therefore found in this study might have been stronger, but not weaker, if a more reliable measure had been available. Second, we used a small sample with limited statistical power. Third, self-report measures of empathy could have contaminated our findings, especially with regard to cognitive empathy in boys with ODD/CD and co-occurring ASD symptoms. There is evidence to suggest that children with disruptive behavior disorders have poor self-referential abilities (Pardini, Barry, Barth, Lochman, & Wells, 2006), and poor self-referential abilities, in turn, are found to be associated with poor mentalizing abilities in adults with ASD (Lombardo, Barnes, Wheelwright, & Baron-Cohen, 2007). In the current study, therefore, ODD/CD children with high levels of ASD symptoms may have had problems reporting on their empathic experiences without being aware of these problems.

In sum, findings suggest that CU traits and ASD symptoms are associated with distinct empathy deficits, and that poor empathic sadness is more typical of CU traits than ASD symptoms. Future studies should build up on our study by trying to replicate results with state measures of empathy that also assess underlying mechanisms of empathy-related responding in ODD/CD children and adolescents.

Chapter IV

Executive Attention and Empathy-related Responses in Boys with Oppositional Defiant Disorder or Conduct Disorder, With and Without Comorbid Anxiety Disorder

Pijper, J., De Wied, M., Van Rijn, S., Swaab, H., Van Goozen, S., & Meeus, W. (2018). Executive attention and empathy-related responses in boys with oppositional defiant disorder or conduct disorder, with and without comorbid anxiety disorder. *Child Psychiatry and Human Development.* Retrieved from https://doi.org/10.1007/s10578-018-0810-z

J.P. and M.d.W. conceptualized the study. J.P. analyzed the data and wrote the manuscript. M.d.W., S.v.R., H.S., S.v.G. and W.M. provided feedback on the analyses and manuscript.

Abstract

This is a first study that investigated the relationships between executive attention – as an important aspect of emotion regulation – and state empathy and sympathy in ODD/CD boys with (*N* = 31) and without (*N* = 18) comorbid anxiety disorder (7 – 12 years). Empathic reactions were evoked using three sadness-inducing film clips. One clip was highly evocative involving a bear cub losing his mother, whilst two other clips were mildly evocative involving children in common childhood situations. Self-reports of empathy and sympathy were collected and executive attention was assessed with a performance task. Poor executive attention skills were associated with less empathy and sympathy, particularly in ODD/CD boys with anxiety and under conditions of a highly evocative stimulus. Our findings support the view that different mechanisms may be involved in empathy problems of ODD/CD children.

Empathy problems have been associated with oppositional defiant disorder (ODD) and conduct disorder (CD; De Wied, Gispen-De Wied, & Van Boxtel, 2010). Children with ODD/CD constitute a heterogeneous group, however, and research suggests that there are individual differences in the mechanisms underlying empathy deficits in children with ODD/CD (De Wied et al., 2010; Pijper, De Wied, Van Goozen, & Meeus, 2017). Poor emotion regulation is common in children with ODD/CD (Hobson, Scott, & Rubia, 2011; Matthys, Vanderschuren, Schutter, & Lochman, 2012), and studies conducted with normal samples suggest that emotion regulation is a factor in empathy, especially in people who are highly sensitive to negative emotions (Eisenberg, Fabes, & Spinrad, 2006). Furthermore, studies with clinical samples show that ODD/CD boys exhibiting relatively high levels of anxiety (indicated by high resting heart rate) and poor emotional control (indicated by low levels of resting respiratory sinus arrhythmia) are selectively impaired in empathy-related responses with negative (not positive emotions; De Wied, Van Boxtel, Posthumus, Goudena, & Matthys, 2009; De Wied, Van Boxtel, Zaalberg, Goudena, & Matthys, 2006). Poor emotional control has been put forward as a factor that might be involved in their empathic responding (De Wied et al., 2010). Empirical evidence for this hypothesis is lacking, however. The current study takes up this issue and examines whether emotion regulation is involved in empathic responses to sadness inducing stimuli in boys with ODD/CD, with and without comorbid anxiety disorder.

Empathy, generally defined as the ability to understand and share another person's feelings (Eisenberg & Strayer, 1987), is a complex construct, encompassing traits (a stable disposition), states (transient reactions), and affective and cognitive components (Davis, 1996). Affective empathy is examined in this study, which refers to "the vicarious affective response to another person" (Hoffman, 2000, p.29) The literature often distinguishes empathy, sympathy and personal distress (Eisenberg & Eggum, 2009), although the constructs are closely related and often part of the same emotional experience. Empathy refers to a matching of emotions (feeling *with* the target), sympathy refers to feelings of sorrow or concern (feeling *for* the target), and personal distress is a self-focused aversive reaction evoked *by* the emotions of another person. Eisenberg and colleagues (1994) hypothesized that individuals who cannot adequately regulate their emotions are more likely than others to become empathically over-aroused when they witness another person in distress, and to experience personal distress rather than sympathy. Well-regulated individuals are thought to maintain optimal levels of empathic arousal and to experience high levels of empathy/sympathy. This hypothesis has been confirmed by findings from numerous studies with children from community samples, using various measures of emotion regulation and empathy-related responses (Eisenberg, 2000, 2010; Eisenberg et al., 2006).

Eisenberg, Hofer and Vaughan (2007) define emotion regulation as 'processes used to manage and change if, when, and how (e.g., how intensely) one experiences emotions and emotion-related motivational and physiological states, as well as how emotions are expressed behaviorally' (p. 288). One of these processes involved occurs at the cognitive level by deliberately shifting attention away from distressing stimuli and refocusing attention to

positive or non-threatening ideas or objects. This deliberate use of attention processes is known as *executive attention* and can be subsumed under the larger construct of effortful control (a dimension of temperament related to the modulation of emotions and behaviour; Eisenberg et al., 2007; Eisenberg, Smith, & Spinrad, 2011; Rothbar & Rueda, 2005). Because executive attention could help regulating emotional reactivity, it is thought to be particularly important in the modulation of empathic arousal (Eisenberg, Fabes, Nyman, Bernzweig, & Pinuelas, 1994).

Despite the suggested importance of executive attention in the regulation of empathic arousal, few empirical studies have addressed the relationship between executive attention and empathy or sympathy. In agreement with predictions, studies with community samples of school-aged children show positive relationships between behavioural measures of children's executive attention and state indexes of sympathy concurrently (Gurthrie et al., 1997) and over time with trait empathy/sympathy (Eisenberg et al., 1996, 1998). The proposed relationships have further been supported by empirical studies demonstrating positive links between the broader construct of effortful control (e.g., inhibitory control) and indexes of trait empathy (Rothbart, Ahadi, & Hershey, 1994) and sympathy (Eisenberg et al., 2007; Murphy, Shepard, Eisenberg, Fabes, & Guthrie, 1999) as well as with conscience development (related to sympathy; Kochanska, & Knaack, 2003) in community samples.

The modulation of empathic arousal may be particularly important in highly sensitive people (Eisenberg et al., 1994, 2006), who are expected to be more susceptible for vicariously induced negative emotions. If they lack the ability to efficiently regulate themselves they may become overwhelmed, rendering them at risk for self-focused rather than other-focused attention and, in turn, feel lower levels of empathy/sympathy. Using different behavioural measures of emotion regulation, Eisenberg and her colleagues have put this hypothesis to the test in at least two studies with community samples of school-aged children (Eisenberg et al., 1996, 1998). Inhibition, impulsivity and self-control were positively related to trait empathy/sympathy among children *high* in emotional sensitivity (Eisenberg et al., 1996, 1998), whilst executive attention was positively related to trait empathy/sympathy among those *low* in emotional sensitivity (Eisenberg et al., 1998). Results are thus still far from conclusive.

Children with ODD/CD constitute a heterogeneous group (Frick, Ray, Thornton, & Kahn, 2013), including children who may show different neurocognitive dysfunctions associated with low threat sensitivity (e.g., those with callous-unemotional traits) or with high threat sensitivity (Blair, Leibenluft, & Pine, 2014). Heightened threat sensitivity is thought to occur in ODD/CD children and adolescents without CU traits, and those with comorbid anxiety disorder. ODD/CD children with comorbid anxiety disorder may be highly susceptible for vicariously induced negative emotions, as they have been associated with hypersensitivity to perceived threat (Blair et al., 2014) and increased autonomic arousal (Bubier & Drabick, 2009). For instance, male adolescent offenders with high levels of anxiety exhibited increased attentional bias to distressing stimuli than those with low levels of anxiety (Kimonis, Frick,

Cauffman, Goldweber, & Skeem, 2012). Furthermore, ODD/CD children with higher levels of anxiety exhibited higher cortisol stress reactivity than those with lower levels of anxiety (Van Goozen, Matthys, Cohen-Kettenis, Buitelaar, & Van Engeland, 2000), and ODD/CD boys with high rates of internalizing problems (including anxiety) had higher resting heart rate (HR) than normal controls (De Wied et al., 2009; Lahey, Loeber, Burke, Rathouz, & McBurrnett, 2000). Moreover, children with ODD/CD have been found to show impairments in executive functions, including problems with attention shifting (Ter-Stepanian et al., 2016). Consequently, the interplay between increased sensitivity to negative emotions and poor attentional regulation can render ODD/CD children with anxiety particularly susceptible to become over-aroused in response to other's distress and show little empathy/sympathy for others, accordingly.

The main purpose of the present study was to examine whether executive attention is a factor in state empathy/sympathy in ODD/CD boys, with and without comorbid anxiety disorder. To evoke empathic reactions we used three sadness inducing film clips: one film clip portraying a bear cub in distress after his mother dies and two film clips involving children who experience sadness in common childhood situations (De Wied, Goudena, & Matthys, 2005). In a prior study with ODD/CD boys, the bear clip was found to be more evocative than the human clips (De Wied et al., 2005).

Theory (Eisenberg et al., 1994) and empirical evidence (Eisenberg et al., 2006) suggest that more efficient emotion regulation is associated with stronger empathy or sympathy. Therefore, we predicted that ODD/CD boys with stronger executive attention skills would report more empathy and sympathy. In addition, because aspects of emotion regulation are especially likely to be a factor in empathy among those highly sensitive to negative emotions (Eisenberg et al., 1994) and under conditions of strong vicarious arousal (Eisenberg, 2010), we expected the proposed relationship to be particularly evident within the group of ODD/CD boys with comorbid anxiety disorder and particularly under conditions of the most challenging stimulus (i.e., the bear clip). Finally, given the importance of CU traits in the ODD/CD literature (Blair, 2013), we investigated the effects of CU traits in the relationship between executive attention and empathic responses. Based on the assumption that heightened threat sensitivity is more likely to occur in ODD/CD children with low rather than high CU traits (Blair et al., 2014), we may expect a stronger role of emotion regulation in empathic responses amongst those with low rather than high CU traits.

Method

This study was approved by the Medical Ethical Committee of Leiden University Medical Centre (LUMC), and parents gave written consent prior to participation according to the declaration of Helsinki.

Recruitment and Participants

An initial group of 58 ODD/CD boys (7-12 years) was recruited via clinical health centers (n = 23) and special education (n = 35). The presence of psychopathology, as set out by the DSM-IV criteria, was determined by the parent-version of the Dutch Diagnostic Interview Schedule for Children (DISC-IV; Ferdinand & Van der Ende, 2002). Boys were excluded from the sample if they had an estimated intelligence quotient (IQ) below 70 (n = 3) or missed data on estimated IQ (n = 2). Estimated IQ was assessed with the subtests Block Design and Vocabulary of the Dutch Wechsler Intelligence Scale for Children (WISC-III-NL; Kort et al., 2005). Four additional participants were excluded from the sample because of missing data on executive attention (n = 2), CU traits (n = 1) and ASD symptoms (n = 1). ASD symptoms were, among other variables, used to verify distinction between subgroups.

Our sample consisted of 49 ODD/CD boys (M_{age}= 10.35, SD = 1.27; M_{IQ} = 95.74, SD = 12.19). Those with comorbid anxiety disorder according to the DISC-IV (social phobia (n = 9), separation anxiety disorder (n = 10), specific phobia (n = 25), panic disorder (n = 1), agoraphobia (n = 1), generalized anxiety disorder (n = 9), obsessive compulsive disorder (n = 2), and/or post traumatic stress disorder (n = 3)) were assigned to the ODD/CD anxious group (ODD/CD+ANX), whereas those without were assigned to the ODD/CD non-anxious group (ODD/CD-ANX). The ODD/CD+ANX group consisted of 31 boys with ODD (n = 20) or CD (n = 11), of which 26 had comorbid attention deficit hyperactivity disorder (ADHD) and five comorbid depression. Eleven boys used psycho stimulants, one boy used anti-psychotics and one used both. The ODD/CD-ANX group consisted of 18 boys with ODD (n = 14) or CD (n = 4), of which nine had comorbid ADHD and one comorbid depression. Seven boys used psycho stimulants. Subgroups showed no differences in age or IQ. Further, no differences were obtained between boys with or without psycho-pharmacological treatment on main study variables.

Stimuli

Empathy-inducing film clips. To evoke empathic reactions, participants were exposed to three sadness-inducing film clips: one clip involving a girl (Anja) feeling depressed because she is ignored and badgered by her classmates (length: 57s), one clip involving a boy (Mohammed) who fails at selection training for a soccer tournament (length: 148s), and one clip involving a bear cub in distress after his mother dies (length 164s). The clips have been used before to evoke empathic sadness in studies with ODD/CD boys (De Wied et al., 2006) and adolescents (De Wied, Van Boxtel, Matthys, & Meeus, 2012). A longer version of the bear clip (length: 256s) was used in the study with ODD/CD boys mentioned above (De Wied et al., 2005). In the current study, a shorter version of the bear clip was used to keep in time with the human clips.

Relaxing video. Because previous studies have documented that ODD/CD children with high rates of anxiety show increased autonomic arousal (De Wied et al., 2009), we compared resting HR to verify distinction between subgroups. Prior to the empathy task,

resting HR was assessed during a 5-min fragment from the video Coral Sea Dreaming (Small World Music, Inc.), found to promote relaxation (Piferi, Kline, Younger, & Lawler, 2000; for a detailed description of the assessment of HR, see De Wied et al., 2012). Prior to each empathy clip, a 1-min fragment of the relaxing video was used to ensure recovery from emotional arousal induced by the previous clip.

Apparatus and stimulus presentation. Participants were individually tested in a laboratory room. All empathy-inducing clips were randomly presented on a 17-inch color monitor (Philips 109E50) that was placed on a desk. Following a 1-min aquatic video, the title of the clip (i.e., the name of the protagonist) appeared on the screen, and a female voice over introduced the clip. A program written with Delphi 6 controlled stimulus presentation and collected self-report data.

Outcome Measures

Clinical measures. To verify group distinction, subgroups were compared on level of 1) externalizing and internalizing problem behaviour, using the externalizing and internalizing scales (including subscales rule-breaking, aggressive behaviour, anxious/depressed, withdrawn/depressed and somatic complaints) of the Dutch *Child Behaviour Checklist (*CBCL*6-18*; Verhulst & Van der Ende, 2013), 2) CU traits, using combined parent and teacher ratings on the CU scale of the Dutch *Antisocial Process Screening Device* (APSD; De Wied, Van der Baan, Raaijmakers, De Ruiter, & Meeus, 2014), and 3) ASD symptoms, using the total scale of the Dutch *Social Responsiveness Scale* (SRS; Roeyers, Thys, Druart, De Schryver, & Schittekatte, 2011). In the current study, internal consistency was acceptable for the externalizing (α = .89) and internalizing (α = .87) scales of the CBCL, poor for the CU scale (α = .56) of the APSD and good for the total scale of the SRS (α = .94). Of all clinical measures, T-scores were used.

Empathy. Following each empathy clip, participants had to identify the *quality* and *intensity* of the emotions of the protagonists and their own experienced emotions. The quality was established by marking one or more cartoon faces visualizing fear, anger, happiness, sadness, surprise, or neutral (i.e., no emotion). The intensity was established by marking one out of four boxes increasing in size. If the participant identified the target emotion, the participant's experienced (target) emotion was scored on a 5-point scale (0 = no empathy to 4 = very much). The participant received a 0 score if they incorrectly identified the target emotion(s), or did not experience the target emotion themselves. In response to the bear, all participants identified the target emotions (sadness or fear). In response to Mohammed 4 participants did not identify the target emotion (sadness) and in response to Anja 2 participants did not identify the target emotion (sadness). The correlation between the empathy scores obtained for Mohammed and Anja was significantly positive (r = .57). Both scores were combined to create one empathy score for the human clips, accordingly.

Sympathy. Following the empathy questions, participants were asked if they felt sorry for the protagonist by marking one of two boxes that represented yes or no. If they

marked yes, participants were asked how much they felt sorry by marking one of four boxes increasing in size. Sympathy was scored on a 5-point scale (0 = no sympathy to 4 = very much). The sympathy scores of Mohammed and Anja were significantly related (r = .53), and were combined to create one sympathy score for the human clips.

Manipulation check. The bear clip was thought to be more evocative than the human clips not only because of its theme, but also because cute young animals are likely to elicit strong positive feelings in children (Endenburg, 1995) and adults (Archer & Monton, 2011), which may minimize potential confounding effects of negative dispositions. In line with previous findings (De Wied et al., 2006), a repeated measures ANOVA revealed that ODD/CD boys in the current study reported higher levels of empathy and sympathy to the bear clip than to the human clips, $F(1,48)= 25.72$, $p<.001$, $F(1,48)= 68.03$, $p<.001$, respectively. We therefore considered it legitimate to separately analyze the empathic responses of the bear clip and human clips.

Executive attention. Executive attention was assessed with the *Shifting Attentional Set – Visual (SSV)* subtest of the Amsterdam Neuropsychological Tasks program (De Sonneville, 2014). The SSV measures attention shifting over three consecutive trials using a within task manipulation by correcting the recorded number of errors and reaction times of trial three from those of trial one. In the first trial, a constantly presented bar appears on the screen with a green block randomly jumping to the left or the right. The participant is instructed to follow the green block with the corresponding mouse key (left or right). In the second trial, a red block appears on the bar also randomly jumping to the left or the right. This time, however, the participant is instructed to respond in the opposite direction. In the third trial, the first and second trials are randomly mixed, which requires attention shifting. Although the SSV is primarily intended to measure attention shifting, it also taps into attention focusing and is therefore a good measure of executive attention. The SSV has been successfully employed in clinical samples (Jahja, Huijbregts, De Sonneville, Van der Meere, & Van Spronsen, 2014; Van Rijn & Swaab, 2015) and has satisfactory psychometric properties (De Sonneville, 2005).

Number of errors and reaction time were significantly related (r = -.38). We controlled for reaction time in the analyses, revealing no significant influences to the findings. Accordingly, we only used number of errors in the analyses: more errors represented weaker executive attention.

Procedures

Participants were invited to visit Leiden University for one day with one of their parents. During this day, parents signed informed consent, filled out questionnaires and completed the DISC-IV interview. Boys completed the empathy-task. Within two weeks, a second session took place either at the school or clinical health center of the participants. During this session, boys were administered to the subtests for estimated IQ and executive attention.

Statistical Analyses

In *pre-analyses,* distinction between subgroups were verified by conducting independent samples t-tests, using ODD/CD subgroups as independent variable and scores on internalizing problem behaviour (anxious/depressed, withdrawal, somatic complaints), externalizing problem behaviour (aggressive, rule-breaking), CU traits and ASD symptoms as well as resting levels of HR as dependent variables.

