STOP HURTING
START HELPING

Empathy in children with disruptive behavior,
attention-deficit and autism spectrum disorders

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Title: Stop Hurting Start Helping
Subtitle: Empathy in children with disruptive behavior, attention-deficit and autism spectrum disorders.
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ISBN: 978-94-91082-06-1
Cover design and book layout: Ruth Visser, VisserVisuals, Amsterdam, the Netherlands
Printed by: Ridderprint Drukkerij BV, Ridderkerk, the Netherlands

The studies described in this thesis were performed at the Rudolf Magnus Brain Center, Department of Psychiatry, University Medical Center Utrecht, The Netherlands.

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Empathie bij kinderen met disurptieve gedragsstoornissen,
ADHD en autisme spectrum stoornissen
(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht
op gezag van de rector magnificus prof. dr. G.J. van der Zwaan,
ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen
op dinsdag 3 juni 2014 des ochtends te 10.30 uur

door

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geboren op 1 juli 1976 te Hasselt, België

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It takes a village to raise a child

Contents

Chapter 1

Introduction

Introduction

To date, various psychiatric disorders such as disruptive behavior, attention-deficit and autism spectrum disorders have been associated with deficits in empathy in school-aged children and adolescents (Bons et al., 2012). As will be explained in more detail later, there are reasons to assume that empathy enhances prosocial behavior such as helping, sharing, and comforting. Empathy is also thought to contribute to the inhibition of antisocial and aggressive behavior (Eisenberg, Eggum, & Di Giunta, 2010). In this thesis, a series of studies will be described on empathy in six and seven year old children with these disorders. A better understanding of the nature of empathy deficits in children with psychiatric disorders ultimately may help in better differentiating between children with these disorders and may serve as a guidance for developing novel treatment approaches.

Empathy

Empathy is the ability to understand and share emotions of other people with whom we interact (Cohen & Strayer, 1996; Feshbach, 1997). Empathy is assumed to be initiated by the observation of another's emotional state (Hofelich & Preston, 2012). This observation is followed by a cascade of phenomena (Bons et al., 2012; Hofelich & Preston, 2012) that have been studied on the emotional (e.g., experiencing another's emotional state), cognitive (e.g., understanding another's emotional state), behavioral (e.g., targeted helping) and physiological level (e.g., facial mimicry) (Dadds et al., 2007; de Waal, 2008; Eisenberg et al., 2010). Empathy is distinguished from other emotional responses such as sympathy or personal distress (Cohen & Strayer, 1996; Eisenberg et al., 2010; Feshbach, 1997). Personal distress is defined as an aversive affective reaction such as discomfort or anxiety in response to another's distress. It is primarily self-focused (Eisenberg et al., 2010; Hofelich & Preston, 2012) and it makes the affected party selfishly seek to alleviate its own distress (de Waal, 2008). Sympathy, on the other hand, is defined as an affective response that consists of feelings of sorrow or concern for a distressed or needy other (rather than sharing the emotion of the other). It is believed to involve an other- oriented, altruistic motivation (de Waal, 2008; Eisenberg et al., 2010). Thus, a child that observes another child's sadness might experience empathic sadness or personal distress, recognize and understand why the other child is sad, feel sympathetic concern for the other child and finally engage in helping or comforting behavior (Eisenberg et al., 2010).

Empathy and behavior

Empathy-related responding is associated with prosocial behavior such as helping, sharing, and comforting another individual (see for reviews Eisenberg et al., 2010; Eisenberg &

Miller, 1987) and contributes to the inhibition of antisocial and aggressive behavior (Miller & Eisenberg, 1988). Empathy is believed to influence whether or not children help or hurt (Eisenberg et al., 2010).

The proposed mechanisms underlying this association have focused on the central role of the behavioral expression of sadness and distress. Based on the inhibition of aggressive behavior in animals upon distress signals of a conspecific, a mechanism has been described labeled as the violence inhibition mechanism (Blair, 1995; Blair, Jones, Clark, & Smith, 1997). Likewise, children witnessing sadness or distress in another person as a consequence of their own behavior have been proposed to become distressed themselves and stop harming the other in order to reduce their personal distress (Pouw, Rieffe, Oosterveld, Huskens, & Stockmann, 2013). On the other hand, witnessing distress in mammals like apes and rats evokes sharing, helping and comforting behaviors (de Waal, 2008). Similarly, empathy has been found to lead to prosocial behaviors in humans (Eisenberg et al., 2010).

Research methods applied to study empathy

A distinction has been proposed between dispositional (i.e., trait) and situational (i.e., state) empathy. In order to study empathic traits in children, self- and other report questionnaires on feelings, thoughts, and behavior have been applied (Bryant, 1982). Furthermore, to study situational empathy-related responding, experimental paradigms have been designed to evaluate the understanding of another's emotional state (i.e. cognitive empathy), elicit emotional responses (i.e. affective empathy) and empathy induced behavior (e.g. targeted helping) (Eisenberg & Miller, 1987; Lovett & Sheffield, 2007). In these paradigms children typically are exposed to either someone expressing distress (e.g., Fabes, Eisenberg, Karbon, Troyer, & Switzer, 1994; Knafo, Zahn-Waxler, Van Hulle, Robinson, & Rhee, 2008; Zahn-Waxler & Radke-Yarrow, 1992) or a film/video/picture showing emotion inducing events or emotional expressions of others (e.g., Eisenberg, Fabes, Miller, Shell, & Shea, 1990; Holmgren, Eisenberg, & Robin, 1998). In response to these stimuli, empathic emotions are reported by the children themselves (e.g. de Wied, Goudena, & Matthys, 2005) or children's behavioral responses are observed. In addition, physiological responses including hearth rate (de Wied, van Boxtel, Posthumus, Goudena, & Matthys, 2009; de Wied, van Boxtel, & Matthys 2012; de Wied, van Boxtel, Zaalberg, Goudena, & Matthys, 2006) skin conductance (Levenson, Ekman, & Friesen, 1990) or facial electromyographic responses (de Wied et al., 2006; 2009; 2012) in response to emotion evoking stimuli have been recorded.

In the study of empathy, special attention has been paid to the role of emotional facial expressions. As Darwin already pointed out in his book on the expression of emotion in man and animals, facial expressions play an important role in emotion processing and social interaction (Darwin, 1998).

Facial expressions seem to induce facial mimicry, concordant changes in the autonomic nervous system and affect matches. Taken together, the results in empathic behavior and deficits in any of these components could yield in impaired empathy in children with psychiatric disorders (Bons et al., 2012). Hence, it has been argued that the study of facial mimicry is an important method to assess a component of empathy during childhood and that empathy deficits and the lack of emotional reciprocity in children with psychiatric disorders might be a consequence of impaired processing and mimicry of emotional expressions (e.g. Beall, Moody, McIntosh, Hepburn, & Reed, 2008; de Wied, Gispen-de Wied, & van Boxtel, 2010).

Empathy in disruptive behavior disorders

Deficits in empathy have been reported in children and adolescents with a disruptive behavior disorder (DBD) who exhibit oppositional, defiant and aggressive behavior. DBD includes oppositional defiant disorder (ODD), which is characterized by a recurrent pattern of negativistic, defiant, disobedient, and hostile behavior toward authority figures. ODD can be a precursor to conduct disorder (CD), characterized by a persistent pattern of violation of basic rights of others and disregard or major age-appropriate societal rules (American Psychiatric Association, 1994).

Indeed, lower scores on self-reported empathic traits are found in adolescents (Cohen & Strayer, 1996) and school-aged children with DBD (Anastassiou-Hadjicharalambous & Warden, 2008; de Wied et al., 2005). Similarly, most studies assessing empathy in DBD in experimental paradigms have agreed on a central role for affective empathy deficits in DBD (Anastassiou-Hadjicharalambous & Warden, 2008; Cohen & Strayer, 1996; de Wied et al., 2005; 2012; Schwenck et al., 2012). Cognitive empathy, however, in these experimental studies, was generally found to be intact in DBD (Schwenck et al., 2012; Woodworth & Waschbusch, 2008). In sum, it seems that reduced sharing of feelings of others is associated with disruptive and aggressive behavior in children and adolescents.

Furthermore, the hypothesis that DBD children show reduced responding to emotions of others compared to healthy developing children was confirmed by studies assessing autonomic responses (Anastassiou-Hadjicharalambous & Warden, 2007; de Wied et al., 2009; 2012) and facial mimicry (de Wied et al., 2006; 2009; 2012) in response to emotional stimuli. Both are thought to be associated with affective empathy and were decreased in school aged boys and adolescents with DBD. In addition, neuroimaging studies have found preliminary evidence that areas that play a role in affective responding are reduced in volume (anterior insula and amygdala) in DBD (Sterzer, Stadler, Poustka, & Kleinschmidt, 2007). Similarly, it seems that there is reduced activation in response to emotional stimuli in the anterior cingulate cortex (Sterzer, Stadler, Krebs, Kleinschmidt, & Poustka, 2005) and the amygdala (Jones, Laurens, Herba, Barker, & Viding, 2009; Marsh et al., 2008; Sterzer et al., 2005) in adolescents with DBD.

Empathy in attention-deficit and hyperactivity disorders

High co-morbidity of attention-deficit/hyperactivity disorder (ADHD) and DBD (Angold, Costello, & Erkanli, 1999) and high co-occurrence of ADHD symptoms exists in children with DBD and of DBD symptoms in children with ADHD (Martel, Gremillion, Roberts, Eye, & Nigg, 2010). In children with ADHD, problems in social functioning and rejection by peers have been associated with the core pattern of inattention and/or hyperactivity-impulsivity (American Psychiatric Association, 1994). Furthermore, reduced empathy has also repeatedly been found in children and adolescents with ADHD. First, parents have reported reduced empathic traits in children with ADHD (Marton, Wiener, Rogers, Moore, & Tannock, 2009). Next, reduced affective empathy was found in ADHD compared to healthy controls in a study that asked ADHD children how emotionally affected they felt by watching video vignettes with emotional content (Braaten & Rosen, 2000). Furthermore, cognitive empathy scored either as emotion recognition (Pelc, Kornreich, Foisy, & Dan, 2006; Sinzig, Morsch, & Lehmkuhl, 2008; Williams et al., 2008) or as the understanding and interpretation of emotional situations (Dyck, Ferguson, & Shochet, 2001; Marton et al., 2009) was less in ADHD as compared to healthy children. In sum, both affective and cognitive empathy seems to be affected in children with ADHD. Possibly, deficits in attending to relevant emotional stimuli in children with ADHD might influence their empathic ability.

Empathy in autism spectrum disorders

Deficits in empathy have also been considered in autism spectrum disorder (ASD) (Bons et al., 2012). Impairment of social responsiveness is one of the core components of autism spectrum disorders (ASD), which can further be characterized by deficits in communication and stereotyped, repetitive behaviors (American Psychiatric Association, 1994). In recent years, growing consensus has been achieved regarding an imbalance between cognitive and affective empathy in ASD (Schwenck et al., 2012).

First, using self- and other-report questionnaires, impairments in cognitive empathy have consistently been found (Dziobek et al., 2007; Greimel et al., 2011; Pouw, Rieffe, Oosterveld, Huskens, & Stockmann, 2013; Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007; Silani et al., 2008), whereas most studies found no differences in affective empathy between ASD and a healthy control group (Dziobek et al., 2007; Pouw et al., 2013; Rogers et al., 2007; Silani et al., 2008).

Second, experimental paradigms in numerous studies on cognitive empathy in adolescents and adults with ASD have shown impairments in emotion recognition as a component of cognitive empathy using a variety of pictures and short film clips of emotional facial expressions (see for a review, Bons et al. 2012). On the other hand, studies of affective empathy that have applied emotionally loaded scenarios to induce an affect match found that ASD children (mean age ±13 years) (Jones, Happe, Gilbert, Burnett, & Viding, 2010; Schwenck et al., 2012) and adults (Dziobek et al., 2008) reported to be as emotionally affected as their TD peers.

In sum, cognitive but not affective empathy seems to be affected in children with ASD. However, reduced facial mimicry has been suggested in school-aged children and adolescents with ASD (Beall et al., 2008; McIntosh, Reichmann-Decker, Winkielman, & Wilbarger, 2006; Oberman, Winkielman, & Ramachandran, 2009).

Aim of the thesis

Further understanding of empathy-related processes and prosocial as well as antisocial and aggressive behavior in children with disruptive behavior, attention deficit and autism spectrum disorders deserves attention for several reasons. First, it remains unclear at what age empathy deficits may already be present. Studies suggest that aggressive school-aged children and adolescents (Eisenberg et al., 2010; Miller & Eisenberg, 1988), but not preschoolers (Feshbach & Roe, 1968; Gill & Calkins, 2003), show less signs of affective empathy in response to stories (Feshbach & Feshbach, 1969) or a distressed adult in a laboratory situation (Gill & Calkins, 2003) compared to their healthy developing peers. While empathy might already be impaired at the beginning of school age, systematic studies assessing empathy in clinical populations with ADHD and DBD at this early age have not yet been performed. This will be addressed in **Chapters 3 and 4** of this thesis where we report on differences in empathy between 6- and 7-year old children with ADHD and DBD and typically developing children. Likewise, in ASD, most studies on empathy have been conducted in older school-aged children, adolescents and adults (e.g. Greimel et al., 2011; Pouw et al., 2013; Schwenck et al., 2012) and it remains unclear whether or not findings also hold true in younger school-aged children. **Chapters 6 and 7** will focus on empathy in 6- and 7-year olds with ASD. Additionally, reduced empathy at an early age might be predictive for a persistent and severe pattern of aggressive behavior (Moffitt, Arseneault, Jaffee, et al, 2008). In **Chapter 5** the results are presented of a longitudinal study on the association between empathy and proactive aggressive behavior.

Second, empathy deficits might help in differentiating between children who share aggressive behavior problems, but differ in etiology, e.g. ASD versus DBD (Blair, 2008). Interestingly, it has been argued that deficits in responding to emotions of others in children with ADHD are at least partially accounted for by the co-existence of DBD (Marton et al., 2009). Similarly, in boys with DBD, deficits in empathy might at least partially be related to ADHD symptoms such as problems in attending to emotions of others. In **Chapters 3 and 4**, the association between empathy in children with DBD or ADHD will be studied while considering the role of comorbidity and associated symptoms.

Third, not much is known yet about empathy-related prosocial behavior in clinical populations. In children with ASD, intact helping and comforting behavior has been observed in experimental settings, despite parent report of reduced prosocial behavior. With regard to ADHD, two studies indicate that in community samples, ADHD symptoms are negatively correlated with pro-social behavior. These studies used ratings of pro-social behavior by teachers or peers of how helpful and cooperative children were in classroom situations (Diamantopoulou, Henricsson, & Rydell, 2005; Tseng et al., 2012). However, to date no studies in children diagnosed with ADHD or DBD have assessed pro-social behavior specifically in response to sadness and distress of others using an experimental paradigm. In sum, the literature on prosocial behavior in clinical populations is sparse and heterogeneous. New experimental methods designed to elicit and assess a pro-social behavioral response, like computer tasks (Dadds et al., 2007), have yet to be applied in clinical populations. In this thesis, the results will be reported of a computer game that aims to induce empathic prosocial behavior in response to sadness and distress of another child in ADHD and DBD (**Chapter 4**) and ASD (**Chapter 7**). Eventually, knowledge of possible deficits in empathy-induced prosocial behavior may lead to new interventions that not only aim to reduce antisocial but also to increase pro-social behaviors (Eisenberg et al., 2010).

As clinical investigations of empathy disorders can only be informative if behavioral, dispositional and biological factors are combined (Decety & Moriguchi, 2007), in this dissertation, behavioral and physiological measures were brought together to study empathy in 6-7 year old children with disruptive behavior, attention deficit and autism spectrum disorders. As a first step, a feasibility study was conducted to examine whether facial mimicry in response to emotional facial expressions can be reliably assessed in 6- and 7-year old children (**Chapter 2**). In the following studies presented in this thesis, children with DBD, ADHD and ASD were compared to typically developing children on parent and teacher reported empathic traits (**Chapter 4 and 7**). Next, differences in empathy between these groups were examined using three experimental paradigms: facial mimicry (**Chapters 2, 3, 6 and 8**), child report of empathy in response to story vignettes (**Chapters 4 and 7**) and empathy induced pro-social behavior assessed with a computer task (**Chapters 4 and 7**). In addition, a one year follow-up study was conducted to explore empathy assessed with various methods as a risk factor in the persistence of aggressive behavior (**Chapter 5**). Finally, it should be noted that the clinical children that participated in the present study were all asked to cease stimulant medication prior to assessment. However, some children with ADHD had accidentally taken methylphenidate (MPH) on the day of testing. This allowed an exploration of the influence of MPH on fear mimicry in an ad hoc fashion (**Chapter 8**).

Outline of the thesis

Chapter 2 describes the feasibility of using facial electromyography (EMG) as a method to study facial mimicry responses in children aged 6-7 years to emotional facial expressions of other children.

Chapter 3 presents the results of a study that examined facial mimicry in 6-7 year old children with DBD and ADHD in comparison to a healthy control group.

Chapter 4 examined parent and teacher reported empathic traits as well as empathy induced pro-social behavior in response to sadness and distress in 6-7 year old children with DBD and ADHD.

Chapter 5 addresses the association between empathy in response to sadness and distress of others and pro-active aggressive behavior both cross-sectionally and longitudinally.

Chapters 6 and 7 report two studies aimed to examine facial mimicry, parent and teacher reported empathic traits as well as empathy induced pro-social behavior in 6-7 year old children with autism spectrum disorder (ASD) and explored whether these were related to the severity of impairment in social responsiveness.

Chapter 8 is a brief report of an exploration of the potential influence on fear processing by methylphenidate (MPH).

Chapter 9 provides a summary and discussion of these experimental studies as well as some limitations, clinical implications and suggestions for further study.

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Chapter 2

Electromyographic responses to emotional facial expressions in six- and seven year olds: A feasibility study

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International Journal of Psychophysiology
2012; 85(2), 195–199

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Abstract

Preliminary studies have demonstrated that school-aged children (average age 9-10 years) show mimicry responses to happy and angry facial expressions. The aim of the present study was to assess the feasibility of using facial electromyography (EMG) as a method to study facial mimicry responses in younger children aged 6-7 years to emotional facial expressions of other children. Facial EMG activity to the presentation of dynamic emotional faces was recorded from the corrugator, zygomaticus, frontalis and depressor muscle in sixty-one healthy participants aged 6-7 years. Results showed that the presentation of angry faces was associated with corrugator activition and zygomaticus relaxation, happy faces with an increase in zygomaticus and a decrease in corrugator activation, fearful faces with frontalis activation, and sad faces with a combination of corrugator and frontalis activation. This study demonstrates the feasibility of measuring facial EMG response to emotional facial expressions in 6-7 year old children.

Keywords

children, electromyography, emotional responsiveness, facial mimicry

At the beginning of school age, social demands in peer interactions are increasing rapidly. Adequate responding to basic emotional expressions of others plays an important role in the development of prosocial behavior, and the inhibition of antisocial and aggressive behavior (Eisenberg, Eggum, & Di Giunta, 2010). However, emotional responses are hard to assess reliably by means of self report in young children (Dadds et al., 2007). Study of facial mimicry in children in response to facial expressions of other children may provide ecologically valid information on emotional phenomena in social interactions between peers.

Mimicry occurs when an individual imitates the facial, vocal or postural expressions of others with whom the person interacts (e.g. Bourgeois & Hess, 2008). Its existence has been confirmed in studies using multiple paradigms, in both adults (Bernieri, Reznick, & Rosenthal, 1988; Cappella & Planalp, 1981; Dimberg, 1990) and children (Chisholm & Strayer, 1995; de Wied, van Boxtel, Posthumus, Goudena, & Matthys, 2009; de Wied, van Boxtel, Zaalberg, Goudena, & Matthys, 2006; Haviland & Lelwica, 1987). It has been suggested that facial mimicry responses to emotional stimuli provide information on the emotional status of the observer (Buck, 1994; Cacioppo, Petty, Losch, & Kim, 1986; Dimberg, 1990). Others have suggested particularly facial mimicry to be a motor matching process, influencing later emotional and social processes (Chartrand & Bargh, 1999). In both views, investigation of facial electromyographic responses to facial expressions can be considered a method to assess responses to emotionally relevant information.

In school-aged children, four previous facial EMG studies assessed emotional facial mimicry (Beall, Moody, McIntosh, Hepburn, & Reed, 2008; de Wied et al., 2006; 2009; Oberman, Winkielman, & Ramachandran, 2009). Two studies compared facial EMG reactions in 22 healthy controls (average age 10 years) to boys with conduct problems (de Wied et al., 2006; 2009). Two other studies assessed facial mimicry in 13 and 15 typically developing children to children with autism spectrum disorders (average age 9-10 years) (Beall et al., 2008; Oberman et al., 2009). Taken together, these studies show that specific mimicry to angry faces (an increase in activity in the corrugator supercilii muscle which frowns the brows) and happy faces (an increase in the zygomaticus major muscle which pulls up the corners of the mouth) is developed in healthy children at least starting from 9-10 years old congruent with previous results in adults.

While studies using facial recognition paradigms describe raising of inner brows to fearful facial expressions, no frontalis activation (raises inner brows) has yet been shown in facial EMG studies (Ekman & Friesen, 1978; Kohler et al., 2004). However, frontalis activation was found in children in response to angry faces of adults, which was interpreted as an indication of a fearful reaction (Beall et al., 2008). Facial recognition studies show a combination of inner eyebrows raised and drawn together, and lip corners pulled down is associated with sad facial expressions (Ekman & Friesen, 1978; Kohler et al., 2004). In facial EMG studies, thus far corrugator activation was shown (de Wied et al., 2009), but activation in the frontalis and depressor anguli oris muscle (pulls down corners of the lips) has not yet been demonstrated.

The present study was designed to determine the feasibility of using facial EMG as a method to study facial mimicry responses in young children aged between 6-7 years old, to emotional facial expressions of other children. Notably, to explore the occurrence of mimicry following the presentation of emotional expressions, two slightly different methodological lines of approach can be followed. Firstly, the activation in a certain facial muscle during the presentation of an emotional condition can be tested against the activity in that facial muscle during another emotional condition. For example, it has been shown that happy faces evoke more zygomatic major activity than angry faces, whereas angry faces evoke more corrugator supercilii activity than happy faces (e.g. Bourgeois & Hess, 2008; Dimberg, 1990; Dimberg & Thunberg, 1998; Oberman et al., 2009; Weyers, Muhlberger, Hefele, & Pauli, 2006). Secondly, activity over a facial muscle during the emotional facial expression can be compared to previous baseline activity in an interval with a neutral facial expression (e.g. de Wied et al., 2006; 2009).

Based on previous studies using facial EMG or facial recognition paradigms, we made the following predictions on basis of emotion differences within each assessed facial muscle, and EMG responses between emotional facial expressions (summarized in Figure 2). We hypothesized angry faces to be associated with an increase in corrugator activity (Dimberg, 1990; Dimberg & Thunberg, 1998) as well as a decrease in zygomaticus activity (Bourgeois & Hess, 2008). In response to happy faces, we hypothesized an increase in zygomaticus (Dimberg, 1990; Dimberg & Thunberg, 1998) as well as a decrease in corrugator activity (Bourgeois & Hess, 2008; Hermans, 2006; Weyers et al., 2006). In response to fearful faces, we hypothesized an increase in frontalis (Moody, McIntosh, Mann, & Weisser, 2007) together with an increase in corrugator activity (Ekman & Friesen, 1978; Kohler et al., 2004). In response to sad faces, we hypothesized an increase in corrugator (Kreibig, Wilhelm, Roth, & Gross, 2007; Sonnby-Borgström, Jonsson, & Svensson, 2008; Weyers, Muhlberger, Kund, Hess, & Pauli, 2009) as well as depressor and frontalis activity (Ekman & Friesen, 1978; Kohler et al., 2004).

Methods

Participants

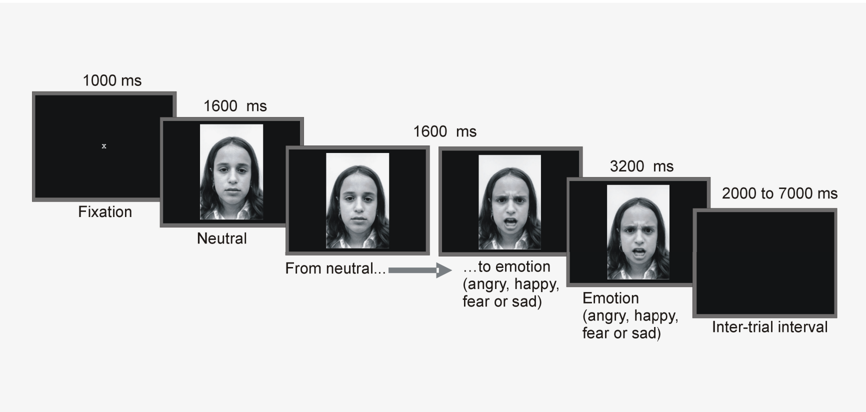
Sixty-one children (33 boys) aged between 6 and 7 years old (mean ± SD 7.19 ± 0.49 years) were recruited from regular elementary schools in the vicinity of Utrecht. All subjects had IQ scores above 70 (mean ± SD 119 ± 26), estimated with the Vocabulary and Block Design subtests of the Wechsler Intelligence Scale for Children III-Dutch version (WISC-III) (Kort et al., 2005; Sattler, 1992). The Medical Ethics Committee of the University Medical Center Utrecht approved the study, and parents gave written informed consent prior to participation.

Stimulus materials

Emotional film clips were created in our laboratory with image morphing software (Morpheus for Mac) based on a set of black-and-white pictures of children showing emotional facial expressions (Camras & Rappaport, 1993; Camras et al., 1988). In a previous study, the photographs were inspected by two raters trained in Ekman and Friesen's (1978) Facial Action Coding System to ensure that the requisite facial expressions had been produced. Also, recognition rates were obtained showing recognition of the intended emotion after presentation to be on average 90% (see Camras et al., 1988 for details).

In these film clips, each with a total duration of 6400 ms, five different children (two boys and three girls) expressed anger, happiness, fear and sadness. The size of the pictures was 21.5 cm height by 16 cm wide. They were viewed from a distance of 95 cm. As shown in figure 1, clips started with a 1600 ms still of a neutral expression which served as baseline, followed by a 1600 ms dynamic emotional expression and ended with a 3200 ms still of the full-blown emotion. Each film clip was preceded by an inter-stimulus interval (a black screen), followed by a central fixation cross with a duration of 1000 ms. Average inter-trial intervals vary widely in previous adult facial EMG literature and time frames between 1000 ms (Magnee, de Gelder, van Engeland, & Kemner, 2007) as well as 30 sec have been reported (Dimberg & Thunberg, 1998). Due to the young age of the children in our study, an inter-stimulus interval randomly ranging between 2000 and 7000 was chosen to limit total task duration.

Figure 1. Example trial of the passive viewing task



All stimuli were presented once in each of two blocks, in a separate semi-random sequence for each block. Thus, each block contained 20 clips (5 children by 4 emotions). The two blocks were preceded by a short practice round showing 4 different emotional film clips to assure children were at ease with the electrodes on their faces, and equipment was functioning properly. To assure the participants paid proper attention to the stimulus material, a cartoon figure appeared twice in each block during a clip. Participants were told to pay attention and push a response button when the cartoon was shown. Practice trials were used to assure children understood the instruction to push a button when a popular cartoon character (Pokemon) appeared on the screen. Trials including the cartoon were removed from further analysis.

Procedure

EMG data were collected while the children were seated in a chair in front of a computer screen in a dimly lit, familiar room at their own school. To assure participants were at ease, they first had a small talk with the experimenter and completed the two WISC-III subtests. Children were instructed to watch the film clips carefully and to push a button when a Pokemon appeared on the screen. Total duration of the facial EMG task was approximately 12 minutes. Upon finishing the task, participants received a small reward.

Apparatus and Physiological Recordings

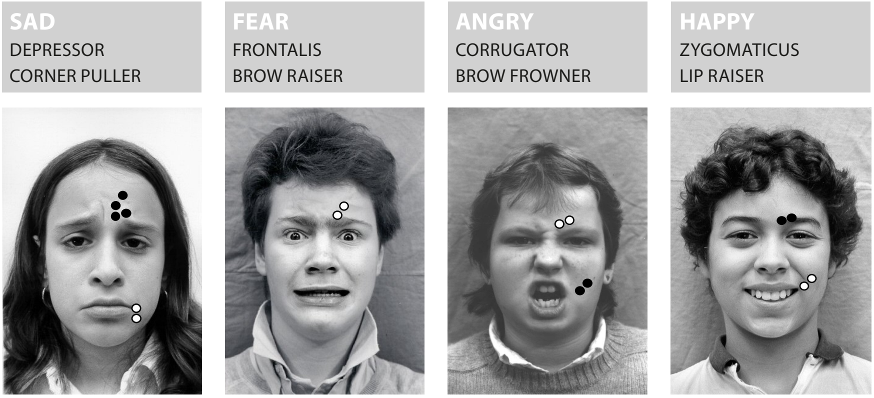
EMG activity was recorded from bipolar montages from the corrugator supercilii, zygomaticus major, frontalis medialis and depressor anguli oris, according to the guidelines given by Fridlund and Cacioppo as shown in figure 2 (Fridlund & Cacioppo, 1986).

Ag-AgCl electrodes with a diameter of 4 mm recording surface were placed on the left side of the face to obtain maximal reactions (Dimberg, Thunberg, & Elmehed, 2000). Raw EMG recordings were made with the ActiveTwo system (BioSemi, Amsterdam, The Netherlands) relative to the common mode sense (CMS). The ground consisted of the active CMS and passive driven right leg (DRL) electrode that form a feedback loop driving the subject's average potential as close as possible to the analog-to-digital converter (i.e., the amplifier "zero") reference voltage in the A/D-box. The EMG signal was sampled at 2048 Hz (bandwith 0.1 to 417Hz).

Data reduction

Differential EMG signals were filtered offline (high-pass 20 Hz, 48dB/octave) and rectified using Brain Vision Analyzer Software (Brain Products GmbH, Munich). Trials, in which a participant was not looking at the screen were marked by the experimenter during the task and these trials were excluded from further analysis (average trials removed per participant

Figure 2. Response selectivity: prediction of specific facial EMG site muscle activation after presentation of facial emotion expressions based on previous literature.



	depressor	frontalis	corrugator	zygomaticus
SAD	+	+	+	
FEAR		+		
ANGRY			+	-
HAPPY			-	+

1.72 +/- 2.78 trials). Raw EMG data were segmented into 100 ms epochs. All values were expressed as a percentage of individual baseline activity (average activity during 1600 ms neutral facial expression preceding morph). An average of the activity during the interval starting 500 ms after the beginning of the morphed dynamic expression and ending 500 ms after the beginning of the static expression at the end of the morphed clip was used for further analyses (total time 1600 ms). Previous findings using dynamic emotional stimuli suggest that in typical individuals, spontaneous mimicry begins around 500 ms after the start of the morphed clip and peaks around the end of the morph (Hermans, 2006; Rymarczyk, Biele, Grabowska, & Majczynski, 2011; Weyers et al., 2006). For each site in every emotion condition, data from trials with change scores calculated across the 1600ms period that were 3 SD above or below the grand mean change score were considered outliers and removed (average 5.6%, range in four emotion conditions 4.8-6.0% of trials) (Larsen & Norris, 2009). Mean EMG responses as expressed in percentage change from baseline activity were calculated for each emotion (averages of all stimuli for that emotion in the two blocks).

Data analysis

The hypotheses were tested using two lines of analysis. First, the activation during stimulus presentation between the four emotional conditions was compared. A repeated measures ANOVA was conducted with average EMG percentage change from baseline as dependent variables and EMOTION (angry, happy, fear, sad) and MUSCLE SITE (corrugator, zygomaticus, frontalis, depressor) as within subjects factors. This repeated measures ANOVA was followed in case of a significant interaction effect by four analyses of variance (ANOVAs), one for each of the four muscle sites, using a repeated measure design with EMOTION as within subjects variable and average EMG percentage change from baseline as dependent variable. Greenhouse–Geisser corrections were applied if necessary. Post-hoc planned contrasts were made to investigate specific differences in muscle activity between different emotional conditions for each of the EMG muscle sites.

In a second line of analyses, the activation during stimulus presentation was compared to the preceding neutral face baseline activation. One-sample t-tests (two-tailed) were conducted to compare the EMG activity in the predefined interval compared to baseline for each muscle within each emotional condition. In all tests, the alpha level of significance was set at $p<0.05$ (two-tailed), except the t-tests, where Bonferroni correction was applied and the alpha level was set at $p<.003$ (two-tailed).

Results

Due to technical problems and unwillingness to participate, four subjects (two boys and two girls) were excluded from the study. In total, data from 57 children was analyzed.

Activation during stimulus presentation in four emotional conditions

The GLM showed a significant main effect of EMOTION, [$F(3,168) = 5.41$, $p<0.05$, $\varepsilon= 0.89$] and EMG SITE [$F(3,168) = 20.68$, $p<0.001$, $\varepsilon= 0.60$]. The EMOTION*EMG SITE interaction was also significant [$F(9,504) = 16.76$, $p<0.001$, $\varepsilon= 0.61$], indicating that the presentation of emotional faces resulted in EMG activity that differed across muscles or that different patterns of facial muscle activations were obtained in response to the presentation of different emotional faces.

Corrugator EMG

The results of the follow-up ANOVA showed that corrugator muscle activity was significantly affected by the type of facial expression presented in the movie clips [$F(3, 168) = 21.27$, $p< 0.001$, $\varepsilon= 0.728$]. Post-hoc contrasts showed that this effect could be explained by significant differences between the angry (increase) and the happy (decrease) condition ($p< 0.001$) as well as between the angry (increase) and the fear condition (no change) ($p< 0.005$). Besides, corrugator activation was significantly different in the sad (increase) versus the happy (decrease) condition ($p=0.01$) and the fear condition ($p<.001$).

Zygomaticus EMG

The type of facial expression also significantly influenced zygomaticus activity [$F(3,168) = 13.66$, $p<0.001$, $\varepsilon =.810$]. This main effect was likely due to significant differences in zygomaticus muscle activity between an increase in happy and decreases in angry, sad and fear conditions (all $p< 0.005$).

Frontalis EMG

Frontalis activity was significantly affected by the type of facial expression presented [$F(3, 168) = 31.35$, $p< 0.001$, $\varepsilon =.799$]. Post-hoc contrasts showed this effect could be explained by differences in frontalis EMG activity in fear (increase) versus happy and angry (both $p<0.001$). Also, frontalis activity was different in sad (increase) versus happy and angry (both $p< 0.001$).

Depressor EMG

There was no main effect of emotion on depressor activitation, [$F(3, 168) = 1.893$, $p>0.10$.

Activation during stimulus presentation compared to pre-stimulus baseline

Angry

The presentation of angry facial expressions in children showed a significant increase in corrugator activity compared to the pre-stimulus neutral face baseline [$t(56)=4.16$, $p<0.001$, $d=0.55$] and a significant decrease in zygomaticus activity [$t(56)=-6.20$, $p<0.001$, $d=0.82$]. Frontalis activity was not significantly increased for angry faces ($p> 0.95$). Children also showed an unexpected significant decrease in depressor activity [$t(56)=-4.21$, $p<0.001$, $d=0.56$].

Happy

Following presentation of happy facial expressions, children showed a significant decrease in corrugator activity [$t(56)=-4.90$, $p<0.001$, $d=0.56$] and a non-significant increase in zygomaticus activity [$t(56)=1.94$, $p=0.057$, $d=0.26$]. Children also showed an unpredicted significant decrease in depressor activity [$t(56)=-5.33$, $p<0.001$, $d=0.71$] and frontalis activity [$t(56)=-3.93$, $p<0.001$, $d=0.52$].

Fear

Presentation of fearful facial expressions led to an increase in frontalis activity compared to baseline [$t(56)= 5.38$, $p< 0.001$, $d=0.71$], in line with predictions. Children also showed an unexpected significant decrease in zygomaticus activity [t(56)=-2.59, p<0.05, d=0.34]. No other effects were observed.

Sad

Sad facial expressions induced a significant increase in corrugator [t(56)=5.03, p<0.001, d=0.66] and frontalis [t(56)=6.96, p<0.001, d=0.92] activity compared to baseline. Also, zygomaticus activity decreased compared to baseline [t(56)= -4.89, p<0.001, d=0.65]. Compared to baseline, however, depressor muscle activity was not significantly increased for the sad condition.

Table 1. Facial EMG activation following emotional expressions compared to neutral face baseline activity

Presented emotion	EMG muscle site	Baseline (mV)	Mean Difference	SD	t	p
Angry	corrugator	8.42	12.01*	21.80	4.16	<.001
	zygomaticus	4.53	-8.51*	10.37	-6.20	<.001
	frontalis	7.14	-.044	6.13	-.054	.957
	depressor	10.41	-7.82	14.02	-4.21	<.001
Happy	corrugator	8.73	-6.06*	9.33	-4.90	<.001
	zygomaticus	3.92	3.74	14.51	1.94	.057
	frontalis	7.38	-3.07	5.89	-3.93	<.001
	depressor	9.59	-9.12	12.92	-5.33	<.001
Fear	corrugator	8.59	2.52	11.83	1.61	.114
	zygomaticus	3.93	-3.49	10.17	-2.59	.012
	frontalis	7.00	4.63*	6.49	5.38	<.001
	depressor	9.04	-4.61	19.17	-1.82	.075
Sad	corrugator	8.44	7.13*	10.71	5.03	<.001
	zygomaticus	3.82	-5.65	8.73	-4.89	<.001
	frontalis	7.13	6.44*	6.99	6.96	<.001
	depressor	9.28	-4.11	16.65	-1.86	.068

Note: Mean difference shown is the mean percentage difference from individual baseline activity set at 100 percent averaged across all subjects. Values marked with * are significant expected increases/decreases in line with hypothesis.

Discussion

The aim of the present study was to assess the feasibility of using EMG recordings as a method to study facial mimicry responses in 6-7 year old children to emotional facial expressions of other children. Results show that 6-7 year old children exhibit increased corrugator activation during angry and sad conditions as compared to happy and fear conditions. Furthermore, in line with our hypotheses, zygomaticus activation was larger during happy as compared to all other conditions and frontalis was larger during fearful and sad conditions. No EMG responses were observed in the depressor muscle. Moreover, the presentation of angry faces was associated with corrugator activition and zygomaticus relaxation, happy faces with a decrease in corrugator activation, fearful faces with frontalis activation, and sad faces with a combination of corrugator and frontalis activation.

The findings on the muscle activation patterns following presentation of angry and happy emotional stimuli in the present study are largely in line with previous facial EMG research in older children and adults (Beall et al., 2008; Bourgeois & Hess, 2008; de Wied et al., 2006; Dimberg, 1990; Dimberg & Thunberg, 1998; Hermans, 2006; Oberman et al., 2009). However, although activity in zygomaticus was significantly larger in response to happy facial expressions when compared to the other emotional conditions, this increase did not differ significantly from the neutral face baseline preceding the stimulus presentation. Possibly, the reactions to happy faces, with less muscular activity for the corrugator, the frontalis and the depressor, can be interpreted as a global relaxation effect. Happy faces presented by peers could convey a message of positive social interaction.

In response to the presentation of fearful facial expressions, the present study is to our knowledge the first facial EMG study that directly confirms brow raising activity. This is in line with previous facial EMG studies that found increased frontalis activation after fear induction with music in adults (Moody et al., 2007) and in children in response to angry faces of adults, which was interpreted as an indication of a fearful reaction (Beall et al., 2008).

The presentation of sad faces resulted in frowning in accordance with previous facial EMG studies in adults (Kreibig et al., 2007; Sonnby-Borgström et al., 2008; Weyers et al., 2009) and children (de Wied et al., 2009). Besides, brow raising appeared following presentation of sad facial expressions, in line with the facial emotion recognition literature (Ekman & Friesen, 1978; Kohler et al., 2004). Presently, we unfortunately could not demonstrate depressor activity to sad faces. It remains unclear whether the unexpected findings in the depressor muscle site in the present study are due to the young age of our participants or result from more general methodological issues in the adult literature. Notably, the lack of muscular activity involved in pulling the corners of the mouth is in agreement with other EMG studies that have failed to show increases in depressor activity following sad stimuli (Mass et al., 2008; Oberman et al., 2009; Schwartz, Fair, Salt, Mandel, & Klerman, 1976). Future studies should reconsider recording activation in the depressor muscle, even more since our results suggest that a differentiation between mimicry in response to negative emotional facial expressions can also be made when recording a combination of corrugator and frontalis activity.

Finally, it should be noted that the present stimuli differ from previous research in children. Only one other study examined facial EMG responses to child stimuli (de Wied et al., 2009). While stimuli of adults are useful to study emotional responsiveness in adult-child interactions, they may be limited in providing information on social interactions between children. However, the children in our stimuli were late-elementary school children while participants were young-elementary school children. It would be an interesting topic for future study to compare facial mimicry reactions in children to stimuli of different age groups.

In conclusion, this study, for the first time, provides evidence in support of the feasibility of recording facial EMG responses to angry, happy, fear and sad facial expressions in 6-7 year old children. Our findings suggest that facial EMG response to emotional faces may be a valuable tool to study the development of mimicry and emotional responsiveness to specific emotions throughout childhood. This is particularly relevant as deficits in mimicry in older children with child psychiatric disorders like disruptive behavior disorders and autism spectrum disorders have already been shown (Beall et al., 2008; de Wied et al., 2006; 2009; Oberman et al., 2009). These disorders, characterized by problems in social interactions, already may be identified at the beginning of school age (Barbaro & Dissanayake, 2009; Moffitt et al., 2008; Steiner & Remsing, 2007). Future investigations in these early onset psychiatric disorders can be more informative if multiple methods of assessment are used (Decety & Moriguchi, 2007). We propose facial EMG may be added as a procedure to assess emotional responsiveness in young elementary school children.

Author notes

Dennis J.L.G Schutter was supported by an Innovational Research Grant (VIDI 452-07-012) from the Netherlands Organization for Scientific Research (NWO).

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Chapter 3

Facial mimicry in six- and seven year old children with disruptive behavior disorder and ADHD

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PloS One
2014; 9(1), e84965. doi:10.1371/journal.pone.0084965

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Abstract

Impairments in facial mimicry are considered a proxy for deficits in affective empathy and have been demonstrated in 10 year old children and in adolescents with disruptive behavior disorder (DBD). However, it is not known whether these impairments are already present at an earlier age. Emotional deficits have also been shown in children with attention-deficit/hyperactivity disorder (ADHD). The aim of the present study was to examine facial mimicry in younger, 6-7 year old children with DBD and with ADHD. Electromyographic (EMG) activity in response to emotional facial expressions was recorded in 47 children with DBD, 18 children with ADHD and 35 healthy developing children. All groups displayed significant facial mimicry to the emotional expressions of other children. No group differences between children with DBD, children with ADHD and healthy developing children were found. In addition, no differences in facial mimicry were found between the clinical group (i.e., all children with a diagnosis) and the typically developing group in an analysis with ADHD symptoms as a covariate, and no differences were found between the clinical children and the typically developing children with DBD symptoms as a covariate. Facial mimicry in children with DBD and ADHD throughout the first primary school years was unimpaired, in line with studies on empathy using other paradigms.

Keywords

children, emotional responsiveness, facial mimicry, ADHD, DBD

Empathy is the ability to share and understand the emotions of other people with whom we interact and plays an important role in the development of prosocial behavior and inhibition of antisocial and aggressive behavior (Eisenberg & Miller, 1987; Miller & Eisenberg, 1988). It is assumed that empathy is initiated by the observation of another's emotional state, followed by a cascade of phenomena (Hofelich & Preston, 2012) that have been studied on an emotional (sharing another's emotional state), cognitive (understanding another's emotional state) and behavioral level (e.g., targeted helping) (de Waal, 2008). Although the precise mechanism, how mimicry is related to the development of individual differences in empathy, remains unclear (Hofelich & Preston, 2012), adequate responses to the emotional states of others also involve the activation of corresponding facial, vocal or postural expressions, called mimicry. Previous facial mimicry studies in school-aged children (mean age 10 years) and adolescents (mean age 13 years) with disruptive behavior disorder (DBD) suggest deficits in response to negative but not positive emotions (de Wied, van Boxtel, Posthumus, Goudena, & Matthys, 2009; de Wied, van Boxtel, & Matthys, 2012 ; de Wied, van Boxtel, Zaalberg, Goudena, & Matthys, 2006).

Several important issues concerning facial mimicry responses in children with DBD need further exploration. First, it remains unclear how early in development abnormalities in responses to emotional expressions start to emerge. The empathic ability of aggressive children may become increasingly impaired as social demands in peer interactions rapidly increase. Hence, deficits in facial mimicry might already be present in children with DBD at the start of school age (6-7 years old). On the other hand, studies using paradigms other than facial electromyography (facial EMG) (e.g., behavioral observation) suggest that aggressive preschoolers do not differ from their healthy developing peers in their response to the emotions of others (Feshbach & Roe, 1968; Gill & Calkins, 2003). The primary goal of the present study was to determine whether 6 to 7 year old children with DBD already show facial mimicry impairment. Second, despite high co-morbidity of attention-deficit/hyperactivity disorder (ADHD) and DBD and high co-occurrence of ADHD symptoms in children with DBD and DBD symptoms in children with ADHD, little attention has been paid to the influence of ADHD on emotion perception and processing in children with DBD (Martel, Gremillion, Roberts, Eye, & Nigg, 2010; Sterba, Egger, & Angold, 2007). Several studies in children with ADHD have shown that emotion processing might also be impaired, to some extent, in boys with ADHD (Braaten & Rosen, 2000; Dyck, Ferguson, & Shochet, 2001; Marton, Wiener, Rogers, Moore, & Tannock, 2009; Pelc, Kornreich, Foisy, & Dan, 2006; Sinzig, Morsch, & Lehmkuhl, 2008; Williams et al., 2008). Interestingly, it has been argued that deficits in responding to the emotions of others in children with ADHD are at least partially accounted for by the co-existence of DBD (Marton et al., 2009) and that in boys with DBD, deficits might at least partially be related to ADHD (Yuill & Lyon, 2007).

The present study aimed to address these issues by examining facial mimicry responses to emotional facial expressions in a sample of 6-7 year old children with DBD, in children with ADHD, and in healthy developing children. Two lines of approach were followed. First, three groups were compared, i.e., children with DBD, children with ADHD, and typically developing children. Second, while comparing the clinical group (i.e., all children with a diagnosis) to the typically developing group, first the effect of DBD on facial mimicry was examined with ADHD symptoms as a covariate, and second the effect of ADHD was examined with DBD symptoms as a covariate.

Method

Participants

A sample of 100(*) children ranging from six to seven years old with a previous clinical diagnosis of DBD (i.e., either oppositional defiant disorder (ODD) or conduct disorder (CD)) and/or ADHD was recruited at the Outpatient Clinic of the Department of Child and Adolescent Psychiatry, University Medical Center Utrecht. Children were excluded from participating if a clinical diagnosis of ADHD or DBD was not confirmed (n=3) in the Diagnostic Interview Schedule for Children (DISC module E) (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) or when they had an estimated IQ below 70 (n=8) based on the vocabulary and block design subsets of the Wechsler Intelligence Scale for Children III-Dutch version (Kort et al., 2005; Sattler, 1992). Eighteen children were excluded as they had taken methylphenidate (n=18) on the day of testing, despite instructions to cease medication prior to assessment. Furthermore, in six children from the clinical groups no EMG data were collected, either caused by technical difficulties, lack of cooperation or anxiety in the children. The final patient group for analyses comprised 65 children.

The healthy developing control group consisted of 37 children from regular elementary schools in the vicinity of Utrecht who did not meet criteria for a clinical diagnosis of ADHD

Note:

(*) The total study sample described in this thesis consisted of 104 patients. In this chapter, four children were accidentally excluded from data-analysis. They were treated as if no EMG data had been collected. This did not affect the conclusions of this study (see footnote 2). Of the total sample of the 104 children, children were excluded if: (a) a clinical diagnosis could not be confirmed (n=3); (b) their estimated IQ was below 70 (n=7, including one child with no EMG data); (c) they had taken medication on the day of testing (n=18: 16 methylphenidate including 3 children with no EMG data, 2 atomoxetine including 1 child with no EMG data) and (d) no EMG data were collected (n=11, including 4 children who were accidentally treated as if no EMG data was collected and 1 child that was originally described as excluded for reason of low IQ). The final patient group for analysis comprised 65 children.

or DBD on the DISC and had an estimated IQ within the normal range. No EMG data were collected in three children from the control group due to technical difficulties or anxiety. The Medical Ethics Committee of the University Medical Center Utrecht approved the study protocol and parents gave written informed consent prior to participation.

Measurements

The DISC module E interview (Shaffer et al., 2000) was used to distinguish patient groups. For our first categorical approach, we pooled children with DBD with ADHD (n=41) and children with DBD without comorbid ADHD (n=6) in one DBD group. The other patient group consisted of children with ADHD without a comorbid DBD diagnosis (n=18). Because of the small sample size of the DBD-only group, an analysis comparing this group to other groups was not appropriate. The group of children with DBD (n=47) included both children with ODD (n=41) and those with CD (n=6). For our second approach, a total patient group was analyzed including 65 children with a diagnosis of DBD (n=6), ADHD (n=18) or DBD with comorbid ADHD (n=41).

Table 1. Descriptives

Characteristics	TD (*n*=34) *M (SD)*	ADHD (*n*=18) *M (SD)*	DBD (*n*=47) *M (SD)*	F (df=96)	Contrasts
Age	7.1 (0.5)	7.1 (0.7)	6.7 (0.5)	6.90*	TD, ADHD > DBD
Sex: male/female	17/17	8/10	11/36	6.65*	TD ≠ ADHD, DBD
estimated IQ	110 (20)	103 (17)	100 (19)	3.20*	TD > ADHD, DBD
SES	7.0 (2.1)	5.1 (1.9)	5.6 (1.5)	8.27*	TD > ADHD, DBD
CBCL T score					
-Attention	52.7 (4.0)	67.0 (8.4)	66.8 (7.9)	47.07*	TD < ADHD, DBD
-Rule-breaking	53.0 (4.3)	58.0 (6.8)	61.9 (6.4)	22.73*	TD < ADHD < DBD
-Aggression	53.5 (5.6)	63.4 (8.9)	70.8 (7.8)	55.34*	TD < ADHD < DBD
TRF T score					
-Attention	52.0 (3.1)	59.9 (9.7)	61.6 (7.5)	19.71*	TD< ADHD, DBD
-Rule-breaking	50.9 (2.6)	54.9 (5.4)	58.8 (7.7)	16.66*	TD < ADHD < DBD
-Aggression	52.2 (3.7)	60.8 (5.6)	64.5 (10.8)	22.03*	TD< ADHD, DBD

Note: * p<0.05

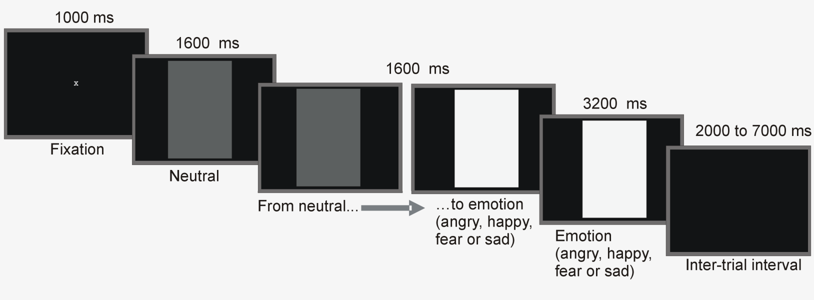
The Child Behavior Checklist 6-18 (CBCL) and Teacher Report Form (TRF) (Achenbach & Rescorla, 2001) were collected and used to quantify attention problems and rule-breaking/aggressive behavior.

Table 1 shows the characteristics of the sample used for final data analyses, divided in the DBD group with and without comorbid ADHD, ADHD only group and healthy control group. Analyses presented in Table 1 show that children in the DBD group were on average 4 months younger than the TD children. Furthermore children in the DBD and ADHD groups contained fewer girls, and these children had lower estimated IQ and lower socio-economic status (SES) than children in the control group. Children in the DBD group did not differ from children in the ADHD group in sex, estimated IQ or SES, but were significantly younger. As expected, the three groups significantly differed on attention problems and rule-breaking/aggressive behavior.

Facial EMG data collection

Film clips with dynamic emotional facial expressions, created at our laboratory, were used in the present study (Deschamps, Schutte, Kenemans, Matthys, & Schutter, 2012). In these film clips, each with a total duration of 6400 ms, five different children (two boys and three girls) expressed anger, sadness, fear and happiness as illustrated in Figure 1. Clips started with a 1600 ms static of a neutral expression which served as baseline, followed by a 1600 ms morph into a dynamic emotional expression and ended with a 3200 ms static of the full-blown emotion. Each film clip was preceded by an inter-stimulus interval (a black

Figure 1. Example trial of the passive viewing task.



Note: Each trial started with a central fixation cross, followed by a film clip. The clips started with a neutral expression (in the figure represented by a gray rectangle), followed by a morph into a dynamic emotional expression and ended with a still of the full-blown emotion (in the figure represented by a white rectangle). Each trial ended with an inter-stimulus interval.

screen), followed by a central fixation cross with a duration of 1000 ms. In total 32 movie clips were presented, once in a semi-random sequence in a first block (16 clips, 4 children x 4 emotions), and once in a semi-random sequence in a second block (16 clips, 4 children x 4 emotions). The size of the pictures was 21.5 cm height by 16 cm width. They were viewed from a distance of 95 cm. Furthermore, during the task, there were four trials in which a cartoon character was presented during an emotional film clip. Children were instructed to push a response button when the character appeared on screen in order to maintain the child's attention to the faces. The data collected during these trials and during the four familiarization trials were excluded from further analyses.

EMG activity was recorded from bipolar montages from the corrugator supercilii (corrugator), zygomaticus major (zygomaticus), frontalis medialis (frontalis) and depressor anguli oris (depressor), according to the guidelines given by Fridlund and Cacioppo (Fridlund & Cacioppo, 1986). Ag-AgCl electrodes with a diameter of 4 mm, filled with conductive electrode gel (Signa gel, Parker Laboratories, Inc., Fairfield, New Jersey, U.S.A.), were placed on the left side of the face to obtain maximal reactions (Dimberg & Petterson, 2000). Raw EMG recordings were made with the ActiveTwo system (BioSemi, Amsterdam, The Netherlands) relative to the common mode sense (CMS). The ground consisted of the active CMS and passive driven right leg (DRL) electrode placed on the forehead that form a feedback loop driving the subject's average potential as close as possible to the analog-to-digital converter (i.e., the amplifier "zero") reference voltage in the A/D-box. The EMG signal was sampled at 2048 Hz.

Procedure

EMG data were collected while the child was seated in a chair in front of a computer screen in a dimly lit room at their own school. To ensure participants were at ease, they first had a small talk with the experimenter and completed the two WISC-III subtests. Children were instructed to watch the film clips carefully and to push a button when a popular cartoon character appeared. They were told they would receive a small present as a reward upon finishing the task. Between the two blocks of the passive viewing task, the experimenter ensured that the child was both comfortable and motivated. Additionally, during the task an experimenter encouraged the children to pay attention and recorded the time segments when the child was not looking at the computer screen to provide a measure of visual inattention. Total duration of the facial EMG task was approximately 12 minutes.

Data reduction and analysis

EMG signals were filtered offline (high-pass 20 Hz, 48dB/octave) and full wave rectified using Brain Vision Analyzer Software (Brain Products GmbH, Munich). Trials marked by the experimenter during the task indicating that the child was not looking at the computer screen, were excluded from further analysis. The average number of trials removed per participant was 1.82 (SD 0.41) out of 32 trials in the typically developing group, 3.68 (SD 0.60) in the DBD with/without ADHD group and 4.95 (SD 1.16) in the ADHD only group.

Raw EMG data were segmented into 100 ms epochs. All values were expressed as a percentage of individual baseline activity, defined as the mean activity during 1600 ms neutral facial expression preceding onset of the morph. Averaged activity during the interval starting 500 ms after the beginning of the morphed dynamic expression and ending 500 ms after the beginning of the static expression at the end of the morphed clip was used for further analyses (total time 1600 ms). Mean EMG responses across this 1600 ms period, expressed as a percentage change from baseline activity, were calculated for each emotion-muscle combination (averages of all stimuli for that emotion-muscle combination in the two blocks). Data points that exceeded 3 SD above or below the grand mean change score of the emotion condition were marked as outliers and excluded from further analysis (Larsen & Norris, 2009). Mean EMG responses as expressed in percentage change from baseline activity were calculated for each emotion-muscle combination (averages of all responses for that emotion-muscle combination in the two blocks).

Based on previous research of our group (Deschamps et al., 2012), facial EMG composite scores were calculated on basis of the absolute mimicry response to all four emotional presentations. Since mimicry to happy facial expressions consists of both smiling activity (i.e., increase in zygomaticus muscle) and relaxation of frowning activity (i.e., decrease in corrugator muscle), to calculate the total mimicry response to happy facial expressions (HAPPY), we used the following formula: [happy mimicry= (% change in zygomaticus activation during happy stimulus presentation compared to neutral face baseline - % change in corrugator activation during happy stimulus presentation compared to neutral face baseline)/2]. Thus, we calculated the overall mean of the positive change in zygomaticus and the negative change in corrugator activity in response to happy facial expressions compared to neutral face baseline. Likewise, angry facial mimicry consists of an increase in frowning and a decrease in smiling activity, the total angry score (ANGRY) consisted of the overall mean of the positive change in corrugator and the negative change in zygomaticus activity in response to angry facial expressions (formula: [angry mimicry= (% change in corrugator activation during stimulus presentation compared to baseline- % change in zygomaticus presentation during stimulus presentation compared to baseline)/2)]. The total fear score (FEAR) consisted of the positive change of frontalis activity in response to fearful facial expressions, and the total sad score (SAD) consisted of the positive change in frontalis, corrugator and depressor activity in response to sad facial expressions (formula: [sad mimicry= (% change in frontalis + % change in corrugator + % change in depressor compared to neutral face baseline)/3]).

Statistical analyses were performed using PASW Statistics 18.0 (IBM Company, Chicago, Illinois). Initially, we validated the composite scores within the healthy control group, as this group was not identical to the group used in our previous study (Deschamps et al., 2012). Using one-sample t-tests, we checked whether the separate muscles of the composite scores changed significantly during presentation of the emotional film clips, compared to the activity during the neutral face baseline.

First, a multivariate analysis of variance (MANOVA) was conducted to examine whether facial mimicry differed in children with DBD, children with ADHD only, and healthy controls. Dependent variables were the facial mimicry response composite scores to sad, fearful, angry and happy facial expressions (SAD, FEAR, ANGRY and HAPPY MIMICRY). MIMICRY was entered as a within subjects factor with two levels (baseline and activation during stimulus presentation). GROUP was entered as between subjects variable with three levels (DBD with or without ADHD, ADHD and healthy controls).

Second, multivariate analyses of variance (MANOVA) were conducted to compare the facial mimicry response scores (SAD, FEAR, ANGRY and HAPPY MIMICRY) in the overall patient group with the typically developing children (GROUP) with the parent and teacher reported attention and aggression symptom scores entered as covariates.

In all tests, the alpha level of significance was set at $p < 0.05$ (two-tailed).

Results

The independent sample t-tests within the healthy control group showed that all four composite scores consisted of the hypothesized muscle activation patterns (all p-values <0.05). In particular, in line with predictions, the presentation of angry facial expressions showed a significant increase in corrugator activity compared to the pre-stimulus neutral face baseline (t(33)=3.03, p=0.005) and a significant decrease in zygomaticus activity (t(33)=-2.31, p=0.027). Following presentation of happy facial expressions, children showed an expected significant decrease in corrugator activity (t(33)=-3.98, p<0.001) and a significant increase in zygomaticus activity (t(33)=3.41, p=0.002). Presentation of fearful facial expressions led to an increase in frontalis activity compared to baseline (t(33)=4.64, p< 0.001). Sad facial expressions induced a significant increase in corrugator (t(33)=4.57, p<0.001), frontalis (t(33)=4.45, p<0.001) and depressor (t(33)=2.21, p=0.034) activity compared to baseline.

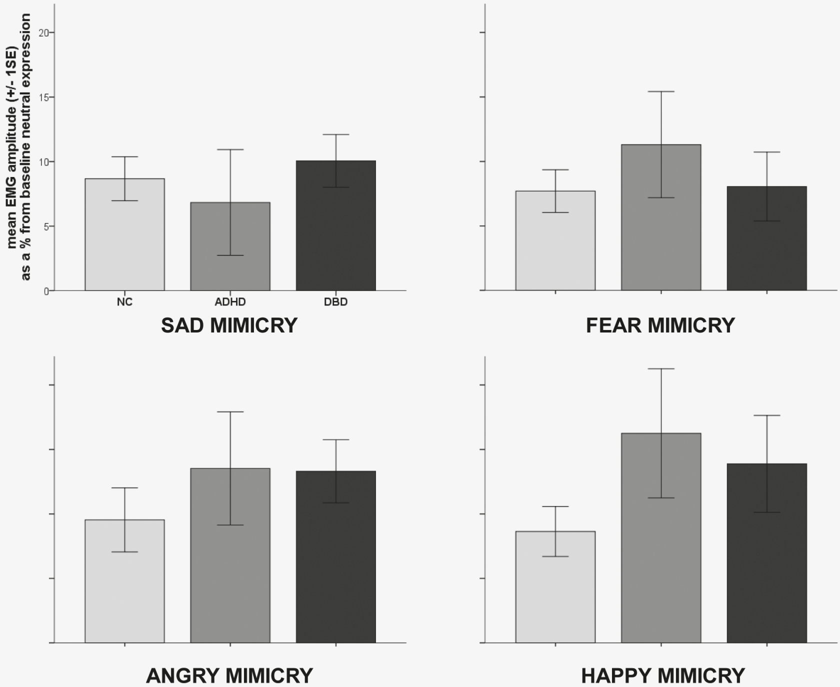
A significant main effect of MIMICRY was found, demonstrating that overall, the presented stimuli resulted in facial mimicry (F(4,93) =21.49, p<0.001).

Univariate analyses showed a significant effect of MIMICRY in response to SAD

(F(1,96)=33.90, p<0.001), FEAR (F(1,96)=27.89, p<0.001), ANGRY (F(1,96)=46.45, p<0.001) and HAPPY (F(1,96)=32.00, p<0.001) facial expressions.

We did not find a significant multivariate main effect of GROUP (F(8,188)=0.80, p=0.60), indicating no differences in facial mimicry between clinical groups and healthy developing children (see Figure 2)(**).

Figure 2. Facial mimicry response to emotional facial expressions in DBD, ADHD and healthy controls.



Note: No significant differences were shown between groups in mean EMG amplitude as a percentage from baseline neutral expression for SAD, FEAR, ANGRY and HAPPY MIMICRY presented for healthy controls, children with attention-deficit/hyperactivity disorder (ADHD) and children with disruptive behavior disorder (DBD). Error bars represent +/- 1 standard error.

Note:
(**) Because the group main effect for n=100 was highly insignificant (p=0.60), we did not consider a re-analysis with n=104 (see first note).

An additional MANOVA comparing the activation of the individual muscles (i.e., zygomaticus and corrugator in response to happy and angry expressions, frontalis in response to fear and corrugator, frontalis and depressor in response to sad) between the three groups showed no multivariate effect of group ($F(16,180)=0.740$, $p=0.75$) meaning that the absence of a group effect in the main analysis was not due to the use of composite scores.

Next, a second additional analysis was conducted within the boys to assure the imbalance of sex in our groups could not explain the lack of a group difference. This analyses yielded similar results as the main analysis and showed no main effect of group ($F(8,116)=0.92$, $p>0.50$).

Finally, four analyses were conducted to examine the effect of GROUP (all patients versus typically developing children) on facial mimicry with attention and aggression symptom scores as covariates respectively, reported by either parents (CBCL attention and CBCL aggression t scores) or teachers (TRF attention and TRF aggression t scores). No significant multivariate effect of GROUP was found in any of the MANOVAs with these individual factors entered as covariate (all $p>0.15$). Of note, no significant correlations were found between facial mimicry and the CBCL Attention t score ($F(4,93)=0.87$, $p=0.48$), CBCL Aggression t score ($F(4,93)=1.40$, $p=0.24$), TRF Attention t score ($F(4,91)=0.62$, $p=0.65$), TRF Aggression t score ($F(4,91)=1.11$, $p=0.36$).

Discussion

In the present study no evidence was found for impaired facial mimicry in 6-7 year old children with ADHD as compared to healthy controls. Also, no differences were found in facial mimicry between children with DBD and healthy controls. However, since the group of children with DBD without ADHD in our study sample was not sufficiently large, we had to pool the children with DBD with and without comorbid ADHD. Nevertheless, no differences in facial mimicry were found between the clinical group (i.e., all children with a diagnosis) and the typically developing group in an analysis with ADHD symptoms as a covariate, and no differences were found between the clinical children and the typically developing children with DBD symptoms as a covariate.

Results of an absence of facial mimicry deficits in our sample of 6-7 year olds with DBD are in keeping with studies using other paradigms (e.g., behavioral observation) that suggest that aggressive school-aged children and adolescents (Eisenberg, Eggum, & Di Giunta, 2010; Miller & Eisenberg, 1988) but not younger children and preschoolers (Feshbach & Roe, 1968; Gill & Calkins, 2003) respond less to the emotions of others compared to their healthy developing peers. Since in 10 year old children and adolescents with DBD diminished facial EMG responses have been demonstrated (de Wied et al., 2006; 2009; 2012), one may speculate that EMG responses to emotional facial expressions are still intact in 6-7 year old children and that decreases in mimicry responses start after the beginning of school age.

However, there are other possible explanations why we did not find a group difference. Children in our study were younger than those in previous studies that showed facial mimicry deficits in DBD (de Wied et al., 2006; 2009; 2012). Since throughout development into late childhood and adolescence, symptoms of DBD are known to persist in certain, and decline in other children (Frick & Loney, 1999; Lahey et al., 1995), our sample might have included children with less severe psychopathology. The symptom scores on the CBCL filled in by parents and the TRF in the present study indeed were lower as compared to those in previous studies (de Wied et al., 2006; 2009; 2012). Also, children in our study were recruited from an outpatient population, whereas in previous studies children were recruited from inpatient and day-treatment settings (de Wied et al., 2006; 2009) or special schools for adolescents with severe behavioral problems (de Wied et al., 2012). Importantly, the present study sample contained only a few children with CD and the others were diagnosed with ODD, whereas in other studies twenty percent (de Wied et al., 2006; 2009) to almost half of the DBD sample consisted of CD children (de Wied et al., 2012). Recently, it has been suggested that the neurobiology of ODD may be different from CD (Matthys, Vanderschuren, & Schutter, 2013; Matthys, Vanderschuren, Schutter, & Lochman, 2012) as ODD differs from CD in symptomatology, comorbidity and development (Nock, Kazdin, Hiripi, & Kessler, 2007; Rowe, Costello, Angold, Copeland, & Maughan, 2010; Stringaris & Goodman, 2009a; 2009b). Overall, this points towards less severe and different psychopathology in our young outpatient group as a possible explanation for the lack of a group difference.