In *main analyses*, separate multiple hierarchical regression analyses were conducted with outcome measures empathy and sympathy of the bear clip, and empathy and sympathy of the human clips. In step 1, we entered group (coded as a dummy: 0= ODD/CD-ANX, 1= ODD/CD+ANX) and executive attention as predictors. In step 2, we entered the product term anxiety X executive attention to examine interaction effects. Significant interactions were dismantled by testing whether simple slopes were significantly different from zero for each subgroup (Hayes & Mattes, 2009). To test for confounding effects of ADHD (DISC-IV diagnosis) and ASD symptoms (SRS total score), regressions were re-analyzed with ADHD and ASD symptom severity as covariates.

In *post-hoc* analyses, we re-analyzed the data with CU traits as a moderator. In addition, because of a potential lack of power due to our small sample size, we checked the main significant findings with bootstrap analyses by drawing 1000 resamples from our original sample (Davison & Hinkley, 1997).

Prior to regression analyses variables were standardized (M = 0; SD = 1). Probabilities of all tests were two-tailed using a significance level of 0.05.

Results

Pre-analyses

There were no differences between the subgroups in externalizing problems, with both groups scoring in the clinical range of the externalizing problem behaviour scale (T > 60). As expected, the ODD/CD+ANX group had significantly higher scores on the CBCL internalizing scale than the ODD/CD-ANX group; the ODD/CD+ANX group scored in the clinical range (T > 60), whereas the ODD/CD-ANX group scored in the normal range. Further, the ODD/CD+ANX group had significantly higher resting HR and significantly more ASD symptoms than ODD/CD-ANX, even though both scored in the moderate range (60 < T < 74; Roeyers et al., 2011). Unexpectedly, however, no differences were obtained between subgroups in terms of CU traits; both scored in the slightly atypical range (56 < T < 60; Frick & Hare, 2001). Overall, these results confirm the distinction between ODD/CD boys with and without anxiety. Table 1 represents an overview of means and standard deviations of the clinical measures and resting HR.

Table 1. *Means and Standard Deviations of Resting HR and Clinical Measures of ODD/CD subgroups*

	ODD/CD-ANX (*n*=18)		ODD/CD+ANX (*n*=31)		t-values (df=47)
	M	*SD*	*M*	*SD*	
Resting HR	77.11	10.23	83.88	10.03	-2.26*
CBCL					
Internalizing[a]	55.50	9.89	69.23	6.70	-5.23***
Anxious/depressed	56.39	7.66	68.74	7.91	-5.33***
Withdrawn/depressed	60.89	7.13	67.65	8.34	-2.88**
Somatic complaints	54.17	5.58	62.71	8.76	-3.71**
Externalizing	66.61	9.88	67.81	8.32	-.45
Rule breaking	62.94	7.22	61.71	7.45	.57
Aggressive	70.17	10.92	71.16	10.59	-.31
CU traits	58.78	6.91	58.26	9.46	.20
ASD symptoms	61.78	11.56	73.45	13.81	-3.02*

Note. df= degrees of freedom; HR= heart rate; CBCL=Child Behavior Checklist; CU= callous unemotional.
[a]df=26.21.
*$p < .05$.**$p < .01$.***$p < .001$.

Main Analyses

Table 2 represents means and standard deviations of main study variables and Table 3 represents bivariate correlations between main study variables.

Table 2. *Means (M) and Standard Deviations (SD) of Main Study Variables (total sample and subgroups)*

	Total sample		ODD/CD-ANX		ODD/CD+ANX		t-values (df=47)
	M	*SD*	*M*	*SD*	*M*	*SD*	
1. Empathy human[a]	.88	1.16	.39	.72	1.18	1.28	-2.58**
2. Sympathy human	2.26	1.22	2.11	1.32	2.35	1.16	-.67
3. Empathy bear	2.00	1.67	1.56	1.69	2.26	1.63	-1.43
4. Sympathy bear	3.37	.88	3.11	.96	3.52	.81	-1.57
5. Executive attention	3.39	4.84	2.06	2.58	4.16	5.66	-1.78
6. CU traits	6.86	2.25	6.94	1.83	6.81	2.50	.20

Note. CU=callous unemotional raw scores
[a]: df = 46.98
**$p < .01$.

Table 3. *Bivariate Correlations Between Main Study Variables (total sample)*

	1	2	3	4	5
1. Empathy human					
2. Sympathy human	.43**				
3. Empathy bear	.46**	.38**			
4. Sympathy bear	.40**	.65**	.55**		
5. Executive attention	-.12	-.09	-.26	-.22	
6. CU traits	-.06	-.29*	-.11	-.13	.29*

Note. Correlations were based on standardized scores.
CU=callous unemotional.
*$p < .05$.**$p < .01$.

Bear clip. In relation to *empathy*, Table 4 shows that executive attention was a significant negative predictor, $F(2,46)=3.74$, $p=.031$. This suggests that weaker executive attention skills (i.e., more errors on the task) were associated with less empathy. Group was not a significant positive predictor of empathy. Importantly, a significant interaction was obtained between executive attention and anxiety, $F(3,45)=5.05$, $p=.004$. In the ODD/CD+ANX subgroup, executive attention was negatively associated with empathy (B=-.44, SE=.14, $p=.003$), whereas no such association was found in the ODD/CD-ANX subgroup (B=.68, SE=.41, $p=.102$). Model's adjusted R square was .20, representing a small to moderate effect.

In relation to *sympathy*, Table 4 shows that executive attention and group were not significant predictors, although the overall model was significant, $F(2,46)=3.27$, $p=.047$. Importantly, a significant interaction was found between executive attention and group, $F(3,45)=3.69$, $p=.018$. Again, further analyses revealed that in the ODD/CD+ANX subgroup executive attention was negatively associated with sympathy (B=-.37, SE=.14, $p=.013$), whereas no such association was found in the ODD/CD-ANX subgroup (B=.53, SE=.42 $p=.216$). Model's adjusted R square was .14, representing a small to moderate effect.

Human clips. In relation to *empathy*, Table 4 shows that executive attention was not a significant predictor, whereas group was a significant positive predictor, $F(2,46)=3.99$, $p=.025$. The ODD/CD+ANX subgroup reported more empathy than the ODD/CD-ANX subgroup. There was no significant interaction between group and executive attention. In relation to *sympathy*, no significant predictors or interaction were found.

Table 4. *Group and Executive Attention Predicting Empathic Responses of the Bear Clip and Human Clips*

	Bear clip				Human clips			
	Empathy		Sympathy		Empathy		Sympathy	
Predictor	β	$R^2\Delta$	β	$R^2\Delta$	β	$R^2\Delta$	β	$R^2\Delta$
Step 1		.14*		.12*		.15*		.02
Executive attention	-.32*		-.28		-.20		-.11	
Group	.27		.28		.37*		.12	
Step 2		.11*		.07*		.00		.04
Group X executive attention	-1.04*		-.84*		-.18		-.64	
Total R^2		.25		.20		.15		.07

Note. The findings remained the same after controlling for ADHD and ASD symptoms.
* $p < .05$.

Post-Hoc Analyses

CU traits as a moderator in human clips and bear clip. Interestingly, a significant interaction was found between executive attention and CU traits (β=.37, $p=.018$) in relation to empathy (not sympathy; β=.04, n.s.) for the human clips, though the overall model was not significant, $R^2=.13$, $F(3,45)= 2.30$, $p=.091$. At low levels of CU traits, executive attention was significantly negatively associated with empathy (B=-.57, SE=.24, $p=.019$), whereas no such association was found at moderate (B=-.22, SE=.15, n.s.) to high (B= .12,

SE=.17, n.s.) levels of CU traits. Model's adjusted R square was .08, representing a small effect. No other significant effects emerged with respect to the human clips (beta's ranged from -.29 to .00, *p*-values > .06), nor to the bear clip (beta's ranged from -.25 to .16., *p*-values >.10).

Bootstrap analyses. Bootstrap analyses supported main significant findings; that is, significant interactions between executive attention and group in relation to empathy (B = -1.12, SE = .43, bootstrapped SE = .45 and 95% CI = -1.67 – .22) and sympathy (B = -.90, SE = .45, bootstrapped SE = .54 and 95% CI = -1.77 – .56) of the bear clip as well as the interaction between executive attention and CU traits in relation to empathy of the human clips (B = .35, SE = .14, bootstrapped SE = .15 and 95% CI = .11 – .72), demonstrating limited statistical biases between estimates.

Discussion

The current study examined whether executive attention is a factor in empathic responses to sadness inducing film clips amongst ODD/CD boys, with and without comorbid anxiety disorder. In agreement with predictions, executive attention was found to relate significantly to empathy and sympathy, such that those with poor executive attention skills reported less empathy and sympathy. The proposed relationships were evident only under conditions of a highly evocative stimulus (the bear clip) and only among ODD/CD boys with comorbid anxiety disorder. As such, our findings are in agreement with prior evidence that aspects of emotion regulation are associated with empathic responses particularly in highly sensitive children (Eisenberg et al., 1994, 1996, 1998). Our findings imply that strong executive attention is beneficial for ODD/CD children with anxiety disorder, as it may help to maintain optimal levels of empathic arousal and higher levels of empathy/sympathy, accordingly. Poor executive attention, on the other hand, may render them particularly susceptible for empathic over-arousal and personal distress – a self-focused emotion – rather than empathy/sympathy. Indeed, prior studies have demonstrated self-focused behaviour in reaction to other's negative emotions in fearful children (Liew et al., 2011; Spinrad & Stifter, 2006), and inadequate regulation strategies in children with anxiety disorder (Legerstee, Garnefski, Jellesma, Verhulst, & Utens, 2010).

Children with ODD/CD who also meet criteria of anxiety disorder may show heightened threat sensitivity because of an overly responsive *basic threat circuit* (amygdala, hypothalamus, periaqueductal grey; Blair, 2013; Blair et al., 2014). This over-responsiveness is thought to result from early trauma or inadequate regulation. There is indeed empirical evidence indicating that ODD/CD individuals with comorbid mood and anxiety conditions show increased reactivity in neural regions involving the threat circuit (e.g., amygdala) and reduced reactivity in neural regions involving the regulation of the circuit (e.g., ventromedial frontal cortex; Crowe & Blair, 2008). Abnormalities in these regions may be associated with general difficulties in the processing of emotional expressions (Coccaro, McCloskey, &

Fitzgerald, 2007; Park, Van Bavel, Vasey, & Thayer, 2013), which may influence empathy development, accordingly.

Under conditions of mild evocative stimuli (human clips), ODD/CD boys with anxiety reported more empathy than those without anxiety. Children with anxiety have been linked to bully victimization and social exclusion (Bifulco, Schimmenti, Jacobs, Bunn, & Rusu, 2014). Given the content of the emotional stimuli (i.e., a girl being bullied and a boy being excluded from a soccer team), ODD/CD boys with anxiety may have been able to better identify themselves with the targets, leading to more empathy compared to ODD/CD boys without anxiety, accordingly. Alternatively, the content of the stimuli could have induced aversive arousal and more personal distress in those with than without anxiety. Empathy and personal distress are highly related constructs often stemming from the same emotional event (Eisenberg & Eggum, 2009). The self-reports of empathy could have partly captured feelings of personal distress.

Because it is has also been proposed that heightened threat sensitivity is more likely to be present in ODD/CD children with low rather than high CU traits (Blair, 2013; Blair et al., 2014), we expected a stronger effect of emotion regulation in empathic responses amongst those with low rather than high CU traits. In agreement with these expectations, we found preliminary evidence that weaker executive attention skills were significantly related to less empathy in ODD/CD boys with low levels of CU traits but not in those with moderate to high levels of CU traits.

Because ODD/CD children with high levels of CU traits are more likely to belong to the "fearless" rather than "fearful" subtype (Raine, 1993), one would expect higher levels of CU traits in ODD/CD boys without anxiety than in those with anxiety. Nevertheless, in the current study there were no significant differences in CU traits between those with and without comorbid anxiety disorder. This finding is in line with growing evidence that anxiety and CU traits are not necessarily related or mutually exclusive (Fanti, Demetriou, & Kimonis, 2013; Kahn, Frick, Golmaryami, & Marsee, 2017; Kimonis et al., 2012). This evidence, together with the current finding of distinct moderating effects of anxiety and CU traits suggests that studies of empathy in ODD/CD children need to include both anxiety and CU traits measures.

Strengths of our study can be seen in the inclusion of a well-defined sample of ODD/CD children; those with anxiety had higher resting HR and higher scores on indexes of internalizing problems than those without anxiety. Further strengths are the standardized measurements of empathic responses and executive attention. However, some important limitations should be taken into consideration while interpreting our findings. First, we only focused on executive attention, whereas prior community-sample studies have also linked other indexes of emotion regulation to empathic responses, such as impulsivity (Eisenberg et al., 2007) and physiological regulation (Taylor, Eisenberg, & Spinrad, 2015). Second, we did not include a measure of personal distress, thereby only partly testing Eisenberg and colleagues' hypothesis regarding the role of emotion regulation in empathic responses (Eisenberg et al., 1994). Third, there is some evidence that animal-directed empathy does not

necessarily transfer to human-directed empathy (McPhedran, 2009). We should therefore be careful in generalizing the role of executive attention in the modulation of strong vicarious arousal to an inter-human empathy context. Fourth, in the current study we only investigated boys. This limits the generalizability of our findings to girls, as prior studies have shown empathy differences between boys and girls (Van der Graaf et al., 2014). Fifth, the CU scale of the APSD showed poor internal consistency. However, poor internal consistency has previously been found for the CU scale (Pardini, Lochman, & Frick, 2003), and in a prior study conducted with the current ODD/CD sample it showed good concurrent validity with the externalizing scale of the Teacher Report From (Pijper et al., 2016). Finally, we investigated a small sample with limit statistical power.

Our findings offer promising new research leads. For instance, it would be interesting to replicate our findings with physiological markers of emotion regulation and empathic responses. Physiological regulation has been linked to empathic responses in normal children (Taylor et al., 2015), but not yet in children with ODD/CD. In addition, physiological markers of empathic responses could provide an index for personal distress (i.e., heart rate acceleration to emotional stimuli; Eisenberg & Fabes, 1990).

If replicated, the findings of this study could provide important implications for clinical practice. Training attention in children with autism improved their academic performance (Spaniol, Shaley, Kossyvaki, & Mevorach, 2018) and clinical outcomes in children with anxiety disorders (e.g., Bar-Heim, Morag, & Glickman, 2011; Bechor et al., 2014). We therefore speculate that training executive attention in ODD/CD children with poor executive attention might be an initial step towards improving their empathic functioning.

This study provides initial evidence that executive attention is associated with empathic responses under conditions of highly evocative stimuli, especially in ODD/CD boys with comorbid anxiety disorder. It supports current ideas that different mechanisms may be involved in empathy problems in children and adolescents with ODD or CD.

Chapter V

Resting Respiratory Sinus Arrhythmia and Heart Rate Reactivity to Sadness-inducing Stimuli in Boys with Oppositional Defiant Disorder or Conduct Disorder, With and Without Comorbid Anxiety Disorder

Pijper, J., De Wied, M., Van Boxtel, T., Van Goozen, S., & Meeus, W. (2017). *Resting respiratory sinus arrhythmia and heart rate reactivity to sadness-inducing stimuli in boys with oppositional defiant disorder or conduct disorder, with and without comorbid anxiety disorder.* Manuscript to be submitted.

J.P. and M.d.W. conceptualized the study. J.P. analyzed the data and wrote the manuscript. M.d.W., T.v.B., S.v.G. and W.M. provided feedback on the analyses and manuscript.

Abstract

The current study examines the relationship between emotion regulation and empathy-related responding at a physiological level in boys with oppositional defiant disorder (ODD) or conduct disorder (CD), with (*N* = 32) and without (*N* = 18) comorbid anxiety disorder (7 – 12 years). Resting respiratory sinus arrhythmia (RSA) was used as an index of emotion regulation, and heart rate (HR) reactivity in response to sadness inducing film clips as an index of empathy-related responding. Children were exposed to mild and intense sadness-inducing film clips. Findings revealed a significant negative relationship between RSA and HR reactivity, such that those with higher RSA (indicative of more efficient emotion regulation) showed smaller HR deceleration (indicative of empathy or sympathy). The relationship was evident under conditions of mildly sad stimuli and only in ODD/CD boys without anxiety. Under conditions of the intense sad stimulus, a significant positive relationship was observed between RSA and HR reactivity in the total ODD/CD sample. The pattern of findings may indicate that efficient regulation of empathic arousal in those with ODD/CD is limited to mildly sad situations, whereas it may be challenged under intense sad situations.

Children with oppositional defiant disorder (ODD) or conduct disorder (CD) are thought to have little empathy (for reviews, see Blair, 2013; Blair, Leibenluft, & Pine, 2014; De Wied, Gispen-De Wied, & Van Boxtel, 2010). Much research attention has been devoted to empathy problems in a small group of ODD/CD children showing high levels of callous unemotional (CU) traits; that is, those specified by a lack of empathy, lack of guilt and shallow affect (Frick & Hare, 2001). The majority of ODD/CD children, however, show low levels of CU traits (Blair et al., 2014) and we know surprisingly little about their empathy problems (Pijper, De Wied, Van Goozen, & Meeus, 2017). It is thought that their empathy problems may be linked to hostility bias, anxiety and/or poor emotion regulation (de Wied et al., 2010; Pijper et al., 2017). Poor emotion regulation is common in ODD/CD individuals (Masi, Muratori, Manfredi, Pisano, & Milone, 2015), and executive attention (a cognitive index of emotion regulation) has recently been found to be a factor in self-reported empathic responses in ODD/CD boys – particularly amongst those with comorbid anxiety disorder (Pijper, De Wied, Van Rijn, Swaab, Van Goozen, & Meeus, 2018). The main aim of the current study is to replicate these findings, using physiological indexes of emotion regulation (i.e., resting respiratory sinus arrhythmia) and empathy-related responses (i.e., heart rate reactivity) to sadness inducing film clips in ODD/CD boys, with and without comorbid anxiety disorder.

Empathy and Emotion Regulation

Empathy is a complex construct, generally defined as the ability to understand and share another person's feelings (Eisenberg & Strayer, 1987). It involves traits (empathic tendencies), states (interpersonal outcomes) and both affective and cognitive components (Davis, 1996). Affective empathy is central to this study and refers to "the vicarious affective response to another person" (Hoffman, 2000, p. 29). The literature often distinguishes empathy (i.e., feeling *with* the target), sympathy (i.e., feeling *for* the target) and personal distress (i.e., self-focused aversive reaction evoked *by* the target), even though the constructs are closely related and often result from the same emotional experience (Eisenberg & Eggum, 2009; Lamm & Majdandžić, 2015).

Empathy-related responses are thought to vary as a function of emotion regulation abilities (Eisenberg et al., 1994). Individuals who cannot optimally regulate their empathic arousal may be more likely than others to become over-aroused and feel personal distress than empathy/sympathy when witnessing another person in distress. By contrast, those who are well-regulated are thought to maintain optimal levels of arousal and to experience high levels of empathy/sympathy. The hypothesis has received empirical support from community-sample studies predominantly using behavioural measures of emotion regulation (Eisenberg, 2010; Eisenberg, Fabes, & Spinrad. 2006). However, emotion regulation is a broad concept not only referring to behavioural processes by which emotions can be regulated, but also to physiological processes (Bridgett, Burt, Deater-Deckard, & Edwards, 2015).