Facial mimicry in children with ADHD thus far had not been studied, but previous studies using other paradigms had suggested deficits in emotion processing in children with ADHD. Several studies in children with attention problems and ADHD have shown that their facial emotion recognition skills (Pelc et al., 2006; Sinzig et al., 2008; Williams et al., 2008) and empathic responsiveness to emotions (Braaten & Rosen, 2000; Dyck et al., 2001; Marton et al., 2009) tend to be less well developed compared to healthy children. However, we could not show deficits in facial mimicry in ADHD compared to typically developing children.

With regard to the role of sex differences, our study sample differed from previous studies on facial mimicry in children with DBD as those studies did not examine girls. Little is known about the influence of sex on the development of facial mimicry, but studies in adults have suggested females might show more facial mimicry, although only in response to happy facial expressions (Dimberg & Lundquist, 1990; Sonnby-Borgström, Jonsson, & Svensson, 2008). To further examine whether the sex ratio in our study influenced the main findings, we conducted an additional analysis within the group of boys in our study. This analysis showed that, as in the overall sample, boys with DBD or ADHD showed no deficits in facial mimicry. Hence it is unlikely that the presence of girls in our sample influenced our main finding. However, it should be noted that due to the small sample sizes in the subgroup analyses, these analyses were likely to be statistically underpowered to detect this effect.

Finally, there are several methodological differences in our study compared to previous work to consider. First, only one other study examined facial EMG responses to child stimuli (de Wied et al., 2009). While stimuli of adults are useful to study emotional responsiveness in adult-child interactions, they might provide only limited information on social interactions between children. Next, the procedure and analysis in the present study was developed to maximize attention paid to the stimuli. Namely, children were encouraged to pay attention, motivated with the promise of a reward, an instruction was inserted in the paradigm to catch a cartoon character, and trials marked with visual inattention were excluded from further analysis. This could have reduced the influence of attention problems on deficits in facial mimicry. Two other studies found evidence for a positive moderating influence of increased attention on emotion processing in adults with low empathy and antisocial behavior using a fear-potentiated startle paradigm (Newman, Curtin, Bertsch, & Baskin-Sommers, 2010) and in children using a fear recognition task (Dadds et al., 2006). Both studies suggest that deficits in emotion processing can be at least temporarily corrected by instructing subjects to focus on the eyes of other people and guiding their attention towards relevant parts of the presented stimuli. Until future studies assess facial mimicry simultaneously with objective procedures, like eye-tracking, to verify actual attendance to the stimuli, it remains difficult to unravel whether previous findings of impaired mimicry are partly driven by a lack of attention. Further study is needed to explore whether young children with DBD and/or ADHD are only capable to adequately make use of their mimicry system under optimal conditions, i.e., conditions that need not be ecologically valid. It might well be that in children with ADHD a continuous lack of proper attention to relevant parts of emotional facial stimuli in daily live has a negative effect on the development of emotion processing and recognition.

Since in 10 year old children and adolescents with DBD diminished facial EMG responses have been demonstrated (de Wied et al., 2006; 2009; 2012), one may speculate that EMG responses to emotional facial expressions are still intact in 6-7 year old children and decreases in mimicry responses start after the beginning of school age. Longitudinal studies using facial EMG and other physiological assessment methods are needed to shed light on the development of responsiveness to visual and other sensory modalities of emotional stimuli of other children. Further study should identify whether, at what age, and in which subgroups (e.g. those with CD versus those with ODD) children with DBD become impaired in their responding to emotions, and which factors affect altered emotional responsiveness. In conclusion, this study demonstrates that 6-7 year old children with DBD and ADHD exhibit normal facial mimicry to emotional facial expressions.

Acknowledgements
The authors would like to thank Arne Popma and Koen van Lith for their kind assistance in the data collection.

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Chapter 4

Empathy and prosocial behavior in response to sadness and distress in six- and seven year olds diagnosed with disruptive behavior disorder and attention deficit hyperactivity disorder

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2014; doi: 10.1007/s00787-014-0535-x

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Abstract

Empathy has been associated with decreased antisocial and increased prosocial behavior. This study examined empathy and prosocial behavior in response to sadness and distress in disruptive behavior disorder (DBD) and attention deficit hyperactivity disorder (ADHD). Six and seven year old children with DBD (with and without ADHD) (n=67) and with ADHD only (n=27) were compared to typically developing children (TD) (n=37). Parents and teachers rated affective empathy in response to sadness and distress on the Griffith Empathy Measure. Children reported affective empathic ability in response to sad story vignettes. Empathy induced prosocial behavior in response to sadness and distress was assessed with a computer task, the Interpersonal Response Task (IRT). Compared to TD, children with DBD (with and without ADHD) and those with ADHD only were rated as less empathic by their teachers, but not by their parents. No differences between groups were observed in children reported affect correspondence. Children with DBD (with and without ADHD) showed less prosocial behavior in response to sadness and distress compared to TD. Children with ADHD only did not differ from TD. An additional analysis comparing all children with a diagnosis to the TD group revealed that the difference in prosocial behavior remained after controlling for ADHD symptoms, but not after controlling for DBD symptoms. These findings of impaired empathy induced prosocial behavior in response to sadness and distress in young children with DBD suggest that interventions to ameliorate peer relationships may benefit from targeting on increasing prosocial behavior in these children.

Keywords
children, empathy, disruptive behavior disorder, attention deficit hyperactivity disorder, prosocial behavior

Empathy is the ability to understand and share emotions of other people with whom we interact (Cohen & Strayer, 1996; Feshbach, 1997). Empathy is assumed to be initiated by the observation of another's emotional state (Hofelich & Preston, 2012) and consists of an emotional (i.e., experiencing another's emotional state) and a cognitive component (i.e., understanding another's emotional state) (Dadds et al., 2007; de Waal, 2008). In addition, a distinction has been proposed between dispositional (i.e., trait) and situational (i.e., state) empathy. Accordingly, to study empathic traits in children self- and other-report questionnaires on feelings, thoughts, and behavior have been developed (Bryant, 1982). Likewise, experimental paradigms have been designed to evaluate the understanding of another's emotional state (cognitive empathy, CE), to elicit emotional experience (affective empathy, AE), and to elicit empathy induced behavior (Eisenberg & Miller, 1987; Lovett & Sheffield, 2007).

Empathy-related responding tends to be positively associated with prosocial behavior such as helping, sharing, and comforting another individual (see for reviews (Eisenberg & Miller, 1987; Eisenberg, Eggum, & Di Giunta, 2010). Empathy is also thought to contribute to the inhibition of antisocial and aggressive behavior (Miller & Eisenberg, 1988b). Researchers trying to explain the mechanisms involved have focused on the central role of the display of sadness and distress in the inhibition of aggressive behavior (Blair, 1995; Blair, Jones, Clark, & Smith, 1997). For example, children inflicting harm upon another person and witnessing the sadness or distress in this person have been proposed to become distressed themselves and stop harming the other in order to reduce their own personal distress (Pouw, Rieffe, Oosterveld, Huskens, & Stockmann, 2013). Similarly, witnessing distress in mammals evokes sharing, helping and comforting behaviors (de Waal, 2008), analogous to the positive association between empathy and prosocial behaviors in humans (Eisenberg et al., 2010). An important point to consider is that it is especially prosocial behavior that does have no direct material benefits for the actor that seems to be related to empathy for the pain and distress of others (de Waal & Suchak, 2010).

Whereas in developmental and ethological studies attention has been paid to empathy and prosocial behavior, in clinical studies the focus has been mainly on the association between empathy and aggression. In children and adolescents, deficits in empathy have been reported in disruptive behavior disorders (DBD), a disorder characterized by oppositional, defiant and antisocial behavior. Indeed, in school-aged children and adolescents with DBD lower scores were obtained on self-report questionnaires of empathic traits (Anastassiou-Hadjicharalambous & Warden, 2008; Cohen & Strayer, 1996; de Wied, Goudena, & Matthys, 2005). Similarly, most studies assessing empathy in DBD in experimental paradigms have agreed on a central role for affective empathy deficits in DBD patients (Anastassiou-Hadjicharalambous & Warden, 2008; Cohen & Strayer, 1996; de Wied et al., 2005; van Boxtel,

& Matthys, 2012; Schwenck et al., 2012). Cognitive empathy, however, in these experimental studies, was generally found to be intact in patients with DBD (Schwenck et al., 2012; Woodworth & Waschbusch, 2008), although one study suggested otherwise (Cohen & Strayer, 1996). In sum, it seems that reduced sharing of feelings of sadness and distress in others is linked to disruptive and aggressive behavior in children and adolescents.

However, several important issues concerning affective empathy deficits and prosocial behavior in children with DBD need further clarification. First, a useful approach would be to examine affective empathic response patterns specifically in response to signals of sadness and distress of others (de Wied, Gispen-de Wied, & van Boxtel, 2010). In experimental studies, the study of affective empathy in response to vignettes of sadness and distress has shown impairments in children with DBD compared to TD (Anastassiou-Hadjicharalambous & Warden, 2008; de Wied et al., 2005; 2012), whereas results of reduced responses to happiness and anger have been more mixed (de Wied et al., 2005; 2012). With regard to report of empathic traits, studies thus far have not distinguished between empathy in response to feelings of sadness/distress, happiness or anger (Anastassiou-Hadjicharalambous & Warden, 2008; Cohen & Strayer, 1996; de Wied et al., 2005).

Second, with regard to prosocial behavior, two studies using community samples have shown an association between conduct problems and reduced prosocial behavior reported as exemplified in how helpful, nice and cooperative children were in classroom situations as rated by teachers (Diamantopoulou, Henricsson, & Rydell, 2005; Tseng et al., 2012). Conduct problems were negatively correlated with teacher and peer reported prosocial behavior (Diamantopoulou et al., 2005), and physical aggression was negatively correlated with peer-reported prosocial behavior (Tseng et al., 2012). However, to date no studies have investigated prosocial behavior in clinical samples of children diagnosed with DBD, although experimental methods such as a computer game to elicit prosocial behavioral responses have been developed (Dadds et al., 2007).

Third, despite high co-morbidity of attention-deficit/hyperactivity disorder (ADHD) and DBD (Angold, Costello, & Erkanli, 1999), and high co-occurrence of ADHD symptoms in children with DBD and DBD symptoms in children with ADHD (Martel, Gremillion, Roberts, Eye, & Nigg, 2010). Little attention has been paid to the influence of ADHD on emotion perception and processing in children with DBD. Several studies in children with ADHD have shown that affective empathy might also be impaired, to some extent, in boys with ADHD compared to TD children, either assessed as a trait using parent reports (Marton, Wiener, Rogers, Moore, & Tannock, 2009), or as a state assessing affective responses to vignettes (Braaten & Rosen, 2000). With regard to prosocial behavior in ADHD, two studies indicate that in community samples, ADHD symptoms are negatively correlated with prosocial behavior (Diamantopoulou et al., 2005; Tseng et al., 2012). Interestingly, it has been argued that deficits in responding to emotions of others in children with ADHD are at least partially accounted for by the co-existence of DBD (Marton et al., 2009). Likewise, in boys with DBD, deficits might at least partially be related to ADHD.

Finally, it remains unclear whether empathy deficits in school-aged children and adolescents with DBD are already present at a younger age. Studies suggest that, compared to their typically developing peers, aggressive school-aged children and adolescents (Eisenberg et al., 2010; Miller & Eisenberg, 1988), but not preschoolers (Feshbach & Roe, 1968; Gill & Calkins, 2003), show less signs of affective empathy in response to stories (Feshbach & Feshbach, 1969) or to a distressed adult in a laboratory setting (Gill & Calkins, 2003). No systematic studies assessing empathy in clinical populations with ADHD and DBD in early school-aged children have yet been performed, while at this age, social demands in peer interactions rapidly increase.

The present study aimed to address these issues by (1) comparing parent and teacher reports of affective empathy in response to sadness and distress of others; (2) measuring affective empathy in response to sad vignettes; (3) assessing empathy induced prosocial behavior with a computer task, in a sample of 6-7 year old children with DBD or ADHD and a typically developing control (TD) group. Two lines of approach were followed. First, in a categorical approach, three groups were compared, i.e., children with DBD, children with ADHD, and typically developing children. Second, we assessed the influence of dimensions of DBD and ADHD within the spectrum of DBD en ADHD psychopathology. While comparing the clinical group (i.e., all children with a diagnosis) to the typically developing group, first the effect of DBD on empathy and prosocial behavior was examined with ADHD symptoms as a covariate, and second the effect of ADHD was examined with DBD symptoms as a covariate.

In keeping with previous studies in school-aged children and adolescents, we hypothesized that 6-7 year old children with a diagnosis of DBD or ADHD would show less parent and teacher reported affective empathic traits, less affective empathy in response to vignettes, and less empathy induced prosocial behavioral responses as compared to TD children. Furthermore, we hypothesized that children in the clinical group would show less empathy and prosocial behavior and that this difference would remain after controlling for ADHD symptoms, but not after controlling for DBD symptoms.

Methods

Participants

A sample of 103 (*) children aged six and seven years old with a previous clinical diagnosis of DBD and/or ADHD was recruited at the Outpatient Clinic of the Department of Child and Adolescent Psychiatry, University Medical Center Utrecht as part of a project on empathy in children with psychiatric disorders. Children were excluded from analysis in case a clinical diagnosis of ADHD or DBD could not be confirmed (n=3) in the parent version of the Diagnostic Interview Schedule for Children (DISC, module E) (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) or when they had an estimated IQ below 70 based on the vocabulary and block design subsets of the Wechsler Intelligence Scale for Children III-Dutch version (n=7) (Kort et al., 2005; Sattler, 1992). The sample of 93 children included 18 children who had taken methylphenidate on the day of testing, despite instructions to cease medication the day prior to assessment.

The TD group consisted of 37 children from regular elementary schools in the vicinity of Utrecht who did not meet criteria for a clinical diagnosis of ADHD or DBD on the DISC and had an estimated IQ within the normal range. The Medical Ethics Committee of the University Medical Center Utrecht approved the study protocol and parents gave written informed consent prior to participation.

Procedure

The parent version of the DISC interview (module E) was administered during a home visit by a trained interviewer. Parents also completed the Child Behavior Checklist 6-18 (CBCL) (Achenbach & Rescorla, 2001) and the Griffith Empathy Measure (GEM). Teachers completed the Teacher Report Form (TRF) and the GEM. The CBCL and TRF were used to quantify attention problems and rule-breaking/aggressive behavior.

All child data were collected in a quiet room at the children's own school. To assure participants were at ease, they first had a small talk with the experimenter and completed the two WISC-III subtests. Next, subjects were presented a facial mimicry paradigm (Deschamps, Schutte, Kenemans, Matthys, & Schutter, 2012), the Interpersonal Response Task, and the

Note:
(*) The total study sample described in this thesis consisted of 104 patients. In this chapter, one patient (with DBD only) was accidentally excluded from data-analysis. This did not affect the conclusions of this study (see footnote 2 and 3). Of the total sample of the remaining 103 children, children were excluded if: (a) a clinical diagnosis could not be confirmed (n=3); (b) their estimated IQ was below 70 (n=7). The final patient group for analysis comprised 93 children. This group included 18 children who had taken medication on the day of the testing (n=16 methylphenidate, n=2 atomoxetine).

Story Task. Between each task, a short break was allowed and children received a sticker as a reward upon completing each task as well as a small gift upon completing all tasks.

Measures

DISC

The parent version of the DISC (module E) (Shaffer et al., 2000) was used to distinguish patient groups. The patient group of 93 children consisted of children with ADHD without comorbid DBD (n=27), of children with DBD without a comorbid ADHD diagnosis (n=6) and of children with ADHD and DBD (n=60). In line with previous reports, comorbidity of ADHD and DBD in the clinical sample was high while the DBD only group was small (Bird, Gould, & Staghezza, 1993; Lahey, Miller, Gordon, & Riley, 1999). Because of the small sample size of the DBD-only group (n=6) in this study, we pooled children with DBD with ADHD (n=60) and children with DBD without comorbid ADHD (n=6) in one DBD group.

Griffith Empathy Measure

Empathy was measured using the Griffith Empathy Measure (GEM) (Dadds et al., 2007) which is a 23-item parent questionnaire adapted from Bryant's index of Empathy for children and adolescents. The GEM assesses both aspects of cognitive empathy (e.g., "My child doesn't understand why other people cry out of happiness") and affective empathy (e.g., "My child becomes sad when other children are sad", "My child gets upset when he/she sees an animal being hurt") using a 9-point Likert scale (-4 = strongly disagree; +4 = strongly agree). A higher total score represents a higher level of empathy. For the current study, we made a selection of questions relating to affective empathy in response to sadness and distress of others, and removed questions tapping cognitive empathy and empathy in response to other emotions. The GEM-AFFECTIVE-SADNESS scores consisted of 6 items; the Cronbach alpha for this scale for parents in our total study sample was 0.76. For teachers the Cronbach alpha for this scale was 0.82.

No GEM teacher data were collected for 8 children (4 TD, 2 ADHD, 2 DBD), because teachers did not return the forms.

Story Task

The story-narratives used were based on the classic Feshbach Affective Situation Test for Empathy (Feshbach & Roe, 1968). The task has been adapted to assess aspects of emotion recognition as well as affective empathy (affect match between the participant and protagonist in the stories) (Albiero & Coco, 2001). It consists of eight short stories in which the protagonist is involved in an event arousing angry, happy, sad, or fearful emotion. Each emotion is represented by two stories. The version presented to boys involves scenarios with a boy protagonist; the version for girls involves a girl.

In the present study, two sad stories were used. After each vignette, children were interviewed to assess whether they had been able to recognize and share the emotions depicted in the stories. Participants were asked how the protagonist felt (angry, happy, fearful, sad or neutral) and to what extent (a little, average, very much). They reported and indicated their responses on a card showing the emotional categories and intensity. Next the child was asked how he or she felt after listening to the story. Again, the child could choose between the five different emotions and the three intensity levels.

Levels of affect correspondence were evaluated on a four-point scale (0= the child did not report an affect match; 1=the child's emotion was similar to his or her report of the character's emotion; 2=the child's emotion was the same as the character's emotion but different in intensity; 3=both the child's emotion and the intensity were the same as the character's). This resulted in a continuous score for affect match in response to sadness computed by adding the scores on the two sad stories per emotion, ranging between 0 and 6 points.

Interpersonal Response Task

The Interpersonal Response Task (Dadds & Hawes, 2004) is a computer-based task that assesses a prosocial behavioral response of subjects to emotional stimuli in a social context. Subjects play a ball-throwing computer game against two computer-controlled players. Subjects are assigned to choose towards which of two computer-players they will play the ball. They are told that they will receive 'money' (score) for throwing the ball to a particular player, and that each player will show them their feelings through facial expression (photos). The game consists of three rounds. In the first round (10 trials), both computer-players keep a happy facial expression, regardless of whether the ball is passed to them or not. When subjects play the ball towards any of both players, they are displayed a coin rolling towards them on the computer screen with simultaneous sound of coins rolling. In the second round (10 trials), one of the players has run out of money and doesn't give money (no rolling coins or sound). This player continues to show a happy face even when the ball is not thrown to him. In the third round (20 trials), each time the ball is not passed to the player that has ran out of money, the player displays a progressively sad and distressed facial expression. In the current study we used an adapted version of the IRT; the task could be performed twice, once with a girl and once with a boy showing distressed facial expressions.

The number of times the participant throws the ball to the 'sad' player in the third round was the dependent variable in this game. This variable reflects empathy induced prosocial behavior in response to the increasing sadness and distress of the computer player that does not provide the child with a monetary reward. The variable yields a continuous score in which a higher score represents a higher sensitivity to sadness and distress and associated empathy induced prosocial behavior.

Data analysis

First, in a categorical perspective, three groups were compared: children with DBD+/-ADHD (n=66), children with ADHD (n=27), and TD children. Second, we compared the clinical group (n=93) (i.e., all children with a diagnosis) to the typically developing group, first the effect of DBD was examined controlling for ADHD symptoms, and second the effect of ADHD was examined controlling for DBD symptoms.

Statistical analyses were performed using PASW Statistics 18.0 (IBM Company, Chicago, Illinois). For the distribution of demographic variables between groups multiple one-way ANOVA's (i.e., age, IQ and SES) or Chi-Square tests (sex) were performed. First, to examine differences in parent and teacher rated empathy, analyses of variance (ANOVA) were conducted. Dependent variables were the GEM affective sad scores from parent and teacher reports. GROUP was entered as between subjects variable with three levels (DBD with or without ADHD, ADHD, and healthy controls). Statistical significant group differences were followed by simple contrasts, comparing healthy developing children to children with DBD and ADHD. Next, ANCOVA's were conducted to compare the GEM affective empathy scores in the overall patient group with the typically developing children (GROUP) with the parent and teacher reported attention and aggression symptom scores entered as covariates.

Second, to examine differences between groups in affect match in response to sadness in the Story Task, a nonparametric test was used as distributions of mean raw scores across subjects violated the assumptions of normality. To test for group effects, we performed Kruskal-Wallis tests.

Third, to examine differences in empathy induced prosocial behavior, ANOVA was performed with PROSOCIAL RESPONSE as dependent variable and GROUP as a between-subject factor. Statistical significant group differences were followed by simple contrasts, comparing TD children to children with DBD and ADHD. Next, ANCOVA's were conducted to compare the PROSOCIAL RESPONSE scores in the overall patient group with the typically developing children (GROUP) with the parent and teacher reported attention and aggression symptom scores entered as covariates.

In all tests, the alpha level of significance was set at < 0.05 (two-tailed) throughout.

Results

Descriptives

Table 1 shows the characteristics of the sample used for data analyses, separately for the DBD+/-ADHD group, the ADHD group and the TD group. Analyses presented in Table 1 demonstrate that children in the DBD+/-ADHD and ADHD groups contained fewer girls and had lower socio-economic status (SES) than children in the control group. As expected, the three groups differed significantly on attention problems and rule-breaking/aggressive behavior.

Since groups differed in SEX and SES, we first examined whether these variables were related to our outcome variable. The only significant association we retained was between the GEM parent report of affective empathy and SES. Thus SES was included as a covariate in further analysis for the GEM parent sadness scores.

Table 1. Descriptives

Characteristics	TD (*n*=37) *M (SD)*	ADHD (*n*=27) *M (SD)*	DBD+/-ADHD (*n*=66) *M (SD)*	F	Post hoc tests
Age	7.1 (0.5)	7.1 (0.7)	6.8 (0.6)	5.93*	(TD, ADHD)>DBD
Sex[1]	18/19	17/10	55/11	14.02*	
estimated IQ	110 (20)	103 (18)	102 (20)	2.10	
SES	7.0 (2.3)	5.4 (2.1)	5.6 (1.6)	7.14*	TD>(ADHD,DBD)
CBCL T score					
- Attention	52.6 (3.8)	66.4 (8.9)	67.2 (7.3)	58.02*	TD<(ADHD,DBD)
- Rule-breaking	52.9 (4.2)	56.4 (6.3)	62.1 (7.1)	27.97*	(TD,ADHD)<DBD
- Aggression	53.5 (5.5)	61.0 (8.5)	71.6 (8.6)	67.05*	TD<ADHD<DBD
TRF T score					
- Attention	51.9 (3.0)	59.1 (8.6)	60.8 (7.1)	21.90*	TD<(ADHD,DBD)
- Rule-breaking	51.0 (2.6)	54.5 (5.1)	58.6 (7.4)	19.60*	(TD,ADHD)<DBD
- Aggression	52.4 (3.9)	59.6 (5.6)	64.7(10.4)	26.15*	TD<ADHD< DBD

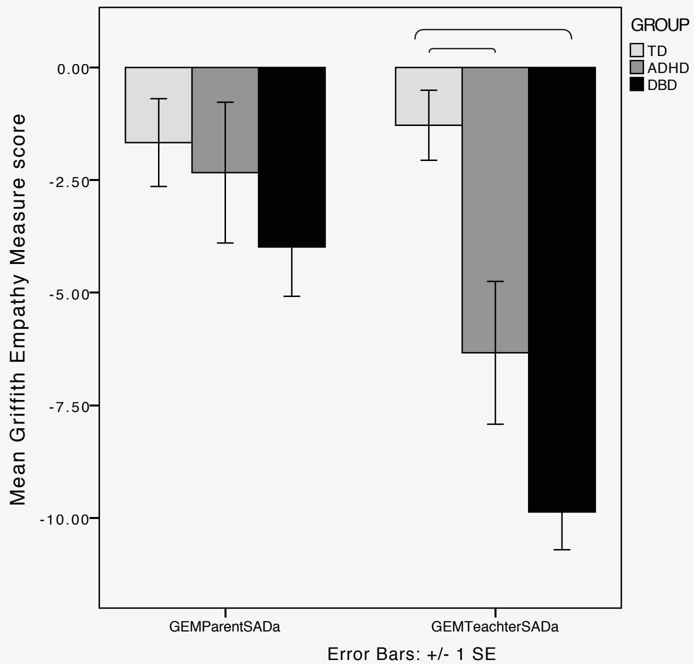
Note: TD= typically developing children; ADHD= ADHD without comorbid DBD; DBD= DBD+/-ADHD; 1: male/female; * p<.05

Griffith Empathy Measure

Results regarding the GEM SAD parent and GEM SAD teacher are demonstrated in figure 1.

For the GEM affective empathy in response to sadness reported by parents, the ANCOVA revealed a significant effect of SES ($p<0.005$). Results showed no significant between-group differences ($F(2,130)=0.98$, $p=0.38$).

Figure 1. Parent and teacher reported empathy in response to sadness/distress



Note: A significant difference was found between the DBD+/-ADHD and the TD group and between the ADHD and TD group for the GEM (Griffith Empathy Measure) Sadness teacher scores; brackets indicate significant differences between groups at the p<.05 level.

For teachers, results showed significant between-group differences ($F(2,122)=19.23$, $p<0.001$)(**). Follow-up analysis using simple contrasts showed that children with DBD+/-ADHD were rated as less empathic to sadness by their teachers compared to TD children ($p<0.001$). Likewise, children with ADHD were rated as less empathic to sadness by their teachers compared to TD children ($p<0.005$).

Next, analyses were conducted to examine the effect of GROUP (all patients versus typically developing children) on reported sadness by parents and teachers controlling for attention and aggression symptom scores respectively, reported by either parents (CBCL attention and CBCL aggression T scores) or teachers (TRF attention and TRF aggression T scores). For parents, no significant effect of GROUP was found in any of the ANCOVA's with the CBCL factors entered as covariate (all $p>.10$). For teachers, a significant effect of GROUP was found in an ANCOVA controlling for TRF attention ($p<0.001$) as well as in an ANCOVA controlling for TRF aggression symptoms ($p=0.001$)(**). Furthermore, an correlation was found between TRF aggression scores and teacher rated affective empathy ($p<0.005$).

Story Task

The Kruskal-Wallis test performed for affect match in response to sadness in the Story Task to examine whether TD children (Mean 2.54, SD 2.4) differed from children with ADHD (Mean 2.33, SD 2.7) and children with DBD+/-ADHD (Mean 2.38, SD 2.3) showed no significant group effect ($p=0.92$). An additional analysis in a subsample that excluded the children who did accidentally take methylphenidate medication on the day of the assessment showed similar results ($p=0.74$). Similarly, no differences were found comparing the overall patient group to the typically developing children ($p=0.75$).

Interpersonal Response Task

First, we entered sex of the computerized player as a within-subject factor (PLAYER GENDER), to explore differences between the tasks in which a boy or girl computer player showed sadness and distress. The ANOVA for PROSOCIAL RESPONSE did not reveal a significant effect of PLAYER GENDER ($p=0.86$). Thus, for our main analyses, the results from the boy and girl task were pooled.

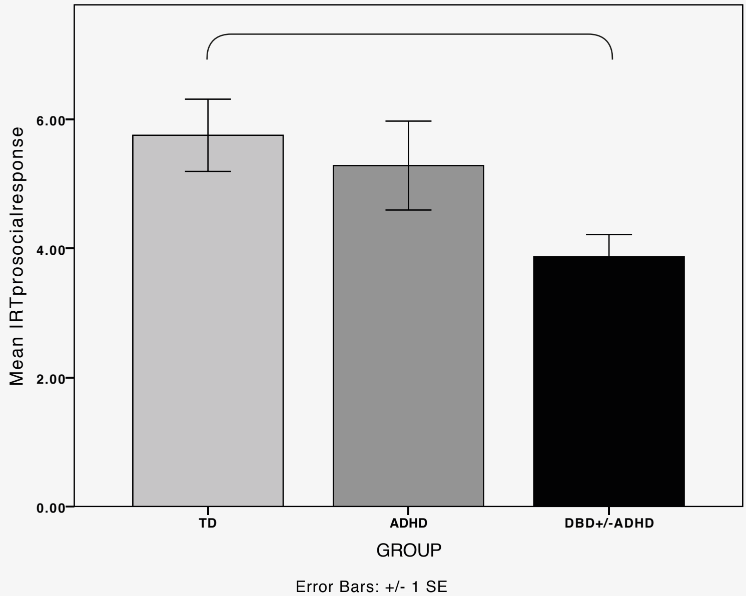
Results of the IRT are shown in figure 2. The ANOVA revealed a significant effect of GROUP ($F(2,126)=4.21$, $p<0.05$) on empathy induced prosocial behavior, indicating differences in scores between the three groups (***).

Note:

(**) The following significant results for n=103 were re-tested with n=104 (new p-values between brackets): GEM teacher overall effect ($p<0.001$); GEM teacher group effect in ANCOVA controlling for TRF attention ($p<0.001$) and in ANCOVA controlling for TRF aggression ($p<0001$).

(***) The following significant results for n=103 were re-tested with n=104 (new p-values between brackets): IRT overall group effect ($p<0.05$); IRT overall group effect in ANCOVA controlling for CBCL attention score ($p<0.05$) and TRF attention score ($p<0.05$).

Figure 2. Mean prosocial response on the IRT task



Note: A significant difference was found between the DBD+/- ADHD and the TD group but not between the ADHD and TD group on the IRT (Interpersonal Response Task); brackets indicate significant differences between groups at the p<0.05 level.

Further analysis using simple contrasts showed that children with DBD+/-ADHD scored significantly lower than TD children (p=0.01). Children with ADHD-only did not show significant differences in empathy induced prosocial behavior when compared to TD children (p=0.78). An additional ANOVA in a subsample that excluded the children who took methylphenidate medication on the day of the assessment showed similar results (effect of GROUP p<0.05, contrast ADHD versus TD p=0.95, contrast DBD+/-ADHD versus TD p< 0.05).

Next, two analyses were conducted to examine the effect of GROUP (all patients versus typically developing children) on prosocial response controlling for attention and aggression symptom scores respectively, reported by either parents (CBCL attention and CBCL aggression T scores) or teachers (TRF attention and TRF aggression T scores). The ANCOVA controlling for CBCL Attention scores (p<0.05) as well as the ANCOVA controlling for

TRF Attention scores (p=0.05) revealed a significant effect of GROUP, whereas the ANCOVA controlling for CBCL Aggression scores as well as the ANCOVA controlling for TRF Aggression scores did not show a significant GROUP effect (both p>0.05).

Discussion

The present study of empathy differs from other studies in that empathy was examined in relation to sadness and distress, while empathy induced prosocial behavior in response to sadness and distress was assessed as well. Teachers reported impairments in affective empathy in response to sadness and distress in 6-7 year old children with DBD with and without ADHD as well as in children with ADHD without a comorbid DBD diagnosis. Furthermore, children with DBD with and without ADHD were impaired in observed empathy induced prosocial behavior in response to sadness and distress. Children with ADHD only, however, did not differ from TD children in prosocial behavior. An additional analysis comparing the clinical group (i.e., all children with a diagnosis) with the TD group revealed that the difference in prosocial behavior remained when controlling for ADHD symptoms but not when controlling for DBD symptoms.

Most studies on empathy in children with aggressive behavior thus far have focused on a theory that underlines the role of sharing of sadness and distress in the inhibition of aggressive behavior (Blair, 1995; Blair et al., 1997). The present study showed that children with disruptive and aggressive behavior indeed have problems in sharing sadness and distress at school. Findings of the present study, however, suggest that we not only should consider the putative role of empathy in inhibiting aggression, but that we also should pay attention to the role of empathy in the induction of prosocial behavior (de Waal & Suchak, 2010; Eisenberg et al., 2010). Notably, the latter notion seems to be a neglected target of interventions in children with DBD (Eisenberg et al., 2010). Interventions to ameliorate peer relationships in children with disruptive behavior may consider targeting not only on decreasing aggressive behavior, but also on increasing empathy induced prosocial behavior.