Resting RSA is considered a physiological marker of emotion regulation (Porges, 2007; Beauchaine, 2015b; Thayer & Lane, 2000). RSA is an index of tonic parasympathetic control of

the heart (or cardiac vagal tone; Berntson et al., 1997) and reflects the natural variation in heart rate that occurs concomitant with breathing, with an HR increase during inhalation and a HR decrease during exhalation. RSA is the high frequency component of heart rate variability (HRV), which is a more global measure of vagal tone (Porges, 2007). RSA is considered an index of emotion regulation because it has been linked to prefrontal cortex (PFC) functioning, which is implicated in the regulation of emotions (Beauchaine, 2015b; Thayer, Hansen, Saus-Rose, & Johnson, 2009). The link between RSA and PFC, described in Thayer's Neurovisceral integration theory (Thayer et al., 2009), receives support from studies showing pathways from the medial PFC to the parasympathetic nervous system (Lane et al., 2009; Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012) and positive relationships between RSA and performance on executive function tasks (Cupuana et al., 2014).

Low resting RSA has been found in a wide range of psychiatric disorders that are characterized by emotion dysregulation, such as depression, anxiety and children and adolescents with ODD/CD (e.g., Beauchaine, Katkin, Strassberg, & Snarr, 2001; De Wied, Van Boxtel, Posthumus, Goudena, & Matthys, 2009).

Community-sample studies in children linking indexes of vagal tone (RSA or HRV) to behavioural measures (i.e., questionnaires and observations) of empathy-related responses reveal that children with higher vagal tone have higher empathic tendencies according to their parents and teachers (Eisenberg et al., 1996; Taylor, Eisenberg, & Spinrad, 2015) and are more likely to show empathy/sympathy (Fabes, Eisenberg, & Eisenbud, 1993; Liew et al., 2011) than personal distress (Fabes, Eisenberg, Karbon, Troyer, & Switzer, 1994; Zahn-Waxler, Cole, Welsh, & Fox, 1995) when observing someone in pain. Some of the community-sample studies have additionally linked vagal tone to autonomic indexes of empathy-related responses. One study revealed that children with high vagal tone showed fewer skin conductance responses (SCR) to a fearful film clip, indicating less personal distress (Fabes et al., 1993). In another study, however, no relationship was observed between vagal tone and SCR to a sadness inducing film clip (Zahn-Waxler et al., 1995). Likewise, no relationship could be established between vagal tone and heart rate (HR) change (indexed by linear slopes) in children while hearing a baby cry (Fabes et al., 1994). Thus, findings from studies on relationships between vagal tone and autonomic indexes of empathy-related responses are far from conclusive.

The role of emotion regulation in modulating empathic arousal is thought to be particularly important for highly sensitive people (Eisenberg et al., 1994, 2006), who are expected to be more susceptible for vicariously induced negative emotions. If they lack the ability to efficiently regulate themselves they may become overwhelmed, rendering them at risk for personal distress. A few community-sample studies with children have put this hypothesis to test with behavioural measures of regulation and empathy, revealing modest empirical evidence (for a review, see Eisenberg et al., 2006).

Empathy and Emotion Regulation in ODD/CD

Children with ODD/CD form a heterogeneous group. Some may show an "insensitive" temperamental style that is characterized by low levels of autonomic arousal at rest and in response to emotional stimuli (Van Goozen, 2015). Others may show a more "sensitive" temperamental style that is characterized by increased autonomic arousal at rest and in reaction to emotional stimuli (Blair, 2013; Frick, 2012). Indeed, there are studies showing that ODD/CD children with high rates of anxiety exhibited higher resting HR than normal controls (De Wied et al., 2009; Lahey, Loeber, Burke, Rathouz, & McBurnett, 2002) and higher cortisol stress reactivity than those with low rates of anxiety (Van Goozen, Matthys, Cohen-Kettenis, Buitelaar, & van Engeland, 2000). Low RSA (indicative of less effective emotion regulation) in ODD/CD children with high rates of anxiety may render them at risk for personal distress rather than that they experience empathy or sympathy.

In an earlier study with the current ODD/CD sample, we investigated this hypothesis using a cognitive measure of emotion regulation and self-reports of empathy and sympathy (Pijper et al., 2018). Findings revealed that ODD/CD boys with poor regulation skills reported lower levels of empathy and sympathy when exposed to an intense sad stimulus – particularly those with comorbid anxiety disorder.

Reporting on one's own emotions may be difficult, especially for ODD/CD children who are known for their relatively low verbal (e.g., Déry, Toupin, Pauzé, Mercier, & Fortin, 1999; Loney, Frick, Ellis, & McCoy, 1998) and self-referential abilities (Pardini, Barry, Barth, Lochman, & Wells, 2006). Using autonomic measures, such as HR, may be less sensitive to such problems. There are conceptual and empirical reasons to expect that HR deceleration may reflect empathy/sympathy, whereas HR acceleration may reflect personal distress (Eisenberg & Fabes, 1990). Empathy and sympathy involve other-oriented reactions, implying an outward focus of attention and intake of information. This kind of information processing has been related to HR deceleration (e.g., Abercombie, Chambers, Greischer, & Monticelli, 2008; Graham, 1992). Personal distress involves feelings of anxiety and discomfort (Eisenberg & Eggum, 2009). Such feelings are generally associated with HR acceleration (Williams, Veldhuijzen van Zanten, Trotman, Quinton, & Ginty, 2017). This differentiation in empathy-related responses based on HR reactivity has received empirical support from several community-sample studies (e.g., Eisenberg et al., 1988a; Eisenberg et al., 1988b; Fabes et al., 1994).

The Current Study

The current study investigated whether emotion regulation is a factor in empathy-related responding at the level of autonomic functioning in ODD/CD boys with and without anxiety, using resting RSA as a measure of emotion regulation and HR reactivity as a measure of empathy. Children were exposed to three sadness inducing film clips: two film clips involving children who experience sadness in common childhood situations and one film clip involving a bear cub in distress after his mother dies. In a prior study with ODD/CD boys, the

bear clip was found to evoke higher levels of self-reported empathy/sympathy than the human clips (De Wied, Goudena, & Matthys, 2005). The emotional impact of the bear clip is possibly stronger, because of its theme and because cute little animals are likely to elicit strong positive feelings in children (Endenburg, 1995), potentially minimizing negative dispositions. As such, the bear-clip may be considered a stronger, more challenging stimulus than the human-clips.

Theory (Eisenberg et al., 1994) and empirical evidence (Eisenberg et al., 2006) suggest that more efficient emotion regulation is associated with stronger empathy or sympathy. Therefore, we predicted that those with higher RSA (indicative of more efficient emotion regulation; Thayer & Lane, 2000) would show greater HR deceleration (indicative of stronger empathy or sympathy; Eisenberg & Fabes, 1990). Thus, we predicted a negative relationship between RSA and HR reactivity. In addition, because emotion regulation is especially likely to be involved in empathy under conditions of strong vicarious arousal (Eisenberg, 2010), we expected the proposed relationship to be particularly evident within the group of ODD/CD boys with comorbid anxiety disorder and particularly under conditions of the most challenging stimulus (i.e., the bear clip). Finally, given the importance of CU traits in the ODD/CD literature, and its link with reduced responsiveness to fear and sadness (Blair, 2013), we investigated the effects of CU traits in the relationship between RSA and HR reactivity.

Methods

This study was approved by the Medical Ethical Committee of Leiden University Medical Centre (LUMC), and parents gave written consent prior to participation according to the declaration of Helsinki.

Participants and Recruitment

An initial group of 58 ODD/CD boys was recruited via clinical health centers (n = 23) and schools for special education (n = 35). The presence of psychopathology was determined by the parent-version of the Diagnostic Interview Schedule for Children following DSM-IV criteria (DISC-IV, Dutch version; Ferdinand & Van der Ende 2002). Participants were excluded from the study if they had an estimated intelligence quotient (IQ) below 70 (n = 3) or missed data on estimated IQ (n = 2). Estimated IQ was assessed with Dutch translations of the subtests Block Design and Vocabulary of the Wechsler Intelligence Scale for Children (WISC-III-NL; Kort et al., 2005). Three additional participants were excluded from the sample because of missing data on HR (n = 1), CU traits (n = 1) and autism spectrum disorder (ASD) symptoms (n = 1). ASD symptoms were, alongside other variables, used in analyses to verify distinction between subgroups.

The final ODD/CD sample consisted of 50 boys (M_{age}= 10.30, SD = 1.31; M_{IQ} = 95.47, SD = 12.21) with ODD (n = 34) or CD (n = 16). Those with comorbid anxiety disorder according to the DISC-IV (social phobia (n = 9), separation anxiety disorder (n = 10), specific phobia (n = 25), panic disorder (n = 1), agoraphobia (n = 1), generalized anxiety disorder (n = 9), obsessive

compulsive disorder (*n* = 2), and/or post-traumatic stress disorder (*n* = 3)) were assigned to the ODD/CD anxious group (ODD/CD+ANX), whereas those without were assigned to the ODD/CD non-anxious group (ODD/CD-ANX).

The ODD/CD+ANX group consisted of 32 boys with ODD (*n* = 20) or CD (*n* = 12), of which 27 had comorbid attention deficit hyperactivity disorder (ADHD) and six comorbid depression. Twelve boys used psychostimulants, two boys used anti-psychotics and one used both. The ODD/CD-ANX group consisted of 18 boys with ODD (*n* = 14) or CD (*n* = 4), of which nine had comorbid ADHD and one comorbid depression. Seven boys used psychostimulants. Subgroups showed no differences in age or IQ (see Table 2 for means and standard deviations). Further, no differences were obtained between boys with or without psychopharmacological treatment on all study variables.

Stimuli

Relaxing video. Resting HR and resting RSA were assessed during exposure to a five minutes video fragment of the *Coral Sea Dreaming* (Small World Music, Inc.). The video has previously been found to be more effective in lowering resting cardiovascular activity than a period of inactive rest and thus better represents the "basal" resting condition (Piferi, Kline, Younger, & Lawler, 2000).

Empathy clips. To evoke empathy, children were exposed to three sadness-inducing film clips: one clip involving a girl (Anja) feeling depressed because she is ignored and badgered by her classmates (duration: 57 s), one clip involving a boy (Mohammed) who fails at selection training for a soccer tournament (duration: 148 s), and one clip involving a bear cub in distress after his mother has died (duration: 164 s). In a prior study with the current ODD/CD sample, the clips were found to successfully evoke empathic sadness (Pijper et al., 2018).

A female voice-over sketching the situation introduced each film clip. The most evocative parts of the clips in which the characters portrayed intense facial and vocal expressions of sadness (human clips) or clear signals of distress and helplessness (bear clip) were used as targets. The first ten seconds of the opening scene (after the introduction by the voice-over) served as baseline. The target episodes varied in length (boy clip 35 s, girl clip 6 s, bear clip 49 s). Furthermore, prior to each film clip the participants watched a one-minute fragment of a relaxing video (described above) to ensure recovery from emotional arousal induced by the preceding film clip. HR was analyzed during baseline and target episodes of each empathy clip.

Apparatus and stimulus presentation. A laboratory room at the university was equipped with two computers: a personal computer with a 17-inch color monitor (Philips 109E50) for stimulus presentation (placed on a desk in front of participants) and a laptop for online control of physiological data collection (placed on a trolley behind the participants). Both computers were connected to a small portable digital recorder for the preprocessing and storage of physiological data (Vitaport II, TEMEC Instruments B.V., Kerkrade, The

Netherlands). A program written with *Delphi 6* controlled stimulus presentation and generated signals marking stimulus onset and offset, which were saved on the digital recorder.

Outcome Measures

Problem behaviour. In order to verify group distinction, subgroups were compared on 1) externalizing and internalizing problem behaviour, using the externalizing and internalizing scales (including subscales rule-breaking, aggressive behaviour, anxious/depressed, withdrawn/depressed and somatic complaints) of the Dutch *Child Behaviour Checklist (*CBCL*6-18*; Verhulst & Van der Ende, 2013), 2) CU traits, using combined parent and teacher ratings on the CU scale of the Dutch *Antisocial Process Screening Device* (APSD; De Wied, Van der Baan, Raaijmakers, De Ruiter, & Meeus, 2014), and 3) ASD symptoms, using the total scale of the Dutch *Social Responsiveness Scale* (SRS; Roeyers, Thys, Druart, De Schryver, & Schittekatte, 2011.). For all measures, T-scores were employed as outcome measure.

Physiological recordings. HR and RSA were measured via electrocardiogram (ECG). The ECG was recorded with electrodes on the chest (sternum-V6 lead). The ECG signal was anti-aliasing filtered (512 Hz lowpass filter), digitized at a rate of 1024 Hz, and digitally bandpass filtered (5-30 Hz) to suppress baseline signal shifts, exceptionally large T-waves, and high-frequency artifacts such as electromyogram potentials. A computer-assisted procedure was executed to detect ECG R-waves and to make corrections for (a) prolonged R-R intervals due to missing R-waves and (b) short R-R intervals due to false R-waves (for details, see De Wied et al., 2009).

Mean HR was assessed during the baseline and target periods of each empathy clip. Resting HR and resting RSA were calculated during the relaxing video. Resting RSA was determined by applying power spectral analysis on the R-R intervals using the computer program CARSPAN for Windows 1.34 (Mulder, Hofstetter, & Van Roon, 2007). The 5-min presentation period was divided into five 50% overlapping data segments of 100 s duration consisting of a series of R-wave events as a function of time. Each 100-s data segment was cross-multiplied with a cosine window tapering 5% of each end of the segment. Next, it was subjected to power spectral analysis using the Sparse Direct Fourier Transform algorithm (Rompelman, Snijders, & Van Spronsen, 1982) that was directly applied on the arrival times of the R-waves in the ECG without interpolation of the non-equidistant time series. Spectral power was determined in the 0.15-0.40 Hz frequency band, averaged across the five data segments, and subjected to natural logarithmic transformation. The power in this frequency band is associated with RSA.

HR responses to film clips were expressed as mean HR during the target period minus mean HR during baseline of the empathy clips (i.e., HR reactivity). Mean HR during baseline and target of the two human clips were significantly correlated (baseline: $r = .71$, $p < .001$, target: $r = .90$, $p < .001$), and therefore averaged as to create one score for the human clips.

Procedure

Participants and their parents were invited to visit Leiden University for one day. During that day, parents signed an informed consent and completed the DISC-interview and questionnaires. The participants were individually seen by a female experimenter, who familiarized them with the setting and research procedures. Next, the experimenter placed electrodes for ECG recordings while the participant was sitting in an armchair in front of the stimulus computer. After checking the signals, the lights were dimmed and participants watched the relaxing video and were exposed to the empathy clips.

Data Analyses

Preliminary analyses. To check whether the bear clip was more intense than the human clips, HR reactivity to the bear clip was compared with HR reactivity to the human clips, using a paired samples t-test. Prior studies have shown that ODD/CD boys experienced more empathy and sympathy in response to the bear clip than to human clips (De Wied et al., 2005; Pijper et al., 2018). Because empathy or sympathy can be indexed by HR deceleration (Eisenberg & Fabes, 1990), stronger HR deceleration may be expected in response to the bear clip than to human clips. Alternatively, the intensity of the bear clip may also elicit feelings of discomfort and aversive arousal and therefore evoke less HR deceleration or even more HR acceleration (indicative of personal distress) than the human clips.

To verify the distinction between the ODD/CD+ANX group and ODD/CD-ANX group, a series of independent samples t-tests were carried out using group (i.e., ODD/CD+ANX and ODD/CD-ANX) as independent variable and externalizing and internalizing problem behaviour, CU traits, and ASD symptoms as well as resting levels of HR as dependent variables. As we distinguished participants on comorbid anxiety disorder, group differences were particularly expected to occur on variables related to anxiety. Therefore, group differences were not necessarily expected on externalizing problem behaviour. Group differences were expected on internalizing problem behavior, with higher scores for the ODD/CD+ANX than for the ODD/CD-ANX group. Further, because of positive associations between anxiety and ASD symptoms (Mayes, Calhoun, Murray, Ahuja, & Smith, 2011), higher ASD symptoms were expected in the ODD/CD+ANX than in the ODD/CD-ANX group. Moreover, because prior studies have found increased arousal in ODD/CD children with high levels of anxiety (De Wied et al., 2009; Lahey et al., 2009), higher resting HR was expected in the ODD/CD+ANX than in the ODD/CD-ANX group. Finally, because of negative associations between anxiety and CU traits (Frick, 2012), lower CU traits were expected in the ODD/CD+ANX than in the ODD/CD-ANX group.

Main analyses. The main hypothesis was tested by running two separate multiple hierarchical regression analyses, using outcome measures HR reactivity to the human clips and HR reactivity to the bear clip. In step 1, medication usage (coded as dummy variables: 0 = no, 1= yes) was entered to test for potential confounding effects of medication on RSA and HR (Alvares, Quintana, Hickie, & Guestella, 2016). In step 2, we entered RSA and group (also

coded as a dummy variable: 0 = ODD/CD-ANX, 1 = ODD/CD+ANX) as predictors. In step 3, we entered the product term RSA X Group to test for interaction effects. Significant interactions were further analyzed by testing whether simple slopes differed significantly from zero for each subgroup (Hayes & Matthes, 2009). To test for confounding effects of ADHD (DISC-diagnosis) and ASD symptoms (SRS total score), we re-analyzed regression analyses with ADHD and ASD symptoms as covariates in step 1.

Post-hoc analyses. Data was re-analyzed with CU traits as a moderator. Furthermore, as the small sample size likely reduced power, we checked main significant findings with bootstrap analyses by drawing 1000 resamples from our original sample (Davison & Hinkley, 1997).

Prior to regression analyses, all variables (except dummy variables) were standardized (M = 0; SD = 1), and correlations were computed between main study variables. Probabilities of all tests were two-tailed using a significance level of .05.

Results

Preliminary Analyses

In agreement with expectations, the bear clip evoked less HR deceleration (M = -2.60, SD = 4.69) than the human clips (M = -4.01, SD = 4.29), but not significantly, t(49) = -1.66, p = .103.

In agreement with expectations, no differences emerged between the subgroups in externalizing problems; both groups scored within the clinical range on the externalizing problem behaviour scale (T > 60). Moreover, conform expectations the ODD/CD+ANX group had significantly higher scores on the CBCL internalizing scale (see Table 1 for scores on syndrome scales) than the ODD/CD-ANX group; the ODD/CD+ANX group scored within the clinical range (T > 60), whereas the ODD/CD-ANX group scored within the normal range. Furthermore, the ODD/CD+ANX group had significantly more ASD symptoms than the ODD/CD-ANX group, even though both scored within the moderate range (60 < T < 74; Constantino & Gruber, 2005), and the ODD/CD+ANX group showed higher resting HR than the ODD/CD-ANX group. In contrast to expectations, no differences were found between the two subgroups in terms of CU traits, with both groups scoring in the slightly atypical range (56 < T < 60; Frick & Hare, 2001). Taken together, the pattern of findings supports our group distinction. See Table 1 for means and standard deviations.

Table 1. *Means and Standard Deviations of Resting HR and Clinical Measures of the ODD/CD subgroups*

	ODD/CD-ANX (*n*=18)		ODD/CD+ANX (*n*=32)		t-values (df=48)
	M	*SD*	*M*	*SD*	
Resting HR[a]	77.12	10.23	84.27	10.11	-2.38*
CBCL					
Internalizing[b]	55.50	9.89	69.28	6.60	-5.29**
Anxious/depressed	56.39	7.66	68.91	7.83	-5.47**
Withdrawn/depressed	60.89	7.13	67.47	8.26	-2.83**
Somatic complaints	54.17	5.58	62.84	8.66	-3.82**
Externalizing	66.61	9.88	68.00	8.25	-.53
Rule-breaking	62.94	7.22	61.88	7.39	.50
Aggressive	70.17	10.92	71.41	10.51	-.40
ASD symptoms	61.78	11.56	73.34	13.60	-3.04**
CU traits	58.78	6.91	58.63	9.53	.06

Note. HR=heart rate; CBCL=Child Behavior Checklist; ASD = autism spectrum disorder; CU=callous unemotional.
[a]df = 35.00. [b]df = 25.69.
*$p < .05$. **$p < .01$. ***$p < .001$.

Associations. Under conditions of the human clips, the expected negative correlation was found between RSA and HR reactivity; though, the correlation did not reach significance (r = -.15, p = .29). Unexpectedly, however, a significant *positive* correlation was found between RSA and HR reactivity in response to the bear clip (r = .34, p = .02).

Main Analyses

Table 2 represents means and standard deviations of main study variables.

Human clips. After controlling for medication, resting RSA and group were not significant predictors of HR reactivity, $F(3,46) = 1.04$, p = .384. Interestingly, however, a significant interaction occurred between RSA and group, though the overall model was non-significant, R^2 = .14, $F(4,45) = 1.89$, p = .129. Adjusted R square was .07, reflecting a small effect. In the ODD/CD-ANX group, RSA showed the expected negative relationship with HR reactivity (B= -.52, SE= .23, p = .025), whilst no such relationship was found in the ODD/CD+ANX group (B= .06, SE= .15, p = .681). Controlling for ADHD and ASD symptoms did not change the pattern of findings. Table 2 displays means and standard deviations of main study variables. Table 3 provides an overview of standardized and unstandardized betas as well as standard errors, and Figure 1 visualizes the interaction effect.

Table 2. *Means and Standard Deviations of Main Study Variables (total group and subgroups)*

	Total sample		ODD/CD-ANX		ODD/CD+ANX		t-values (df=48)
	M	*SD*	*M*	*SD*	*M*	*SD*	
1. RSA	8.44	.82	8.50	.77	8.40	.86	.42
2. HR reactivity human	-2.60	4.69	-5.18	3.73	-3.35	4.49	-1.46
3. HR reactivity bear	-4.01	4.29	-4.30	4.10	-1.65	4.79	-1.97
4. CU traits	6.92	2.28	6.94	1.83	6.91	2.52	.06

Note. RSA=respiratory sinus arrhythmia; HR=heart rate; CU=callous unemotional raw scores

Table 3. *RSA, Group and RSA X Group Predicting HR reactivity of the Human Clips*

Predictor	B	SE	β	$R^2\Delta$
Step 1				.00
Medication	-.07	.29	-.03	
Step2				.06
RSA	-.14	.14	-.14	
Group	.41	.30	.20	
Step 2				.08*
RSA X Group	.63	.30	.52*	

Note. RSA: respiratory sinus arrhythmia.
*p<.05. **p<.01.

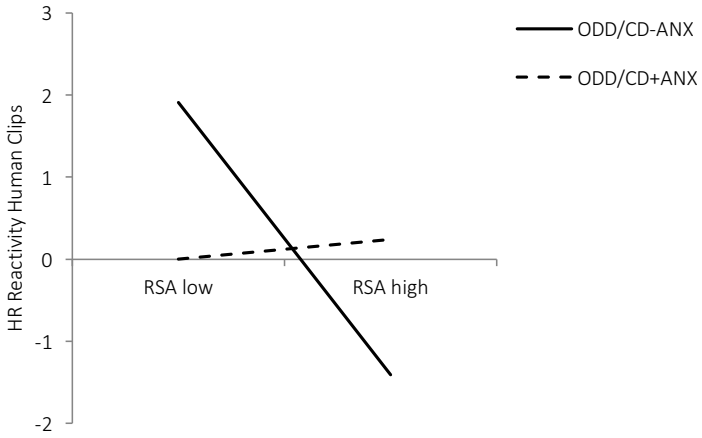

Figure 1. Interaction Between Respiratory Sinus Arrhythmia (RSA) and Group Predicting Heart Rate (HR) Reactivity of the Human Clips

Bear clip. After controlling for medication, RSA and group were both significant positive predictors of HR reactivity, R^2 = .29, $F(3,46)$= 6.35, p = .001. Adjusted R square was .25, reflecting a medium effect size. Different from expectations, higher levels of RSA were found to be associated with lower levels of HR deceleration. Moreover, the ODD/CD+ANX group showed a smaller HR deceleration than the ODD/CD-ANX group. There was no significant interaction between RSA and group, indicating no differences in relationships between the subgroups. Controlling for ADHD and ASD symptoms did not change the pattern of findings. See Table 4 for an overview of standardized and unstandardized betas as well as standard errors.

Table 4. *RSA, Group and RSA X Group Predicting HR reactivity of the Bear Clip*

Predictor	B	SE	β	$R^2\Delta$
Step 1				.06
Medication	-.47	.28	-.23	
Step 2				.24**
RSA	.39	.13	.39**	
Group	.66	.26	.32*	
Step 3				.00
RSA X Group	-.13	.28	-.11	

Note. RSA: respiratory sinus arrhythmia.
*p<.05. **p<.01.

Post-hoc Analyses

CU traits. Whilst re-analyzing the effect of CU traits as a moderator, CU traits appeared to be a significant negative predictor (β = -.33, p = .01) of HR reactivity in the *bear clip*, R^2= .30, F(3, 46)= 6.50, p = .001. Higher levels of CU traits were associated with greater HR deceleration. No significant interaction occurred between RSA and CU traits (β = .18, p = .482), and no significant findings were obtained with the human clips. Controlling for ADHD and ASD symptoms did not change the above pattern of findings.

Bootstrap analyses. The results confirmed the main significant findings; that is, a significant interaction between RSA and group in relation to the human clips as well as RSA, group and CU traits as significant predictors of HR reactivity in reaction to the bear clip (betas ranging from -.06 to .03, demonstrating limited statistical biases between estimates).

Discussion

This study examined the relationship between resting RSA (as an index of emotion regulation) and HR reactivity (as an index of empathy or sympathy) to sadness inducing film clips in ODD/CD boys, with and without comorbid anxiety disorder. We expected to find an inverse relationship between resting RSA and HR reactivity, particularly in the group of ODD/CD boys *with* comorbid anxiety disorder and particularly under conditions of the intense sad stimulus. In agreement with expectations, we found a significant inverse relationship between RSA and HR reactivity, but only for ODD/CD boys without comorbid anxiety disorder under conditions of a *mildly* sad stimulus (human clips). Under more intense sad conditions, an unexpected positive relationship was observed between RSA and HR reactivity, such that ODD/CD boys with high RSA showed little HR deceleration.

The inverse relationship between RSA and HR reactivity is in agreement with expectations based on theory (Eisenberg et al., 1994) and prior empirical evidence (Eisenberg et al., 2006) on the role of regulation in empathy/sympathy. Starting from the assumption that HR deceleration reflects empathy/sympathy, the inverse relationship suggests that more effective emotion regulation is associated with stronger empathy or sympathy. Although we

expected to find this pattern under conditions of a highly (rather than mildly) intense sad stimulus, the current pattern of results is actually in line with literature suggesting that efficient regulation is limited to situations that are perceived as non-stressful. In such situations, the body increases vagal influences on the heart, which slows down HR fostering calm and vegetative activities as well as social engagement behaviours (Porges, 2007), which may facilitate empathy. Because the mildly sad stimuli may be less stressful, in particular for those without anxiety, it is understandable that we found the negative relationship under conditions of mild stressful stimuli (human clips) and only in ODD/CD boys without anxiety. Under perceived stressful conditions, however, it has been suggested that, despite good efforts of the vagus to regulate HR, activation of the sympathetic nervous system is additionally necessary to meet with external demands (Porges, 2007). Sympathetic activation will lead to an increase in HR and other bodily processes to prepare the body for mobilization (i.e., fight/flight response). Because the more intense sad stimulus may be experienced as more stressful, it is understandable that we found that those with high levels of resting RSA (reflecting good vagus functioning) showed less HR deceleration (reflecting reduced parasympathetic activation and/or enhanced sympathetic activation).

It is important to note that in our prior study with the current ODD/CD sample, stronger cognitive regulation skills (i.e., executive attention) were associated with more self-reported empathy and sympathy under intense sad conditions (Pijper et al., 2018). No such a relationship occurred at the physiological level. These findings may indicate that the regulation of empathic arousal occurs gradually via several regulatory mechanisms. When efficient physiological regulation is challenged in intense empathy-inducing situations, higher-order cognitive regulation may take over to manage strong vicarious arousal. This 'step by step' way of regulating emotions may be interesting to study in future research.

Findings from exploratory analyses with CU traits revealed an inverse relationship between CU traits and HR reactivity in response to the intense sad stimulus (bear clip); ODD/CD boys with the highest CU traits showed more HR deceleration. Considering the assumption that HR deceleration reflects empathy/sympathy, results would seem to suggest that high CU boys are more empathic than low CU boys, which seems counterintuitive. There are conceptual and empirical reasons to expect that HR deceleration reflects empathy or sympathy in empathy-inducing situations. Empathy and sympathy are other-oriented reactions and thus involve an outward focus of attention. Outward focus of attention has consistently been linked to HR deceleration (Graham, 1992), which may therefore be expected to reflect empathy or sympathy. This indeed has received empirical support from community-sample studies (Eisenberg & Fabes, 1990). However, the literature suggests that HR deceleration occurs in various situations. For instance, during orientation (for a review, see Reynolds & Richards, 2008), freeze-like behaviour (Alban & Pocknell, 2017), and during different types of mood inductions (Davis, Suveg, Whitehead, Jones, & Shaffer, 2016). Moreover, in a community-sample study, not only children who showed concern for others demonstrated HR deceleration in response to other people in distress, but also children who

showed disregard to others (Van Hulle et al., 2013). Hence, HR deceleration seems to involve attention for stimuli that may not always indicate more empathy or sympathy. This has previously been discussed in the study of Van Hulle and his colleagues (2013), and they suggest that increased attention for stimuli (indicated by HR deceleration) may be the result of different reasons; the observer may feel sorry for someone else in distress, derive pleasure from its suffering or because of attention to non-affective features of the stimuli, such as novelty. Given the consistent link between HR deceleration and outward focus of attention and because empathy involves an outward focus of attention, we believe there are currently no reasons to suggest that HR deceleration would be an invalid index of empathy. Nevertheless, future research should try to clarify this, especially in ODD/CD samples.

Limitations

It is critical to acknowledge some limitations. First of all, some children in our sample used medication during assessments. The use of psychostimulants and anti-psychotics can influence cardiovascular responses (Alvares et al., 2016) and may have therefore resulted in less reliable measures of RSA and HR responses in the current study. Second, because we measured regulation and empathic responses in isolation, we are unaware of the actual regulation processes during the experience of vicarious arousal. To circumvent this problem, future studies may want to use RSA reactivity, reflecting RSA change from baseline to emotional challenge (El-Sheikh et al., 2009). Third, considering evidence that animal-directed empathy does not necessarily transfer to human-directed empathy (McPhedran, 2009) and the differential findings under conditions of the human clips versus bear clip, we should be cautious in generalizing the findings obtained with the bear clip to an inter-human empathy context. Fourth, we used a small sample size, limiting statistical power.

Conclusion

Our findings indicate that ODD/CD children may be able to efficiently regulate empathic arousal in mildly empathy-inducing situations but that their physiological regulation may be challenged in more intense empathy-inducing situations. Future research should examine to what extent this affects their empathic behaviour.

Chapter VI

General Discussion

Empathy problems are often associated with oppositional defiant disorder (ODD) and conduct disorder (CD; De Wied, Gispen-De Wied, & Van Boxtel, 2010). It is thought that some may show a lack of empathy because of *under* responsiveness to other's distress cues, whilst others may show a lack of empathy because of *over* responsiveness to other's distress cues, hostility and/or poor emotion regulation abilities (De Wied et al., 2010). The current dissertation aimed to elucidate the nature of empathy impairments in ODD/CD subtypes, and to explore possible mechanisms involved. In **Chapter II** we investigated the assumption that ODD/CD children and adolescents with CU traits show a selective impairment in affective empathy and whether a lack of empathy can differentiate between those with and without CU traits. In **Chapter III** we investigated the assumption that CU traits and ASD symptoms are associated with distinct empathy impairments. In **Chapters IV** and **V** we investigated the assumption that emotion regulation is involved in empathy-related responding in ODD/CD boys, at a cognitive and physiological level, respectively. In this final chapter, the main findings of the current dissertation will be summarized, integrated and discussed, after which implications and directions for future research will be provided. The chapter closes with general strengths and limitations of the studies and a general conclusion.

Summary of Main Research Findings

Table 1 provides an overview of the current dissertation's main research findings.

Chapter II involved a literature review on the nature of empathy impairments in ODD/CD children and adolescents and whether a lack of empathy contributes to a differentiation between those with and without CU traits. Findings revealed that the relatively few studies conducted with clinical ODD/CD samples differentiating and not differentiating on CU traits, provide consistent evidence for affective empathy deficits in children and adolescents with ODD/CD. As for cognitive empathy, the overall pattern of results is less consistent. Significant differences between ODD/CD subtypes emerged on autonomic indexes of affective state empathy; that is, ODD/CD children/adolescents with high CU traits show less HR change from baseline than those with low CU traits, indicating less empathic responsiveness. No differences were reported between ODD/CD subtypes on self-report and facial indexes of affective state empathy.

Chapter III involved an empirical study on the additive and interactive effects of CU traits and ASD symptoms in relation to affective and cognitive trait empathy in ODD/CD boys. Findings revealed that higher levels of CU traits were associated with lower levels of empathic sadness and that higher levels of ASD symptoms were associated with lower levels of cognitive empathy. Interestingly, ASD symptoms significantly moderated the relationship between CU traits and empathic sadness. Higher CU traits were associated with lower levels of empathic sadness at *low* levels of ASD symptoms.

Chapter IV involved an empirical study on the relationship between emotion regulation and empathy-related responding in ODD/CD boys with and without anxiety. We

investigated relationships between executive attention (a cognitive index of emotion regulation) and self-reports of empathy and sympathy in response to sadness inducing film clips among ODD/CD boys with and without anxiety. The effects of CU traits in the relationship between executive attention and empathic responses were also investigated. Results showed that executive attention was significantly related to empathy and sympathy, such that those with stronger executive attention skills reported more empathy and sympathy. The proposed relationships were evident only under intense sad conditions and only among ODD/CD boys with comorbid anxiety disorder. Analyses with CU traits reveal some evidence that the positive relationship between executive attention and empathic responses is particularly evident at low levels of CU traits.

Chapter V also involved an empirical study on the relationship between emotion regulation and empathy-related responding in ODD/CD boys with and without anxiety. We investigated relationships between resting RSA (a physiological index of emotion regulation) and HR reactivity (a physiological index of empathic responsiveness) to sadness inducing film clips. The effects of CU traits in the relationship between RSA and HR reactivity were also investigated. In agreement with expectations, results showed a significant inverse relationship between RSA and HR reactivity: higher RSA was associated with greater HR deceleration. However, different from expectations, the relationship was evident under mildly sad conditions and only among ODD/CD boys without comorbid anxiety disorder. Under intense sad conditions, a significant positive relationship appeared between RSA and HR reactivity: higher RSA was associated with less HR deceleration. Analyses further revealed a negative relationship between CU traits and HR reactivity under intense sad conditions: higher levels of CU traits were associated with greater HR deceleration.

Table 1. *Summary of Main Research Findings*

Chapter	Research Aims	Study	Predictors	Outcome Measures	Main-effects	Interaction-effects
II	a) Examine the nature of empathy problems in clinical samples of ODD/CD children and adolescents with CU traits b) examine whether a lack of empathy contributes to a differentiation between ODD/CD subtypes.	Literature review	-	-	a) Consistent evidence for impaired affective empathy. Inconsistent evidence for impaired cognitive empathy. b) No differences between ODD/CD subtypes on self-report and facial indexes of affective state empathy. Significant differences emerged on autonomic indexes of affective state empathy; that is, ODD/CD children/adolescents with CU traits showed less HR change from baseline than those without CU traits.	
III	Examine additive and interactive effects of CU traits and ASD symptoms in relation to trait empathy in a clinical sample of ODD/CD boys.	Empirical study	CU traits ASD symptoms	Empathic sadness Affective empathy Cognitive empathy	Higher CU traits, lower empathic sadness. Higher ASD symptoms, lower cognitive empathy.	Higher CU traits, lower empathic sadness (not affective empathy) at *low* to *moderate* ASD symptoms (not high).
IV	Examine relationships between executive attention and self-reports of empathy and sympathy to sadness inducing stimuli in ODD/CD boys, with and without comorbid anxiety disorder.	Empirical study	Executive attention Comorbid anxiety (yes/no)	Empathic sadness Sympathy	Under intense sad conditions: a) stronger executive attention, more empathy (not sympathy) Under mildly sad conditions: a) those with anxiety reported more empathy than those without anxiety	Under intense sad conditions: a) stronger executive attention, more empathy in those *with* comorbid anxiety disorder (not without). Under mildly sad conditions: a) poor executive attention, less empathy at *low* CU traits.
V	Examine relationships between resting RSA and HR reactivity to sadness inducing film clips in ODD/CD boys, with and without comorbid anxiety disorder.	Empirical study	RSA Comorbid anxiety (yes/no)	Empathic sadness	Under intense sad conditions: a) higher RSA, less HR deceleration b) higher CU traits, greater HR deceleration.	Under mildly sad conditions: a) higher RSA, greater HR deceleration in those *without* comorbid anxiety disorder (not with).

Note. ODD = oppositional defiant disorder; CD = conduct disorder; CU = callous unemotional; ASD = autism spectrum disorder; RSA = respiratory sinus arrhythmia; HR = heart rate.

Conclusions, Implications and Future Directions

The Nature of Empathy Impairments in ODD/CD

The literature review in **Chapter II** reveals consistent evidence for affective empathy impairment in ODD/CD children and adolescents with high levels of CU traits on measures of both state (Anastassiou-Hadjicharalambous & Warden, 2008b; Cheng, Hung, & Decety, 2012; De Wied, Van Boxtel, Matthys, & Meeus, 2012; Marsh et al., 2011; Marsh et al., 2013; Schwenck et al., 2012) and trait empathy (Anastassiou-Hadjicharalambous & Warden, 2008b; Jones, Happé, Gilbert, Burnett, & Viding, 2010; Pasalich, Dadds, & Hawes, 2014). Moreover, studies with ODD/CD children and adolescents not taking CU traits into account also show consistent evidence for affective empathy impairment on measures of both state and trait empathy (e.g., Cohen & Strayer, 1996; Decetey, Michalska, Akitsuki, & Lahey, 2009; De Wied, Goudena, & Matthys, 2005; De Wied, Van Boxtel, Zaalberg, Goudena, & Matthys, 2006; De Wied, Van Boxtel, Posthumus, Goudena, & Matthys, 2009; Sterzer, Stadler, Poustka, & Kleinschmidt, 2007). Together these findings suggest that affective empathy impairment is common across the broader range of disruptive behaviour disorders.