Furthermore, the present study aimed to examine whether previously reported empathy deficits in older school-aged children and adolescents with DBD would already be present at a younger age. First, with regard to empathic traits assessed with questionnaires, we found impaired teacher rated empathy. It should be noted that all previous studies in school-aged children and adolescents with DBD have used self-report questionnaires of empathic traits (Anastassiou-Hadjicharalambous & Warden, 2008; Cohen & Strayer, 1996; de Wied et al., 2005). Since the ability of young children to reliably report on their empathic traits using questionnaires has been questioned (Dadds et al., 2007), in the present study in young children parent as well as teacher reports were obtained, which complicates comparison with previous reports. Second, we found intact affective empathy in response to vignettes whereas impairment was found in studies in older school-aged children (Anastassiou-Hadjicharalambous & Warden, 2008; de Wied et al., 2005; Schwenck et al., 2012) and adolescents (Cohen & Strayer, 1996; de Wied et al., 2012) with DBD. The finding of the present study regarding reported affective empathy in children with DBD seems to be in line with the observation that the association of empathy and antisocial behavior in children is most consistent when empathy is measured using questionnaires (i.e., dispositional empathy), but not using experimental paradigms (i.e., measures of situational empathy) (Eisenberg et al., 2010; Lovett & Sheffield, 2007). In addition, the inverse relations between empathy and aggression have been proposed to become stronger with age (Eisenberg et al., 2010; Lovett & Sheffield, 2007). Finally, since throughout development into late childhood and adolescence, symptoms of DBD are known to persist in certain, and decline in other children (Frick & Loney, 1999; Lahey et al., 1995), our sample might have included children with less severe psychopathology. Attention and aggression assessed with CBCL and TRF symptom checklists in the present study indeed were lower as compared to those in some previous studies (de Wied et al., 2005).

The difference between parent and teacher reported empathy in response to sadness and distress in DBD is not easy to interpret. In the study of child and adolescent psychopathology and related constructs, discrepancies often arise among multiple informants' reports and yield important information regarding where children express behaviors (De Los Reyes, 2011).Teachers typically supervise a large group of children simultaneously, whereas parents will have much more one on one interaction with their children. Possibly, school settings are socially more demanding and therefore putative impairments in empathy become more manifest in the school environment.

Children with ADHD without comorbid DBD showed impaired empathy in response to sadness and distress according to their teachers but not according to their parents. The absence of parent reported deficits in empathy in ADHD is consistent with a study in older children that showed that children with ADHD were rated to be less empathic than controls by their parents, but differences between children with ADHD and controls in that study were exclusively explained by comorbid conduct problems (Marton et al., 2009). In the present study, however, teacher rated affective empathy deficits were present in the ADHD group without a comorbid DBD diagnosis and persisted after controlling for conduct problems. This seems to suggest that in young ADHD children, empathic responding to sadness and distress of peers is impaired regardless of conduct problems, but only in a socially highly demanding school setting. This converges with our finding that ADHD, in contrast to DBD, was not associated with reduced empathic responding to sadness and distress and subsequent prosocial behavior in a setting where the interaction with only one peer in a quiet environment was simulated. Mainly in a socially demanding school setting, the core pattern of inattention and/or hyperactivity-impulsivity seems to influence social functioning and rejection by peers that have been associated with ADHD (Hoza et al., 2005; Mrug, Hoza, & Gerdes, 2001).

Finally, several limitations should be noted. First, most of DBD children had ADHD symptoms, and we did not succeed in including a large enough group of DBD only children to reliably distinguish DBD with comorbid ADHD from DBD only children. Therefore, an additional analysis was conducted comparing the clinical group (i.e., all children with a diagnosis) and the TD group taking the impact of both symptom-clusters into account. Second, the affective empathy dimension of the Story Task showed low affect correspondence in all groups. The lack of a group difference on this measure may have been driven by the fact that the task did not sufficiently lead to an affective empathic response in this age group. It has been proposed that the hypothetical character of most experimental paradigms such as the Story Task as well as the rapid changes in affective content, together with the probability of social desirable answers, limits the validity to detect affective empathy deficits using these paradigms (Miller & Eisenberg, 1988). Third, the IRT we applied to assess empathy induced prosocial behavior is a complex measure, the outcome most likely to be related not only to empathy, but also to several other relevant processes including the specific context (e.g., monetary versus social reward). For example, evidence has been provided showing that empathic healthy children tended to benefit more from social reward than monetary reward on an outcome measure of response inhibition (Kohls, Peltzer, Herpertz-Dahlmann, & Konrad, 2009). Further study is needed to examine whether decreased prosocial responses in DBD children are accounted for by an increased dependency on monetary reward.

In conclusion, findings of impaired empathy induced prosocial behavior in response to sadness and distress in young children with DBD suggest that interventions to ameliorate peer relationships in these children could benefit from targeting on increasing empathy induced prosocial behavior.

Acknowledgements

The authors would like to thank Arne Popma and Koen van Lith for their kind assistance in the data collection.

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Chapter 5

Empathy in response to sadness and distress, and proactive aggression in early school-aged children

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Abstract

Empathy in response to sadness and distress of others may be relevant for the course of proactive aggressive behavior. In the present study at baseline (T1) and 12 months later (T2) parents and teachers completed the Instrument for Reactive and Proactive Aggression in 6-7 year old children (n=150). At T1, parents and teachers reported empathy in response to sadness and distress on the Griffith Empathy Measure. Empathy was also assessed using three experimental paradigms: child-report of empathy to sad vignettes, empathy-induced prosocial behavior during a computer game, and facial mimicry in response to sad facial expressions. At T1, findings showed that low levels of parent-reported empathy, but not empathy assessed with any of the three experimental paradigms, was associated with high parent-reported proactive aggression. Similarly, only teacher-reported empathy was negatively related to teacher-reported proactive aggression. At T2, a higher level of parent-reported empathy at T1 was associated with a relatively larger decrease in parent-reported proactive aggression at T2. In conclusion, low empathic traits in response to distress of others were cross-sectionally associated with high proactive aggression according to the same informant and predicted change in proactive aggression. This is of interest to the development of new treatment paradigms.

Keywords

empathy, proactive aggression, children

Aggression is behavior deliberately aimed at harming people (Lovett & Sheffield, 2007; Parke & Slaby, 1983). The lack of empathy, that is the sharing and understanding of others' feelings, is one of the many factors that have been shown to be associated with aggression (see for a review Eisenberg 2010). It has been proposed that empathy decreases aggression, because the victim's pain and distress induce similar feelings in the aggressor, and inhibit further aggressive behavior (Blair, 1995; Blair, Jones, Clark, & Smith, 1997; Katsuma & Yamasaki, 2008). Thus, children witnessing sadness or distress in another person as a result of their own behavior are thought to become distressed themselves and stop harming the other in order to reduce their personal distress (Kimonis, Frick, Fazekas, & Loney, 2006; Pouw, Rieffe, Oosterveld, Huskens, & Stockmann, 2013). Numerous studies have examined impairments in empathy of children and adolescents with aggressive behavior, such as those diagnosed with a disruptive behavior disorder (DBD) (e.g. Anastassiou-Hadjicharalambous & Warden, 2008; Cohen & Strayer, 1996; de Wied, Goudena, & Matthys, 2005; de Wied, van Boxtel, Matthys, 2012; Jolliffe & Farrington, 2011; Schwenck et al., 2012; Steffgen, Konig, Pfetsch, & Melzer, 2011). These cross-sectional studies sometimes found a negative association between empathy and aggression, indicating that a lack of empathy was indeed related to high levels of aggressive behavior among children. However, these findings are inconclusive in four ways. First, the strength of this association ranged from low to moderate, depended on the methods used to study both aggression and empathy, and the association was more consistent in adolescence than in (early) childhood (Eisenberg, Eggum, & Di Giunta, 2010; Lovett & Sheffield, 2007; Miller & Eisenberg, 1988; Polman, Orobio de Castro, Thomaes, & van Aken, 2009). Second, there was a wide variety in the exact nature of empathy and the type of emotions (e.g. distress versus happiness) leading to an empathic response. Third, likewise the nature of aggression or behavior problem studied varied between studies. Finally, these cross-sectional studies did not elucidate whether empathy actually plays a role in changes in aggressive behavior over time. In order to examine the role of empathy in the course of aggressive behavior, a longitudinal design is needed as well as further refinement in subtyping of both empathy and aggression (Eisenberg et al., 2010; Pouw et al., 2013).

Empathy is a complex construct that has been studied on several levels and consists of an emotional (i.e., experiencing another's emotional state) and a cognitive component (i.e., understanding another's emotional state) (Dadds et al., 2008; de Waal, 2008; Lovett & Sheffield, 2007). A further distinction has been made between empathy in a specific context directed at a specific individual or individuals (situational or state) on the one hand, and dispositional empathy (trait), on the other (Dustin Pardini, 2013; Eisenberg et al., 2010). Dispositional, rather than state empathy seems most consistently related to aggressive behavior when questionnaires are used to assess empathic traits and aggressive behavior (Eisenberg et al., 2010; Frick, 2009). In order to study situational empathy-related responding, experimental paradigms have been designed to evaluate the understanding of another's emotional state (cognitive empathy, CE), elicit emotional responses (affective empathy, AE), and empathy induced behavior (Eisenberg & Miller, 1987; Lovett & Sheffield, 2007; Pardini, Lochman, & Powell, 2007). In these paradigms children typically are exposed to either someone feigning expressing distress (e.g., Carrasco, Barker, Tremblay, & Vitaro, 2006; Fabes, Eisenberg, Karbon, Troyer, & Switzer, 1994; Knafo, Zahn-Waxler, Van Hulle, Robinson, & Rhee, 2008; Zahn-Waxler & Radke-Yarrow, 1992) or a film/video/picture depicting emotion inducing events or emotional expressions of others (e.g., Achenbach & Rescorla, 2001; Eisenberg, Fabes, Miller, Shell, & Shea, 1990; Holmgren, Eisenberg, & Robin, 1998). In response to these situations and stimuli, either empathic emotions are reported by the children themselves, children's behavioral responses are observed, or facial and physiological responses are recorded. The study of empathy and aggression using these experimental paradigms, however, has provided more mixed results than questionnaire data (Eisenberg et al., 2010; Kort et al., 2005; Sattler, 1992). To clarify these inconsistencies, a multi-dimensional approach deploying measures of state as well as trait empathy in response to sadness and distress of others is needed.

When studying empathy in relation to aggression it seems particularly relevant to distinguish differences in the various forms of aggression (the 'whats' of aggressive behavior) from differences in the underlying motivation of aggression (or the 'whys' of aggressive behavior) (Little, Henrich, Jones, & Hawley, 2003). Thus, physical, verbal, and relational aggression (Crick & Grotpeter, 1995; Dadds et al., 2007) may be considered different forms of aggression. Here we are particularly interested in differences in the underlying motivation of aggression. In this respect, a distinction has been made between reactive and proactive aggression (for reviews see Dodge, Pepler, & Rubin, 1991; Feshbach & Roe, 1968; Kempes, Matthys, de Vries, & van Engeland, 2005; Vitaro, Brendgen, & Barker, 2006); these two types of aggression refer to different functions of aggression (Albiero & Coco, 2001; Little et al., 2003). Reactive aggression is an impulsive aggressive response to a frustration, a perceived threat, or a provocation. On the other hand, proactive aggression is controlled aggressive behavior in anticipation of a reward. Reactive aggression also has been called defensive or 'hot-blooded' aggression whereas proactive aggression has been called instrumental or 'cold-blooded' aggression (for a review see Kempes et al., 2005). Although reactive aggression and proactive aggression have appeared to be highly correlated when confounded in measures, they are independent or modestly related in observational studies or when a distinction was made between the form and the function of aggression (Dadds & Hawes, 2004; Polman, Orobio de Castro, Koops, van Boxtel, & Merk, 2007).

Several studies have tried to refine the association between empathy and aggression by looking into the specific functions of aggression. Theory proposes that empathy would be more likely to inhibit proactive aggression than reactive aggression (Lovett & Sheffield, 2007). In short, it is not very likely that a reactive and impulsive aggressive response to a threat or frustration is inhibited by empathic feelings induced by the observation of sadness and distress of the other. On the other hand, the experience or anticipation of empathic feelings upon proactive and controlled aggressive behavior are more likely to inhibit further proactive aggressive behavior. A number of studies seem to support this hypothesis. In a community sample of elementary school children (grades four to six), children who reported they were proactive-relationally aggressive felt fewer empathy responses in hypothetical-conflict-situation vignettes compared with non-aggressive children (Katsuma & Yamasaki, 2008). Similarly, in another study among 50 non-referred girls and boys (mean age 9 years) there was a significant association between proactive aggression and reduced responsiveness to distressing stimuli (Kimonis et al., 2006). In further support of the association between empathy and proactive aggression, some have concluded that proactive aggression in the form of bullying is associated with lower levels of empathy (e.g. Jolliffe & Farrington, 2011; Steffgen et al., 2011). However, in a community sample of 10-13 year old children, teacher-reported reactive aggression was negatively associated with self-reported empathy in response to sadness, but surprisingly proactive aggression was not (Polman et al., 2009). Another study in 9-14 year old typically developing children failed to show an association between self-reported empathy and proactive aggression, although lower levels of perspective taking and Theory of Mind were associated with self-reported proactive aggression (Pouw et al., 2013).

Thus, although some preliminary support has been found for a specific cross-sectional association between deficits in empathy in response to sadness and distress, and proactive aggression, a general conclusion based on the existing literature remains difficult due to variations in the operationalization and assessment of both empathy and aggression. Importantly, while theory predicts a specific role for empathy in response to sadness and distress of others, rather than to other emotions (e.g., happiness and anger) in general, not all studies have specified empathy in response to sadness/distress of others. Thus, an examination of the specific relation between empathy to distress and proactive aggression is called for.

Longitudinally, no studies have directly investigated the role of empathy in the persistence or course of aggression (Lovett & Sheffield, 2007). There is, however, some indirect evidence from studies in children high on callous-unemotional traits (CU-traits), a concept that has been included as a specifier in the DSM-5 (American Psychiatric Association, 2013) labeled as limited prosocial emotions and that includes callousness and a lack of empathy and guilt (Pardini et al., 2013). Children and adolescents with CU traits tend to show aggression that is both reactive and proactive, while children and adolescents without CU traits tend to show less aggression overall, and when they do show aggressive behavior, it tends to be largely reactive in nature (Frick et al., 2009). Characteristics of a callous and unemotional interpersonal style were found to be relatively stable across a 1-year period in fifth graders followed over a 1-year period and predicted increases in aggressive behavior over time (Pardini et al., 2007). In addition, Carrasco, Barker, Tremblay, and Vitaro (2006) found that boys with high, stable trajectories for physical aggression or vandalism (but not theft), compared to those with low, declining trajectories, had lower scores on empathy questionnaires (Carrasco et al., 2006). Based on theoretical considerations and the aforementioned studies, empathy in response to sadness and distress of others can be hypothesized to play a role in the change of proactive aggressive behavior over time.

The aim of the present study was to examine empathy in response to sadness and distress and its relation to proactive aggression in 6-7 year old children. First, we examined the cross-sectional association between empathy in response to sadness and distress of others and proactive aggression reported by parents as well as teachers. Empathy was assessed with a wide variety of measures including (a) parent and teacher reported traits of empathy in response to sadness and distress, (b) self-reported affective empathy in response to sad story vignettes, (c) empathy-related prosocial behavior in response to sadness during a computer task, and (d) facial mimicry responses to sad emotion facial expressions. We expected a high level of empathy in response to sadness and distress of others to be associated with a low level of proactive aggressive behavior. Second, the role of empathy in response to sadness and distress of others in the change of proactive aggressive behavior over time was examined. We expected a high level of empathy to be associated with a larger decrease in proactive aggression.

Methods

Participants

The total study sample consisted of 150 children aged 6-7 years, 70 percent boys, with an average estimated IQ of 105. In order to obtain a study sample with sufficient variance in proactive aggressive behavior, we recruited children referred to an Outpatient Clinic for disruptive behavior disorders at the Department of Child and Adolescent Psychiatry, University Medical Center Utrecht (n=106). Furthermore we recruited 47 children from regular elementary schools in the vicinity of Utrecht. Parents completed the Child Behavior Checklist 6-18 (CBCL) and teachers completed the Teacher Report Form (TRF) (Achenbach & Rescorla, 2001) as general dimensional measures of aggressive behavior (CBCL aggression symptom t-score Mean 63.54, SD 11.13, TRF aggression symptom t-score Mean 59.66, SD 9.43).The Medical Ethics Committee of the University Medical Center Utrecht approved the study protocol and parents gave written informed consent prior to participation.

Procedure

At baseline (T1) parents were asked to complete the CBCL and teachers to complete the TRF (see Measures). Both completed the Griffith Empathy Measure (GEM) and the Instrument for Reactive and Proactive Aggression (IRPA). All child data were collected in a quiet room at the children's own school. To assure participants were at ease, they first had a small talk with the experimenter and completed two WISC-III subtests (vocabulary and block design) (Kort et al., 2005; Sattler, 1992). Next, participants were presented a facial mimicry paradigm (Deschamps et al., 2012), the Interpersonal Response Task (IRT), and the Story Task (ST). Between each task, a short break was allowed and children received a sticker as a reward upon completing each task as well as a small gift upon completing all tasks. At follow-up (T2) 12 months later, parents from 124 children (83%) and teachers from 109 children (73%) completed the IRPA questionnaires.

Measures

IRPA

The Instrument for Reactive and Proactive Aggression (Polman et al., 2008) was designed to assess forms and functions of aggression. Parents and teachers rated the frequency of 3 form scales of aggression over the period of a month. The 3 form scales concerned physical, verbal and covert aggression. Ratings were scored on a 5-point scale (0 = never, 1 = once or twice, 2 = weekly, 3 = several times a week, 4 = daily). In case of a score on a form-item of 1 or higher, teachers also rated 7 aggression functions for the specific aggressive behavior. Function-items consisted of 4 proactive items (to get something he/she wanted, to hurt someone or to be mean, to be the boss, because this child takes pleasure in it), and 3 reactive items (because someone teased or upset him/her, because this child felt threatened by someone, because this child was angry). These items were rated on a 5-point scale (0 = never, 1 = rarely, 2 = sometimes, 3 = most of the time, 4 = always). In case of a null-score on a form-item, function-items were coded as 0. A high score on a proactive function means that if this child behaves aggressively, it is often with a proactive function. Seven function-scores were computed by aggregating functions over forms. Total scores for proactive and reactive aggression were calculated by taking the average of the relevant items.

GEM

Empathy was measured using the Griffith Empathy Measure (Dadds et al., 2007) which is a 23-item parent questionnaire adapted from Bryant's index of Empathy for children and adolescents. The GEM assesses both aspects of CE (e.g., "My child doesn't understand why other people cry out of happiness.") and AE (e.g., "My child becomes sad when other children are sad", "My child gets upset when he/she sees an animal being hurt") using a 9-point Likert scale (-4 = strongly disagree; +4 = strongly agree). A higher total score represents a higher level of empathy. For the current study, we selected the questions relating to empathy in response to sadness and distress of others, and removed questions tapping empathy in response to other emotions. We also adapted the scale to a teacher scale, selecting items applicable to classroom or school situation. The GEM-SADNESS scores for parents consisted of 15 items; the Cronbach's alpha for this scale was 0.85. The GEM-SADNESS scores for teacher consisted of 13 items; the Cronbach's alpha for this scale was 0.87.

ST

The story-narratives used were based on the classic Feshbach Affective Situation Test for Empathy (Feshbach & Roe, 1968). The task has been adapted to assess aspects of CE (understanding and decoding of the events in the stories) as well as AE (affect match between the participant and protagonist in the stories) (Albiero & Coco, 2001), and it consists of eight short stories in which the protagonist is involved in an event arousing angry, happy, sad, or fearful emotion. Each emotion is represented by two stories. The version presented to boys involves scenarios with a boy protagonist, whereas the version for girls involves a girl.

In the present study, only the two sad stories were used as we were specifically interested in the relationship between empathy in response to sadness/distress. After each vignette, children were interviewed to assess whether they had been able to recognize and share the emotions depicted in the stories. Participants were asked how the protagonist felt (angry, happy, fearful, sad, or neutral) and to what extent (a little, average, very much). They reported and indicated their responses on a card showing the emotional categories and intensity. Next the child was asked how he or she felt after listening to the story. Again, the child could choose between the five different emotions and the three intensity levels.

Levels of affect match were evaluated on a four-point scale (0= the child did not report an affect match; 1=the child's emotion was similar to his or her report of the character's emotion; 2=the child's emotion was the same as the character's emotion but different in intensity; 3=both the child's emotion and the intensity were the same as the character's). This resulted in a continuous score for affect match in response to sadness computed by adding the scores on the two sad stories per emotion, ranging between 0 and 6 points. Since the scores were not normally distributed and scores of 0 (no affect match) were overrepresented in the sample, we dichotomised the continuous score to 0 (no affect match) or 1 (any report of affect match).

IRT

The IRT (Dadds & Hawes, 2004) is a computer-based task that assesses a prosocial behavioral response of subjects to emotional stimuli in a social context. Participants play a ball-throwing computer game against two computer-controlled players. Subjects are assigned to choose towards which of two computer-players they will play the ball. They are told that they will receive 'money' (score) for throwing the ball to a particular player, and that each player will show them their feelings through facial expression. The game consists of three rounds. In the first round (10 trials), both computer-players keep a happy facial expression, regardless of whether the ball is passed to them or not. When subjects play the ball towards any of both players, they are displayed a coin rolling towards them on the computer screen with simultaneous sound of coins rolling. In the second round (10 trials), one of the players has run out of money and doesn't give money (no rolling coins or sound). This player continues to show a happy face even when the ball is not thrown to him. In the third round (20 trials), each time the ball is not passed to the player that has ran out of money, the player displays a progressively sad and distressed facial expression. In the current study we used an adapted version of the IRT. The task was performed twice, once with a girl and once with a boy showing distressed facial expressions.

As dependent variable for this study we used the number of times the participant throws the ball to the 'sad' player in the third round. This variable reflects empathy induced prosocial behavior in response to the increasing sadness and distress of the computer player who does not provide the child with a monetary reward. The variable yields a continuous score in which a higher score represents a higher sensitivity to sadness and distress and associated empathy induced behavior.

Facial mimicry

Film clips with dynamic emotional facial expressions were used in the present study (Deschamps et al., 2012). In these film clips, each with a total duration of 6400 ms, five different children (two boys and three girls) expressed anger, sadness, fear and happiness. In total 16 movie clips (4 children x 4 emotions) were presented, once in a semi-random sequence in a first block, and once in a semi-random sequence in a second block. The size of the pictures was 21.5 cm height by 16 cm wide. They were viewed from a distance of 95 cm. Furthermore, during the task, there were four trials in which a cartoon character was presented during an emotional film clip. Children were instructed to push a response button when the character appeared on screen in order to maintain the child's attention to the faces. The data collected during these trials and during the four familiarization trials were excluded from further analyses.

Facial electromyographic (EMG) activity was recorded from bipolar montages from the corrugator supercilii (corrugator), zygomaticus major (zygomaticus), frontalis medialis (frontalis) and depressor anguli oris (depressor), according to the guidelines given by Fridlund and Cacioppo (Fridlund & Cacioppo, 1986; Parke & Slaby, 1983). Ag-AgCl electrodes with a diameter of 4 mm, filled with conductive electrode gel (Signa gel, Parker Laboratories, Inc., Fairfield, New Jersey, U.S.A.), were placed on the left side of the face to obtain maximal reactions (Blair, 1995; Blair et al., 1997; Dimberg & Petterson, 2000). Raw EMG recordings were made with the ActiveTwo system (BioSemi, Amsterdam, The Netherlands) relative to the common mode sense (CMS). The ground consisted of the active CMS and passive driven right leg (DRL) electrode placed on the scalp that form a feedback loop driving the subject's average potential as close as possible to the analog-to-digital converter (i.e., the amplifier "zero") reference voltage in the A/D-box. The EMG signal was sampled at 2048 Hz.

EMG signals were filtered offline (high-pass 20 Hz, 48dB/octave) and full wave rectified using Brain Vision Analyzer Software (Brain Products GmbH, Munich). Trials that included marks of visual inattention were excluded from further analysis (average ± SD percentage of trials removed per participant, 3.27 ± 3.97). Raw EMG data were segmented into 100 ms epochs. All values were expressed as a percentage of individual baseline activity, defined as the mean activity during 1600 ms neutral facial expression preceding onset of the morph. Averaged activity during the interval starting 500 ms after the beginning of the morphed dynamic expression and ending 500 ms after the beginning of the static expression at the end of the morphed clip was used for further analyses (total time 1600 ms). For each site, data from trials with change scores were calculated across the 1600 ms period. Activity that exceeded 3 SD above the grand mean change score of the emotion condition were marked as outliers and excluded from further analysis (Larsen & Norris, 2009; Pouw et al., 2013). Mean EMG responses as expressed in percentage change from baseline activity were calculated for each emotion-muscle combination (averages of all stimuli for that emotion-muscle combination in the two blocks).

Based on previous research (Anastassiou-Hadjicharalambous & Warden, 2008; Cohen & Strayer, 1996; de Wied et al., 2005; 2012; Deschamps et al., 2012; Schwenck et al., 2012), a sad facial EMG total composite score was calculated for the absolute mimicry response to sad facial expressions. The total sad score (EMG-SAD) consisted of the positive change in frontalis and corrugator activity in response to sad facial expressions.

Statistical analysis

Bivariate correlations were calculated between all variables measured at T1 using IBM SPSS 20.0 (IBM Company, Chicago, Illinois). Next, to examine the effects of different measures of empathy on the change in proactive aggressive behavior over time, stepwise regression analyses of proactive aggression at T2 on empathy were used, controlling for both proactive and reactive aggression at T1 using Mplus (version 7; Muthén & Muthén, 1998-2012). To reduce the number of statistical tests, predictors of change in aggressive behavior over time were selected based on the correlations at T1. Indicators of empathy that were significantly correlated to proactive aggression at T1 were used as predictors of the change in aggressive behavior over time. For consistency, predictors in parent and teacher models were the same. MLR was used as an estimator in these analyses, since it is robust to non-normality (Muthén & Muthén,1998-2012). To deal with missing data, wave 1 variances were estimated (Enders, 2010).

Results

Correlations between different measures of empathy and proactive aggression at T1

To examine the associations between different indicators of empathy and proactive aggressive behavior, bivariate correlations were estimated at T1. Table 1 shows correlations for different indicators of empathy and both parent- and teacher-reports of proactive aggressive behavior. Parent-reported empathy in response to sadness and distress was negatively correlated with parent-reported proactive aggression. The correlations between the other indicators of empathy, which were measured using experimental paradigms among children themselves, and parent-reported proactive aggression were not significant. Finally, the positive correlation between parent-reported empathy and the child's prosocial response on a computerized task was significant, but no other significant correlations were

Table 1. Bivariate correlations between measures of proactive and reactive aggressive behavior (reported by parent and teacher) and different measures of empathy at wave 1.

	IRPA Proactive Aggr.	IRPA Reactive Aggr.	GEM Trait empathy	IRT Prosocial behavior	EMG Facial mimicry	ST Empathic report
IRPA Proactive Aggr.		.22*	-.33*	-.11	-.10	-.10
IRPA Reactive Aggr.	.17		-.05	-.04	-.04	.02
GEM Trait empathy	-.44*	-.01		.16*	-.08	.04
IRT Prosocial	-.06	-.08	.07		.02	-.03
EMG Facial mimicry	.05	.12	-.04	.02		-.09
ST Empathic report	-.13	-.04	-.03	-.04	-.13	

Note. * p<.05, Correlations above the diagonal represent the correlations between parent-reported proactive and reactive aggression, trait empathy and the child's prosocial behavior, facial mimicry, empathic report, whereas under the diagonal correlations between teacher reports and child behavior are presented. IRPA: Instrument for Reactive and Proactive Aggression; GEM: Griffith Empathy Measure; IRT: Interpersonal Response Task; EMG: electromyography; ST: Story Task.

found between parent-reported empathy, empathy assessed with the ST, the IRT, and facial mimicry in response to sadness. Parent-reported proactive aggression and parent-reported reactive aggression were correlated. As expected, parent-reported reactive aggressive behavior was not significantly correlated with any of the empathy measures.

Among teachers, a significant negative correlation between teacher-reported empathy in response to sadness and distress and proactive aggressive behavior was found. All other correlations with teacher-report measures were non-significant.

Associations between empathy and change in proactive aggression

Parent-reported mean-levels of proactive aggression decreased from M_{wave1}=0.77 to M_{wave2}=0.68, and also among teachers mean-levels of proactive aggression decreased from M_{wave1}=0.67 to M_{wave2}=0.64. The 12 month stability of proactive aggression was moderate, r=.49, p<.001 among parents and r=.37, p<.001 among teachers (Cohen, 1988).

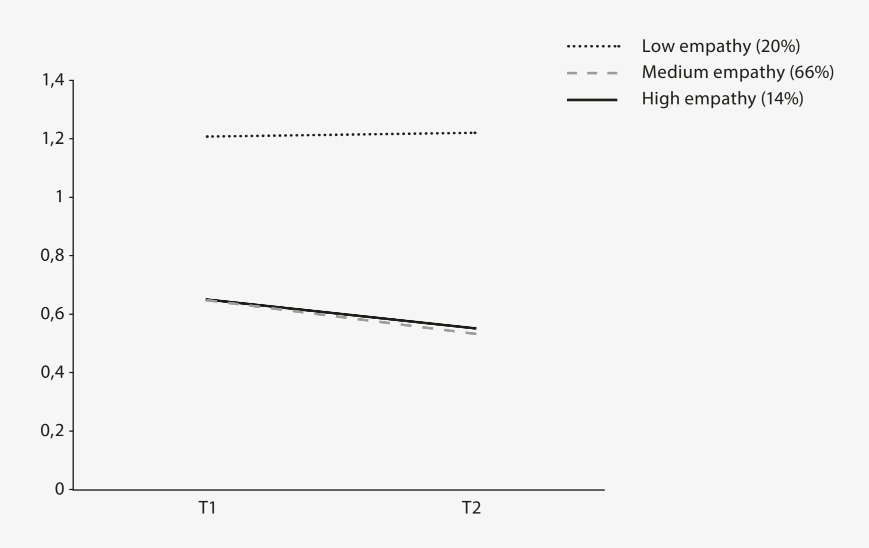
Stepwise regression analyses were used to examine the predictive value of the different measures of empathy for the development of proactive aggression over time. Based on correlations at wave 1, parent-reported trait empathy and parent-reported reactive aggression were used to predict change in proactive aggression over time. Gender and IQ were not included in the models as they did not significantly predict change in proactive aggression in both parent and teacher models. Table 2 shows the results for parent-reports of proactive aggressive behavior. In the first step, parent-reported proactive and reactive aggression at T1 were entered. Results showed that only proactive aggression at T1 was a

Table 2. Stepwise regression model predicting the development in *parent-reported* proactive aggressive behavior over time.

	β	p-value	R2
Model 1			.250
IRPA Proactive aggression T1	0.47*	<.001	
IRAP Reactive aggression T1	0.09	.273	
Model 2			.320
IRPA Proactive aggression T1	0.39*	<.001	
IRPA Reactive aggression T1	0.09	.220	
GEM Parent-reported trait empathy	-0.27*	.001	

Note. * p<.05, IRPA: Instrument for Reactive and Proactive Aggression; GEM: Griffith Empathy Measure significant predictor of proactive aggression at T2, indicating that more proactive aggression at baseline was associated with more proactive aggression at follow-up. In the second step, parent-reported empathy was entered to the model. Parent-reported empathy in response to sadness and distress was predictive of the change in proactive aggression over time, B = -.27. The negative association between parent-reported empathy and proactive aggression at T2 after controlling for proactive aggression at T1 indicates that a higher level of parent-reported empathy in response to sadness and distress at baseline was associated with a relatively larger decrease in parent-reported proactive aggression at follow-up. The increase in explained variance due to the indicators of empathy was 7%.

Figure 1 Means of parent-reported proactive aggression at wave 1 and 2 for children with low, medium, and high parent-reported empathy.



To illustrate the effect of parent-reported empathy on the change in proactive aggression, Figure 1 depicts proactive aggression at T1 and T2 in participants with parent-reported empathy at the mean – 1 SD; at the mean, and at mean + 1SD. Figure 1 shows that decreases in proactive aggression over time were found for children with mean and high levels of parent-reported empathy, whereas stability in proactive aggression over time was found for children with low parent- reported empathy.

Among teachers, proactive aggression at T1 was also found to predict proactive aggression at T2 (see Table 3). However, teacher-reported trait empathy did not significantly predict change in proactive aggressive behavior over time as reported by teachers (p=.10).

Table 3. Stepwise regression model predicting the development in *teacher-reported* proactive aggressive behavior over time.

	β	p-value	R2
Model 1			.134
IRPA Proactive aggression T1	0.36*	<.001	
IRPA Reactive aggression T1	0.02	.832	
Model 2			.151
IRPA Proactive aggression T1	0.30*	.001	
IRPA Reactive aggression T1	0.03	.747	
GEM Teacher-reported trait empathy	-0.13	.102	

Note. * p<.05, IRPA: Instrument for Reactive and Proactive Aggression; GEM: Griffith Empathy Measure

Discussion

The aim of the present study was to examine the cross-sectional and longitudinal association between empathy in response to sadness and distress and proactive aggression in 6-7 year old children. Results show that a lower level of empathy in response to sadness and distress as reported by parents and teachers was cross-sectionally associated with a higher level of proactive aggression according to the same informants. In addition, a higher level of parent-reported empathy in response to sadness and distress at baseline was associated with a relatively larger decrease in parent-reported proactive aggression at follow-up one year later. No associations were found between the experimental empathy measures and proactive aggression.