As for cognitive empathy, the literature review from **Chapter II** reveals inconsistent evidence from studies conducted with ODD/CD samples differentiated and not differentiated on CU traits. At least two studies conducted with undifferentiated ODD/CD samples suggest cognitive empathy impairments in ODD/CD children (Downs & Smith, 2004) and adolescents (Cohen & Strayer, 1996). However, given the limited number of studies and the use of distinct samples and methods it seems too soon to draw conclusions about possible cognitive empathy impairments in ODD/CD children and adolescents. Furthermore, at least three studies suggest a link between CU traits and impairments in cognitive empathy (Anastassiou-Hadjicharalambous & Warden, 2008a; Cheng et al., 2012; Pasalich et al., 2014). Interestingly, however, the studies may have used measures of cognitive empathy that tap into affective components. This suggests that the reported impairments in cognitive empathy may have resulted from the involvement of affective components in the assessment tools. Thus, ODD/CD children and adolescents with high CU traits may have an affective-specific impairment that becomes apparent in poor affective empathy skills as well as poor cognitive empathy skills when it involves emotional components.

The literature review from **Chapter II** further reveals that significant differences between ODD/CD subtypes only emerged in studies using physiological indexes of affective state empathy (not self-reports or facial indexes). CD children and ODD/CD adolescents with CU traits seemed less responsive to other's distress cues (showed less HR change from baseline) than their low CU counterparts. Similar results have been obtained in an earlier study with emotionally disturbed children (classifications of ODD/CD were not reported). Those with psychopathic traits showed reduced skin conductance responses to distressed pictures than those without psychopathic traits and controls (Blair, 1999). It thus seems that

individuals with high and low CU traits from different samples show distinct autonomic patterns to other people's distress cues.

The distinct autonomic patterns may be driven by different underlying impairments in ODD/CD subtypes. Those with CU traits may show less change in arousal to other's distress because they are less sensitive and/or attentive to other's emotions, resulting from abnormalities in the amygdala (Blair, 2013; Blair, Leibenluft, & Pine, 2014).

Chapter II additionally reveals that no studies to date have demonstrated significant differences between ODD/CD subtypes on self-report indexes of affective (or cognitive) trait empathy. Considering the notion that CU traits are associated with a distinct causal pathway to conduct disorder (Frick, Ray, Thornton, & Kahn, 2013), we may expect deficits in both state and trait empathy for those with CU traits. However, self-report questionnaires of empathy may not be sensitive enough to capture differences in trait empathy between the ODD/CD subtypes. This may call for the development of more sensitive questionnaire measures of empathy, but also to adopt a multi-method design while studying empathy in ODD/CD samples, using self-reports and physiological measures of empathy.

Chapter III studied the assumption that CU traits and ASD symptoms are associated with distinct empathy impairments. Based on theory (Baron-Cohen, Leslie, & Frith, 1985; Blair, 2005, 2013; Blair et al., 2014) and prior studies (e.g., Jones et al., 2010; Schwenck et al., 2012) we expected impaired affective empathy for CU traits and impaired cognitive empathy for ASD symptoms. In line with these expectations, we found that boys with higher levels of CU traits reported lower levels of empathic sadness, whilst those with higher levels of ASD symptoms reported lower levels of cognitive empathy. Importantly, the negative relationship between CU traits and empathic sadness was particularly strong at *low* levels of ASD symptoms (not high). This finding is understandable because the inverse relationship between CU traits and empathic sadness at high levels of ASD may be confounded by false positives for CU traits. More specifically, CU traits and ASD symptoms show behavioural overlap; both conditions have been associated with reduced empathic responsiveness (APA, 2013) and disruptive behaviour (Frick et al., 2013; Kaat & Lecavalier, 2013). Some children with high ASD symptoms may therefore be falsely rated with high CU traits. Unlike CU traits, however, ASD symptoms have been linked to sensitivity, even over-sensitivity to other people's feelings (Järvinen et al., 2015; Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007; Smith, 2008). False positives for CU traits thus involve 'sensitive' CU-ers, which may confound the inverse relationship between CU traits and empathic sadness. Accordingly, we find the lowest levels of empathic sadness in ODD/CD boys high on CU traits but low on ASD symptoms and no association in ODD/CD boys high on CU traits and ASD symptoms. Together the findings seem to indicate that low levels of empathic sadness may be more typical for CU traits than for ASD symptoms.

Emotion Regulation and Empathy Impairments in ODD/CD

The role of emotion regulation in empathy-related responding among ODD/CD children has been studied at a cognitive level in **Chapter IV** and at a physiological level in **Chapter V**. Based on theory (Eisenberg et al., 1994) and empirical studies conducted with community samples (Eisenberg et al., 1996, 1998), we expected to find that more efficient regulation would be associated with greater empathy or sympathy. Conforming to these expectations; findings from **Chapter IV** reveal that stronger executive attention skills were associated with more self-reported empathy and sympathy. The relationship was evident only under intense sad conditions and only in ODD/CD boys *with* comorbid anxiety disorder. As such, these findings are in agreement with the literature suggesting that emotion regulation is particularly involved in the regulation of empathic arousal amongst highly sensitive people (Eisenberg et al., 1994, 1996, 1998) and when vicarious arousal is strong (Eisenberg, 2010). Executive attention may be beneficial for ODD/CD children with anxiety disorder, as it may help to maintain optimal levels of empathic arousal, enabling other-focused attention and higher levels of empathy and sympathy for another person, accordingly. By contrast, poor executive attention may place them at risk for empathic over-arousal, leading to self-focused attention and therefore less empathy and sympathy for another person.

At a physiological level, findings from **Chapter V** also reveal associations between emotion regulation and empathy-related responding. In agreement with expectations, we found a negative relationship between resting RSA (a physiological index of regulation) and HR reactivity during the empathy-inducing clip (reflecting empathy/sympathy), in that higher RSA was associated with greater HR deceleration. Assuming that HR deceleration reflects stronger empathy or sympathy (which will be discussed below), the findings indicate that more efficient regulation (higher RSA) was associated with stronger empathy or sympathy (greater HR deceleration). Different from expectations, however, the relationship was obtained only in ODD/CD boys *without* anxiety under mildly sad conditions. Under more intense sad conditions, an unexpected positive relationship appeared between RSA and HR reactivity, such that high RSA was associated with less HR deceleration. Nevertheless, findings seem to be in agreement with literature arguing that efficient physiological regulation is limited to situations that are perceived as non-stressful. In such situations, the body increases vagal influences on the heart, which slows down HR, fostering calm and vegetative activities as well as social engagement behaviours (Porges, 2007), which could facilitate empathy. Because the mildly sad stimuli may be less stressful, in particular for those without anxiety, we can understand why we found the inverse relationship between RSA and HR reactivity under mildly (rather than highly) sad conditions and only in those *without* comorbid anxiety disorder. Under perceived stressful conditions, however, it has been suggested that, despite good efforts of the vagus to regulate HR, activation of the sympathetic nervous system is additionally necessary to meet with external demands (Porges, 2007). Sympathetic activation will lead to an increase in HR and other bodily processes to prepare the body for mobilization. Because the more intense sad stimulus may be experienced as more stressful, this may

explain why those with high RSA (which should reflect good vagus functioning) showed little HR deceleration (possibly indicating sympathetic activation).

Findings from Chapters IV and V thus provide evidence for the notion that more efficient regulation is association with greater empathy and sympathy in ODD/CD individuals. However, the relationship emerged under different conditions. At the cognitive level, more efficient emotion regulation was associated with more empathy/sympathy under intense sad conditions, whilst at the physiological level, more efficient emotion regulation was associated with more empathy/sympathy under mildly sad conditions. The pattern of findings may indicate that the regulation of empathic arousal occurs gradually via several regulatory mechanisms. When vicarious arousal is mild, the body may be able to efficiently regulate itself and does not need the 'help' of any other regulatory mechanisms. However, when vicarious arousal becomes too strong, efficient physiological regulation may be challenged and more is needed to maintain optimal levels of arousal. This could lead to the recruitment of higher-order cognitive regulation skills to regulate vicarious arousal, accordingly. Emotion regulation as a 'step by step' process may be interesting to further elucidate in future research.

HR Deceleration: An Index for Empathy

Results obtained in the current research raise questions about the operationalization and measurement of empathy, more specifically about HR deceleration as a physiological index of empathy or sympathy. In Chapter V, CU traits were found to inversely relate to HR reactivity during the most stressful bear-clip, such that boys with the highest CU traits showed more HR reduction. Starting from the assumption that HR deceleration reflects empathy/sympathy results would seem to suggest that high CU boys are more empathic than low CU boys, which is counterintuitive.

There are conceptual and empirical reasons to suggest that HR deceleration is indicative of empathy or sympathy (Eisenberg & Fabes, 1990). Empathy and sympathy refer to other-oriented emotions (including feelings of tenderness and compassion) and involve an outward focus of attention. In the psychophysiological literature, attention to external stimuli have been linked to HR deceleration (e.g., Abercombie, Chambers, Greischer, & Monticelli, 2008; Graham, 1992). Indeed, empirical evidence from community-sample studies seems to support the notion that HR deceleration reflects empathy or sympathy (e.g., Eisenberg et al., 1988a; Eisenberg et al., 1988b). Nevertheless, HR deceleration may occur for a variety of reasons. For example, during orientation (for a review, see Reynolds & Richards, 2008), freeze like behaviour (Alban & Pocknell, 2017), and during different types of mood inductions (e.g., fear, sadness, and happiness; Davis, Suveg, Whitehead, Jones, & Shaffer, 2016). Moreover, a community-sample study revealed that children who showed concern for others exhibited HR deceleration in response to other people in distress, as did children who showed disregard to others (Van Hulle et al., 2013). Thus, an outward focus of attention may be associated with HR deceleration, but not always with empathic concern. This has previously been discussed by Van Hulle and his colleagues (2013), and they suggest that enhanced attention for stimuli

(indicated by HR deceleration) may be associated with different cognitions. For instance, the observer may feel sorry for the target in distress, derive pleasure from its suffering or feel attracted by the non-affective features of the stimuli, such as novelty. Considering the consistent link between HR deceleration and outward focus of attention and because empathy involves an outward focus of attention (Eisenberg & Fabes, 1990), we believe that there are no reasons to suggest that HR deceleration would be an invalid index of empathy. Nevertheless, future research should further clarify this, especially in ODD/CD samples.

Implications for Clinical Practice and Recommendations for Future Research

First, findings from the current dissertation clearly reveal impairments in empathic distress in children and adolescents with ODD/CD (**Chapter II**), and that these impairments may be more typical for CU traits rather than ASD symptoms (**Chapter III**). This is important information for clinicians as it may help differential diagnostics involving CU traits and ASD. Unfortunately, however, there are limited diagnostic instruments to assess affective empathy. The instruments at hand involve questionnaire measures of trait empathy (e.g., BES and IECA) without norm references. This makes it difficult to conclude anything about the 'level' of affective empathy. It is therefore crucial to provide norm references for the available questionnaires of affective empathy. It is also crucial to develop state measures of affective empathy.

Second, findings from the current dissertation suggest that stronger executive attention skills may be beneficial for ODD/CD children to control strong vicarious arousal. We therefore speculate that training executive attention might be a promising way to improve their empathic responding. However, it is important to gain more insight into emotion regulation as a factor in empathy among ODD/CD individuals. Emotion regulation is a broad construct involving many other aspects than executive attention or RSA. Moreover, in the current dissertation we did not measure emotion regulation during the experience of empathic arousal. It would be interesting to investigate regulation processes during the experience of vicarious arousal via, for instance, observations or RSA reactivity (RSA change from baseline to emotional episode).

Third, whilst it is often assumed that empathy stimulates prosocial behaviour (Eisenberg, 2000) and inhibits aggressive behaviour (Vachon, Lynam, & Johnson, 2014), findings on these relationships are often modest and weak (Eisenberg, 2000; Vachon et al., 2014). A possible reason for this is the influence of moderating variables, such as regulatory skills (Lockwood, Seara-Cardoso, & Viding, 2014; Vachon et al., 2014). Because the current dissertation suggests that emotion regulation is involved in the regulation of empathic arousal, it would be interesting to investigate whether emotion regulation moderates the relationship between empathy and prosocial behaviour as well as aggressive behaviour in clinical ODD/CD samples. Thus, it would be interesting to know whether efficient regulation of empathic arousal is associated with more prosocial and less aggressive behaviour, and whether inefficient regulation of empathic arousal is associated with less prosocial and more

aggressive behaviour. This is important to investigate because it gives us more information as to whether emotion regulation training may be efficient to improve social functioning in ODD/CD children and adolescents.

Fourth, in the current dissertation we only focused on emotion regulation as a factor in empathy-related responses in ODD/CD while other factors, such as hostile attribution biases (De Wied et al., 2010) and environmental factors such as parenting (Guo & Feng, 2017) may also be involved. Community-samples studies have shown relationships between hostile attributions and empathy in students (e.g., Lanzetta & Englis, 1989; Singer, 2006) as well as parenting styles and empathy in children (Guo & Feng, 2017). It would be interesting to investigate whether these findings could be extended to ODD/CD samples.

Fifth, because the meaning of HR deceleration may sometimes be unclear, future research on empathic responses in ODD/CD children would benefit from studies on HR deceleration as an index of empathy/sympathy or attention.

Strengths and Limitations

Strengths of the current dissertation can be seen in the use of a multi-measure approach to study empathy. We studied affective and cognitive trait as well as state empathy (Chapter II), we employed self-reports of affective and cognitive trait empathy (Chapter III), and we employed self-reports (Chapter IV) and physiological indices (Chapter V) of affective state empathy. Further strengths can be seen in the careful description of our ODD/CD sample thereby taking into account the heterogeneity and complexity of the ODD/CD population (Chapter III – V).

Despite its strengths, the current dissertation has several limitations. Besides the limitations that are specific to the individual studies described in the chapters, there are some important general limitations worth mentioning. First, in our empirical studies we only investigated boys. This limits the generalizability of our findings to girls, as prior studies have shown gender differences in empathy (Van der Graaff, Branje, De Wied, Hawk, Van Lier, & Meeus, 2014). Second, findings obtained in our empirical studies were mainly related to empathy for sadness and can therefore not be generalized to other emotions. Third, we often used self-report measures of empathy despite knowing that reporting on one's own emotions can be difficult for ODD/CD children, considering their low verbal (e.g., Déry, Toupin, Pauzé, Mercier, & Fortin, 1999; Loney, Frick, Ellis, & McCoy, 1998) and self-referential abilities (Pardini, Barry, Barth, Lochman, & Wells, 2006). Self-reports may have thus resulted in less reliable reports of empathy in our empirical studies.

General Conclusion

The current dissertation reveals that (1) children and adolescents with ODD/CD show more consistent impairments in affective empathy than in cognitive empathy, (2) that there are differences in empathy impairments among ODD/CD subtypes; that is, (3) those with and without CU traits exhibit distinct autonomic patterns to other's distress cues, (4) those with higher CU traits report lower levels of empathic sadness, whilst those with higher ASD symptoms report lower levels of cognitive empathy, and finally (5) aspects of emotion regulation may be involved in empathy impairments among ODD/CD individuals. Future research should focus on the development of diagnostic instruments for affective empathy and further elucidate the role of emotion regulation in empathy-related responding and how this relates to social functioning in ODD/CD children and adolescents.

References

Abercombie, H. C., Chambers, A. S., Greischar, L., & Monticelli, R. M. (2008). Orienting, emotion, and memory: Phasic and tonic variation in heart rate predicts memory for emotional pictures in men. *Neurobiology of Learning and Memory, 90,* 644-650.

Alban, M. W., & Pocknell, V. (2017). Cognitive factors affecting freeze-like behavior in humans. *The Journal of General Psychology, 144,* 140-156.

Alegria, A. A., Radua, J., & Rubia, K. (2016). Meta-analysis of fMRI studies of disruptive behavior disorders. *The American Journal of Psychiatry, 173,* 1119-1130.

Alvares, G. A., Quintana, D. S., Hickie, I. B., & Guestella, A. J. (2016). Autonomic nervous system dysfunction in psychiatric disorders and the impact of psychotropic medications: a systematic review and meta-analysis. *Journal of Psychiatry and Neuroscience, 41,* 89-104.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders, fifth edition.* Washington: American Psychiatric Association.

Anastassiou-Hadjicharalambous, X., & Warden, D. (2008a). Cognitive and affective perspective-taking in conduct-disordered children high and low on callous-unemotional traits. *Child and Adolescent Psychiatry and Mental Health, 2*(16), 1-11.

Anastassiou-Hadjicharalambous, X., & Warden, D. (2008b). Physiologically-indexed and self-perceived affective empathy in conduct-disordered children high and low on callous-unemotional traits. *Child Psychiatry and Human Development, 39,* 503-517.

Archer, J., & Monton, S. (2011). Preferences for infant facial features in pet dogs and cats. *Ethology, 117,* 217–226.

Austin, G., Bondü, R., & Elsner, B. (2016). Longitudinal relations between children's cognitive and affective theory of mind with reactive and proactive aggression. *Aggressive Behavior, 43,* 440-449.

Barkley, R. A. (2006). *Attention-deficit hyperactivity disorder: A handbook for diagnosis and treatment, third edition*. New York: Guilford press.

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1985). Does the autistic child have a "theory of mind"? *Cognition, 21,* 37-46.

Baron-Cohen, S., & Wheelwright, S. (2004). The empathy quotient: An investigation of adults with Asperger syndrome or high functioning autism, and normal sex differences. *Journal of Autism and Developmental Disorders, 34,* 163-175.

Bar-Haim, Y., Morag, I., Glickman, S. (2011). Training anxious children to disengage attention from threat: a randomized controlled trial. *Journal of Child Psychology andPsychiatry, 52,* 861-869.

Batson, C. D. (2009). These things called empathy: Eight related but distinct phenomena. In J. Decety & W. Ickes (Eds.), *The social neuroscience of empathy* (pp. 3-15). Cambridge, US: MIT Press.

Beauchaine, T. P. (2015a) Future directions in emotion dysregulation and youth psychopathology. *The Joural of Clinical Child and Adolescent Psychology, 44,* 875-896.

Beauchaine, T. P. (2015b). Respiratory sinus arrhythmia: a transdiagnostic marker of emotion dyregulation and psychopathology. *Current Opinion in Psychology, 3,* 43-47.

Beauchaine, T. P., Gatzke-Kopp, L., & Mead, H. K. (2007) Polyvagal theory and developmental psychopathology:Emotion dysregulation and conduct problems from preschool to adolescence. *Biological Psychology, 74,* 174-184.

Bechor, M., Pettit, W., Silverman, W. K., Bar-Heim, Y., Abend, R., Pine, D. S., … Jaccard, J.(2014). Attention bias modification treatment for children with anxiety disorders who do not respond to cognitive behavioral therapy: a case series. *Journal of Anxiety Disorders, 28,* 154-159.

Berntson, G. G., Bigger Jr, J. T., Eckberg, D. L., Grossman, P., Kaufmann, P. G., Malik, M., ... Van der Molen, M. W. (1997). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology, 34*, 623– 648.

Bifulco, A., Schimmenti, A., Jacobs, C., Bunn, A., & Rusu, A. C. (2014). Risk factors and psychological outcomes of bullying victimization: A community-based study. *Child Indicators Research, 7,* 633-648.

Blair, R. J. R. (1999). Responsiveness to distress cues in the child with psychopathic tendencies. *Personality and Individual Differences, 27,* 135-145.

Blair, R. J. R. (2005). Responding to the emotions of others: Dissociating forms of empathy through the study of typical and psychiatric populations. *Consciousness and Cognition, 14,* 698-718.

Blair, R. J. R. (2007). Empathic dysfunction in psychopathic individuals. In T.F.D. Farrow & P.W.R. Woodruff (Eds.), *Empathy in mental illness* (pp. 3-16). New York: Cambridge University Press.

Blair, R. J. R. (2008). Fine cuts of empathy and the amygdala: Dissociable deficits in psychopathy and autism. *The Quarterly Journal of Experimental Psychology, 61,* 157-170.

Blair, R. J. R. (2013). The neurobiology of psychopathic traits in youths. *Nature Reviews Neuroscience, 14,* 786-799.

Blair, R. J. R., Leibenluft, E., & Pine, D. S. (2014). Conduct disorder and callous-unemotional traits in youth. *The New England Journal of Medicine, 371,* 2207-2216.

Blair, R. J. R., Peschardt, K. S., Budhani, S., Mitchell, D. G. V., & Pine, D. S. (2006). The development of psychopathy. *The Journal of Child Psychology and Psychiatry, 47,* 262-275.

Boucher, J. (2012). Putting theory of mind in its place: Psychological explanations of the socio-emotional-communicative impairments in autistic spectrum disorder. *Autism, 16,* 226-246.

Braaten, E. B., & Rosén, L. A. (2000). Self-regulation of affect in Attention Deficit-Hyperactivity Disorder (ADHD) and non-ADHD boys: Differences in empathic responding. *Journal of Consulting and Clinical Psychology, 68,* 313-321.

Bradshaw, C. P., Schaeffer, C. M., Petras, H., & Ialongo, N. (2010). Predicting negative life outcomes from early aggressive-disruptive behavior trajectories: gender differences in maladaptation across life domains. *Journal of Youth and Adolescence, 39,* 953-966.

Bridgett, D. J., Burt, N. M., Deater-Deckard, K., & Edwards, E. S. (2015). Intergenerational transmission of self-regulation: A multidisciplinary review and integrative conceptual framework. *Psychological Bulletin, 141,* 602-654.

Bryant, B. K. (1982). An index of empathy for children and adolescents. *Child Development, 53,* 413-425.

Bubier, J. L., & Drabick, D. A. G. (2009). Co-occurring anxiety and disruptive behavior disorders: The roles of anxious symptoms, reactive aggression, and shared risk processes. *Clinical Psychology Review, 29,* 658–669.

Carr, L., Iacoboni, M., Dubeau, M-C., Mazziotta, J. C., & Lenzi, G. L. (2003). Neural mechanisms of empathy in humans: A relay from neural systems for imitation to limbic areas. *PNAS, 100,* 5497-5502.

Cheng, Y., Hung, A-Y., & Decety, J. (2012). Dissociation between affective sharing and emotion understanding in juvenile psychopaths. *Developmental and Psychopathology, 24,* 623-636.

Coccaro, E. F., McCloskey, M. S., Fitzgerald, D. A., & Phan, K. L. (2007). Amygdala and orbitofrontal reactivity to social threat in individuals with impulsive aggresion. *Biological Psychiatry, 62,* 168-178.

Cohen, D., & Strayer, J. (1996). Empathy in conduct-disordered and comparison youth. *Developmental Psychology, 32,* 988-998.

Cole, P. M., Martin, S. E., & Dennis, T. A. (2004). Emotion regulation as a scientific construct: methodological challenges and directions for child development. *Child Development, 75,* 317-333.

Constantino, J. N., Davis, S. A., Todd, R. D., Schindler, M. K., Gross, M. M., Brophy, S. L., … Reich, W. (2003).Validation of a brief quantitative measure of autistic traits: Comparison of the social responsiveness scale with the autism diagnostic interview-revised. *Journal of Autism and Developmental Disorders, 33,* 427-433.

Constantino, J. N., & Gruber, C. P. (2005). *Social responsiveness scale (SRS).* Los Angeles, CA: Western Psychological Services.

Constantino, J. N., & Todd, R. D. (2003). Autistic traits in the general population: A twin study. *Archives of General Psychiatry, 60,* 524-530.

Crowe, S. L., & Blair, R. J. R. (2008) The development of antisocial behavior: What can we learn from functional neuroimaging studies? *Development and Psychopathology, 20,* 1145-1159.

Cupuana, L. J., Dywan, J., Tays, W. J., Elmers, J. L., Witherspoon, R., & Segalowitz, S. J. (2014). Factors influencing the role of cardiac autonomic regulation in the service of cognitive control. *Biological, Psychology, 102*, 88-97.

Dadds, M. R., Cauchi, A. J., Wimalaweera, S., Hawes, D. J., & Brennan, J. (2012). Outcomes, moderators, and mediators of empathic-emotion recognition training for complex conduct problems in childhood. *Psychiatry Research, 199,* 201-207.

Dadds, M. R., El Masry, Y., Wimalaweera, S., & Guastella, A. J. (2008a). Reduced eye gaze explains "fear blindness" in childhood psychopathic traits. *Journal of the American Academy of Child and AdolescentPsychiatry, 47,* 455-463.

Dadds, M. R., Hunter, K., Hawes, D. J., Frost, A. D. J., Vassallo, S., Bunn, P., ... El Masry, Y. (2008b). A measure of cognitive and affective empathy in children using parent ratings. *Child Psychiatry and Human Development, 39,* 111-122.

Dadds, M. R., Jambrak, J., Pasalich, D., Hawes, D. J., & Brennan, J. (2011). Impaired attention to the eyes of attachment figures and the developmental origins of psychopathy. *The Journal of Child Psychology and Psychiatry, 52,* 238-245.

Dadds, M. R., Perry, Y., Hawes, D. J., Merz, S., Riddel, A. C., Haines, D. J., … Abeygunawardane, A. I. (2006). Attention to the eyes and fear-recognition deficits in child psychopathy. *British Journal of Psychiatry, 189,* 280-281.

Davis, M. H. (1983). Measuring individual differences in empathy: Evidence for a multidimensional approach. *Journal of Personality and Social Psychology, 44,* 113-126.

Davis, M. H. (1996). *Empathy: A social psychological approach.* Boulder, US: Westview Press.

Davis, M. H. (2006). Empathy. In J. E. Stets & J. H. Turner (Eds.), *Handbook of the sociology of emotions* (pp. 443-466). New York, NY: Springer.

Davis, M., Suveg, C., Whitehead, M., Jones, A., & Shaffer, A. (2016). Preschoolers' psychophysiological responses to mood induction tasks moderate the intergenerational transmission of internalizing problems. *Biological Psychology, 117,* 159-169.

Davison, A.C., & Hinkley, D.V. (1997). *Bootstrap methods and their application*. New York, NY: Cambridge University Press.

Decety, J., Michalska, K. J., Akitsuki, Y., & Lahey, B. B. (2009). Atypical empathic responses in adolescents with aggressive conduct disorder: A functional MRI investigation. *Biological Psychology, 80,* 203-211.

Déry, M., Toupin, J., Pauzé, R., Mercier, H., & Fortin, L. (1999). Neuropsychological characteristics of adolescents with conduct disorder: Associations with attention-deficit-hyperactivity and agression. *Journal of Abnormal Child Psychology, 27,* 225-236.

De Sonneville, L. M. J. (2005). Amsterdam Neuropsychological Tasks: Scientific and clinical applications. *Tijdschrift voor Neuropsychologie, 0,* 27-41.

De Sonneville, L. M. L. (2014). Handboek Amsterdamse neuropsychologische taken. Amsterdam: Boomuitgevers.

De Wied, M., Gispen-De Wied, C., & Van Boxtel, A. (2010). Empathy dysfunction in children and adolescents with disruptive behavior disorders. *European Journal of Pharmacology, 626,* 97-103.

De Wied, M., Goudena, P. P., & Matthys, W. (2005). Empathy in boys with disruptive behavior disorders. *The Journal of Child Psychology and Psychiatry, 46*, 867-880.

De Wied, M., Maas, C., Van Goozen, S., Vermande, M., Engels, R., Meeus, W., … Goudena, P. (2007). Bryant's Empathy Index: A closer examination of its internal structure. *European Journal of Psychological Assessment, 23,* 99-104.

De Wied, M., Van Boxtel, A., Matthys, W., & Meeus, W. (2012). Verbal, facial and autonomic responses to empathy-eliciting film clips by disruptive male adolescents with high versus low callous-unemotional traits. *Journal of Abnormal Child Psychology, 40,* 211-223.

De Wied, M., Van Boxtel, A., Posthumus, J. A., Goudena, P. P., & Matthys, W. (2009). Facial EMG and heart rate responses to emotion-inducing film clips in boys with disruptive behavior disorders. *Psychophysiology, 46,* 996-1004.

De Wied, M., Van Boxtel, A., Zaalberg, R., Goudena, P. P., & Matthys, W. (2006). Facial EMG responses to dynamic emotional facial expressions in boys with disruptive behavior disorders. *Journal of Psychiatric Research, 40,* 112-121.

De Wied, M., Van der Baan, H., Raaijmakers, Q., De Ruiter, C., & Meeus, W. (2014). Factor structure and construct validity of the Dutch version of the Antisocial Process Screening Device. *Journal of Psychopathology and Behavioral Assessment, 36,* 84-92.

Dimberg, U. (1990). Facial electromyography and emotional-reactions. *Psychophysiology, 27,* 481-494.

Dimberg, U., Thunberg, M., & Elmehed, K. (2000). Unconscious facial reactions to emotional facial expressions. *Pyschological Science, 11,* 86-89.

Dimberg, U., Thunberg, M., & Grunedal, S. (2002). Facial reactions to emotional stimuli: automatically controlled emotional responses. *Cognition and Emotion, 16,* 449-471.

Dodge, K. A., Price, J. M., Bachorowski, J-A., & Newman, J. P. (1990). Hostile attributional biases in severely aggressive adolescents. *Journal of Abnormal Psychology, 99,* 385-392.

Downs, A., & Smith, T. (2004). Emotional understanding, cooperation, and social behavior in high-functioning children with autism. *Journal of Autism and Developmental Disorders, 34,* 625-635.

Eisenberg, N. (2000). Emotion, regulation, and moral development. *Annual Review of Psychology, 51,* 665-697.

Eisenberg, N. (2010). Empathy-related responding: Links with self-regulation, moral judgement and moral behavior. In M. Mikulincer & P. R. Shaver (Eds.), *Prosocial motives, emotions and behavior: The better angels of our nature* (pp 129-148). Washington, DC: American Psychological Association.

Eisenberg, N., & Eggum, N. D. (2009). Empathic responding: Sympathy and personal distress.

In J. Decety, W. Ickes (Eds.), *The social neuroscience of empathy* (pp 71-83). Cambridge, US: MIT Press.

Eisenberg, N., & Fabes, R. A. (1990). Empathy: Conceptualization, measurement, and relation to prosocial behavior. *Motivation and Emotion, 14,* 131-149.

Eisenberg, N., Fabes, R. A., Bustamante, D., Mathy, R. M., Miller, P. A., & Lindholm, E. (1988a). Differentiation of vicariously induced emotional reactions in children. *Developmental Psychology, 24,* 237-246.

Eisenberg, N., Fabes, R. A., Murphy, B., Karbon, M., Maszk, P., Smith, M., … Suh, K. (1994). The relations of emotionality and regulation to dispositional and situational empathy-related responding. *Journal of Personality and Social Psychology, 66,* 776-797.

Eisenberg, N., Fabes, R. A., Murphy, B., Karbon, M., Smith, M., & Maszk, P. (1996). The relations of children's dispositional empathy-related responding to their emotionality, regulation, and social functioning. *Developmental Psychology, 32,* 195-209.

Eisenberg, N., Fabes, R.A., Nyman, M., Bernzweig, J., & Pinuelas, A. (1994). The relations of emotionality and regulation to children's anger-related reactions. *Child Development, 63,* 109-128.

Eisenberg, N., Fabes, R. A., Shepard, S. A., Murphy, B. C., Jones, S., & Guthrie, I. K. (1998). Contemporaneous and longitudinal prediction of children's sympathy from dispositional regulation and emotionality. *Developmental Psychology, 34,* 910-924.

Eisenberg, N., Fabes, R. A., & Spinrad, T. L. (2006). Prosocial behavior. In N. Eisenberg (Vol. Ed) and W Damon, R. M. Lerner (Series Eds.), *Handbook of child psychology: Vol. 3. Social, emotional, and personality development* (6th ed.; 646–718). New York, NY: Wiley.

Eisenberg, N., Hofer, C., & Vaughan, J. (2007). Effortful control and its socioemotional consequences. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 287–306). New York, NY: Guilford.

Eisenberg, N., Michalik, N., Spinrad, T. L., Hofer, C., Kupfer, A., Valiente, C., ... Reiser, M. (2007). The relations of effortful control and impulsivity to children's sympathy: A longitudinal study. *Cognitive Development, 22,* 544-567.

Eisenberg, N., & Miller, P. A. (1987). The relation of empathy to prosocial and related behaviors. *Psychological Bulletin, 101,* 91-119.

Eisenberg, N., Schaller, M., Fabes, R. A., Bustamante, D., Mathy, R. M., Shell, R., & Rhodes, K. (1988b). Differentiation of personal distress and sympathy in children and adults. *Developmental Psychology, 24,* 766-755.

Eisenberg, N., Shea, C. L., Carlo, G., & Knight, G. P. (1991). Empathy-related responding and cognition: A "chicken and egg" dilemma. In W. M. Kurtines (Ed.), *Handbook of moral behavior and development: Vol. 2. Research* (pp. 63-88). Hillsdale, NJ: Erlbaum.

Eisenberg, N., Smith, C. L., & Spinrad, T. L. (2011). Effortful control: Relations with emotion regulation, adjustment, and socialization in childhood. In K. D. Vohs & R. F. Baumeister (Eds.), *Handbook of self-regulation: Research, theory and applications (*2nd ed.; pp. 263-283). New York, NY: The Guilford Press.

Eisenberg, N., & Strayer, J. (1987). Critical issues in the study of empathy. In N. Eisenberg & J. Strayer (Eds.), *Empathy and its development* (pp 3-13). New York, NY: Cambridge University Press.

Eisenberg, N., & Sulik, M. J. (2012) Emotion-related self-regulation in children. *Teaching Of Psychology, 39,* 77-83.

El-Sheikh, M., Kouros, C., Erath, S., Cummings, E. M., Keller, P., & Staton, L. (2009). Marital conflict and children's externalizing behavior: Pathways involving interactions between parasympathetic and sympathetic nervous system activity. *Monographs of the Society for Research in Child Development, 74,* 1-69.

Endenburg, N. (1995). The attachment of people to companion. *Anthrozoös, 8,* 83-89.

Fabes, R. A., Eisenberg, N., & Eisenbud, L. (1993). Behavioral and physiological correlates of children's reactions to others in distress. *Developmental Psychology, 29,* 655-663.

Fabes, R. A., Eisenberg, N., Karbon, M., Troyer, D., & Switzer, G. (1994). The relations of children's emotion regulation to their vicarious emotional responses and comforting behaviors. *Child Development, 65,* 1678-1693.

Fanti, K. A. (2016). Understanding heterogeneity in conduct disorder: A review of psychophysiological studies. Retrieved from http://dx.doi.org/10.1016/j.neubiorev.2016.09.022

Fanti, K. A., Demetriou, C. A., & Kimonis, E. R. (2013). Variants of callous-unemotional conduct problems in a community sample of adolescents. *Journal of Youth and Adolescence, 42,* 964-979.

Ferdinand, R. F., & Van der Ende, J. (2002). *NIMH-DISC-IV: Diagnostic interview schedule for children (Authorized Dutch version).* Rotterdam: Erasmus MC/Sophia Kinderziekenhuis Rotterdam.

Ford, T., Goodman, R., & Meltzer, H. (2003). The british child and adolescent mental health survey 1999: the prevalence of DSM-IV disorders. *The Journal of the American Academy of Child and Adolescent Psychiatry, 42,* 1203-1211.

Foster, M., & Jones, D. (2005). The high costs of aggression: Public expenditures resulting from conduct disorder. *American Journal of Public Health, 95,* 1767-1772.

Frick, P. J. (2012). Developmental pathways to conduct disorder: Implications for future directions in research, assessment, and treatment. *Journal of Clinical Child and Adolescent Psychology, 41,* 378-389.

Frick, P. J., & Hare, R. D. (2001). *Antisocial process screening device (APSD).* Toronto: Multi-Health Systems.

Frick, P. J., Ray, J. V., Thornton, L. C., & Kahn, R. E. (2013). Can callous-unemotional traits enhance the understanding, diagnosis, and treatment of serious conduct problems in children and adolescents? A comprehensive review. *Psychological Bulletin, 140,* 1-57.

Frick, P. J., & Viding, E. (2009). Antisocial behavior from a developmental psychopathology perspective. *Development and Psychopathology, 21,* 1111-1131.

Frick, P. J., & White, S. F. (2008). Research review: The importance of callous unemotional

traits for developmental models of aggressive and antisocial behavior. *The Journal of Child Psychology and Psychiatry, 49,* 359-375.

Furr, R. M., & Bacharach, V. R. (2008). Psychometrics: An introduction. California, CA: Sage Publications.

Gibbs, J. C., Potter, G. B., & Goldstein, A. P. (1995). *The EQUIP program: Teaching youth how to think and act responsibly through a peer-helping approach.* Champaign, IL: Research Press.

Guo, Q., & Feng, L. (2017). The associations between perceived parenting styles, empathy, and altruistic choices in economic games: A study of Chinese children. *Frontiers in Psychology, 8,* 1-11.

Gurthrie, I. K., Eisenberg, N., Fabes, R. A., Murphy, B. C., Holmgren, R., Mazsk, P., & Suh,K. (1997). The relations of regulation and emotionality to children's situational empathy-related responding. *Motivation and Emotion, 21,* 87-108.

Graham, F. K. (1992). Attention: The heartbeat, the blink, and the brain. In B.A. Campbell, H. Hayne, & R. Richardson (Eds.), *Attention and Information Processing in Infants and Adults. Perspectives from Human and Animal Research* (pp. 3-29). Hillsdale, NJ: Erlbaum, 1992.

Happé, F., & Frith, U. (1996). Theory of mind and social impairment in children with conduct disorder. *British Journal of Development Psychology, 14,* 385-398.

Hatfield, E., Rapson, R. L., & Le, Y. L. (2009). Emotional contagion and empathy. In: J. Decety & W. Ickes (Eds.), *The social neuroscience of empathy* (pp. 19-30). Cambridge, US: MIT Press.