This study hypothesized a relationship between various aspects of empathy in response to sadness and distress and proactive aggression, based on the assumption that the experience or anticipation of empathic feelings of distress upon aggressive behavior are most likely to inhibit further proactive aggressive behavior (Eisenberg et al., 2010; Lovett & Sheffield, 2007; Miller & Eisenberg, 1988). We found that empathy in response to distress and sadness reported by parents as well as teachers indeed was related to proactive aggressive behavior. This finding is in keeping with studies that have shown that proactive aggression is associated with lower levels of empathy in response to sadness and distress in older elementary school children (Eisenberg et al., 2010; Katsuma & Yamasaki, 2008;

Kimonis et al., 2006), and with studies that have shown that bullying as a form of proactive aggression is associated with lower levels of empathy (e.g. Dadds et al., 2008; de Waal, 2008; Jolliffe & Farrington, 2011; Steffgen et al., 2011). Parent-reported proactive aggression was positively related to parent-reported reactive aggression whereas the measures of empathy were not related to parent-reported reactive aggressive behavior. This seems to confirm the hypothesis that empathy is more likely to inhibit proactive aggression than reactive aggression (Eisenberg et al., 2010; Lovett & Sheffield, 2007) already at the beginning of school age.

Interestingly, in the present study empathy assessed with experimental paradigms was not associated with proactive aggressive behavior. Furthermore, whereas some aspects of empathy such as parent-reported empathy were associated with the child's prosocial response on a computerized task, no associations were found neither with facial mimicry in response to sadness of another person nor with self-reported empathy on a story task paradigm. It seems that the way empathy is operationalized is crucial in the study of the relationship between empathy and aggression as has been argued based on previous cross-sectional studies. This underlines that empathy is a complex phenomenon which is initiated by the observation of another's emotional state, followed by a cascade of phenomena (Eisenberg et al., 2010; Hofelich & Preston, 2012) that have been studied on an emotional (sharing another's emotional state), cognitive (understanding another's emotional state), behavioral (e.g., targeted helping) and physiological level (e.g., facial mimicry) (de Waal, 2008; Eisenberg & Miller, 1987; Lovett & Sheffield, 2007). The present findings are in line with previous suggestions that the relationship between aggression and empathic traits is more consistent using parent or teacher reports than the association between aggressive behavior and empathy using experimental paradigms (Eisenberg et al., 2010; Fabes et al., 1994; Knafo et al., 2008; Zahn-Waxler & Radke-Yarrow, 1992). Importantly, though, this may not necessarily be due to experimental paradigms per se, but rather to a mismatch between the exact kinds of empathy that may be expected to decrease proactive aggression and the specific experimental tasks used so far. Possibly, experimental tasks that specifically concern responses to sadness displayed by (potential) victims would provide a more stringent experimental test of the proposed role of lacking empathy in proactive aggression. In fact, a primary motivation of aggression may be to induce feelings of distress in victims as was suggested by the finding that highly aggressive boys frequently mentioned revenge as a moral argument favoring aggressive responses (Orobio de Castro, Verhulp, & Runions, 2012; Eisenberg et al., 1990; Holmgren et al., 1998).

This study adds to the literature by examining the association between empathy in response to sadness and distress and the change in proactive aggressive behavior over time. Results showed that more parent - but not teacher-reported - empathy predicted change in proactive aggressive behavior over time. Importantly, while proactive aggression at the first assessment predicted a relatively large portion of change in proactive aggression one year later, there was an additional and significant predictive value for empathy in response to sadness and distress. This is in keeping with studies that have shown that high CU-traits - a concept that includes limited prosocial emotions, callousness and a lack of empathy and guilt - predicted increases in aggressive behavior over time (Eisenberg et al., 2010; Pardini et al., 2007). Likewise, CU traits have been shown to be associated with high, stable trajectories of antisocial behavior over time in school-aged children (Frick, Stickle, Dandreaux, Farrell, & Kimonis, 2005; Little et al., 2003). Specifically, CU traits have been uniquely related to proactive, but not reactive aggression in children who score high on CU traits and conduct problems at a one-year follow-up in a community sample (Crick & Grotpeter, 1995; Frick, Cornell, Barry, Bodin, & Dane, 2003).

As far as the finding that teacher-reported empathy did not predict proactive aggression is concerned, it should be noted that empathic traits (at T1) and proactive aggression (at T2) were reported by different teachers. Although both empathy and proactive aggression at T1 and proactive aggression at both waves were significantly associated, it is possible that different teachers introduced additional variance in the model that made the effect of empathy on the change in proactive aggression too small to be significant in the current study sample.

This study is characterized by a number of strengths. First, we examined empathy in response to sadness and distress applying multiple methods of assessment: both experimental paradigms as well as multiple informants (i.e., parents and teachers) of empathic traits. Second, rather than testing for global relations between empathy and aggression, we tested relations of specific features of empathy with a specific function of aggression. Third, to our knowledge, this study is the first that examined the relation between empathy in response to sadness and distress and proactive aggressive behavior over a one-year period of time in early elementary school children.

It is also important to highlight several limitations. First, a larger study sample covering a longer follow-up period and repeated measurements are needed to confirm the current findings. Second, for the finding that parent-rated empathy was associated with parent-reported proactive aggressive behavior, common method variance may have been a source of measurement error. Third, empathy was measured using questionnaires as well as experimental paradigms while aggression measures were all based on parent and teacher report. Finally, the nature of the stimuli of sadness and distress in the various experimental paradigms was quite heterogeneous.

In conclusion, results of the study suggest that in 6-7 year old children report of low empathic traits in response to sadness and distress of others is associated with more proactive aggressive behavior and predicts change in proactive aggression over time. If these results are replicated, they are of interest to the development of new treatment paradigms. Future development of appropriate prevention and intervention programs should consider taking the role of empathy in response to distress of others into account and further examine whether subgroups of children can be identified that are at risk for a more stable and persistent course of proactive aggression. This is relevant since children who conduct aggressive behavior before the age of 12 are at risk to continue showing problem behaviors into (early) adulthood (Dodge et al., 1991; Kempes et al., 2005; Mannuzza, Klein, Abikoff, & Moulton, 2004; Nagin & Tremblay, 1999; Vitaro et al., 2006) and these 'early-starters' are at high risk of becoming persistent offenders (Domburgh, Loeber, Bezemer, Stallings, & Stouthamer-Loeber, 2009; Little et al., 2003), which makes their behavior highly detrimental to these individuals, their environment, and society (e.g.Frick & Loney, 1999; Polman et al., 2007).

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Chapter 6

Electomyographic responses to emotional facial expressions in six- and seven year olds with autism spectrum disorders

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Journal of Autism and Developmental Disorders
2013; doi:10.1007/s10803-013-1890-z

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Abstract

This study aimed to examine facial mimicry in 6-7 year old children with autism spectrum disorder (ASD) and to explore whether facial mimicry was related to the severity of impairment in social responsiveness. Facial electromyographic activity in response to angry, fearful, sad and happy facial expressions was recorded in twenty 6-7 year old children with ASD and twenty-seven typically developing children. Even though results did not show differences in facial mimicry between children with ASD and typically developing children, impairment in social responsiveness was significantly associated with reduced fear mimicry in children with ASD. These findings demonstrate normal mimicry in children with ASD as compared to healthy controls, but that in children with ASD the degree of impairments in social responsiveness may be associated with reduced sensitivity to distress signals.

Keywords

children, emotional responsiveness, facial mimicry, autism spectrum disorders

Impairment of social responsiveness is one of the core components of autism spectrum disorders (ASD), which can further be characterized by deficits in communication and stereotyped, repetitive behaviors (American Psychiatric Association 1994). In the last decades, social neuroscience has tried to unravel the mechanisms that might account for the various behavioral characteristics found in ASD, using a range of assessment methods (Volkmar 2011). Most research paradigms have first focused on adolescents and adults with autism, and confirm findings later in younger children (Courchesne et al. 2011), as this is where behavioral symptoms of ASD first become present.

The development of social responsiveness to the emotional states of others is assumed to be facilitated via the activation of corresponding facial, vocal and/or postural expressions, called mimicry (de Waal 2008). Mimicry in children has been reliably established across different studies using multiple paradigms (Chisholm & Strayer 1995; de Wied et al. 2006; de Wied et al. 2009; Haviland & Lelwica 1987). Specifically, mimicry of facial emotional expressions is thought to be a critical aspect in the primary reaction to emotional stimuli. It has been argued that the study of facial mimicry is an important method to assess processes of typical and atypical social–emotional engagement during childhood, and that the lack of emotional reciprocity and social deficits among individuals with ASD are a consequence of impaired processing of emotional expressions (Beall et al. 2008). Facial mimicry can be assessed using electromyographic responses (facial EMG) and has been done successfully in children at the age of six and seven years old (Deschamps et al. 2012).

In recent years, four previous facial EMG studies have explored facial mimicry responses in individuals with ASD. McIntosh et al. (2006) found ASD participants did not automatically mimic facial expressions to happy and angry facial expressions in eleven adolescents and adults (age range 13-64) with ASD, whereas the typically developing participants did (McIntosh et al. 2006). In eleven school-aged children with ASD, Beall et al. (2008) could not demonstrate consistent facial mimicry to happy or angry faces, and found a pattern of activation that appeared to be different from that of the typically developing children. Although they did not directly compare ASD children to a healthy control group, their study pointed towards deficient mimicry to happy, angry and fearful facial expressions in ASD (Beall et al. 2008). In contrast, Magnée et al. (2007) presented data on thirteen adults with high functioning ASD in which no deficits in facial mimicry to happy and fearful expressions compared to typically developing adults were found. Their study even found some evidence for an increased response to fearful stimuli in ASD (Magnee et al. 2007). Most recently, Oberman et al. (2009) demonstrated no differences in the overall response to emotional facial expressions in thirteen school-aged children with ASD compared to healthy controls. Despite the lack of a difference in overall response, school-aged children with ASD showed a delay in facial mimicry response onset across all emotional expressions together (happy, angry, fear, sadness and disgust) (Oberman et al. 2009). In sum, the literature remains rather inconclusive as to whether individuals with ASD show reduced, delayed or even increased mimicry responses.

Furthermore, several aspects concerning facial mimicry responses to emotional expressions in children with ASD require further exploration. First, facial EMG studies in young children with ASD have not been systematically conducted. Studies using paradigms other than facial EMG conclude that children aged 2-3 years old with ASD symptoms already show decreased signs of facial concern (e.g., brow furrowing) and facial mimicry (Charman et al. 1997; Scambler et al. 2007), and show less signs of empathic concern and prosocial behavior in response to parental social distress signals (McDonald & Messinger 2011). Moreover, an exploration of event-related potentials showed a disordered pattern of neural responses to emotional stimuli in children as young as 3 years of age (Dawson et al. 2004). It seems likely that abnormal facial EMG responses to emotional expressions emerge already early in development.

Second, it remains unclear whether facial mimicry might be selectively altered to some, or rather to all, emotional expressions. The available literature on deficits in the recognition and neural processing of emotional facial expressions suggests a selective, or more severe, impairment in the processing of especially fearful facial expressions in individuals with ASD (Ashwin et al. 2007; Dawson et al. 2004; Howard et al. 2000; Humphreys et al. 2007). This selective impairment in the processing of facial expressions of fear in autism is thought to be associated with abnormal development of the amygdala (Holmes et al. 2001). Facial EMG studies thus far have shown a decreased response to happy and angry (Beall et al. 2008; McIntosh et al. 2006) and an increased (Magnee et al. 2007) or blended response to fear (Beall et al. 2008), while another study assessing responses to a wide range of expressions reported no differences between emotions (Oberman et al. 2009).

Third, there is some uncertainty as to whether it is the magnitude and/or, timing that is altered in ASD. Research on temporal aspects of perceptual and response systems seems to suggest that, even when ASD participants show overall typical levels of responding, their spontaneous mimicry is delayed (Dawson et al. 2004; Oberman et al. 2009). Notably, timing has been argued to play a central role in social interaction (Crown et al. 2002). Nevertheless, only one facial EMG study in ASD assessed mimicry in response to a wide range of emotional expressions and looked beyond differences in magnitude. Their analysis of the temporal aspects of facial mimicry showed an overall delayed response, which was interpreted as a possible problem with automatic engagement of sensory-motor mechanisms involved in timing of social interactions (Oberman et al. 2009).

Finally, no facial EMG study thus far did address the severity of social impairments in relation to mimicry. In DSM-IV, ASD is further categorized into autistic disorder, Asperger's disorder and pervasive developmental disorder not otherwise specified (PDD-NOS). The proposed changes in DSM-V focus on a more dimensional approach in which the social-communication dimension is thought to offer research perspectives on underlying neurobiology, such as mechanisms of the social brain (Lord & Jones 2012). Research in ASD children using fMRI has provided preliminary evidence for an association between subtypes of autism and reduced activity in several brain structures implicated in the processing of emotional facial expressions (Harms et al. 2010). One facial mimicry study that did not use facial EMG, but assessed experimenter-coded facial expressions in ASD, looked into the differences between adolescents with ASD (both with autism and less severe PDD-NOS). They noted that while participants watched a film clip with happy emotional expression, less mimicry was displayed by adolescents with ASD compared to healthy developing controls. No differences between autism and PDD-NOS were found (Stel et al. 2008). Another study, however, did find a significant correlation between autism symptom severity and response to parental social distress signals, assessed by signs of empathic concern and prosocial behavior (McDonald & Messinger 2011). It remains therefore unclear whether more severe social impairment in ASD is related to deficits in facial mimicry.

To further address these issues, the present study was conducted in a sample of six and seven year old children with ASD. We assessed facial EMG responses to four basic emotional facial expressions and analyses examining both the differences in magnitude and timing of emotional mimicry were pursued in light of the study by Oberman et al. (2009). The study also explored the association between impairment in social responsiveness and facial mimicry to emotional facial expressions. We anticipated that children with ASD would show a general decrease or delay in facial mimicry compared to typically developing children, which would be most pronounced for fear. In addition we explored the hypotheses that more severe deficits in social responsiveness would be related with decreased facial mimicry.

Method

Participants

A sample of 27 children ranging from six to seven years old with a previous clinical diagnosis of ASD was recruited at the Outpatient Clinic of the Department of Child and Adolescent Psychiatry, University Medical Center Utrecht. The clinical ASD diagnosis was given, according to DSM-IV, by a child and adolescent psychiatrist. Patients were excluded from the study if a clinical diagnosis of ASD was not confirmed with the Social Responsiveness Scale (SRS) (n=2) or if they had an estimated IQ below 70 (n=3) based on the vocabulary and block design subsets of the Wechsler Intelligence Scale for Children III-Dutch version (Kort et al. 2005;

Sattler 1992). Furthermore, for some children no EMG data was collected (n=2), which was either caused by technical difficulties or lack of cooperation/anxiety in the children. The final patient group for the analysis included 20 children.

The healthy control group consisted of 29 six and seven year old children matched on sex from regular elementary schools in the vicinity of Utrecht who did not have a history of clinical diagnosis of ASD, and did have an SRS total score in the normal range (total SRS T-score<60) and an estimated IQ within the normal range. No EMG data could be collected in 3 children.

The Medical Ethics Committee of the University Medical Center Utrecht approved the study. Parents gave written informed consent prior to participation.

Measurements

Parents completed the Social Responsiveness Scale (SRS) (Constantino & Gruber 2005). Total SRS scores have been shown to reliably distinguish children with ASD from those with other psychiatric disorders (Constantino et al. 2003) and the SRS has been shown to be strongly associated with the social deficits criterion of the Autism Diagnostic Interview—Revised (Murray et al. 2011). The 65 items are rated on a 4-point scale from "not true" to "almost always true" and completed by the parent, based on the child's behavior over the past 6 months. The SRS yields a total score that serves as an index of severity of social deficits in the autism spectrum. Gender-based T-scores are available derived from the general population, 4–18 years of age, in the Netherlands (Roeyers et al. 2012). T-scores of 60 through 75 are in the "mild to moderate" range for autism spectrum disorders and are

Table 1. Descriptive statistics for all participants.

	Controls	ASD	ASD SRS severe
Sample Size *(n)*	27	20	9
Age M *(SD)*	7.2 (0.6)*	6.8 (0.6)*	6.8 (0.7)
Sex males	22	16	5
Estimated IQ *M (SD)*	119 (27)	115 (24)	112 (24)
SRS total *M (SD)*	46.5 (5.2)**	76.5 (10.4)**	85.6 (7.8)**

Note: ASD= Autism Spectrum Disorder; SRS= Social Responsiveness Scale; M=Mean; SD= Standard Deviation; IQ= Intelligence Quotient
***:** Controls and participants with ASD had a significant difference ($p \leq 0.05$) in age
****:** Both participants with ASD and participants with ASD + severe SRS had a significant difference ($p \leq 0.001$) in SRS total score compared to controls

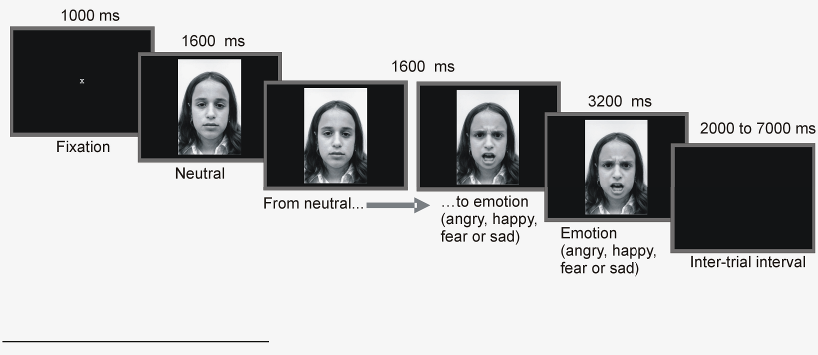
typical for children with mild or 'high functioning' autism spectrum conditions, such as PDD-NOS and higher functioning children with Asperger's Disorder (Constantino & Gruber 2005, p. 15). T-scores of 76 or higher are in the "severe" range. Based on the SRS total T-scores, patients were stratified into subgroups with low-moderate or severe SRS scores.

Table 1 shows the characteristics of the sample used for the final data analyses, both for the healthy controls and ASD group. Table 1 demonstrates that the patient group was significantly younger. No differences in sex or estimated IQ were found. As expected, the two groups differed significantly on SRS total scores.

Facial EMG data collection

Film clips with dynamic emotional facial expressions, created at our laboratory, were used in the present study (Deschamps et al. 2012). In these film clips, each with a total duration of 6400 ms, five different children (two boys and three girls) expressed anger, sadness, fear and happiness as illustrated in Figure 1. In total 16 movie clips (4 children x 4 emotions) were presented, once in a semi-random sequence in a first block, and once in a semi-random sequence in a second block. The size of the pictures was 21.5 cm height by 16 cm wide. They were viewed from a distance of 95 cm. Furthermore, during the task, there were four trials in which a cartoon character was presented during an emotional film clip. Children were instructed to push a response button when the character appeared on screen in order to maintain the child's attention to the faces. The data collected during these trials and during the four familiarization trials were excluded from further analyses.

Figure 1. Example trial of the passive viewing task



Note: The morphing of facial expressions started 1600ms after onset of the neutral facial expression and lasted for 1600ms, after which the full-blown emotional expression was presented for 3200ms.

EMG activity was recorded from bipolar montages across the corrugator supercilii (corrugator), zygomaticus major (zygomaticus), frontalis medialis (frontalis) and depressor anguli oris (depressor), according to the guidelines given by Fridlund and Cacioppo (Fridlund & Cacioppo 1986). Ag-AgCl electrodes with a diameter of 4 mm, filled with conductive electrode gel (Signa gel, Parker Laboratories, Inc., Fairfield, New Jersey, U.S.A.), were placed on the left side of the face to obtain maximal reactions (Dimberg & Petterson 2000). Raw EMG recordings were made with the ActiveTwo system (BioSemi, Amsterdam, The Netherlands) relative to the common mode sense (CMS). The ground consisted of the active CMS and passive driven right leg (DRL) electrode placed on the scalp that form a feedback loop driving the subject's average potential as close as possible to the analog-to-digital converter (i.e., the amplifier "zero") reference voltage in the A/D-box. The EMG signal was sampled at 2048 Hz.

Procedure

EMG data were collected while the child was seated in a chair in front of a computer screen in a dimly lit room at their own school. To assure participants were at ease, they first had a small talk with the experimenter and completed the two WISC-III subtests. Children were then instructed to watch the film clips carefully and to push a button when a popular cartoon character appeared. They were told they would receive a small prize upon finishing the task. Between the two blocks of the task, the experimenter ensured that the child was both comfortable and motivated. Additionally, during the task an experimenter watched the child and recorded the time segments when the child was not looking at the computer screen to provide a measure of visual inattention. Data collected during periods of inattention were removed from further analysis. Total duration of the facial EMG task was approximately 12 minutes.

Data reduction and analysis

EMG signals were filtered offline (high-pass 20 Hz, 48dB/octave) and full wave rectified using Brain Vision Analyzer Software (Brain Products GmbH, Munich). Trials that included marks of visual inattention were excluded from further analysis (average ± SD percentage of trials removed per participant 10.03 ± 13.20). Raw EMG data was segmented into 100 ms epochs. All values expressed were baseline corrected, defined as the mean activity during the 1600 ms neutral face preceding the onset of the morph, and expressed as a percentage over /under the individual's baseline. Mean EMG responses, expressed as a percentage change from baseline activity, were calculated for each emotion-muscle combination (averages of all stimuli for that emotion-muscle combination in the two blocks). Data from trials with scores that were 3 SD above the grand mean change score of the emotion condition were considered outliers and removed (Larsen & Norris 2009). An average of the activity during three time intervals after the beginning of the morphed dynamic expression was calculated. In the first time interval of 600 ms, no mimicry was expected due to lack time to respond to the start of morph. Average activity within the time window of 600 ms to 1400 ms (early time window) as well as 1400 ms to 2400 ms after the start of the morph (late time window) (Oberman et al. 2009) was calculated.

Facial EMG total composite scores were calculated for the absolute mimicry response to all four emotional presentations (Deschamps et al. 2012). As mimicry to happy facial expressions consists of both smiling activity (increase in zygomaticus muscle) and relaxation of brow frowning activity (decrease in corrugator muscle) both muscles are examined. To calculate the total mimicry response to happy facial expressions (HAPPY), we added the positive changes from baseline in zygomaticus and the negative changes from baseline in corrugator activity in response to happy facial expressions. Likewise, since angry facial mimicry consists of an increase in brow frowning and a decrease in smiling activity, the total angry score (ANGRY) consisted of the positive changes in corrugator and the negative changes in zygomaticus activity in response to angry facial expressions. The total fear score (FEAR) consisted of the positive changes in frontalis activity in response to fearful facial expressions. Finally, the total sad score (SAD) consisted of the positive changes in frontalis, corrugator and depressor activity in response to sad facial expressions.

Statistical analyses were performed using PASW Statistics 18.0 (IBM Company, Chicago, Illinois). As a first step, we validated the composite scores within the healthy control group, as this group was not identical to the group used in our previous study (Deschamps et al. 2012). Using one-sample t-tests, we checked whether the composite scores changed significantly during presentation of the emotional film clips, compared to the activity during the neutral face baseline.

To explore our first hypothesis, a multivariate analysis of variance (ANOVA) was conducted to examine whether facial mimicry differed in children with ASD and healthy controls. Dependent variables were the facial mimicry response scores to happy, angry, fearful and sad facial expressions (HAPPY, ANGRY, FEAR and SAD), and were combined in a compound multivariate test statistic. The time interval, referred to as window, was entered as a within subjects factor with 2 levels (800 ms early and 1000 ms late mimicry). The two groups were entered as a between subjects variable with 2 levels (ASD and healthy controls). To explore our second hypothesis, we excluded children with ASD who did not have an SRS total score within the severe range from analysis and conducted a similar MANOVA with healthy controls and ASD with severe SRS as a between subjects factor.

Additionally, we examined the correlations between the SRS total T score and the facial mimicry composite scores within the ASD group across the overall time frame. In all tests, the alpha level of significance was set at $p < .05$ (two-tailed).

Results

In line with our expectations results of the independent sample t-tests within the control group showed that all four composite scores used to measure facial mimicry differed significantly from baseline (all p-values ≤ 0.05). This indicates that facial mimicry, assessed with the composite scores, was present in the healthy control group in response to all presented emotions.

Facial EMG in ASD and healthy developing children

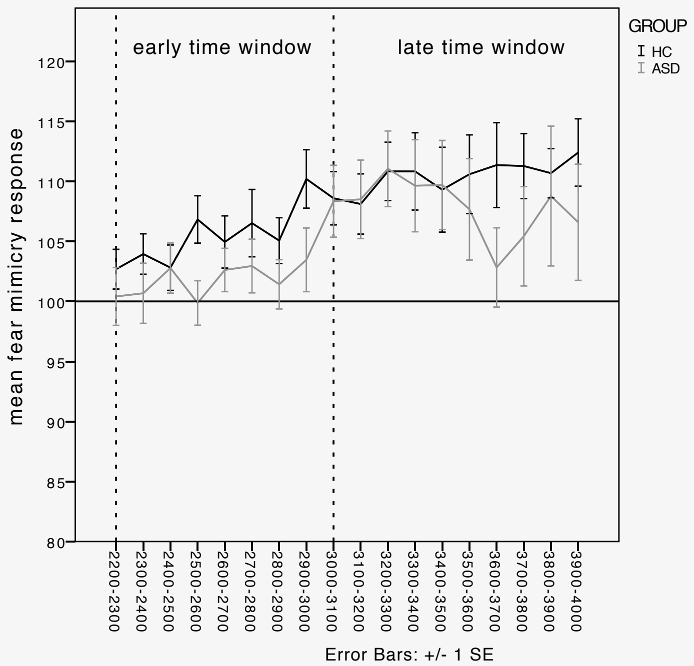
A significant main effect of window was found ($F(4,42)$ =10.06, p <0.01), demonstrating the facial stimuli resulted in more facial mimicry in the late as compared to the early time window. Univariate analyses showed a significant effect of time window in response to happy ($F(1,45)$= 29.44, p < 0.001), fear ($F(1,45)$= 13.80, p = 0.001), sad ($F(1,45)$= 22.86, p < 0.001) but not to angry ($F(1,45)$= 0.21, p = 0.65) expressions. The crucial between group effect was not significant ($F(4,42)$= 1.70, p = 0.17). The group x time window interaction ($F(4,31)=0.64$, p =0.63) was also not significant. These results indicate that children with ASD do not differ from healthy developing children on facial mimicry (see table 2 and figure 2).

Table 2. Facial mimicry in healthy controls versus participants with autism spectrum disorder.

	Time 1		Time 2	
	Controls (*n*=27)	ASD (*n*=20)	Controls (*n*=27)	ASD (*n*=20)
ANGRY *M (SD)*	5.27 (10.65)	8.87 (13.00)	7.44 (18.56)	8.86 (25.14)
HAPPY *M (SD)*	2.95 (9.84)	5.39 (16.70)	12.58 (18.56)	14.03 (21.56)
FEAR *M (SD)*	5.38 (7.73)	1.78 (7.18)	10.40 (11.92)	7.86 (14.32)
SAD *M (SD)*	5.44 (10.49)	-2.43 (11.38)	10.27 (14.66)	6.49 (15.33)

Note: ASD= Autism Spectrum Disorder; N= Sample Size; M=Mean; SD= Standard Deviation.

Figure 2. Time course of fear mimcry in children with ASD and healthy controls.



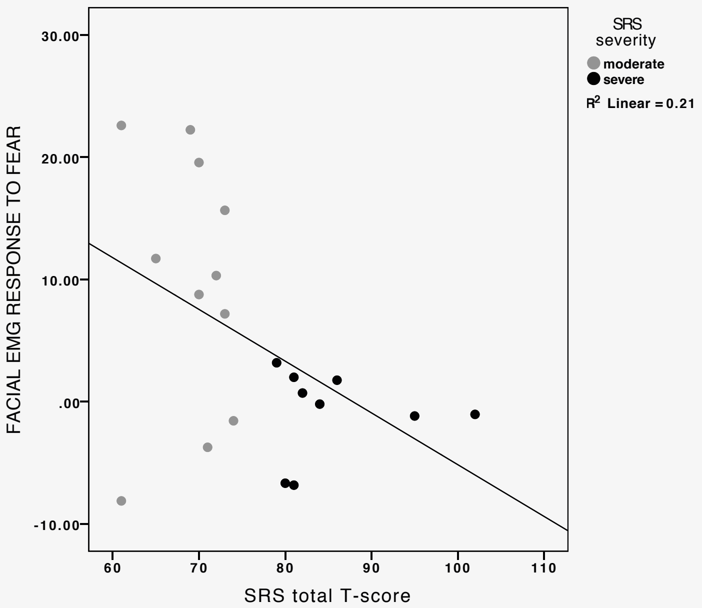
In a direct comparison between the severe SRS ASD children and healthy developing children, a significant main effect of time window (*F(4,31)*= 3.63, p <0.05) and of ASD severe group (*F(4,31)*= 2.72, p <0.05) was found, whereas the interaction effect of window by ASD severe group was not significant (*F(4,31)*= 0.67, p = 0.62). These results indicate a difference between facial mimicry in healthy developing children and participants with ASD and severe impairment in social responsiveness. Additional univariate analyses showed a significant effect of ASD severe group only for facial mimicry in response to FEAR (*F(1,34)*= 7.82, p <0 .01), but not to the other emotional expressions (all p>0.05) (see table 3).

Table 3. Facial mimicry in healthy controls versus participants with autism spectrum disorders with a severe range on the social responsiveness scale.

	Time 1 Controls (*n*=27)	Time 2 SRS severe (*n*=9)	Time 1 Controls (*n*=27)	Time 2 SRS severe (*n* =9)
ANGRY *M (SD)*	5.27 (10.65)	9.57 (11.50)	7.44 (18.56)	8.81 (13.65)
HAPPY *M (SD)*	2.94 (9.84)	2.48 (8.77)	12.58 (18.57)	7.63 (13.19)
FEAR *M (SD)*	5.38 (7.73) *	-1.61 (4.11) *	10.40 (11.92) *	-0.21 (4.52) *
SAD *M (SD)*	5.44 (10.49)	1.07 (7.06)	10.27 (14.66)	6.29 (16.19)

Note: SRS= Social Responsiveness Scale, M=Mean, SD= Standard Deviation
***:** Significant differences were found on the total Fear mimicry between the two groups ($p \leq 0.01$)

Figure 3. Fear mimicry and Social Responsiveness Scores in ASD



Note: Facial EMG response to fear shown is the average activity of the early and late time window.

Facial EMG and SRS symptom severity in ASD children

Moreover, a negative correlation was found between SRS severity score and facial mimicry to fear across the entire group of participants with ASD ($r(20) = -0.46$, $p = 0.04$) (see figure 3). No significant correlations were found between mimicry in response to happy, angry or sad facial expressions and SRS total scores (all p-values >0.5).

Discussion

This study focused on investigating differences in both the magnitude and timing of facial mimicry response between six and seven year old children with ASD and healthy controls. Results demonstrated no significant differences in facial EMG responses to any emotional condition between participants with ASD and healthy controls. The results did not provide support for the hypothesis of delayed facial mimicry in participants with ASD. However, the results did show that ASD patients who scored in the severe range of the SRS had significantly reduced facial mimicry in response to fearful expressions compared to healthy controls. This finding was bolstered by the fact that within the total group of participants with ASD, there was a significant inverse correlation between the SRS severity and fear mimicry.

The observed reductions in fear mimicry specifically in the most severely impaired ASD children is in keeping with previous findings of altered facial EMG responses in school-aged children and adolescents (Beall et al. 2008; McIntosh et al. 2006; Oberman et al. 2009). Results are also in line with studies using other paradigms, showing young children and toddlers with ASD symptoms to display decreased emotional responsiveness to facial signs of distress at a behavioral level (Charman et al. 1997; McDonald & Messinger 2011; Scambler et al. 2007) and lowered neural responsivity to fearful facial expressions (Dawson et al. 2004).

It has been suggested that the decrease in the behavioral difficulties experienced by individuals with ASD throughout adolescence and adulthood is correlated with increased motor mimicry (Bastiaansen et al. 2011). An increase in motor simulation is thought to play a crucial role in age-related improvements in social functioning in autism and the improved responsiveness to other's distress evidenced throughout adolescence. One facial EMG study found a positive correlation between age and mimicry to happy faces in a group of 8 to 13 year old children with ASD (Beall et al. 2008). Another study showed that inferior frontal gyrus activity during the perception of facial expressions increased with age in subjects with autism, but not in control subjects. This was taken as evidence for a deficit in the mirror neuron system in ASD, a system that contains neurons that are activated both in preparation of a movement and by observing that movement in a conspecific (Bastiaansen et al. 2011). A cross-sectional ERP study also suggested maturation of face processing in response to pictures of fearful and neutral faces in 3- to 8-year old children (Vlamings et al. 2010). It may well be that, over the years, patients with ASD cease to have problems in facial mimicry, which would be in line with the results of Magnee, who showed no deficits and even found an increased sensitivity to fearful faces in adults with ASD (Magnee et al., 2007).