Hayes, A. F., & Matthes, J. (2009). Computational procedures for probing interactions in OLS and logistic regression: SPSS and SAS implementations. *Behavior Research Methods. 41,* 924-936.

Herpers, P. C. M., Rommelse, N. N. J., Bons, D. M. A., Buitelaar, J. K., & Scheepers, F. E. (2012). Callous-unemotional traits as a cross-disorders construct. *Social Psychiatry and Psychiatric Epidemiology, 47,* 2045-2064.

Hill, E. L., & Frith, U. (2003). Understanding autism: Insights from mind and brain. *Philosophical Transactions of the Royal Society B: Biological Sciences, 358,* 281-289.

Hobson, C. W., Scott, S., & Rubia, K. (2011). Investigation of cool and hot executive function in ODD/CD independently of ADHD. *The Journal of Child Psychology and Psychiatry, 52,* 1035-1043.

Hoffman, M. L. (2000). *Empathy and moral development: Implications for caring and justice*. Cambridge, UK: Cambridge University Press.

Hoffman, M. L. (2008). Empathy and prosocial behavior. In M. Lewis, J.M. Haviland-Jones, & L. F. Barrett (Eds.), *Handbook of Emotions, third edition* (pp. 440-455). New York: The Guilford Press.

Iacoboni, M. (2005). Understanding others: Imitation, language, and empathy. In S. Hurley & N. Chater (Eds.), *Perspectives on imitations: From neuroscience to social science -*

Volume 1: Mechanisms of imitation and imitation in animals (pp. 77-101). Cambridge, US: MIT Press.

Ickes, W., & Hodges, S. D. (2013). Empathic accuracy in close relationships. In J. Simpson & L. Campbell (Eds.), *The Oxford Handbook of Close Relationships* pp. 348-373). New York, NY: Oxford University Press.

Jahja, R., Huijbregts, S. C. J, De Sonneville, L. M. J, Van der Meere, J. J., & Van Spronsen, F. J. (2014). Neurocognitive evidence for revision of treatment targets and guidelines for phenylketonuria. *The Journal of Pediatrics, 164,* 895-899.e2.

Järvinen, A., Ng, R., Crivelli, D., Neumann, D., Grichanik, M., Arnold, A.J., … Bellugi, U. (2015). Patterns of sensitivity to emotion in children with Williams syndrome and autism: Relations between autonomic nervous system reactivity and social functioning. *Journal of Autism and Developmental Disorders, 45,* 2594-2612.

Jolliffe, D., & Farrington, D.P. (2006). Development and validation of the Basic Empathy Scale. *Journal of Adolescence, 29,* 589-611.

Jones, A. P., Happé, F. G. E., Gilbert, F., Burnett, S., & Viding, E. (2010). Feeling, caring, knowing: Different types of empathy deficit in boys with psychopathic tendencies and autism spectrum disorder. *The Journal of Child Psychology and Psychiatry, 51,* 1188-1197.

Jones, A. P., Laurens, K. R., Herba, C. M., Barker, G. J., & Viding, E. (2009). Amygdala hypoactivity to fearful faces in boys with conduct problems and callous-unemotional traits. *American Journal of Psychiatry, 166,* 95-102.

Kaat, A. J., & Lecavalier, L. (2013). Disruptive behavior disorders in children and adolescents with autism spectrum disorders: A review of the prevalence, presentation, and treatment. *Research in Autism Spectrum Disorders, 7,* 1579-1594.

Kahn, R. E., Frick, P. J., Golmaryami, F. N., & Marsee, M. A. (2017). The moderating role of anxiety in the associations of callous-unemotional traits with self-report and laboratory measures of affective and cognitive empathy. *Journal of Abnormal Child Psychology, 45,* 583-596.

Kerig, P. K., & Stellwagen, K. K. (2010). Roles of callous unemotional traits, narcissism, and machiavellianism in childhood aggression. *Journal of Psychopathology and Behavioral Assessment, 32,* 343-352.

Kimonis, E. R., Frick, P. J., Cauffman, E., Goldweber, A., & Skeem, J. (2012). Primary and secondary variants of juvenile psychopathy differ in emotion processing. *Development and Psychopathology, 24,* 1091-1103.

Kochanska, G., & Knaack, A. (2003). Effortful control as a personality characteritic of young children: Antecedents, correlates, and consequences. *Journal of Personality, 6,* 1087-1112.

Kort, W., Schittekatte, M., Dekker, P. H., Verhaege, P., Compaan, E. L., Bosmans, M., & Vermeir, G. (2005). Manual Wechsler Intelligence Scale for Children – Dutch edition (WISC-III-NL) (Third ed.). Amsterdam: Hartcourt Test Publishers/Nederlands Instituut

voor Psychologen.

Lahey, B. B., Loeber, R., Burke, J., Rathouz, P. J., & McBurnett, K. (2002). Waxing and waning in concert: Dynamic comorbidity of conduct disorder with other disruptive and emotional problems over 17 years among clinic-referred boys. *Journal of Abnormal Child Psychology, 111,* 556-567.

Lamm, C., & Majdandžić, J. (2015). The role of shared neural activations, mirror neurons, and morality in empathy – A critical comment. *Neuroscience Research, 90,* 15-24.

Lane, R. D., McRae, K., Reiman, E. M., Chen, K., Ahern, G. L., & Thayer, J. F. (2009). Neural correlates of heart rate variability during emotion. *Neuroimage, 44,* 213-222.

Lanzetta, J. T., & Englis, B. G. (1989). Expectations of cooperation and competition and their effects on observers' vicarious emotional responses. *Journal of Personality and Social Psychology, 56,* 543-554.

Legerstee, J. S., Garnefski, N., Jellesma, F. C., Verhulst, F. C., & Utens, E. M. W. J. (2010) Cognitive coping and childhood anxiety disorders. *European Child and Adolescent Psychiatry, 19,* 143-150.

Liew, J., Eisenberg, N., Spinrad, T. L., Eggum, N. D., Haugen, R. G., Kupfer, ... Baham, M. E. (2011). Physiological regulation and fearfulness as predictors of young children's empathy-related reactions. *Social Development, 20,* 111-134.

Lockwood, P. L., Seara-Cardoso, A., & Viding, E. (2014). Emotion regulation moderates the association between empathy and prosocial behavior. *PLOS one, 9,* 1-6.

Lockwood, P. L., Sebastian, C. L., McCrory, E. J., Hyde, Z. H., Gu, X., De Brito, S. A., & Viding, E. (2013). Association of callous traits with reduced neural response to others' pain in children with conduct problems. *Current Biology, 23,* 901-905.

Loeber, R., Burke, J. D., Lahey, B. B., Winters, A., & Zera, M. (2000). Oppositional Defiant and Conduct Disorder: A review of the past 10 years, Part I. *American Academy of Child and Adolescent Psychiatry, 39,* 1468-1484.

Lombardo, M. V., Barnes, J. L., Wheelwright, S. J., & Baron-Cohen, S. (2007). Self-referential cognition and empathy in autism. *PLOS ONE, 2*(9), 1-11.

Loney, B. R., Frick, P. J., Ellis, M., & McCoy, M. G. (1998). Intelligence, callous-unemotional traits, and antisocial behavior. *Journal of Psychopathology and Behavioral Assessment, 20,* 231-247.

Lovett, B. J., & Sheffield, R. A. (2007). Affective empathy deficits in aggressive children and adolescents: A critical review. *Clinical Psychology Review, 27,* 1-13.

Lynam, D. R., Caspi, A., Moffitt, T. E., Loeber, R., & Stouthamer-Loeber, M. (2007). Longitudinal evidence that psychopathy scores in early adolescence predict adult psychopathy. *Journal of Abnormal Child Psychology, 116,* 155-165.

Lynam, D. R., & Gudonis, L. (2005). The development of psychopathy. *Annual Review of Clinical Psychology, 1,* 381-407.

Marsh, P., Beauchaine, T. P., & Williams, B. (2008a). Dissociation of sad facial expressions and autonomic nervous system responding in boys with disruptive behavior disorders.

Psychophysiology, 45, 100-110.

Marsh, A. A., Finger, E. C., Fowler, K. A., Adalio, C. J., Jurkowitz, I. T. N., Schechter, J. C., … Blair, R. J. R. (2013). Empathic responsiveness in amygdala and anterior cingulate cortex in youths with psychopathic traits. *The Journal of Child Psychology and Psychiatry, 54,* 900-910.

Marsh, A. A., Finger, E. C., Mitchell, D. G. V., Reid, M. E., Sims, C., Kosson, D. S., … Blair, R. J. R. (2008b). Reduced amygdala response to fearful expressions in children and adolescents with callous-unemotional traits and disruptive behavior disorders. *American Journal of Psychiatry, 165,* 712-720.

Marsh, A. A., Finger, E. C., Schechter, J. C., Jurkowitz, I. T. N., Reid, M. E., & Blair, R. J. R. (2011). Adolescents with psychopathic traits report reductions in physiological responses to fear. *The Journal of Child Psychology and Psychiatry, 52,* 834-841.

Martin-Key, N., Brown, T., & Fairchild, G. (2017). Empathic accuracy in male adolescents with conduct disorder and higher versus lower levels of callous-unemotional traits. *Journal of Abnormal Child Psychology, 45,* 1385-1397.

Marton, I., Wiener, J., Rogers, M., Moore, C., & Tannock, R. (2009). Empathy and social perspective taking in children with Attention-Deficit/Hyperactivity Disorder. *Journal of Abnormal Child Psychology, 37,* 107- 118.

Masi, G., Muratori, P., Manfredi, A., Pisano, S., & Milone, A. (2015). Child behavior checklist emotional dysregulation profiles in youth with disruptive behaviour disorders: Clinical correlates and treatment implications. *Psychiatry Research, 225,* 191-196.

Matthys, W., Vanderschuren, L. J. M. J., Schutter, D. J. L. G., & Lochman, J. E. (2012). Impaired neurocognitive functions affect social learning processes in oppositional defiant disorder and conduct disorder: Implications for interventions. *Clinical Child and Family Psychology Review, 15,* 234-246.

Mayes, S. D., Calhoun, S. L., Murray, M. J., Ahuja, M., & Smith, L. A. (2011). Anxiety, depression, and irritability in children with autism relative to other neuropsychiatric disorders and typical development. *Research in Autism Spectrum Disorders, 5,* 474-485.

Mazza, M., Pino, M. C., Mariano, M., Tempesta, D., Ferrara, M., De Berardis, D., … Valenti, M. (2014). Affective and cognitive empathy in adolescents with autism spectrum disorder. *Frontiers in Human Neuroscience, 8,* 1-6.

McPhedran, S. (2009). A review of the evidence for associations between empathy, violence, and animal cruelty. *Aggression and Violent Behaviour, 14,* 1-4.

Miller, P. A., & Eisenberg, N. (1988). The relation of empathy to aggressive and externalizing/antisocial behavior. *Psychological Bulletin, 103,* 324-344.

Molenberghs, P., Cunnington, R., & Mattingley, J. B. (2012). Brain regions with mirror properties: A meta-analysis of 125 human fMRI studies. *Neuroscience and Biobehavioral Reviews, 36,* 341-349.

Mulder, L. J. M., Hofstetter, H., & Van Roon, A. (2007). *CARSPAN for windows: User's manual.*

Groningen: University of Groningen.

Murphy, B. C., Shepard, S. A., Eisenberg, N., Fabes, R. A., & Guthrie, I. K. (1999). Contemporeneous and longitudinal relations of dispositional sympathy to emotionality, regulation, and social functioning. *The Journal of Early Adolescence, 19,* 66-97.

Northover, C., Thapar, A., Langley, K., & Van Goozen, S. (2015). Emotion regulation in adolescent males with attention-deficit hyperactivity disorder: Testing the effects of comorbid conduct disorder. *Brain Sciences, 5,* 369-386.

Olsson, A., & Phelps, E. A. (2007). Social learning of fear. *Nature Neuroscience, 10,* 1095-1102.

Orobio de Castro, B., Veerman, J. W., Koops, W., Bosch, J. D., & Monshouwer, H. J. (2002). Hostile attribution of intent and aggressive behavior: A meta-analysis. *Child Development, 73,* 916-934.

Pardini, D. A., Barry, T. D., Barth, J. M., Lochman, J. E., & Wells, K. C. (2006). Self-perceived social acceptance and peer social standing in children with aggressive-disruptive behaviors. *Social Development, 15,* 46-64.

Pardini, D. A., Lochman, J. E., & Frick, P. J. (2003). Callous/unemotional traits and social-cognitive processes in adjudicated youths. *Journal of the American Academy of Child & Adolescent Psychiatry, 42,* 364-371.

Park, G., Van Bavel, J. J., Vasey, M. W., & Thayer, J. F. (2013). Cardiac vagal tone predicts attentional engagement to and disengagement from fearful faces. *Emotion, 4,* 645-656.

Pasalich, D. S., Dadds, M. R., & Hawes, D. J. (2014). Cognitive and affective empathy in children with conduct problems: Additive and interactive effects of callous-unemotional traits and autism spectrum disorders symptoms. *Psychiatry Research, 219,* 625-630.

Piferi, R. L., Kline, K. A., Younger, J., & Lawler, K. A. (2000). An alternative approach for achieving cardiovascular baseline: Viewing an aquatic video. *International Journal of Psychophysiology, 37,* 207-217.

Pijper, J., De Wied, M., Van Goozen, S., & Meeus, W. (2017). Empathy problems in youth with disruptive behavior disorders, with and without callous unemotional traits. In L.C. Centifanti & D.M. Williams (Eds.), *The Wiley Handbook of Developmental Psychopathology* (pp.161-178). United Kingdom, UK: John Wiley and Sons Inc.

Pijper, J., De Wied, M., Van Rijn, S., Van Goozen, S., Swaab, H., & Meeus, W. (2016). Callous unemotional traits, autism spectrum disorder symptoms, and empathy in boys with oppositional defiant disorder or conduct disorder. *Psychiatry Research, 245,* 340-345.

Pijper, J., De Wied, M., Van Rijn, S., Swaab, H., Van Goozen, S., & Meeus, W. (2018). Executive attention and empathy-related responses in boys with oppositional defiant disorder or conduct disorder, with and without comorbid anxiety disorder. *Child Psychiatry and Human Development.* Retrieved from https://doi.org/10.1007/s10578-018-0810-z

Porges, S. W. (2007). The polyvagal perspective, *Biological Psychology, 74,* 116-143.

Pouw, L. B. C., Rieffe, C., Oosterveld, P., Huskens, B., & Stockmann, L. (2013). Reactive/proactive aggression and affective/cognitive empathy in children with ASD. *Research in Developmental Disabilities, 34,* 1256-1266.

Raine, A. (1993). *The psychopathology of crime: criminal behavior as a clinical disorder.* San Diego: Academic Press.

Reynolds, G. D., & Richards, J. E. (2008). Infant heart rate: A developmental psychophysiological perspective. In L.A. Schmidt & S.J. Segalowitz (Eds.),*Developmental Psychophysiology: Theory, Systems, and Applications* (173-212). Cambridge University Press.

Rizzolatti, G. (2005). The mirror neuron system and imitation. In S. Hurley & N. Chater (Eds.), *Perspectives on imitation: From neuroscience to social science – Volume 1: Mechanisms of imitation and imitation in animals* (pp. 55-76). Cambridge, US: MIT Press.

Roeyers, H., Thys, M., Druart, C., De Schryver, M., & Schittekatte, M., 2011. Screeningslijst voor autismespectrumstoornissen: Handleiding. Amsterdam: Hogrefe Uitgevers.

Rogers, K., Dziobek, I., Hassenstab, J., Wolf, O.T., & Convit, A. (2007). Who cares? Revisiting empathy in Asperger syndrome. *Journal of Autism and Developmental Disorders, 37,* 709-715.

Rogers, J., Viding, E., Blair, R.J., Frith, U., & Happé, F. (2006). Autism spectrum disorder and psychopathy: Shared cognitive underpinnings or double hit? *Psychological Medicine, 36,* 1789-1798.

Rompelman, O., Snijders, J. B. I. M., & van Spronsen, C. J., (1982). The measurement of heart rate variability spectra with the help of a personal computer. *IEEE Transactions on Biomedical Engineering, 29*, 503-510.

Rothbart, M. K., Ahadi, S. A., & Hershey, K. L. (1994). Temperament and social behavior in childhood. *Merrill-Palmer Quarterly, 40,* 21-39.

Rothbart, M. K., & Rueda, M. R. (2005). The development of effortful control. In U. Mayr, E. Awh & S. Keele (Eds.), *Developing individuality in the human brain: A tribute to Michael I. Posner* (pp. 167-188). Washington, DC: American Psychological Association.

Sánchez-Pérez, N., Fuentes, L. J., Jolliffe, D., & González-Salinas, C. (2014). Assessing children's empathy through a Spanish adaptation of the Basic Empathy Scale: Parent's and child's report forms. *Frontiers in Psychology, 5,* 1-13.

Sattler, J.M., 1992. *Assessment of children (3rd edition).* San Diego, CA: Jerome M. Sattler, Publisher.

Schwenck, C., Mergenthaler, J., Keller, K., Zech, J., Salehi, S., Taurines, R., … Freitag, C. M. (2012). Empathy in children with autism and conduct disorder: group-specific profiles and developmental aspects. *The Journal of Child Psychology and Psychiatry, 53,* 651-659.

Sebastian, C. L., McCrory, E. J. P., Cecil, C. A. M., Lockwood, P. L., De Brito, S. A., Fontaine, N. M. G., & Viding, E. (2012). Neural responses to affective and cognitive theory of mind

in children with conduct problems and varying levels of callous-unemotional traits. *Archives of General Psychiatry, 69,* 814-822.

Shamay-Tsoory, S. G. (2009). Empathic processing: Its cognitive and affective dimensions and neuroanatomical basis. In: J. Decety & W. Ickes (Eds.), *The social neuroscience of empathy* (pp. 215-232). Cambridge, US: MIT Press.

Shamay-Tsoory, S. G., Harari, H., Aharon-Peretz, J., & Levkovitz, Y. (2010). The role of orbitofrontal cortex in affective theory of mind deficits in criminal offenders with psychopathic tendencies. *Cortex, 46,* 668-677.

Singer, T. (2006). The neuronal basis and ontogeny of empathy and mind reading: Review of literature and implications for future research. *Neuroscience and Biobehavioral Reviews, 30,* 855-863.

Skuse, D. (2003). Fear recognition and the neural basis of social cognition. *Child and Adolescent Mental Health, 8,* 50-60.

Smith, A. (2008). The empathy imbalance hypothesis of autism: A theoretical approach to cognitive and emotional empathy in autistic development. *The Psychological Record 59,* 273-294.

Spaniol, M. M., Shalev, L., Kossyvaki, L., & Mevorach, C. (2018). Attention training in autism as a potential approach to improving academic performance: A school-based pilot study. *Journal of Autism and Developmental Disorders, 48,* 592-610.

Sparrow, S., Balla, D., & Cicchetti, D. (1984). *Vineland Adaptive Behavior Scales: Survey Form Manual.* Circle Pines, MN: American Guidance Service.

Spinrad, T. L., & Stifter, C. A. (2006). Toddlers' empathy-related responding to distress: Predictions from negative emotionality and maternal behavior in infancy. *Infancy, 10,* 97-121.