Although the present study was conducted in a sample of children who received an ASD diagnosis following a clinical assessment at our university clinic medical center, and none of the ASD participants had an SRS T-score in the normal range, it is possible that some patients would not have fulfilled criteria for the autism group if we would have performed an ADI (autism diagnostic interview) and ADOS (autism diagnostic observation schedule) to confirm diagnosis. The inclusion of these patients with less severe symptoms in our study might have influenced our negative finding of impaired facial mimicry in the overall autism group, and might explain why we did only find a significant difference between participants with ASD that scored in the severe range of the SRS and healthy controls. Interestingly, in the study conducted by Beall et al. (2008), there was no significant relation between severity of autism and mimicry, however, as they noted, the statistical power for these correlations within their sample of eleven subjects was low. A close look at their results shows a trend of a correlation between specifically fear mimicry and severity of autism (Beall et al. 2008). Likewise, an association has been reported between higher autism symptom severity and impaired response to parental social distress signals (McDonald & Messinger 2011), less emotional contagion (Scambler et al. 2007) and reduced neural activity in mirror neuron areas (Harms et al. 2010). In sum, our results seem to support the idea that different individuals with autism, depending on their symptom severity may have different patterns of functional deviation in processing faces or other socially relevant information (Pierce & Courchesne 2000).

The finding that reduced mimicry in the most severely impaired ASD patients was not general, but rather specific in response to fearful facial expressions is notable. Our study did not replicate previous findings of altered facial EMG responses to happy and angry facial expressions in older children and adolescents (Beall et al. 2008; McIntosh et al. 2006; Oberman et al. 2009) and suggests altered mimicry specifically in response to fearful facial expressions. Similarly, studies that carried out facial emotion recognition paradigms and did find differences between ASD and healthy developing individuals were most obviously in the recognition of fear (Howard et al. 2000; Humphreys et al. 2007). Furthermore, fMRI studies in adults (Ashwin et al. 2007) and an EEG experiment in 3-4-year-old children with ASD (both PDD-NOS and autistic disorder) (Dawson et al. 2004) pointed towards differential brain activity to the processing of fear versus neutral facial expressions. In sum, the literature on deficits in the recognition and neural processing of emotional facial expressions in ASD seems consistent with a selective, or more severe, impairment in the processing of fear.

A methodological issue to consider is that facial mimicry of fear is associated with frontalis (i.e., brow raising) activation which is situated around the eye region. All other emotions we assessed also included mimicry responses of the mouth region (e.g. happy involved mouth corner raising). Notably, an often-debated face-processing anomaly in ASD concerns the salience and processing of information from the eyes (Harms et al. 2010). Individuals with ASD are thought to look less at the eye region of emotionally expressive faces than controls and thus might not to use information from the upper aspects of the face as effectively during emotion identification (Harms et al. 2010). The procedure and analysis in the present study were developed to maximize attention paid to the stimuli. Namely, children were encouraged to pay attention, motivated with the promise of a reward and instructed to catch a cartoon character. Trials marked by visual inattention were excluded from further analysis. Possibly, deficits in emotion processing can be at least temporarily corrected by simply asking subjects to focus on the eyes of other people and guiding their attention towards relevant parts of the presented stimuli, as has been previously shown in conduct disordered populations using a fear-potentiated startle paradigm (Newman et al. 2010) and fear recognition task (Dadds et al. 2006). In sum, a lack of attention to relevant parts of the emotional facial stimuli in children with ASD could at least in part explain group differences in emotional responsiveness.

In our study, these issues related to attention could have contributed to the absence of mimicry deficits in the less severely impaired ASD group and to less severely impaired emotions in the severe ASD group. Until future studies assess facial mimicry simultaneously with objective procedures, like eye-tracking, to verify actual attendance to the stimuli, it remains impossible to unravel whether previous findings of impaired mimicry are partly driven by a lack of attention to the eye region and whether children with ASD.

In conclusion, results show that overall 6-7 year old patients with ASD have no mimicry deficits unless they score in the severe range of the SRS, and that differences in fear mimicry correlate with SRS severity in the ASD group. These results are consistent with the literature of impaired processing of fearful expressions in ASD. As this study is one of the first to examine facial mimicry in young children and had a small sample size, it is imperative that similar studies replicate these results in larger samples. Further studies are needed to explore the relationship between symptom severity and facial mimicry in ASD and shed light on the longitudinal development of mimicry in ASD patients.

Acknowledgements

The authors would like to thank Maurice Magné for his kind advice.

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Chapter 7

Empathy and empathy induced prosocial behavior in six- and seven year olds with autism spectrum disorder

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Journal of Autism and Developmental Disorders
2014; doi: 10.1007/s10803-014-2048-3

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Abstract

The present study aimed to assess empathy and prosocial behavior in six to seven year old children with autism spectrum disorders (ASD). Results showed, first, lower levels of parent- and teacher-rated cognitive empathy, and similar levels of affective empathy in children with ASD compared to typically developing (TD) children. Second, emotion recognition for basic emotions, one aspect of cognitive empathy, in a story task was adequate in ASD children, but ASD children with severe impairments in social responsiveness had difficulties in recognizing fear. Third, prosocial behavior in response to signals of distress of a peer in a computer task was similar in ASD as in TD children. In conclusion, early elementary school children with ASD show specific impairments in cognitive empathy.

Keywords
autism spectrum disorder, children, cognitive empathy, affective empathy, empathy induced prosocial behavior

Being able to share and understand emotions of others, referred to as empathy, is essential in managing successful reciprocal human relationships (Dziobek et al., 2008). A distinction is drawn between a cognitive and an affective component. Cognitive empathy refers to the capacity to take the perspective of others and the understanding of emotions. Affective empathy is defined as the observer's experience of another's emotional state (Baron-Cohen & Wheelwright, 2004; Dadds et al., 2008; Dziobek et al., 2008). In general, empathy is thought to trigger a number of behaviors intended to benefit another like helping, sharing and comforting, together called prosocial behavior (Eisenberg, Eggum, & Di Giunta, 2010). Deficits in both empathy and prosocial behavior have been considered in autism spectrum disorder (ASD) (Bons et al., 2012; Russell et al., 2012), a psychiatric disorder characterized by deficits in social skills and communication (American Psychiatric Association 2000 – DSM-IV-Revised). However results of studies are inconsistent and little is known about the age at which deficits in empathy and prosocial behavior might emerge. In order to develop adequate early interventions aimed at improving the social behavior of children with ASD, further understanding of empathy-related processes and prosocial behavior in young children with ASD seems relevant.

Although some studies in individuals with ASD have focused on empathy as a single construct (Auyeung, Allison, Wheelwright, & Baron-Cohen, 2012; Johnson, Filliter, & Murphy, 2009), most literature has demonstrated the importance of differentiating between the cognitive and affective component of empathy. In recent years, growing consensus has been achieved regarding an imbalance between cognitive and affective empathy in ASD (Schwenck et al., 2012). First, impairments in cognitive empathy have consistently been found in studies using self- and other-report questionnaires in children and adolescents (Greimel et al., 2011; Pouw, Rieffe, Oosterveld, Huskens, & Stockmann, 2013) and in adults with ASD (Dziobek et al., 2008; Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007; Silani et al., 2008) . On the other hand, the evaluation of affective empathy with questionnaires yielded mixed results. Most studies reported no differences between ASD and typically developing (TD) peers in self-reports of affective empathic traits in children and adolescents (Pouw et al., 2013) and in adults with ASD (Dziobek et al., 2008; Rogers et al., 2007; Silani et al., 2008). Conversely, two studies did demonstrate impairments in affective empathy in adults (based on self-report) (Lombardo, Barnes, Wheelwright, & Baron-Cohen, 2007) and adolescents (based on parent report) (Greimel et al., 2011). To our knowledge, no studies examined affective empathic traits by means of parent report in younger children with ASD. In sum, studies of empathic traits in ASD using questionnaires consistently found deficits in cognitive empathy throughout development, whereas findings regarding impaired affective empathy in ASD thus far remain inconsistent, and the presence of deficits in affective empathy in young children with ASD remains unstudied.

Second, experimental paradigms have also been applied to evaluate cognitive and affective empathy in response to emotional stimuli in ASD. Numerous studies on cognitive empathy in adolescents and adults with ASD have shown impairments in emotion recognition as a component of cognitive empathy using a variety of pictures and short film clips of emotional facial expressions (see for a review, Bons et al. 2012). The only study on emotion recognition in young children, aged five- to seven-years-old, found difficulties in recognition of fear and anger (Rump, Giovannelli, Minshew, & Strauss, 2009). Furthermore, children with ASD aged about twelve years old showed deficits in actually understanding someone else's emotions when they were asked to explain why a person felt as he did (Schwenck et al., 2012). However, findings are not always consistent and a recent review on impairments in emotion recognition in older children and adolescents with ASD suggested impairments mainly in complex emotions (Bons et al., 2013). On the other hand, studies of affective empathy that have applied emotionally loaded scenarios to induce an affect match found that ASD children (mean age ±13 years) (Jones, Happe, Gilbert, Burnett, & Viding, 2010; Schwenck et al., 2012) and adults (Dziobek et al., 2008) reported to be as emotionally affected as their TD peers. In sum, studies using experimental paradigms to assess empathy seem to support impaired cognitive empathy, but not impaired affective empathy. Since research in young children with ASD on cognitive empathy is scarce and on affective empathy is lacking, it remains unclear how early in development cognitive empathy deficits emerge.

Although impairment in social interaction and behavior in ASD has been extensively reported as a main characteristic of ASD (see for a review McConnell, 2002), only a few studies have specifically focused on prosocial behavior in children with ASD, and results are inconsistent. First, by means of the prosocial subscale of the parent- and teacher-rated Strength and Difficulties Questionnaire (SDQ), three studies found reduced scores in children with ASD aged between 4- and 13-years-old compared to TD children (Iizuka et al., 2010; Jones & Frederickson, 2010; Russell et al., 2012). Second, in experimental settings children's behavior was observed in response to situations where the experimenter either needed help (e.g., to put a heavy tray on the table but the table was covered with objects) (Liebal, Colombi, Rogers, Warneken, & Tomasello, 2008; Travis, Sigman, & Ruskin, 2001) or wanted to share something (e.g., food or photos) (Travis et al., 2001). Travis et al. (2001) found reduced helping and sharing behavior in children with high-functioning autism compared to a control group of older children and adolescents with developmental delay (mean age 13 years). Liebal et al. (2008) performed a similar experiment in a group of two- to five-year-olds where the experimenter could not reach a certain object (e.g., he dropped a pen), but found no significant differences between ASD and children with developmental delay. Similarly, the study of McDonald and Messinger (2012) was not able to find differences in prosocial behavior, defined as the child's attempt to comfort or relieve parental distress, between toddlers at risk for ASD who eventually were diagnosed with ASD and the ones at risk who were not diagnosed (McDonald & Messinger, 2012). In sum, despite indications based on parent report of reduced prosocial behavior in ASD, intact helping and comforting behavior in young children with ASD has been observed in experimental settings.

Several issues concerning empathy and empathy induced prosocial behavior in ASD require further clarification. First, most studies of empathic traits are based on self-reports (Dziobek et al., 2008; Lombardo et al., 2007; Pouw et al., 2013; Rogers et al., 2007; Silani et al., 2008). However, prior to about the age of eight, children are thought to lack the cognitive and/or verbal abilities to reliably report on their internal states (Dadds et al., 2008). Moreover, difficulties in perceiving inner psychological processes have been suggested in ASD (Lombardo et al., 2007), which might lead to inappropriate evaluation of one's own empathic traits. Thus, in ASD reliability of self-reported empathic traits seems to be limited, as illustrated by findings of reduced parent report of empathic traits while adolescents themselves reported no empathy deficits (Greimel et al., 2011; Johnson et al., 2009). Furthermore, it has been suggested that teacher report is valuable in addition to parent report in studying children's emotional and behavioral capacities, as teachers have greater opportunities to observe their pupils within the classroom or playground where social interaction abounds (Iizuka et al., 2010). It may be assumed that classroom situations are more likely to reveal empathy deficits than home situations, as social impairments of children with ASD are specifically pronounced in social interaction with peers (Frankel, Gorospe, Chang, & Sugar, 2011).

Second, in studying prosocial behavior, an important distinction can be drawn between prosocial behavior with knowable benefits to the actor versus prosocial behavior that offers the actor no knowable rewards. It is especially the second category that seems to be related to empathy for the pain and distress of others (de Waal & Suchak, 2010). However, most experimental paradigms thus far focused mainly on helping behavior in response to a situation without emotional distress (Liebal et al., 2008; Travis et al., 2001). Only in one study responses of ASD children towards actual distress of parents were examined (McDonald & Messinger, 2012), and no studies have been conducted on prosocial behavior in response to peers. Furthermore, between the age of four and twelve years old a progression in the development of prosocial behavior in children with ASD has been suggested (Russell et al., 2012). While previous studies have examined either toddlers (McDonald & Messinger, 2012), pre-schoolers (Liebal et al., 2008) or adolescents (Travis et al., 2001), research examining elementary school children is lacking.

Finally, children with ASD are a heterogeneous group, with differences in severity and symptom levels (Hu & Steinberg, 2009). If deficits in empathy and empathy induced prosocial behavior play a role in problems in social responsiveness in various social situations, it is relevant to examine the association between empathy and empathy induced prosocial behavior on the one hand, and severity of problems in social responsiveness in ASD children on the other.

The present study aimed to address these issues. First, we studied early elementary school children, since social demands in peer interactions rapidly increase at this age. We aimed to examine differences in cognitive and affective empathy between children with ASD compared to typically developing children using parent and teacher reports of empathic traits, as well as an experimental story task paradigm. In keeping with previous studies in school-aged children and adolescents, we hypothesized that cognitive empathy levels would be lower in the ASD group compared to the control group, while affective empathy would remain unimpaired. Second, empathy induced prosocial behavior in ASD children was examined using a computer-based ballgame that provides direct observation of children's prosocial behavioral responses to emotional stimuli from distressed peers in a social context. We hypothesized that no differences in prosocial behavior between groups would be found. As an additional goal, we hypothesized the severity of social impairment would be associated with parent- and teacher-reported cognitive empathy levels.

Methods

Participants

A sample of 27 children ranging from six- to seven-years-old with a previous clinical diagnosis of ASD was recruited at the Outpatient Clinic of the Department of Child and Adolescent Psychiatry, University Medical Center Utrecht. The clinical diagnosis of ASD was given, according to DSM-IV, by a child and adolescent psychiatrist. Patients were excluded from the study if a clinical diagnosis of ASD was not confirmed with the Social Responsiveness Scale (SRS) (Constantino & Gruber, 2005) using a cut-off score of 60 (n=2) or if they had an estimated IQ below 70 (n=3) based on the vocabulary and block design subsets of the Wechsler Intelligence Scale for Children III-Dutch version (Kort et al., 2005; Sattler, 1992). The final patient group for the analysis included 22 children with ASD. The typically developing (TD) control group consisted of 29 six- and seven-year-old children matched on gender from regular elementary schools in the vicinity of Utrecht who did not have a history of clinical diagnosis of ASD, and who had a total SRS score within the normal range (total SRS<60) and an estimated IQ within the normal range (IQ>70).

The Medical Ethics Committee of the University Medical Center Utrecht approved the study. Parents gave written informed consent prior to participation.

Procedure

Parents completed the Griffith Empathy Measure (GEM) (Dadds et al., 2008) as well as the SRS (Constantino & Gruber, 2005) at home and teachers completed the teacher version of the GEM. All child data were collected in a quiet room at the child's own school. To assure participants were at ease, they first had a small talk with the experimenter and completed the two WISC-III subtests. Next, subjects were presented the Interpersonal Response Task (Dadds & Hawes, 2004) and the Story Task. Between each task, a short break was allowed and children received a sticker as a reward upon completing each task as well as a small gift upon completing all tasks.

Measurements

SRS scores were completed by parents. Total SRS scores have been shown to reliably distinguish children with ASD from those with other psychiatric disorders (Constantino et al., 2003) and the SRS has been shown to be strongly associated with the social deficits criterion of the Autism Diagnostic Interview—Revised (Murray, Mayes, & Smith, 2011). The 65 items are rated on a four-point scale from "not true" to "almost always true" and completed by the parents, based on the child's behavior over the past 6 months. The SRS yields a total score that serves as an index of severity of social deficits in the autism spectrum. Gender-based T-scores are available derived from the general population, for 4–18 years of age, in the Netherlands (Roeyers, Thys, Druart, De Schryver, & Schittekatte, 2012). T-scores of 60 through 75 are in the "mild to moderate" range for ASD and are typical for children with mild or high-functioning autism spectrum conditions, such as Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) and higher functioning children with Asperger's Disorder (Constantino & Gruber 2005, p. 15). T-scores of 76 or higher are in the "severe" range. Based on the total SRS T-scores, patients were stratified into subgroups with low-moderate or severe SRS scores.

Griffith Empathy Measure

Empathy was measured using the GEM (Dadds et al., 2008) which is a 23-item parent-reporting questionnaire, adapted from Bryant's Index of Empathy for children and adolescents. The GEM assesses both cognitive empathy (e.g., "My child doesn't understand why other people cry out of happiness") and affective empathy (e.g., "My child becomes sad when other children are sad", "My child gets upset when he/she sees an animal being hurt") using a nine-point Likert scale (-4 = strongly disagree; +4 = strongly agree). A higher total score represents a higher level of empathy. In the present study the two sub scores for cognitive empathy (6 items) and for affective empathy (9 items) were used for analysis. In addition, for the current study we adapted the scale to a teacher scale, omitting 2 CE-items that are not applicable to classroom or school situations. Internal consistencies in our total study sample for the parent reports were 0.73 for cognitive empathy and 0.82 for affective empathy, and for the teacher reports internal consistencies were 0.68 for cognitive empathy and 0.76 for affective empathy. No GEM scores of two patients and five TD controls were obtained from teachers.

Story task

The story-narratives of the Story Task are based on the classic Feshbach Affective Situation Test for Empathy (Feshbach & Roe, 1968). The task has been adapted to assess aspects of cognitive empathy (understanding and decoding of the events in the stories) as well as affective empathy (affect match between the participant and protagonist in the stories) (Albiero & Coco, 2001). It consists of eight short stories in which the protagonist is involved in an event arousing angry, happy, sad or fearful emotions. Each emotion is represented by two stories. The version presented to boys involves scenarios with a boy protagonist; the version for girls involves a girl.

After each vignette, children were interviewed to assess whether they had been able to recognize and share the emotions depicted in the stories. Participants were asked how the protagonist felt (angry, happy, sad, fearful or neutral) and to what extent (a little, average, very much). They reported and indicated their responses on a card showing the emotional categories and intensity. Next, the child was asked how he or she felt after listening to the story, as a measure for AE. Again, the child could choose between the five different emotions and the three intensity levels.

Levels of affect match were evaluated on a four-point scale (0 = the child did not report an affect match; 1 = the child's emotion was similar to his or her report of the character's emotion; 2 = the child's emotion was the same as the character's emotion but different in intensity; 3 = both the child's emotion and the intensity were the same as the character's). This resulted in a continuous score for each emotion, computed by adding the scores on the two stories per emotion, ranging between 0 and 6 points.

Interpersonal Response Task

The Interpersonal Response Task (Dadds & Hawes, 2004) is a computer-based task that assesses a prosocial behavioral response of subjects to emotional stimuli in a social context. Subjects play a ball-throwing computer game against two computer-controlled players. Subjects are assigned to choose towards which of two computer-players they will play the ball. They are told that they will receive 'money' (reward) for throwing the ball to a particular player and that each player will show them their feelings through facial expression. The game consists of three rounds. In the first round (10 trials), both computer-players keep a happy facial expression, regardless of whether the ball is passed to them or not. When subjects play the ball towards any of both players, they are displayed a coin rolling towards them on the computer screen with a simultaneous sound of coins rolling. In the second round (10 trials), one of the players has run out of money and doesn't 'give money' (no rolling coins or sound). This player continues to show a happy face even when the ball is not thrown to him. In the third round (20 trials), each time the ball is not passed to the player that has run out of money, the player displays a progressively distressed facial expression. In the current study we used an adapted version of the IRT; the task could be performed twice, once with a girl and once with a boy showing distressed facial expressions.

As dependent variable for this study we used the number of times the participant threw the ball to the 'sad' player in the third round. This variable reflects behavior in response to the increasing distress of the computer player that does not provide the child with a monetary reward. The variable yields a continuous score in which a higher score represents a higher sensitivity to sadness and distress and associated empathy induced prosocial behavior.

Analysis

Statistical analyses were performed using SPSS Statistics 20.0.0 (IBM Company, Chicago, Illinois). For the distribution of demographic variables between groups independent samples t-tests (age, estimated IQ and SRS) were performed. First, to analyze differences between ASD and TD in GEM scores two multivariate analyses of variance (MANOVA), separate for parent and teacher scores, were performed. Total cognitive and affective empathy scores were entered as dependent variables and GROUP was entered as a between-subjects variable with two levels (ASD and TD). In addition, the same analyses were performed to examine differences between TD and the severely affected ASD children (SRS score > 75). To examine the association between the severity of impairments in social responsiveness and empathy bivariate Pearson's correlations were conducted between total SRS scores and parent- and teacher-rated cognitive and affective empathy within the ASD group. Second, to examine differences in emotion recognition on the Story Task between ASD and TD and additionally between severe ASD and TD, Fisher's exact tests were performed. For differences in affect match non-parametric Mann-Whitney U tests were performed as distributions of mean scores across subjects failed to meet assumptions of normality. Spearman's correlations were conducted within the ASD children to examine an association between scores on the Story Task and SRS scores. Finally, in the IRT, prosocial responses were examined for differences between ASD and TD and between severe ASD and TD with Mann-Whitney U tests, because results in both groups did not meet assumptions of normality. For the association between IRT scores and SRS scores Spearman's correlations were conducted within the ASD group.

Results

Descriptive characteristics

Descriptive characteristics of the children in both groups included in analysis are shown in Table 1. Analysis showed a significant difference in age, such that the TD controls were on average four months older. However, since all children in our study were six or seven years old, no influence on our data analysis was expected from this difference. No differences in estimated IQ were found. As expected, significant differences were found in SRS scores between the ASD and TD groups. In the ASD group eleven children had low/moderate SRS scores (60-75) and eleven children had SRS scores in the severe range (>75).

Table 1. Participant information by diagnostic group.

	ASD	TD
n	22	29
Gender (female/male)	4/18	5/24
Age in years *M* (*SD*)	6.8 (0.58)	7.2 (0.56)
Estimated IQ *M* (*SD*)	114 (24.8)	119 (27.8)
SRS total T score *M* (*SD*)	77 (10.2)	46 (5.0)
<60	0	29
60-75	11	0
>75	11	0

Note: ASD autism spectrum disorder, TD typically developing controls, IQ intelligence quotient, SRS social responsiveness scale: scores were derived from parents. Diagnostic groups were significantly different on age ($p<0.05$) and mean SRS scores ($p<0.01$).

Griffith Empathy Measure

Table 2 demonstrates the results of parent and teacher scores on the GEM. Both analyses for parent and teacher scores on the cognitive and affective subscales of the GEM revealed a significant effect of GROUP (parents: $F(2,48)=15.17$, $p<0.001$; teachers: $F(2,41)=9.19$, $p=0.001$). Children with ASD were rated as less empathic compared to TD children by both their parents and teachers on the cognitive (parents: $F(1,49)=30.48$, $p<0.001$; teachers: $F(1,42)=18.25$, $p<0.001$), but not on the affective subscale (parents: $F(1,49)=1.36$, $p=0.249$; teachers: $F(1,42)=3.77$, $p=0.059$). An additional analysis to compare the group of ASD children with the most severe SRS scores to the TD children showed a similar pattern with differences between groups for cognitive empathy (p<0.001) but not for affective empathy (p=0.063; p=0.125). Finally, a significant negative correlation between parent-rated cognitive empathy scores and total SRS scores (r=-0.641, p<0.001) was found within the ASD group, but not between teacher-rated cognitive empathy and SRS scores (r=-0.287, p=0.208) nor between affective empathy and SRS scores (r=-0.113, p=0.617; r=-0.099, p=0.671).

Table 2. Griffith Empathy Measure

	TD	ASD	F [a]	p-value	Severe ASD	F [b]	p-value
Parent scores	(*n* =29)	(*n* =22)			(*n* =11)		
CE *M (SD)*	9.90 (6.3)	-0.91 (7.7)	30.48	0.000*	-6.18 (5.5)	55.55	0.000*
AE *M (SD)*	1.31 (8.0)	-2.27 (13.8)	1.36	0.249	-6.00 (16.2)	3.68	0.063
Teacher scores	(*n* =24)	(*n* =20)			(*n* =10)		
CE *M (SD)*	7.00 (4.2)	-0.75 (7.6)	18.25	0.000*	-3.30 (6.8)	29.08	0.000*
AE *M (SD)*	2.00 (5.3)	-3.25 (11.9)	3.78	0.059	-3.00 (13.4)	2.49	0.125

Note: TD typically developing controls, ASD autism spectrum disorder, CE cognitive empathy, AE affective empathy. a: comparison between TD and ASD. b: comparison between TD and severe ASD. * significant difference.

Story task

Results of the Story Task are shown in Table 3. For emotion recognition, no differences were found between ASD and TD children using a Fisher's exact test (all p > 0.05). When only severely affected children in the ASD group were compared to TD, a significant difference was found for fear recognition (p=0.021), but not for recognition of any of the other emotions (all p>0.05). For affect match, a Mann-Whitney U test revealed no differences in AE between the ASD group and the TD children of between the most severely affected ASD subgroup and TD children (all p-values > 0.05). Finally, no significant correlations between cognitive and affective empathy scores on the Story Task and total SRS scores were found within the ASD group (all p-values > 0.15).

Table 3. Story Task

	TD (*n*=29)	ASD (*n* =22)	p-value [a]	Severe ASD (*n* =11)	p-value [b]
CE: emotion recognition					
Angry			0.844		0.800
0	1	1		1	
1	4	2		1	
2	24	19		9	
Happy			0.341		0.061
0	0	2		2	
1	4	2		0	
2	25	18		9	
Sad			0.383		0.479
0	0	1		1	
1	1	2		0	
2	28	19		10	
Fear			0.066		0.021*
0	0	4		3	
1	5	4		2	
2	24	14		6	
AE: affect match					
Angry	2.21 (2.5)	2.55 (2.6)	0.672	2.82 (2.5)	0.530
Happy	2.79 (2.0)	2.82 (2.4)	1.000	2.91 (2.6)	0.905
Sad	2.62 (2.3)	1.95 (2.4)	0.317	2.36 (2.4)	0.788
Fear	1.66 (2.1)	1.45 (2.1)	0.839	1.91 (2.4)	0.765

Note: CE cognitive empathy scores: accurate emotion recognition in 0, 1 or 2 out of 2 presented story vignettes. AE affective empathy scores: mean (SD) scores based on the average of two stories for each emotion condition. a: comparison between TD and ASD. b: comparison between TD and severe ASD. * significant difference.

Interpersonal Response Task

Results of the IRT are shown in Table 4. Mann-Whitney U tests revealed no significant differences between the ASD and TD group (p=0.125; p=0.688). Likewise, no significant differences in IRT scores were found between the severely affected ASD subgroup and the TD children (p=0.103; p=0.952). Finally, correlations between total SRS score and IRT score within the ASD group were not significant (Spearman's rho=-0.140, p=0.533; r=0.132, p=0.559).

Table 4. Interpersonal Response Task

	TD	ASD	p-value [a]	Severe ASD	p-value [b]
IRT(b)	5.45 (4.3)	3.36 (3.5)	0.125	2.82 (3.2)	0.103
IRT(g)	5.69 (4.4)	5.91 (3.3)	0.688	5.64 (3.6)	0.952

Note: TD typically developing controls, ASD autism spectrum disorder, IRT(b) Interpersonal Response Task: playing against a boy, IRT(g) playing against a girl.
a: comparison between TD and ASD. b: comparison between TD and severe ASD.

Discussion

Results of the present study in six- and seven-year-old children with ASD showed, first, lower levels of parent- and teacher-rated cognitive empathy and similar levels of affective empathy compared to typically developing children. Second, impairment in social responsiveness according to the parents was associated with reduced parent rated, but not teacher rated cognitive empathy in children with ASD. Third, emotion recognition for basic emotions, i.e., one aspect of cognitive empathy, in the story task was adequate in ASD children, but ASD children with severe impairments in social responsiveness had difficulties in recognizing fear compared to TD children. Finally, prosocial behavior in response to signals of distress of a peer in the computer task was similar in ASD as in TD children.

Our findings of reduced levels of parent- and teacher-reported cognitive empathy, but intact affective empathy in six- and seven-year-olds are consistent with previous research that has applied empathy questionnaires in older children and adults with ASD by means of self-report (Dziobek et al., 2008; Pouw et al., 2013; Rogers et al., 2007). This study is the first to assess parent-reported empathy in a sample of young children with ASD. A previous study in adolescents with ASD by Greimel et al. (2011) applied the parent version of the GEM as well as the original self-report questionnaire it is based on (Bryant's Empathy Index (Bryant, 1982). This allowed them to compare parents' perception of the empathic traits of their autistic child to the child's own perception (Greimel et al., 2011). Interestingly, they found cognitive empathy as well as affective empathy to be impaired according to parent rates while self-reports did not show any deficits. Besides raising the possibility of inaccuracy of self-reports of empathic traits in ASD, the authors proposed that impaired parent-reported affective empathy could be explained by the fact that individuals with ASD do actually feel an affective response, but are less able to display their emotions, so that others (in this case their parents) tend to underestimate their affective empathic traits (Dziobek et al., 2008; Greimel et al., 2011). Obviously, in our sample of young ASD children parents did rate adequate affective empathic responding.

The inverse correlation that we found between parent-rated cognitive empathy and severity of impairments in social responsiveness suggests that besides the consistent finding of impaired cognitive empathy in ASD, severity of social impairments is associated with severity of impairments in cognitive empathic understanding. It should be noted that cognitive empathy and SRS scores were both based on parent report. Thus, common method variance may have been a source of measurement error. Correlations between impaired empathy and emotion processing and severity of social impairments, however, are in line with experimental and neurobiological studies (Dapretto et al., 2006; McDonald & Messinger, 2012). McDonald and Messinger (2012), who studied empathy and ASD symptoms in toddlers at risk for ASD, found that the overall quality of the child's empathic responding (which included observed empathic concern as well as prosocial behavior and level of arousal) was predictive for ASD severity. In addition, in an fMRI study about mirror neuron dysfunction in children with ASD similar inverse correlations were found between autism symptom severity and activity of specific parts of the mirror neuron system, which is proposed to be involved in emotion processing (Dapretto et al., 2006).

As far as affective empathy responding is concerned, no differences were observed between ASD and TD children in the extent to which children felt affected by the emotion of the child in the story. This is in line with previous studies that found children with ASD were equally affected in response to emotional stimuli as TD children (Dziobek et al., 2008; Jones et al., 2010; Schwenck et al., 2012). For cognitive empathy we found that, although empathic traits were perceived as less developed by their parents and teachers, children with ASD were equally capable in adequately recognizing the four basic emotions anger, fear, happiness and sadness, as compared to TD peers. In a recent review of Bons et al. (2012) impairments in emotion recognition were found in about 50% of the reviewed studies in juveniles with ASD, while in another review on emotion recognition of Harms et al. (2010) 70% of the studies reported impairments (Bons et al., 2012; Harms, Martin, & Wallace, 2010). Our findings of unimpaired recognition of basic emotions are in line with studies reviewed by Bons et al. (2012) that used simple basic emotional expression pictures (Piggot et al., 2004; Tracy, Robins, Schriber, & Solomon, 2011), whereas studies that reported emotion recognition deficits mostly included stimuli that were more difficult to recognize (Bolte & Poustka, 2003; Wallace et al., 2011) . In the current study, we choose to examine basic emotion recognition, as we studied six- to seven-year-olds. However, in adults (Golan, Baron-Cohen, Hill, & Golan, 2006) and adolescents (Golan, Baron-Cohen, & Golan, 2008) with ASD, recognition of complex emotions and mental states, e.g. annoyed, awkward, bitter, concerned, in film scenes has been shown to be impaired.

Interestingly, indications were found that a subgroup of ASD children with the most severe problems in social responsiveness showed deficits in recognizing fear, one aspect of cognitive empathy. In a study of Rump et al. (2009) recognition of the same basic emotional expressions were examined in a sample of five- to seven-year-olds with ASD using dynamic, facial emotional stimuli that morphed from subtle to more explicit expressions (Rump et al., 2009). They found that children with ASD were able to accurately recognize most stimuli, but that specifically for fear and anger they needed significantly more time (i.e. more explicit facial expressions) compared to TD children. Likewise, studies that have carried out an emotion recognition paradigm in adults with ASD using morphing faces found that differences between ASD and TD controls were most obvious in the recognition of fear (Humphreys, Minshew, Leonard, & Behrmann, 2007). An explanation that has been proposed for the particular difficulties in recognizing fear, involves the consistent finding that ASD individuals pay less attention to the eyes, while the most relevant parts of facial expressions of fearful emotions are situated around the eyes (Bons et al., 2012; Harms et al., 2010). Similarly, in a previous study conducted in the same sample of six- to seven-year-old ASD and TD children, reduced facial mimicry specifically in response to fearful facial expressions was found in the most severely affected children with ASD (Deschamps, Coppes, Kenemans, Schutter & Matthys, 2013).

Cognitive empathy and the understanding of emotions of others are closely related to a broader concept about inferring mental states in others, also described as the ability to take perspective of another person's situation. This is also referred to as Theory of Mind, our ability to understand mental states such as intentions, goals and beliefs (Singer, 2006), which has consistently been argued to be deficient in ASD (see for a review Gaigg, 2012). Several studies in children and adolescents with ASD have interpreted impairments in first- and second-order false believe Theory of Mind tasks ("he thinks that she thinks") as reduced cognitive empathy (Jones et al., 2010; Pouw et al., 2013).

Results of the IRT that showed that children with ASD did not differ from TD children in their empathy induced prosocial behavior. This is in line with the study of McDonald & Messinger (2011) who found that, while toddlers at risk for ASD had overall reduced empathic responding, their prosocial behavior, defined as the child's attempt to comfort parent's distress (after he/she pretended to got something in his/her eye), did not differ. Two other studies that used experimental settings (Liebal et al., 2008; Travis et al., 2001) investigated behavior that was less triggered by empathy-related responding to distress cues, but instead simulated situations where the experimenter needed help from a practical concern. One found reduced helping behavior in adolescents (Travis et al. 2001), whereas the other found no significant differences in two- to five-year-olds (Liebal et al., 2008). Although comparing experimental behavioral paradigms to a computer based task is difficult, we would argue that the IRT endeavors to trigger prosocial behavior that is more explicitly motivated by the desire to reduce actual distress of the opponent, i.e., it is empathy induced. Our results that children with ASD did not significantly differ in their attempts to comfort the progressively sad player, may be associated with these children's intact affective empathic abilities.

A number of issues should be taken into account when interpreting our findings. First, participants were included based on their history of ASD diagnosis and parent-rated SRS scores within the clinical range (>60), while no ADI (autism diagnostic interview) or ADOS (autism diagnostic observation schedule) was performed to confirm diagnosis. Second, the sample of participants used in this study was fairly small. Particularly in order to detect the influence of the severity of impairments in social responsiveness it would have been desirable to include more children with ASD and create larger groups with low/moderate and high SRS-scores. Third, as far as the affective empathy dimension of the Story Task is concerned, it should be noted that in ASD as well as in the typically developing group, more than half of the children did not report an affect match. Possibly, as the stories were fairly short and followed each other rapidly, little time was left to actually be able to empathize with the child in the story. Likewise, simply listening to a short story is less likely to trigger a corresponding emotion than for example viewing a film where emotions of the actor are more pronounced (Barnes, Lombardo, Wheelwright, & Baron-Cohen, 2009). Finally, the IRT that we used to examine empathy induced prosocial behavior has not been extensively validated and the outcome is likely to be related to other processes than empathy, like the tendency to depend on monetary versus social reward. We would argue that further development of an ecologically valid experimental paradigm that investigates empathy induced prosocial behavior, particularly in response to peers, is necessary.

In conclusion, the present study confirmed that cognitive empathy is impaired in early elementary school children with ASD as compared to TD children, according to both parent and teacher reports, while no impairments in affective empathy were reported. These cognitive impairments seem to be associated with severity of social responsiveness, which is supported by our finding of reduced emotion recognition for fear only in severely affected ASD children. Despite well-established social deficits in ASD individuals, we were unable to demonstrate differences in empathy induced prosocial behavior in young children with ASD.

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Chapter 8

Brief report: Exploring possible effect of methylphenidate on mimicry in ADHD.

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Abstract

Although stimulant medications offer benefits for most children, there is also concern that these agents reduce emotional responsiveness. This report presents preliminary data on the possible influence of stimulants on emotion processing in attention deficit hyperactivity disorder (ADHD). Participants were recruited in the scope of a larger study project on facial mimicry in 6-7 year old children. During this project, some children with ADHD had accidentally taken MPH on the day of testing, and allowed us to explore the influence of MPH on fear mimicry in an ad hoc fashion. We compared electromyographic responses to facial expressions of children tested with MPH (n=13) to children with ADHD who were MPH-naïve (n=32), to patients who were on MPH treatment and ceased their medication prior to assessment (n=37) and to typically developing (TD) children (n=37). Results show ADHD MPH-naïve children displayed increased fear mimicry compared to TD (p = .046). ADHD children tested with MPH did not differ from the TD (p = .757), but showed less fear mimicry than the MPH-naïve ADHD group (p = .005). Children with ADHD who were treated with MPH, but who ceased MPH before assessment did not differ in fear mimicry from TD (p-values = 1.00). However, ADHD children did show a significant decrease in fear mimicry as compared to the ADHD patients who were MPH-naïve (p = .034). In conclusion, despite the small sample size and the naturalistic design, the findings point toward conducting systematic studies on the influence of methylphenidate on fear mimicry in children with ADHD.

Keywords
children, emotional responsiveness, facial mimicry, ADHD, DBD

Although stimulant medications are widely used and offer benefits for most children with attention deficit hyperactivity disorder (ADHD), there is concern that these agents influence emotional responsiveness (Manos et al., 2011). Irritability, blunting, depression and dysphoria have been proposed to reflect some of the negative side-effects of stimulants, whereas others have proposed that stimulants can also have positive effects on emotion processing (Manos et al., 2011). These positive effects could be either direct, like an increase in emotional expression. Effects could also be more secondary to reductions in symptoms and/or to the altered behavior of caretakers who tend to use less controlling behavior when symptoms of ADHD are reduced (Manos et al., 2011). In addition, in clinical practice, parents sometimes report emotional side effects of stimulant treatment. This made us explore the possible influence of methylphenidate on facial mimicry in an ad hoc fashion. Indeed, in a project on empathy in children with ADHD, participants were asked to cease stimulant medication prior to assessment. However, some children with ADHD had accidentally taken MPH on the day of testing. This allowed us to explore the influence of MPH on fear mimicry in a naturalistic, non-randomized design.

In the literature, the emotion processing deficits in ADHD have been proposed to reflect a failure to attend to salient emotional signals (Sinzig, Morsch, & Lehmkuhl, 2008). Likewise, a lack of attention to the eyes has been hypothesized to play a central role in abnormal emotional responsiveness in children with conduct problems (Bons et al., 2012). In these children, who often have comorbid ADHD symptoms, a positive moderating influence of increased attention to the eyes on fear recognition has been found (Dadds et al., 2006). This suggests that deficits in emotion processing could be at least temporarily corrected by instructing subjects to guide their attention towards relevant parts of the presented stimuli, and that stimulant treatment results in an increase in attending to salient emotional signals.

Interestingly, recent reports suggest that stimulants in ADHD may have a positive influence on emotion processing. A recent study by Posner and colleagues found increased activity in the amygdala and elevated functional connectivity between the amygdala and lateral prefrontal cortex during the presentation of fearful faces in ADHD adolescents compared to typically developing adolescents. Stimulants had a reducing effect on both activity and functional connectivity. Importantly, in this study subliminal stimuli were used to diminish the effects of differences in supraliminal attention as a potential confound (Posner et al., 2011). On the other hand, a reduction in emotion processing related electric brain potentials and emotion recognition for fearful and angry expressions in adolescents with ADHD has been shown compared to typically developing adolescents (Williams et al., 2008). These reductions were associated with both negative mood and emotional lability. Treatment with MPH brought an improvement in brain activity, which was associated with improvements in emotional lability, while negative mood persisted after treatment. However, it could not be ruled out that improvements in general cognitive functions contributed to improvements in emotion-related neural activity (Williams et al., 2008).

Here we report an exploration of the possible effect of methylphenidate (MPH) in children with ADHD on fear processing. Participants were recruited in the scope of a study on facial mimicry in 6-7 year old children. As an overall result in this study we did not find deficits in fear processing in children with ADHD compared to typically developing children (Deschamps et. al. 2013). During this project, however, some children with ADHD had accidentally taken MPH on the day of testing. This allowed us to explore in an ad hoc fashion the influence of MPH on fear mimicry. In line with previous reports in adolescents, we hypothesized MPH would have a positive effect on fear processing assessed using facial electromyographic responses to fearful facial expressions in children with ADHD. Based on the sparse available literature, we hypothesized that no effect of methylphenidate would be found on happy, angry and sad mimicry.

Methods

Participants were recruited at the outpatient clinic of the Department of Psychiatry, University Medical Center Utrecht in the scope of a project on empathy and facial mimicry in children with externalizing disorders. A clinical diagnosis of ADHD was confirmed with the Diagnostic Interview Schedule for Children (DISC, module E) (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000)). During this project, some children with ADHD had accidentally taken MPH on the day of testing (daily MPH dosage in mg/kg Mean 0.93, SD 0.28). The total study sample consisted of 104 patients. Children were excluded if: (a) a clinical diagnosis of ADHD could not be confirmed (n=10: 7 children had a DISC diagnosis of DBD only without ADHD and 3 children had a DISC diagnosis of neither ADHD nor DBD) and (b) no EMG data were collected (n=12). In the total sample, 16 children had accidentally taken methylphenidate at the day of testing, but 3 of them were excluded as no EMG data were collected. The final patient group for analysis comprised 82 children. This allowed us to explore in an ad hoc fashion the influence of MPH on fear mimicry by comparing these MPH-tested children (n=13) to the children with ADHD who were MPH-naïve (n=32), to patients who were on MPH treatment and ceased their medication prior to assessment (MPH-ceased, n=37). The study sample included children with an estimated IQ below 70 (n=6). The healthy developing control group consisted of 43 children from regular elementary schools in the vicinity of Utrecht who did not meet criteria for a clinical diagnosis of ADHD or DBD on the DISC.

Patient groups did not differ significantly on symptom severity (attention, rule breaking and aggression) measured with the Child Behavior Checklist 6-18 (CBCL) and the Teacher

Report Form (TRF) (Achenbach & Rescorla, 2001). No differences between the clinical groups were found in comorbidity with disruptive behavior disorders, estimated IQ, age, sex or socio-economic status (all p values > .09). Differences between groups were found in CBCL anxiety and depression and TRF anxiety and depression scores (all $p<0.05$). ADHD MPH-naïve patients had higher scores of anxiety and depression compared to TD children (all $p<0.05$). CBCL anxiety and depression did not differ between the ADHD MPH-tested and the other patient groups (all p values > .05). However, the ADHD MPH-naïve group was reported to have more anxiety and depressive symptoms as compared to the ADHD MPH-ceased group ($p = .02$).

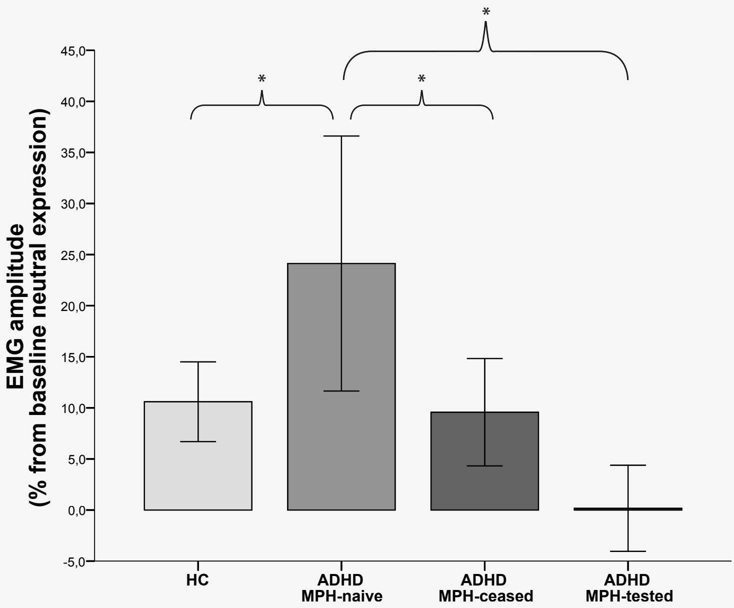
Facial mimicry to fear was assessed using electromyographic responses (facial EMG) of the frontalis muscle in response to film clips with dynamic fearful facial expressions. Furthermore, facial mimicry was assessed in response to happy (increase in zygomaticus and decrease in corrugator activation), angry (increase in corrugator and decrease activation) and sad (increase in depressor, corrugator and frontalis activation). Film clips with dynamic emotional facial expressions were used in the present study (Deschamps, Schutte, Kenemans, Matthys, & Schutter, 2012). In these film clips, each with a total duration of 6400 ms, five different children (two boys and three girls) expressed fearful facial expressions. The size of the pictures was 21.5 cm height by 16 cm wide. They were viewed from a distance of 95 cm. Children were instructed to push a response button when the character appeared on screen in order to maintain the child's attention to the faces. The data collected during these trials were excluded from further analyses. EMG data collection and reduction procedures have been described in a previous feasibility study on facial mimicry in 6-7 year old children (Deschamps et al., 2012).

Results

Fear mimicry

An ANOVA with fear-mimicry as dependent variable and GROUP as between subjects variable (HC, ADHD MPH-naïve, ADHD MPH-ceased and ADHD MPH-tested) showed a significant main effect of GROUP ($F(1,3) = 4.93$, $p = .003$) (Figure 1). Bonferroni corrected post hoc analyses showed that the ADHD MPH-naïve children displayed increased fear mimicry compared to healthy developing children ($p = .046$). ADHD children tested with MPH showed less fear mimicry than the MPH-naïve ADHD group ($p = .005$), but did not differ from HC ($p = .757$). Likewise, the children with ADHD who were treated with MPH, but who ceased MPH before assessment did show less fear mimicry than the MPH-naïve ADHD group ($p = .034$), but did not differ from HC ($p=1.00$) (figure 1).

Figure 1. Fear mimicry.



Note: Figure represents mean EMG amplitude (+/- 2SE); HC=healthy controls; MPH=methylphenidate; * $p < .05$. Children with ADHD who were MPH-naïve (ADHD MPH-naïve) showed more fear mimicry in response to fearful facial expressions than the healthy control group (HC). Children with ADHD who were treated with MPH showed less fear mimicry than the ADHD MPH-naïve children. This was the case for both those who ceased MPH before testing (ADHD MPH-ceased) as well as those who were tested with MPH (ADHD MPH-tested).

Mimicry in response to angry, happy and sad expressions

The ANOVA's for happy (p=0.67) and angry (p=0.32) mimicry showed no significant effect of GROUP. However, the ANOVA for mimicry in response to sad facial expressions did show a significant effect of GROUP (p=0.015). Post-hoc analyses show that children with ADHD who were MPH-naïve showed more mimicry in response to sad expressions compared to children with ADHD who took MPH, both those who ceased (p<0.05) and those who accidentally took medication at the time of assessment (p<0.05).

Discussion

The presented study explored in an ad hoc fashion the possible effects of methylphenidate on fear mimicry. Preliminary findings suggest that children with ADHD who were not treated with methylphenidate show increased fear mimicry compared to healthy developing children. However, those children who were tested with methylphenidate did not show increased fear processing. This may indicate that fear processing is increased in children with ADHD and that this increase may no longer be present after stimulant treatment, as has been previously suggested (Posner et al., 2011). Since the study had a naturalistic and non-randomized design, it is well possible that the differences found in fear processing can be explained by other characteristics that could have influenced the choice of parents to start or cease methylphenidate treatment.

Although patient groups did not differ significantly on any level of symptom severity or comorbid conditions, the ADHD MPH-naïve group was reported to have more anxiety symptoms as compared to the ADHD MPH-ceased group. Thus, the unexpected difference in fear mimicry response between these two groups could well have been driven by differences in anxiety and not by MPH treatment status. Similarly, it cannot be ruled out that parents of children who observed their children as having higher anxiety levels preferred other treatment methods than stimulant medication. This could have been a confounding factor leading to increased fear mimicry in MPH-naïve children. Alternatively, MPH could be an important contributor to reduced fear processing. The present results suggest that in that case chronic MPH treatment is critical, and acute withdrawal is without effect. To further investigate the possible effect of methyphenidate on fear processing a placebo controlled randomized control trial is needed.

In addition to comorbid anxiety levels, co-occurring disruptive behavior disorders should also be carefully considered, although in our sample no difference between the MPH treated children and MPH naïve children in conduct problems was found. There is high co-occurrence of ADHD symptoms in children with DBD and DBD symptoms in children with ADHD (Martel, Gremillion, Roberts, Eye, & Nigg, 2010), and deficits in emotion processing and facial mimicry have also been established in these disorders (de Wied, Gispen-de Wied, & van Boxtel, 2010).

Finally, no differences were found between groups in the facial mimicry of happy and angry facial expressions. However, ADHD children tested with methylphenidate did show less sad mimicry than MPH-naïve ADHD children although unlike fear mimicry, sad mimicry was not found to be increased in MPH-naïve ADHD children compared to healthy developing children. Questions remain on the specificity of a possible effect of methylphenidate on fear processing.

In conclusion, these findings are preliminary due to the small sample size and the naturalistic design. However, the results appear to be in line with previous findings in adolescents that suggest that fear processing is different in ADHD compared to a healthy control group and that administration of MPH might have an effect on these differences. Further research on the effects of MPH on emotion processing is needed, including a double-blind, cross-over, placebo-controlled study within a larger sample of ADHD patients. Future studies should also take comorbid anxiety and conduct problems into account. Another point of interest is whether the effects of MPH on emotion processing are driven by its effect on increased attention or that MPH also has specific effects on emotional brain systems in ADHD. Finally, the influence of possible long-term effects of MPH on fear processing in children with ADHD needs further attention.

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Chapter 9

General discussion

General discussion

The aim of the present dissertation was to examine empathy-related processes in six and seven year old children with disruptive behavior, attention deficit and autism spectrum disorders. The intention was to study whether empathy deficits previously found in older children and adolescents with these disorders would also be present at the age of 6-7 years and a one-year follow-up study was conducted to examine empathy as a risk factor in the persistence of aggressive behavior. Children with DBD as well as ADHD and ASD were compared to typically developing children to increase knowledge on differences in empathy deficits in children with these disorders. An attempt was made to add to the literature on impairment in empathy and empathy-induced prosocial behavior in response to sadness and distress of others, as this may be relevant for interventions.

To this end parent and teacher reported empathic traits were obtained and empathy in children was assessed using three experimental paradigms: facial mimicry, child report of empathy in response to story vignettes and empathy induced pro-social behavior assessed with a computer task.

Summary of main results

In Chapter 2, it was demonstrated that facial mimicry, as a psychophysiological marker of empathy, can be reliably assessed using facial electromyography. Children aged 6-7 years old showed emotion-specific facial EMG activity following the presentation of happy, angry, fearful and sad expressions.

In Chapters 3 and 4 on empathy in children with disruptive behavior and attention deficit/ hyperactivity disorder, inconsistent results were found. Teachers reported reduced affective empathy in response to sadness and distress in children with DBD as well as in children with ADHD. Parents, however, did not report empathy deficits of their child. In the experimental paradigms children with DBD or ADHD showed no deficits in facial mimicry, nor in their self-report of empathic feelings in response to sad story vignettes.

Taken together, based on a combination of positive and negative findings presented in Chapters 3 and 4 results point toward the idea that young children with ADHD and DBD show affective empathic responding in laboratory situations where attention to the relevant stimuli is maximized, as well as in more natural settings observed by parents. On the other hand, teachers reported impaired empathic responding based on their ratings on observations of children in a school environment. At school, the environment is either highly structured during instruction and task performance or much less structured during breaks with fluctuating social demands. Furthermore, at school children typically interact with multiple peers simultaneously, while at home, children play with one or a few friends with whom they have a positive relationship. It is not unlikely that at school problems in attending to relevant emotional stimuli as well as impulsive behavior in larger peer groups at least to some extend influence empathic ability. Interestingly, in **Chapter 8** some preliminary indications were found that empathic responding might be influenced by medication (methylphenidate) that influences attention deficits and impulsivity in children with ADHD. Together this suggests that attention problems may influence the ability of children with ADHD and/or DBD to attend to emotional stimuli as a first and important step in the empathic process.

With regard to empathy induced prosocial behavior, results obtained in **Chapter 4** seem to indicate that impairment is more related to symptoms of DBD and not to symptoms of ADHD. It should be noted that the prosocial response paradigm as with the other paradigms in this dissertation was assessed in a quiet environment. Emotional stimuli of only one child at a time were displayed and children were stimulated to pay attention to the stimuli and the task. This limits the generalizability of our finding of unimpaired prosocial behavior in children with ADHD to more naturalistic settings. On the other hand, the prosocial response task did not allow exclusion of data of trials in which children did not pay attention as was done in the facial mimicry paradigm. Thus, attention problems could have still played a role in the reduced performance on the prosocial task in children with DBD and ADHD, although this is less likely to be the case since no association was found between prosocial empathic behavior and symptoms of ADHD.

In **Chapter 5**, an attempt was made to explore empathy in response to sadness and distress of others assessed with multiple measures as a risk factor in the persistence of proactive aggressive behavior. In order to obtain a study sample with sufficient variance in proactive aggressive behavior, children with ADHD and DBD were combined with typically developing children. At baseline, low levels of parent-reported empathic traits in response to distress of others were associated with high parent-reported proactive aggression. Similarly, teacher-reported empathy was negatively related to teacher-reported proactive aggression. At follow-up one year later, a higher level of parent-reported empathy at baseline was associated with a relatively larger decrease in parent-reported proactive aggression. However, no associations were found between pro-active aggression and empathy assessed with any of the three paradigms in children.

Results described in **Chapters 6 and 7** show that 6-7 year old children with ASD have deficits in fear recognition and fear mimicry, but only when they have severe deficits in social responsiveness. In line with the empathy imbalance theory that predicts impairment in cognitive, but not affective empathy, lower levels of parent- and teacher-rated cognitive empathy were found, and similar levels of affective empathy in children with ASD compared to typically developing children. Finally, prosocial behavior in response to distress signals of a peer was similar in ASD as in TD children.

Before the clinical significance of the results of this project can be further interpreted, several limitations need to be considered regarding the characteristics of the sample recruited in this project as well as in the measures applied to assess empathy.

Considerations related to sample characteristics

Age

In this project, children of 6-7 years old at the beginning of school age were included. It was examined whether deficits in empathy found in older school-aged children and adolescents would already be present at this younger age. Since it is well possible that impairments in some aspects of empathy already emerge in early childhood, future studies should consider examining empathy in toddlers and preschoolers.

Comorbidity between ADHD and DBD

In general, there is high co-morbidity of attention-deficit/hyperactivity disorder (ADHD) and DBD (Angold, Costello, & Erkanli, 1999). In the present study, although 104 children with ADHD and DBD were recruited from our outpatient clinic, only 7 children were included with a diagnosis of DBD without comorbid ADHD. Thus, in data-analysis a categorical approach distinguishing DBD from ADHD was not feasible. In an attempt to distinguish between the effects of attention and conduct problems, a more dimensional approach was also applied. An additional analysis was conducted to compare the clinical group (i.e. all patients with ADHD and/or DBD) to the healthy developing children, first entering attention problems and next entering aggression as a covariate. Although these analyses indicated the same pattern of results as the categorical analysis in which ADHD and DBD+/-ADHD groups were compared, it should be noted that the CBCL and TRF symptom scores were used as measures to assess ADHD and DBD related behaviors. To thoroughly assess dimensions of ADHD and DBD clusters in a clinical population, other questionnaires that are more sensitive and specific could have been applied. Besides, experimental tasks to measure attention problems, impulsivity and executive functioning in children could have been more appropriate.

Severity of psychopathology

Our sample might have included children with less severe psychopathology, since throughout development into late childhood and adolescence, symptoms of DBD are known to persist in certain, but decline in other children (Frick & Loney, 1999; Lahey et al., 1995). Thus, it is possible that our sample of young children included less severely affected children that would show a decline in symptoms at a later age. Indeed, the symptom scores on the CBCL filled in by parents and the TRF in the present study were lower as compared to those in previous studies (de Wied, van Boxtel, Posthumus, Goudena, & Matthys, 2009; de Wied, van Boxtel, Matthys, 2012; de Wied, van Boxtel, Zaalberg, Goudena, & Matthys, 2006). Also, children in our study were recruited from an outpatient population, whereas in previous studies children were recruited from inpatient and day-treatment settings (de Wied et al., 2006; 2009) or special schools for adolescents with severe behavioral problems (de Wied et al., 2012). Overall, this points towards less severe and somewhat different psychopathology in our young outpatient group and can provide possible explanation for the inconsistent results on the measures of empathy. With regard to the ASD children in our sample, it should be noted that the sample size was relatively small. Furthermore, no ADI (autism diagnostic interview) or ADOS (autism diagnostic observation schedule) was administrated to confirm an ASD classification, but participants were included based on their history of an ASD diagnosis and parent-rated SRS scores within the clinical range (>60). Nevertheless, it is possible that part of our sample consisted of less severely affected ASD children.

Heterogeneity in DBD

DBD is a heterogeneous disorder. It has been suggested that although ODD can be a precursor to conduct disorder (CD), ODD also differs from CD in symptomatology, comorbidity and development (Nock, Kazdin, Hiripi, & Kessler, 2007; Rowe, Costello, Angold, Copeland, & Maughan, 2010; Stringaris & Goodman, 2009a; 2009b). In addition, the neurobiology of ODD has been proposed to be different from CD (Matthys, Vanderschuren, & Schutter, 2013; Matthys, Vanderschuren, Schutter, & Lochman, 2012). For example, impaired fear conditioning and amygdala hypo-reactivity to negative stimuli have been found in CD (Matthys et al., 2013), but it needs to be further examined whether this is also the case in ODD. Importantly, the present study sample contained only a few children with CD and the majority were diagnosed with ODD, whereas in some other studies on empathy in older children and adolescents twenty percent (de Wied et al., 2006; 2009) to almost half of the DBD sample consisted of CD children (de Wied et al., 2012).

Another important distinction that has been made in DBD is between children with high versus low callous-unemotional traits (CU-traits). CU-traits include callousness and a lack of empathy and guilt and have been introduced as limited prosocial emotions in the DSM-5 (American Psychiatric Association, 2013). In children with conduct problems and high CU traits, a reduced level of emotional reactivity has been found compared to children with disruptive behavior but lower levels of CU traits (Frick, Ray, Thornton, & Kahn, 2013). It has been proposed that the mechanisms underlying empathy problems in DBD children with CU traits (fearless (emotionally cold) type) may be different from those encountered in DBD children without these traits (fearful type) (de Wied, Gispen-de Wied, & van Boxtel, 2010). An attempt to distinguish DBD children with high and low CU-traits in the present study failed because of low internal consistency in the parent and teacher reports on the CU-trait subscale of the Antisocial Process Screening Device that was collected.

Treatment

Some children already participated in a previous project on the assessment of ADHD and DBD at an early age. These children had previously been examined and treated at our outpatient clinic, whereas others had only been recently evaluated and a treatment plan had just been made at the time of assessment. This also holds for some children in our ASD sample. The effects of various forms of treatment, like e.g. parent training and medication, in some of these children were not entered as an additional variable in our analyses and their effect on empathy remains unknown. Finally, the recruitment from an outpatient clinic at a University Medical Center could have resulted in a selection bias and further limits the generalizability of our findings to other patient populations.

Considerations related to the assessment of empathy

A reliable and ecologically valid assessment of empathy in young children is challenging. As empathy-related responding is a complex construct, a nuanced understanding of empathy deficits is most likely to be obtained when multiple measures are applied (Eisenberg, Eggum, & Di Giunta, 2010). Therefore, in this dissertation, parent and teacher report of empathic traits were brought together with the assessment of empathy in children using three experimental paradigms. Here, the advantages as well as limitations of the different methods that were applied will be discussed as well as the consistency of the results obtained from different measures.

Questionnaires

Questionnaires that ask participants to self-report on empathic traits are unlikely to be suitable for the study of empathy in young children (Dadds et al., 2008; Lovett & Sheffield, 2007). Thus, parent- or teacher-report seems fundamental to the accurate measurement of empathy (Dadds et al., 2008). There are a number of issues when teachers and parents report empathy. First, teachers might be better able to compare children with typically developing peers. On the other hand, parents might have more thorough knowledge of their children's empathic responding. Second, questionnaires thus far have made no distinction between for example empathy in response to emotions of adults, other children, possible victims or friends. Finally, it should be noted that especially in Chapter 5, where an association was found between questionnaires on empathy and proactive aggression, both were parent-rated and common method variance could have occurred.

Facial mimicry

Children were presented a facial mimicry paradigm since numerous studies have suggested that facial mimicry is an important component in empathic responding. In children with DBD as well as in those with ASD, there were inconsistencies in the results of empathic traits and facial mimicry. In children with DBD, at the level of facial mimicry, emotional responsiveness was unimpaired (**Chapter 3**) while teachers reported reduced empathic traits and an experimental paradigm showed reduced empathy induced prosocial behavior (**Chapter 4**). On the other hand, in ASD, facial mimicry of fearful stimuli was impaired (**Chapter 6**) while no differences in parent or teacher rated affective empathy were found (**Chapter 7**). Furthermore, in **Chapter 5**, no significant correlation between facial mimicry and reported empathic traits in response to sadness was found. Together, these findings raise questions on the association between facial mimicry and other components of empathy in children.

Interestingly, in adults, there is a growing body of research regarding the existence of links between facial mimicry, emotion induction and emotion recognition (Sato, Fujimura, Kochiyama, & Suzuki, 2013). For example, when participants were instructed to suppress their facial expressions, this reduced their mimicry as well as their self-reported subjective emotional reactions while they viewed comedy films (Bush, Barr, McHugo, & Lanzetta, 1989). In addition, facial mimicry responses to emotional stimuli predicted the strength of the emotion felt by participants upon perceiving the stimuli a second time (Sato et al., 2013). Similarly, emotion recognition may be enhanced by facial feedback signals that are generated when we automatically mimic expressions of others' faces (Neal & Chartrand, 2011; Oberman, Winkielman, & Ramachandran, 2007). Emotion perception was significantly impaired in people who had received a cosmetic procedure that reduces muscular feedback from the face (Botox) (Neal & Chartrand, 2011) or while biting on a pen and chewing gum (Oberman et al., 2007). Also, emotion perception was increased using a procedure that enhanced muscle contractions (Neal & Chartrand, 2011). These findings suggest a correlation between affective and cognitive aspects of empathy as well as facial mimicry. Nevertheless, thus far, only two studies in healthy volunteers have shown a relationship between individual differences in facial mimicry responses and empathic traits (Balconi & Canavesio, 2012; Sonnby-Borgström, 2002). In sum, questions remain on how the different components of empathy relate to facial mimicry in children with various psychiatric conditions, but the assessment of facial mimicry seems to be both a feasible and an important method to assess empathy during early childhood.

Another important point to consider is that in the facial mimicry paradigm in the present study, the procedure and analysis were developed to maximize attention paid to the stimuli. That is, children were encouraged to pay attention, motivated with the promise of a reward, an instruction was inserted in the paradigm to catch a cartoon character, and trials marked with visual inattention were excluded from further analysis. This could have reduced the influence of attention problems on deficits in facial mimicry. Two other studies found evidence for a positive moderating influence of increased attention on emotion processing in adults with low empathy and antisocial behavior using a fear-potentiated startle paradigm (Newman, Curtin, Bertsch, & Baskin-Sommers, 2010) and in children using a fear recognition task (Dadds et al., 2006). Both studies suggest that deficits in emotion processing can be at least temporarily corrected by instructing subjects to focus on the eyes of other people and guiding their attention towards relevant parts of the presented stimuli. Furthermore, there is evidence of decreased dopaminergic functioning in DBD that may be associated with reduced salience of environmental stimuli (Matthys et al., 2013). More studies are needed to explore whether young children with DBD and/or ADHD are only capable to adequately make use of their mimicry system under optimal conditions that are not necessarily ecologically valid.

Child report of empathy in response to story vignettes

In the affective empathy dimension of the Story Task, children were asked how they felt after listening to a story in which the protagonist is involved in an emotion-arousing event. Overall, scores of an affect match on this task were low which could have resulted from the fact that the task did not sufficiently lead to an affective empathic response in this age group. It has been previously proposed that the hypothetical character of most experimental paradigms such as the Story Task as well as the rapid changes in affective content, together with the probability of social desirable answers, limits the validity to detect affective empathy deficits using these paradigms (Miller & Eisenberg, 1988). Furthermore, in these tasks, children are asked to report on their own experienced feelings, which depends on their ability to perceive and recognise their own emotions. Hence, the lack of a group difference on affective empathy between children with DBD, ADHD or ASD and TD children on this measure may have been driven by the fact that the task did not lead to a sufficient affective empathic response in TD.

Prosocial behavior

Prosocial behavior was assessed with the Interpersonal Response Task (IRT), a computer game in which children decide to play a ball towards one of two computer players. The main outcome variable reflects empathy induced prosocial behavior in response to the increasing sadness and distress of a computer player who does not provide the child with a symbolic monetary reward. The results obtained from the IRT should be interpreted with caution, as the validity and reliability of the IRT has not been extensively investigated.

First, the pictures of emotional faces of the computer players presented during the task may be limited in their arousal-eliciting properties. Second, only one study has looked into the convergence between performance on the IRT and empathic traits. In this study, the IRT task was presented to a sample of 23 clinically referred children aged 7-12 years old with various disorders in the scope of a larger study on empathic traits (Dadds et al., 2008). It was demonstrated that the IRT measure was correlated with parent report of empathic traits (Dadds et al., 2008). Similarly, in **Chapter 5** a positive correlation between parent-reported empathy in response to sadness and the child's prosocial response to sadness on the IRT was found. Finally, whether or not children show prosocial behavior during this computer task is likely to be related to other relevant processes like a relative preference for monetary reward. Preliminary findings suggest that empathic children tend to benefit more from social reward than monetary reward on an outcome measure of response inhibition (Kohls, Peltzer, Herpertz-Dahlmann, & Konrad, 2009). However, it is unknown whether children with ADHD and DBD differ in their response to monetary reward. Hence, it remains unclear whether our findings of impaired prosocial response to distress in the presence of a monetary reward on the IRT in children with DBD compared to typically developing children could have been driven by their preference for monetary reward.

General considerations

Inconsistent results between the different measures were found in **Chapters 3 and 4**, where deficits in empathy in children with DBD and ADHD compared to the TD children were reported, as well as in **Chapters 6 and 7** in a comparison between children with ASD and typically developing children. Moreover, an analysis in **Chapter 5** of the correlations between various empathy measures in our sample indicated that only parent-reported empathy and the child's prosocial response on a computerized task were significantly associated, whereas other measures were not.