Sterzer, P., Stadler, C., Poustka, F., & Kleinschmidt, A. (2007). A structural neural deficit in adolescents with conduct disorder and its association with lack of empathy. *NeuroImage, 37,* 335-342.

Taylor, Z. E., Eisenberg, N., & Spinrad, T. L. (2015). Respiratory Sinus Arrhythmia, effortful control, and parenting as predictors of children's sympathy across early childhood. *Developmental Psychology, 51,* 17-25.

Ter-Stepanian, M., Grizenko, N., Cornish, K., Talwar, V., Mbekou, V., Schmitz, N., & Joober, R. (2016). Attention and executive function in children diagnosed with attention deficit hyperactivity disorder and comorbid disorders. *Journal of the Canadian Academy of Child and Adolescent Psychiatry, 26*, 21-30.

Thayer, J. F., Åhs, F., Fredrikson, M., Sollers, J. J., & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience and Biobehavioral Reviews, 36,* 747-756.

Thayer, J. F., Hansen, A. L., Saus-Rose, E., & Johnsen, B. H. (2009). Heart rate variability, prefrontal cortex function, and cognitive performance: The neurovisceral integration

perspective on self-regulation, adaption, and health. *Annals of Behavioral Medicine, 37,* 141-153.

Thayer, J. F., & Lane, R. D. (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders, 61,* 201-216.

Tremblay, R. E., Mâsse, B., Perron, D., LeBlanc, M., Schwartzman, A. E., & Ledingham, J. E. (1992). Early disruptive behavior, poor school achievement, delinquent behavior, and delinquent personality: Longitudinal analyses. *Journal of Consulting and ClinicalPsychology, 60,* 64-72.

Vachon, D. D., Lynam, D. R., & Johnson, J. A. (2014). The (non)relation between empathy and aggression: surprising results from a meta-analysis. *Psychological Bulletin, 140,* 751-773.

Van der Graaff, J., Branje, S., De Wied, M., Hawk, S., Van Lier, P., & Meeus, W. (2014). Perspective Taking and Empathic Concern in Adolescence: Gender Differences in Developmental Changes. *Developmental Psychology*, *50*, 881-888.

Van Goozen, S. H. M. (2015). The role of early emotion impairments in the development of persistent antisocial behavior. *Child Development Perspectives, 9,* 206-210.

Van Goozen, S. H. M., Matthys, W., Cohen-Kettenis, P. T., Buitelaar, J. K., & Van Engeland, H. (2000). Hypothalamic-pituitary-adrenal axis and autonomic nervous system activity in disruptive children and matched controls. *Journal of the American Academy of Child and Adolescent Psychiatry, 39,* 1438–1445.

Van Hulle, C., Zahn-Waxler, C., Robinson, J. L., Rhee, S. H., Hastings, P. D., & Knafo, A. (2013). Autonomic correlates of children's concern and disregard for others. *Social Neuroscience, 8,* 275-290.

Van Rijn, S., & Swaab, H. (2015). Executive dysfunction and the relation with behavioral problems in children with 47,XXY and 47,XXX. *Genes, Brain and Behavior, 14,* 200-208.

Verhulst, F. C., & Van der Ende, J. (2013). *Handleiding ASEBA-Vragenlijsten voor leeftijden 6 t/m 18 jaar: CBCL/6-18, YSR en TRF.* Rotterdam: ASEBA Nederland.

Viding, E., Fontaine, N. M. G., & McCrory, E. J. (2012). Antisocial behaviour in children with and without callous-unemotional triats. *Journal of the Royal Society of Medicine,105,* 195-200.

Viding, E., & McCrory, E. J. (2012). Genetic and neurocognitive contributions to the development of psychopathy. *Development and Psychopathology, 24,* 969-983.

Viding, E., Sebastian, C. L., Dadds, M. R., Lockwood, P. L., Cecil, C. A. M., De Brito, S. A., & McCrory, E. J. (2012). Amygdala response to preattentive masked fear in children with conduct problems: The role of callous-unemotional traits. *American Journal of Psychiatry, 169,* 1109-1116.

Völlm, B. A., Taylor, A. N. W., Richardson, P., Corcoran, R., Stirling, J., McKie, S., … Elliott, R. (2006). Neuronal correlates of theory of mind and empathy: A functional magnetic resonance imaging study in a nonverbal task. *NeuroImage, 29,* 90-98.

Waller, R., Gardner, F., & Hyde, L. W. (2013). What are the associations between parenting, callous-unemotional traits, and antisocial behavior in youth? A systematic review of evidence. *Clinical Psychology Review, 33,* 593-608.

Walter, H. (2012). Social cognitive neuroscience of empathy: concepts, circuits, and genes. *Emotion Review, 4,* 9-17.

Wechsler, D. (1991). *Wechsler Intelligence Scale for Children – Third Edition.* Sant Antonio, TX: The Psychological Corporation.

White, S. F., Williams, W. C., Brislin, S. J., Sinclair, S., Blair, K. S., Fowler, K. A., … Blair, R. J. (2012). Reduced activity within the dorsal endogenous orienting of attention network to fearful expressions in youth with disruptive behavior disorders and psychopathic traits. *Development and Psychopathology, 24,* 1105-1116.

Williams, S. E., Veldhuijzen van Zanten, J. J. C. S., Trotmanm G. P., Quinton, M. L., & Ginty, A. T. (2017). Challenge and threat imagery manipulates heart rate and anxiety responses to stress. *International Journal of Psychophysiology, 117,* 111-118.

Zahn-Waxler, C., Cole, P. M., Welsh, J. D., & Fox (1995). Psychophysiological correlates of empathy and prosocial behavior in preschool children with behavior problems. *Development and Psychopathology, 7,* 27-48.

Zhou, Q., Valiente, C., & Eisenberg, N. (2003). Empathy and its measurement. In: S. J. Lopez & C. R. Snyder (Eds.), *Positive psychological assessment: A handbook of models and measures* (pp. 269-284). Washington, DC: American Psychological Association.

Samenvatting (Summary in Dutch)

Empathie is het mee voelen met en begrijpen van andermans emoties (Eisenberg & Strayer, 1987). Het is een belangrijke sociale vaardigheid dat zou bijdragen aan meer prosociaal gedrag (Hoffman, 2008) en minder ongewenst gedrag, zoals agressie (Austin, Bondü, & Elsner, 2017). Empathie problemen worden vaak in verband gebracht met kinderen en adolescenten met een oppositioneel opstandige stoornis (ODD) en normoverschrijdend gedragsstoornis (CD; APA, 2013). Dit promotieonderzoek was erop gericht om meer inzicht te krijgen in de aard van het empathiegebrek van jongens met ODD/CD en welke mechanismen hier mogelijk een rol bij spelen. Kinderen en adolescenten met ODD/CD zijn heel verschillend en er wordt daarom ook wel gedacht dat er individuele verschillen zijn in de mechanismen die ten grondslag liggen aan hun empathie problemen (De Wied, Gispen-De Wied, & Van Boxtel, 2010; Pijper, De Wied, Van Goozen, & Meeus, 2017).

Empathie is een multidimensioneel construct. Het omvat de neiging die je hebt om met empathie te reageren in verschillende situaties (trait empathie), psychologische toestanden tijdens empathie-inducerende situaties (state empathie), maar ook affectieve en cognitieve componenten (Davis, 1996). *Affectieve empathie* is het psychologische proces dat ervoor zorgt dat je meer mee voelt met andermans emoties dan met je eigen emoties (Hoffman, 2000). Er wordt vaak een onderscheid gemaakt tussen *empathie, sympathie* en *personal distress* (Eisenberg & Eggum, 2009). Empathie is een aansluiting van gevoelens tussen jezelf en die van de geobserveerde ander; je voelt *mee* met andermans emoties. Sympathie is een emotionele reactie gericht op de ander dat bestaat uit gevoelens van bezorgdheid en verdriet voor de ander; je voelt *voor* andermans emoties. Personal distress is een emotionele reactie gericht op jezelf dat bestaat uit gevoelens van angst en ongemakkelijkheid; je voelt *door* andermans emoties (Batson, 2009). *Cognitieve empathie* is het vermogen andermans emoties te begrijpen (Walter, 2012). Theory of Mind (ToM) kan gezien worden als een aspect van cognitieve empathie.

Er wordt verondersteld dat kinderen met ODD/CD én callous unemotional (CU) traits – gekenmerkt door een gebrek aan empathie, een gebrek aan schuldgevoelens en vlakke emoties (Frick & Hare, 2000) – selectief beperkt zijn in affectieve empathie voor negatieve emoties (zoals angst en verdriet). Dit wordt in verband gebracht met onderliggende deficiënties in de amygdala (Blair, 2013; Blair, Leibenluft, & Pine, 2014), wat kan leiden tot verminderde gevoeligheid (Blair, 2013) en/of aandacht (White et al., 2011) voor andermans negatieve emoties. Hoewel er toenemend bewijs is voor stoornissen in affectieve empathie bij CU traits (Blair, 2008, 2013; Blair et al., 2014), zijn er weinig onderzoeken gedaan met klinische steekproeven van kinderen en/of adolescenten met ODD/CD. Daarnaast zijn de empathie problemen van degene met en zonder CU traits weinig met elkaar vergeleken. Het is daarom nog onduidelijk of een gebrek aan empathie verschillend is voor degene met en zonder CU traits. In **Hoofdstuk II** is hier nader onderzoek naar gedaan.

Een gebrek aan empathie is niet alleen kenmerkend voor CU traits, het is ook kenmerkend voor autismespectrumstoornissen (ASS; Baron-Cohen et al., 1985). Daarnaast worden beiden in verband gebracht met destructief gedrag (Frick, Ray, Thornton, & Kahn,

2013, Kaat & Lecavalier, 2013); op gedragsniveau kunnen de stoornissen elkaar dus overlappen. Er zijn conceptuele en empirische redenen om aan te nemen dat er een onderscheid kan worden gemaakt tussen de 'empathie stoornissen' op basis van de aard van het empathiegebrek. De sociale tekorten die kenmerkend zijn voor ASS worden vaak verklaard vanuit problemen in ToM (Baron-Cohen, Leslie, & Frith, 1985). Omdat ToM nauw verwant is aan cognitieve empathie (Baron-Cohen & Wheelwright, 2004), relateren onderzoekers ASS aan beperkingen in cognitieve empathie en niet affectieve empathie. Gezien de overlap tussen CU traits en ASS kenmerken op gedragsniveau, lijkt het belangrijk om met beiden rekening te houden wanneer empathie problemen worden onderzocht. Dit is echter nog maar weinig gedaan waardoor er beperkt bewijs is voor de veronderstelling dat de aard van het empathiegebrek verschillend is voor CU traits en ASS kenmerken. In **Hoofdstuk III** is hier daarom nader onderzoek naar gedaan.

Empathie problemen bij de kinderen met ODD/CD zónder CU traits worden in verband gebracht met andere factoren zoals negatieve attributiestijlen, angst en/of zwakke emotieregulatie (de Wied et al., 2010). Zwakke emotieregulatie komt vaak voor bij kinderen met ODD/CD (Masi, Muratori, Manfredi, Pisano, & Milone, 2015; Northover, Thapar, Langley, & van Goozen, 2015) en er is bewijs dat mensen met een zwakke emotieregulatie moeite hebben gevoelens van empathie onder controle te houden. Ze lopen daardoor het risico overspoeld te raken door andermans emoties en hun aandacht te richten op zichzelf (personal distress) in plaats van op de ander (Eisenberg et al., 1994). Verhoogde gevoeligheid voor negatieve emoties én slechte emotieregulatie, kan kinderen met ODD/CD extra gevoelig maken voor personal distress in plaats van empathie of sympathie voor de ander. Er is echter tot nu toe geen bewijs voor deze hypothese. Daarom is deze hypothese onderzocht in **Hoofdstuk IV** en **V** waarbij emotieregulatie respectievelijk op cognitief (executieve aandacht) en fysiologisch (respiratory sinus arrhythmia (RSA)) niveau is gemeten.

Het review beschreven in **hoofdstuk II** onderzocht de aard van het empathiegebrek bij kinderen en adolescenten met ODD/CD en of een gebrek aan empathie bijdraagt aan een differentiatie tussen degene met en zonder CU traits. Uit de resultaten van relatief weinig onderzoeken bleek consistent bewijs voor een gebrek aan affectieve empathie bij kinderen en adolescenten met ODD/CD. Voor cognitieve empathie waren de resultaten minder consistent. Significante verschillen tussen ODD/CD-subtypes zijn gerapporteerd op autonome maten van affectieve state empathie. Kinderen en adolescenten met ODD/CD en CU traits lieten minder hartslag verlaging zien vanaf baseline (wat kan duiden op minder empathie) dan degene zonder CU traits in reactie op verdrietige en angstige stimuli. Er zijn geen verschillen gerapporteerd tussen ODD/CD-subtypen op zelfrapportage maten (trait empathie) en gezichtsmaten van affectieve state empathie. Het lijkt er dus op dat beperkingen in affectieve empathie algemeen zijn voor kinderen en adolescenten met ODD/CD en dat degene met en zonder CU traits verschillende autonome patronen laten zien in reactie op andermans negatieve emoties.

Het empirische onderzoek beschreven in **hoofdstuk III** onderzocht de onafhankelijke en interactieve bijdrage van CU traits en ASS kenmerken in relatie tot affectieve en cognitieve empathie bij jongens met ODD/CD. Meer CU traits waren gerelateerd aan minder empathie voor verdriet en meer ASS kenmerken waren gerelateerd aan minder cognitieve empathie. Interessant was dat ASS kenmerken van invloed waren op de relatie tussen CU traits en empathie voor verdriet; meer CU traits waren gerelateerd aan minder empathie voor verdriet bij weinig ASS kenmerken. De resultaten geven bewijs voor de veronderstelling dat het empathiegebrek verschillend is voor CU traits en ASS. De resultaten geven ook aan dat een gebrek aan empathie voor verdriet meer kenmerkend lijkt voor CU traits dan ASS bij jongens met ODD/CD.

Het empirische onderzoek beschreven in **hoofdstuk IV** onderzocht de relatie tussen emotieregulatie en empathie bij jongens met ODD/CD, met en zonder comorbide angst. We onderzochten relaties tussen executieve aandacht (een cognitieve maat van emotieregulatie) en zelfrapportages van empathie en sympathie in reactie op verdrietige film clips. De resultaten toonden aan dat executieve aandacht significant gerelateerd was aan empathie en sympathie; degenen met zwakkere executieve aandacht rapporteerden minder empathie en sympathie. Deze relatie was alleen zichtbaar onder conditie van een intens verdrietige film clip (een beertje verliest zijn moeder) en alleen bij jongens met ODD/CD en angst. De resultaten zijn in overeenstemming met het idee dat emotieregulatie met name betrokken is bij het reguleren van empathie bij hoog gevoelige mensen (Eisenberg et al., 1994, 1996, 1998) en wanneer de empathie reactie sterk is (Eisenberg, 2010).

Het empirische onderzoek beschreven in **hoofdstuk V** onderzocht ook de relatie tussen emotieregulatie en empathie bij jongens met ODD/CD, met en zonder angst. Dit keer onderzochten we de relatie op fysiologisch niveau door te kijken naar de relatie tussen RSA in rust (een fysiologische index van emotieregulatie) en hartslag (een fysiologische index van empathie) in reactie op verdrietige film clips. In overeenstemming met verwachtingen werd een significant negatieve relatie gevonden tussen RSA en hartslag; een hogere RSA (efficiëntere regulatie) was gerelateerd aan een sterkere hartslag verlaging (indicatie voor meer empathie). Anders dan verwacht, was de relatie alleen zichtbaar onder condities van relatief milde verdrietige film clips en alleen bij ODD/CD-jongens zonder angst. Onder condities van de intens verdrietige stimulus, bleek er een significant positieve relatie te bestaan tussen RSA en hartslag reacties: hogere RSA was gerelateerd aan minder hartslag verlaging. De resultaten lijken in overeenstemming te zijn met het idee dat efficiënte fysiologische regulatie beperkt is tot situaties die als niet stressvol worden ervaren terwijl dit mogelijk onder druk komt te staan in situaties die als stressvol worden ervaren (Porges, 2007).

Al met al wijzen de resultaten van deze dissertatie erop 1) dat kinderen en adolescenten met ODD/CD meer consistent problemen laten zien in affectieve empathie dan in cognitieve empathie, 2) dat er verschillen zijn in empathie problemen tussen ODD/CD-subtypes; 3) degene met en zonder CU traits laten verschillende autonome patronen zien in

reactie op andermans verdriet, 4) degene met meer CU traits rapporteren minder empathie voor verdriet terwijl degene met meer ASS kenmerken minder cognitieve empathie rapporteren, en als laatste 5) dat aspecten van emotieregulatie een rol lijken te spelen bij empathie problemen van kinderen met ODD/CD. Toekomstig onderzoek zou zich moeten richten op de ontwikkeling van diagnostische instrumenten voor affectieve empathie en zou verder de rol van emotieregulatie moeten uitdiepen en op welke manier dit van invloed is op het sociaal functioneren van kinderen en adolescenten met ODD/CD.

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About the Author

Curriculum Vitae

Jarla Pijper werd geboren op 3 februari 1987 in Schiedam. Na het behalen van haar VWO diploma op het Groen van Prinsterer Lyceum in Vlaardingen is ze in 2006 gestart met de bachelor Pedagogische Wetenschappen aan de Universiteit Leiden waar ze aansluitend de reguliere Master Education and Child Studies heeft gedaan. In deze periode heeft ze een klinische stage doorlopen bij Rijndam Revalidatie centrum en is ze altijd werkzaam geweest als begeleider van kinderen en volwassenen met een (licht) verstandelijke beperking bij ASVZ. Tevens heeft ze in deze periode besloten meer verdieping te zoeken door de Research Master 'Developmental Psychopathology in Education and Child Studies' (track: Clinical Practice and Research) te volgen. Gedurende deze opleiding heeft ze een klinische stage doorlopen op het Ambulatorium van de Universiteit Leiden waar ze haar Basis Aantekening Diagnostiek behaalde. Na het succesvol afronden van de opleiding in 2012 is ze werkzaam geweest als junior docent bij de Universiteit Leiden (afdeling Orthopedagogiek) waar ze onderwijs verzorgde binnen het bachelor- en masteronderwijs (o.a. thesis begeleiding, werkgroep docent klinische en statistische vakken). Tegelijkertijd was ze werkzaam als junior onderzoeker op de Universiteit Utrecht (afdeling Jeugd en Gezin) op het onderzoeksproject waar ze later in 2013 begon als promovendus, onder begeleiding van prof. dr. Wim Meeus, prof. dr. Stephanie van Goozen en dr. Minet de Wied. Het doel van het onderzoek was om meer inzicht te krijgen in de aard van het empathiegebrek bij kinderen en adolescenten met gedragsstoornissen en welke factoren hierbij mogelijk een rol spelen. De resultaten van dat onderzoek staan beschreven in dit proefschrift. Tijdens haar promotietraject heeft ze regelmatig gesproken op zowel nationale als internationale congressen en verzorgde ze (klinisch) onderwijs. Na de afronding van haar proefschrift is ze gestart als basis orthopedagoog bij MEE Rotterdam Rijnmond waar ze actief is binnen de wijkteams van Barendrecht en Stedelijke zorg van Rotterdam. Jarla is zowel NVO als SKJ geregistreerd.

List of Publications

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