These results point towards deficits at some but not on other levels of empathy and are in line with critical reviews that have pointed out that the relationship between aggression and empathy seems to depend on the methods and perspectives chosen to examine empathy (Eisenberg et al., 2010; Lovett & Sheffield, 2007). Furthermore, in the literature there is little evidence available on the correlations between various empathy-assessment methods. In general, in most studies that have applied multiple empathy measures, correlations between these different methods of assessment have not been reported (e.g. (de Wied et al., 2006; de Wied, Goudena, & Matthys, 2005; Schwenck et al., 2012)).

Taken together, questions remain on the reliability and validity of the instruments currently used to assess empathy and much is unknown about how stable they reflect empathic traits throughout development (Lovett & Sheffield, 2007). This also holds for the measures that were used in the current study. In conclusion, the assessment of the different features of empathy seems to resemble the Indian story in which a group of blind men touch an elephant to learn what it is like. Each one feels a different part, but only one part, such as the side, the trunk or the ears. They then compare notes and learn that they are in complete disagreement. In the present dissertation, an attempt was made to obtain a view of some parts of the empathy-elephant, but results remain inconsistent. As the story continues, in some versions a sighted man walks by and sees the entire elephant all at once, and the other men also learn that they are blind. In other versions however, the men stop talking, start listening and collaborate to "see" the full elephant. It seems that a nuanced understanding of possible manifestations of empathy-related responding is needed (Eisenberg et al., 2010) and that further research with multiple measures is likely to be the only way to reveal a completer picture of empathy deficits in children with psychiatric disorders.

Taking all these considerations regarding sample characteristics and the assessment of empathy into account, the results from the present thesis suggest several clinical implications regarding a better understanding of empathy deficits in young children, fine-cutting between disorders and the development of future interventions.

A better understanding of empathy deficits and trajectories in young children

Reduced empathy has been suggested to be predictive for a persistent and severe pattern of aggressive behavior (Moffitt, Arseneault, Jaffee, et al, 2008). Interestingly, some sparse longitudinal data suggests that the negative relation between empathy as well as sympathy and aggression/externalizing becomes more consistent with age (Eisenberg et al., 2010). One longitudinal study that started in 4-5 year olds found that the ones high and low in risk for behavioral problems did not differ at that age in their observed concern for others. However, in children with behavioral problems, there was a significant decrease in concern for others from age 4–5 years to age 6–7 years (Hastings, Zahn-Waxler, R, Usher, & Bridges, 2000).

The results from our longitudinal data suggest that in a sample that included both typically developing and clinical 6-7 year old children there is a subgroup of children with low empathic traits that do not show a decline in pro-active aggression. More longitudinal research is needed to better define subgroups, identify unique characteristics and track the trajectories of children with DBD and reduced empathy (Frick & White, 2008).

Implications for differentiating between disorders

The results presented in Chapters 3 and 4 on DBD and ADHD and in Chapters 6 and 7 on ASD allow for some inferences based on the differences found between the various patient groups and typically developing children, although groups of children with these various disorders were not directly compared. First, at the level of facial mimicry, it seems that while children with ADHD or DBD did not show reduced facial mimicry compared to typically developing children, children with ASD and severe deficits in social responsiveness did show reduced mimicry in response to fearful facial expressions. Second, empathy induced prosocial behavior in response to sadness and distress of another child was unimpaired in children with ADHD and ASD compared to typically developing children, while children with DBD did show less prosocial responses. As for the parent and teacher reported traits and emotion recognition and self-reported empathy in response to story paradigms, the results presented in this thesis do not allow a comparison between the different patient groups since different approaches of data analysis were chosen in line with previous studies and theoretical considerations. In sum, the presented studies hint that some aspects of empathy are uniquely affected in attention deficit, disruptive behavior and autism spectrum disorders.

A role for prosocial behavior in further development of interventions

Although low empathy and callous and unemotional features in youth were previously found to be relatively stable from childhood to adolescence (Frick & White, 2008), there is no reason to assume that these traits are unchangeable (Belgrave, Nguyen, Johnson, & Hood, 2010; Frick & White, 2008). A better understanding of impaired empathic functioning may lead to more comprehensive and individualized approaches to treatment interventions aiming to reduce antisocial and to increase pro-social behaviors (Eisenberg et al., 2010). It has been proposed that a comprehensive program targeting prosocial behaviors could also involve the development of skills and activities directed at helping children to learn to be empathic (Belgrave et al., 2010). In the future development of these therapeutic interventions, several important questions need to be addressed. What components of empathy should we aim to influence? At what stage in development will our interventions most likely have a positive effect? And what will the effect of improved empathy be on aggressive and prosocial behavior? Although much remains unclear, some guidance on which ingredients of effective interventions in subgroups of children with empathy deficits could be further examined can be inferred based on the presented studies.

First, the present study adds to the literature in showing that children with DBD, already at the age of 6-7 years old, show less empathy induced prosocial behavior compared to their healthy developing peers. This finding suggests that future interventions should target on increasing empathy induced prosocial behavior. In healthy developing children, existing studies suggest that empathy can be used to foster prosocial behavior in children (Eisenberg et al., 2010). Several studies like the Empathy Training Program and the Child Development Project have made an attempt to assist children in identifying emotions, discriminating emotions in oneself and others, and developing the ability to take the perspective of another (Eisenberg et al., 2010). Other studies have shown an effect of e.g. listening to prosocial lyrics and music (Greitemeyer, 2009) and playing prosocial video games (Gentile et al., 2009) on an increase in helping and other prosocial behavior in typically developing children. However, in clinical populations, efforts have thus far mainly been made to reduce antisocial behavior and examine the effect of low empathy on the treatment of conduct problems and aggression (Eisenberg et al., 2010; Frick et al., 2013). Besides, no studies thus far have focused on the enhancement of prosocial behavior in ecologically valid interactions with peers where children could learn positive consequences of prosocial behavior in a structured and protected environment.

Second, empathic responding was found unimpaired in ADHD and DBD as reported by parents, during a facial mimicry paradigm and on a story task. These three assessment measures, although hard to compare, share that they assessed empathy in less demanding settings, where attention to relevant stimuli could be optimal. Emotion processing and empathy is likely to be increased when attention is directed towards relevant parts of emotional stimuli. For example for facial stimuli, the eyes convey relevant information. Instructing children with empathy deficits to direct their attention to the eyes of others might thus have a positive influence on fear recognition and emotion processing (Dadds et al., 2006). It is a hopeful possibility that interventions at an early age aimed at increasing the healthy components of empathy could have an effect on other aspects of empathy as well as on empathy related prosocial behavior and the inihibition of aggression in the long term.

Third, dimensions of parenting like harsh punishment and low parent–child warmth seem to be associated (Pardini, Lochman, & Powell, 2007) and prospectively related to changes in empathy and callous-unemotional traits (Waller, Gardner, & Hyde, 2013). Importantly, children with reduced empathy and high CU-traits were less responsive to the disciplinary component of parenting interventions but responded equally to positive reinforcement to encourage prosocial behavior (Hawes & Dadds, 2005; Waschbusch, Carrey, Willoughby, et al, 2007). Furthermore, parenting-focused interventions appear to be effective in reducing the level of both aggressive behavior and CU traits (Waller et al., 2013). In sum, interventions should be considered that also focus on empathy and prosocial behavior and not only on the reduction of aggressive behavior. Interestingly, in the present study it was found that parents did not perceive their children as less empathic, whereas teachers did report deficits. This could mean that in interventions on young children with DBD, a first step might be that parents need to be made aware that the setting is of influence on the ability of children to empathize with others. Next, they could be advised to consider to allow children to further improve their empathic skills at home and try to create an environment that makes other settings like the school less socially demanding.

Fourth, in ASD, cognitive empathy but not affective empathy was found to be unimpaired.

A previous study in 4-7 year old children with ASD has proposed that emotion recognition can be trained in ASD (Golan et al., 2010). However evidence that children became more willing to discuss emotions, and became more interested in facial expressions in daily live remained anecdotal (Baron-Cohen, Golan, & Ashwin, 2009) and another study in older and more seriously affected ASD children could not show additional value of emotion recognition training (Dadds, Cauchi, Wimalaweera, Hawes, & Brennan, 2012). In short, a focus on cognitive empathy and improvement in emotion recognition in ASD seems justified but further study is needed. Interestingly, in ASD deficits in both facial mimicry and emotion recognition of fear were found. Since emotion recognition may be enhanced by facial feedback signals that are generated when we automatically mimic expressions of others' faces (Neal & Chartrand, 2011; Oberman et al., 2007) it could also be explored whether an approach aimed to enhance facial could improve emotion recognition in ASD children.

Finally, it has been suggested that stimulant medication can also have positive effects on emotion processing (Manos et al., 2011). These effects could be either direct (e.g., increased emotional expression) or more secondary to reductions in symptoms and/or improvement in others' responses to the child (Manos et al., 2011). Thus far, only a few studies have addressed the role of medication on empathy and prosocial behavior in clinical populations. An early study in children with ADHD found an effect of methylphenidate on a reduction in aggression, but no effect on prosocial behavior (Hinshaw, Henker, Whalen, Erhardt, & Dunnington, 1998). Conversely, in a recent study it was found that in children with ADHD callous-unemotional traits declined alongside other behavioral improvements treatment with a combination of a family-focused behavioral intervention and stimulants (Blader et al., 2013). Our preliminary findings that seem to support a possible influence of methylphenidate on fear processing seem to suggest that further studies examining the role of methylphenidate on emotion processing and empathy are worthwhile. In addition, some studies have considered a possible role for oxytocin administration in the treatment of emotion processing in ASD e.g. (Bartz & Hollander, 2008; Guastella et al., 2010). In sum, more research is needed to examine the role of psychopharmacologic treatment on emotion processing and empathy in children with psychiatric disorders.

Implications for further studies

In order to obtain a consistent view of empathy, first, new instruments are needed to examine deficits in different features of empathic functioning (de Wied et al., 2010; Lovett & Sheffield, 2007). These new paradigms should present ecologically valid and engaging stimuli. They could for example present a combination of facial, postural and vocal emotional content and should consider moving away from passive viewing tasks towards more engaging social interaction paradigms. These paradigms could be designed in a way that different affective and behavioral responses to an emotional stimulus in the participant might provoke different patterns of new emotional stimuli and thus simulate social interaction. Investigators should further take into account that children may lack empathy for certain victims but not for all individuals, especially those they consider part of their in-group (Eisenberg et al., 2010).

Next, the simultaneous assessment of various levels of empathy in response to the same stimulus materials should be considered (Lovett & Sheffield, 2007). Candidates for methodological approaches that could be applied simultaneously are eye tracking to assess whether attention is directed towards relevant parts of the emotional stimulus, fMRI and/or event related potentials to measure neural activity and facial mimicry to assess mimicry responses.

Third, future studies should also take other characteristics in clinical groups into account that are likely to influence empathic responding like limited prosocial emotions, anxiety, impulse control, attention problems and reward dependence. Another interesting trait that has been neglected thus far is the influence of emotion-regulation skills on empathy and prosocial behavior.

Fourth, longitudinal studies are needed to evaluate reduced empathy at different points in development.

Finally, an interesting point for further study lies in the disentanglement of the association between empathy and aggressive behavior and in further refinement of prosocial and aggressive behavior. Does empathy for sadness and distress of others that arise upon an act of aggression indeed prevent further escalation of aggression? If so, both reactive and proactive aggression could be influenced by increasing empathy. Or does the anticipation of empathic feelings of distress also inhibit the initiation of aggression? In that case, a stronger influence of empathy on pro-active versus reactive aggressive behavior would be hypothesized. Likewise, much remains unclear on how empathy is related to prosocial behavior. An important point to consider is that it is especially prosocial behavior that offers the actor no direct knowable rewards that seems to be related to empathy for the pain and distress of others (de Waal & Suchak, 2010). It remains unclear how empathy influences prosocial behavior when other rewards and benefits are present.

Research addressing these issues can help us in the development of new treatment paradigms aimed specifically at inducing empathy in response to sadness and distress of others and prosocial behaviors.

Conclusion

In this thesis, a series of studies on empathy in six and seven year old children with disruptive behavior, attention-deficit and autism spectrum disorders have been presented. It was examined whether previously found impairments in empathy in older children and adolescents would already be present at this age. The nature of empathy deficits in children with these various psychiatric disorders was explored to help better differentiating. Special attention was paid to empathy induced prosocial behavior as this may be relevant for developing novel treatment approaches. In summary, the studies presented in this dissertation show that:

- Children with DBD and ADHD show no impairments in empathy in paradigms and situations where the influence of problems in attending to relevant emotional stimuli is limited.
- Future studies that aim to examine interventions to increase empathy and decrease antisocial behavior in children with DBD and ADHD should take the role of empathy on prosocial behavior and a possible effect of treatment of attention problems into account.
- Children with ASD with severe problems in social responsiveness show deficits in cognitive empathy and emotion recognition of fear as well as in fear mimicry.
- Future studies that aim to enhance empathy in ASD could focus on aspects of cognitive empathy, emotion recognition and facial mimicry.
- High empathic traits predict a reduction in proactive aggressive behavior.

At the end of this dissertation, some questions have been answered and new questions have been raised on the influence of empathy on aggressive and prosocial behavior in children with disruptive behavior, attention deficit and autism spectrum disorders. Obviously, much remains unknown on the complex phenomenon of empathy in children with psychiatric disorders. Some directions have been provided for further study on how we can stimulate empathy and provide environments and treatments that help children in clinical population to hurt less and help more.

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Nederlandse Samenvatting

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Achtergrond en vraagstelling

Empathie is het vermogen om met emoties van anderen mee te voelen en om deze te begrijpen. Eerder onderzoek heeft uitgewezen dat er bij kinderen in de schoolleeftijd of adolescentie een verband bestaat tussen empathie aan de ene kant en agressief en antisociaal gedrag aan de andere kant. De theorie veronderstelt dat als kinderen agressief gedrag vertonen, zij meevoelen met de pijn of het verdriet van andere kinderen als gevolg van dit agressieve gedrag. Daardoor stoppen zij met dit agressieve gedrag. Daarnaast kan het meevoelen met en het begrijpen van emoties en verdriet van anderen er ook voor zorgen dat kinderen prosociaal gedrag vertonen zoals helpen of troosten.

In dit onderzoek hebben we gekeken of kinderen van 6 en 7 jaar met diverse kinder- en jeugdpsychiatrische stoornissen (disruptieve gedragsstoornissen, ADHD en autisme spectrum stoornissen) verschillen van kinderen zonder deze stoornissen in empathie en in prosociaal gedrag. Ook hebben we onderzocht of het vertonen van veel empathie ertoe leidt dat kinderen een jaar later minder agressief gedrag vertonen.

Methode

Empathie is een ingewikkeld concept dat uit verschillende onderdelen bestaat. Er wordt een onderscheid gemaakt tussen affectieve empathie (meevoelen met de emoties van anderen) en cognitieve empathie (herkennen en begrijpen van emoties van anderen). Om empathie te onderzoeken moesten we een manier vinden om empathie betrouwbaar te meten. Empathische kenmerken kunnen gemeten worden met vragenlijsten die door kinderen zelf, ouders of leerkrachten worden ingevuld. Daarnaast kunnen aspecten van empathie worden gemeten in een testsituatie waarbij kinderen naar bijvoorbeeld foto's of filmpjes kijken en geobserveerd worden. Er wordt hen gevraagd hoe ze zich voelen en of ze de emoties van anderen herkennen en begrijpen.

In dit onderzoek hebben we ouders en leerkrachten vragenlijsten laten invullen over het empathisch vermogen van kinderen. Ook hebben we bij de kinderen 3 taken afgenomen. Als eerste hebben we hen verhalen voorgelezen waarin andere kinderen dingen meemaakten. Na de verhalen hebben we gevraagd hoe zij dachten dat de kinderen zich voelden en hoe ze zich zelf voelden tijdens het luisteren naar het verhaal. Ten tweede hebben we onderzocht of ze de emoties van andere kinderen spiegelden door de elektrische spieractiviteit in hun gezicht te meten terwijl ze naar filmpjes met emoties keken. Tot slot hebben we ze een computerspel laten spelen waarbij ze de bal konden toespelen aan 2 andere kinderen. Van een van deze kinderen kregen ze geen munten, waardoor ze de bal vaker naar het andere kind gingen spelen. Daardoor werd het kind zonder munten verdrietig. In dit computerspel konden we meten of ze dit kind alsnog de bal toe gingen spelen.

Resultaten

Hoofdstuk 2 wijst allereerst uit dat 6-7 jarige kinderen zonder psychiatrische stoornis bij het kijken naar gezichten van andere kinderen deze emotionele gezichtsuitdrukkingen spiegelen en dat dit betrouwbaar te meten is met elektromyografie.

De resultaten in **hoofdstukken 3 en 4** tonen dat 6-7 jarige kinderen met disruptieve gedragsstoornissen (met en zonder ADHD) in sommige situaties verschillen van kinderen zonder deze stoornissen. Zo gaven leerkrachten aan dat kinderen met gedragsproblemen minder empathisch reageren. Diezelfde kinderen toonden bij het computerspel minder prosociaal gedrag. Maar we vonden geen verschillen in de vragenlijsten van ouders, de verhalentaak en tijdens het spiegelen van gezichten tussen kinderen met en zonder disruptieve gedragsstoornis.

Voor kinderen met alleen ADHD zonder disruptieve gedragsstoornis kwamen we in **hoofdstukken 3 en 4** tot bijna dezelfde resultaten. Ook over hen rapporteerden alleen leerkrachten dat ze minder empathisch waren, terwijl geen verschil werd gevonden bij de vragenlijsten van ouders, de verhalentaak of het spiegelen van gezichten. In tegenstelling tot de kinderen met disruptieve gedragsstoornis en ADHD toonden de kinderen met ADHD zonder gedragsstoornis tijdens het spelen van het computerspel evenveel prosociaal gedrag als kinderen zonder stoornis. We denken dat dit komt omdat deze kinderen in een onrustige omgeving, zoals die er op school vaak is, moeilijker empathisch kunnen reageren dan wanneer ze thuis zijn of wanneer wij ze in een rustige kamer allerlei taken laten doen. We weten immers dat deze kinderen vaak moeite hebben met het richten van hun aandacht, dus misschien ook wel met het kijken naar de gezichten van anderen op het goede moment. Daardoor zouden ze wel eens belangrijke informatie kunnen missen over hoe anderen zich voelen.

Vaak nemen kinderen met aandachtsproblemen medicatie om deze aandachtsproblemen te doen verminderen. In dit onderzoek hadden we aan de kinderen gevraagd om geen medicatie te nemen tijdens de metingen. Toch waren er een paar kinderen die per ongeluk wel medicatie hadden genomen. In **hoofdstuk 8** beschreven we dat we per toeval aanwijzingen vonden dat deze kinderen op de dag van de meting anders reageerden op angstige gezichten dan kinderen die nooit eerder medicatie namen of op de dag van de meting geen medicatie hadden ingenomen. Om te begrijpen of dit ook echt zo is en hoe dit komt is verder onderzoek nodig dat zich speciaal op deze vraag richt.

Bij de kinderen met autisme spectrum stoornissen die veel problemen hebben in de sociale interactie en communicatie toonden we in **hoofdstuk 6** aan dat ze moeite hebben met het spiegelen van angstige gezichten. In **hoofdstuk 7** beschreven we dat deze kinderen in een verhaal minder goed de angst van een ander kind konden herkennen. Ook rapporteerden ouders en leerkrachten dat ze minder goed gevoelens van anderen konden begrijpen, maar niet dat ze ook minder goed met anderen konden meevoelen.

Tot slot hebben we in **hoofdstuk 5** gekeken in een groep kinderen zonder en met gedragsstoornis of ADHD naar de verbanden tussen de verschillende meetmethoden van empathie en proactieve agressie. We hadden verwacht dat de ene meetmethode van empathie goed met de andere zou overeenkomen, maar dat was lang niet altijd het geval. Wel toonden kinderen die door ouders als meer empathisch werden gezien meer empathisch gedrag tijdens het spelen van het computerspel. We hebben daarna onderzocht of een van de methoden waarmee we empathie hadden gemeten kon voorspellen of kinderen een jaar later nog veel pro-actief agressief gedrag vertoonden. We vonden dat het vooral de empathie was die door ouders werd gerapporteerd die ons hielp bij het voorspellen van proactief agressief gedrag, maar niet de empathie gemeten met de andere methoden.

Discussie

De resultaten van dit onderzoek dienen met voorzichtigheid geïnterpreteerd te worden, rekening houdend met een aantal beperkingen. Ten eerste bestond de patiëntengroep uit 6-7 jarige kinderen die bekend waren op de polikliniek van het UMC Utrecht waarvan sommigen al enige tijd behandeld werden voor hun disruptieve gedragsstoornis, ADHD of autisme spectrum stoornis. De resultaten gelden dus niet zonder meer voor andere groepen kinderen die (nog) geen behandeling kregen. Ten tweede hebben de verschillende manieren waarop we empathie hebben gemeten ook allemaal hun beperkingen en was er weinig overeenstemming tussen de verschillende meetmethoden. Ook blijft het onduidelijk welke aspecten van het disfunctioneren van kinderen met deze stoornissen hun empathie en prosociaal gedrag beïnvloeden. We weten bijvoorbeeld nog te weinig over wat de invloed van het impulsieve en snelle reageren is op de empathie en het prosociale gedrag van kinderen. Verder zou het kunnen dat kinderen met ADHD of gedragsstoornissen minder gegrepen worden door emotionele gezichtsuitdrukkingen, mogelijk als gevolg van een geringere dopaminerge functie, en daarom hun aandacht ook minder op emoties van anderen richten. Ook kunnen kinderen met gedragsproblemen, ADHD of autisme misschien minder goed hun eigen gevoelens onderscheiden van die van anderen of hun eigen gevoelens minder goed onder controle houden. Dat is in dit onderzoek niet onderzocht en het is niet te zeggen wat de invloed daarvan is geweest op de gemeten empathie.

Toekomstig onderzoek zou zich kunnen richten op het verder verkennen van welke invloed aandachtsproblemen, de verwerking van emoties in zijn algemeenheid en de omgeving hebben op de ontwikkeling van empathie bij kinderen met psychiatrische stoornissen. De resultaten van dit onderzoek kunnen worden meegenomen bij nieuwe pogingen om empathie te beïnvloeden en te behandelen. Dat zou bijvoorbeeld kunnen door kinderen te leren om te kijken naar en te letten op belangrijke signalen op de gezichten van anderen. Of door ze te helpen gevoelens van anderen beter te herkennen en benoemen. Misschien ook door ze te leren bewust gezichten van anderen te imiteren of door hen te helpen zich in hen in te leven. Ook medicatie zou een rol kunnen spelen. Eerst en vooral de medicatie die erop gericht is om de aandacht te verbeteren, maar ook bijvoorbeeld het hormoon oxytocine, aangezien onderzoek bij volwassenen lijkt te tonen dat oxytocine mogelijk invloed heeft op empathie.

Dit onderzoek heeft alvast aangetoond dat 6-7 jarige kinderen met gedragsproblemen op een paar niveaus wel, maar op andere niveaus ook weer niet verschillen van kinderen zonder deze problemen. Het lijkt erop dat een rustige omgeving met niet te veel prikkels kinderen met ADHD en/of disruptieve gedragsstoornissen helpt om zich beter in te leven in anderen. Dat is anders dan bij kinderen met autisme en ernstige sociale communicatieproblemen, die problemen hebben met onder andere het herkennen en spiegelen van angst. Meer onderzoek is nodig om beter te begrijpen hoe dit ingewikkelde en gelaagde concept zich ontwikkelt en wat de mogelijkheden zijn om daarop met behandeling invloed uit te oefenen.

Dankwoord

Dankwoord

Het kon alleen maar lukken met veel hulp. Dat heeft me veel plezier opgeleverd in de samenwerking en gesteund om in moeilijke momenten door te gaan om dit onderzoek af te maken.

Aan alle kinderen, ouders en leerkrachten, bedankt dat jullie bereid waren om ons te ontvangen thuis en op school. Wat fantastisch dat jullie al die vragenlijsten wilden invullen en taken wilden doen. Dankzij jullie hulp begrijpen we nu iets meer over inlevingsvermogen bij kinderen en hopelijk helpt dat ons om hen in de toekomst verder te helpen.

Beste Walter, van het eerste idee tot de uitvoering en publicatie heb je me geholpen mijn gedachten te scherpen, keuzes te maken en rustig en stabiel verder te werken. Dank je, dat je mijn nieuwsgierigheid en enthousiasme steeds wist te waarderen en waar nodig in goede banen leidde. Dank voor al je snelle en heldere advies op de vele stukken die we schreven. Toen de omstandigheden moeilijk waren heb ik me door en door gesteund gevoeld en dat heeft me deugd gedaan.

Beste Leon, dank voor je adelaarsblik die beschouwing en grote lijnen combineert met oog voor detail. Met je scherpe analytische vermogen heb je meermaals meegedacht en helderheid geschept in de problemen die we tegenkwamen. Bedankt dat je in je drukke agenda snel tijd wist te maken wanneer ik je nodig had. Dank ook, dat je me steeds weet te vinden voor andere interessante projecten.

Beste Dennis, de ping van de lift van verdieping 17 van het van Unnik is de afgelopen vijf jaar synoniem geworden voor steun, hulp, rustig samen nadenken en uiteindelijk altijd tot een goed plan komen om problemen die eerst onoplosbaar leken tot behapbare proporties terug te brengen en er samen met de nodige humor op terug te kijken. Het is aan jouw zorgvuldige correcties te danken dat de vorige zin de enige in dit proefschrift is die echt veel te lang is.

Geachte professoren van Baar, Dorelijers, Boer, Kemner en Durston, leden van de leescommissie, dank voor jullie tijd, inspanning en kritische blik bij het doorlezen en beoordelen van het manuscript.

Beste Raf en Maarten, het is een grote eer dat jullie mijn paranimfem willen zijn, al is het eigenlijk een woord dat niet bij jullie past. Beste Raf, we hadden bij de biefstuk met friet bij de Belgacom niet kunnen bedenken dat we ooit onderzoek zouden doen, laat staan er een boekske over zouden schrijven. Onze dromen van toen hebben we allebei aangepast aan een academisch ziekenhuis. Laten we blijven zoeken, niet om te vinden, maar omdat er voor ons vak en onze patiënten nog veel te zoeken en nog veel te vinden valt. Beste Maarten, je hebt de afgelopen jaren tijdens het spitten, wieden of dieven geluisterd naar mijn enthousiaste verhalen over wat ik nu weer ontdekt dacht te hebben. Vaak heb je lachend vastgesteld dat er toch ook ergens een echte onderzoeker in me schuilt. Dankjewel voor je eeuwige optimisme. Laten we snel ons nieuwe kantoortje gaan halen.

Als iemand zich bij het lezen van dit proefschrift heeft afgevraagd hoe ik er in geslaagd ben om op 2 jaar tijd al die ouders thuis te bezoeken voor een interview, kinderen op school te meten en ook nog alle data tot bruikbare informatie te bewerken dan komt nu het antwoord. Beste Iris, Kim en Cicely, de drie studentenmusketiers van het eerste uur, dank voor jullie bijdrage aan het ontwikkelen en uittesten van alle taken en het samen zoeken naar een betrouwbaar systeem om de data te verwerken. Beste Lucas, Leonie, Lara, Reggie, Timmy, Laura, Karin, Kirsten, Eva, Marije, Laurien, Dieuwertje, Patricia, Siri, Nicolette, Annemieke, Mirjam, Saskia, Jodine, Kirstie, Lara en Sanne, in het tweede en derde jaar van de dataverzameling kon ik rekenen op jullie hulp en mocht ik samen met jullie de eerste verkenning van de data doen bij het begeleiden van jullie thesis of stageverslag. Beste Perrine en Sarah, wat fijn dat jullie precies op de piekmomenten bijsprongen om te coördineren, te stroomlijnen en aan te sturen.

Beste Iris, Lucas en Nicolette. Jullie mogen nog een keer extra in dit dankwoord. Letterlijk door weer en wind gingen jullie voor mij, bus op bus af, zeulen met de zware koffers vol apparatuur (behalve Lucas dan, want voor jou waren ze natuurlijk licht). Samen hebben jullie schat ik bijna 2000 plakkertjes op de gezichten van de deelnemende kinderen geplakt, uren achter de laptop gezeten om de EMG data te bewerken en alsof dat nog niet genoeg was kon ik ook nog op jullie rekenen als waardevolle coauteurs. Beste Bram en Esmee, wat fijn dat jullie wilden helpen met verse inspiratie bij het berekenen en publiceren van de proactieve agressie en follow-up data. Beste Marieke, dankzij je snelle en gestructureerde denken en werken ben je er in geslaagd om op nauwelijks 3 maanden tijd samen een volledig strak en te publiceren artikel te schrijven. Bedankt.

Beste Arne en Koen, jullie gaven de sample size vanuit Amsterdam een laatste zet, ik hoop dat we elkaar in de toekomst nog vaak weten te vinden voor samenwerking. Dear Linda Camras, Paolo Albeiro, Mark Dadds and David Hughes, thank you so much for letting me use and adapt your pictures, stories and tasks. Dear Christina, Felix and Celia, thank you for the fruitfull brainstorms and positive feedback. I hope we can find ways to put our efforts together in future studies. And yes, I promise, I will finally make time to visit Basel.

It takes a village to raise a child en een afdeling om onderzoek te doen. Dank aan al mijn collega's van onze afdeling psychiatrie. Er was voor dit onderzoek geen geld beschikbaar, maar dankzij jullie kreeg ik tijd om in de afgelopen jaren mijn onderzoeksdag aan dit onderzoek te besteden.

Een paar mensen van onze afdeling wil ik bedanken voor hun bijzondere bijdrage. Eerst en vooral receptie 32, ons secretariaat. Tijdens de jaren dat dit onderzoek liep hebben jullie me geholpen om te voorkomen dat mijn agenda ontplofte en er voor gezorgd dat de combinatie van alles wat ik deed op een of andere manier altijd net paste. Mijn collega kinder- en jeugdpsychiaters door de jaren heen, dank voor het voortdurend delen van jullie kennis, de goede samenwerking en jullie waarneming van patiënten op de momenten dat ik even rust en tijd nodig had om te schrijven. Maurice, Jocelyn, Sarah, Patrick, Marieke, Tim, Tamar, Maretha, Kim, Tessa, MarieLies, Heddeke, Wieske en Jeanette, bij jullie kon ik in de verschillende fases van dit onderzoek altijd even binnenspringen om na te denken over EMG plakkers plakken, taken progammeren, een haalbare planning maken, een dataset bouwen, literatuur ordenen, studenten begeleiden, een klooster zoeken, een dankwoord schrijven, een drukker zoeken, even kletsen tussendoor of op tijd naar huis fietsen. Patricia, dank je voor de kansen die je me hebt gegeven om me na mijn afzwaaien als kinder- en jeugdpsychiater op de zorglijn disruptieve stoornissen verder te ontwikkelen. Rob, voor je stabiele en flexibele hulp en je inspringen als het nodig was. Geeke, voor je morele steun en het waardevolle pedagogisch advies om elke week minstens 1 keer knakworst met komkommer te serveren. Mijn mede MT-leden, samen vormen wij sinds 2 jaar het management team van de afdeling psychiatrie. Het was niet altijd makkelijk om mijn functie als medisch hoofd met het afwerken van dit onderzoek te combineren. Gelukkig doen we het samen, dat scheelt een hoop. En jij, Jannie, zonder jou was het al helemaal niet gelukt. Laten we nog lang en goed blijven samenwerken en de uitdagingen die ons te wachten staan in de komende tijd in goede banen leiden.

Beste Ruth, aan het staartje van dit onderzoek kwam jij met hulp om de laatste loodjes te verlichten en er een heel mooi boekje van te maken.

Beste Peter, Marina, Rutger-Jan, Tom, Piet, Harold, Roy, Coby en Herman, dank voor het aanwakkeren van mijn wetenschappelijke interesse, de begeleiding in de eerste stappen en vele tips die nog jaren later erg zinvol blijken. Dank ook aan alle docenten en mede-cursisten van de Corsendonck cursus 2008 en Biostatistiek 2011. Dear Hanneke, thank you so much for your help and advice in scientific writing. Have you noticed the "to dates" as a tribute?

Beste buren, wat wonen we toch op een heerlijke plek waar onze kinderen vrijuit kunnen spelen, we voor elkaar bijspringen als het nodig is en in alle rust kunnen rondhangen in de zon of bij het vuur na een rondje Ruiterberg of Amelisweerd. Beste Arjen, Maarten, Madeline en Frans Peter, Nicole en Bauke. Het is uniek dat jullie zo een actieve bijdrage hebben geleverd aan dit proefschrift. Van juridisch advies tijdens de pilot, jullie kinderen als proefkonijn, advies bij de opbouw van de dataset tot het schrijven van de macro die voor eeuwig en altijd de final file zal heten.

Beste Martijn, Pepijn, David, Sjoerd en Erik, na bijna 11 jaar wordt onze intervisie nog elke keer rijker en groeien onze gesprekken met ons mee. Dank voor de warmte, scherpe analyses en onvoorwaardelijke steun. Beste Gerard, dank voor je bijdrage en steun aan mijn ontwikkeling. Beste Isis, dank je voor de heerlijke, ongecompliceerde, nuchterheid en gezelligheid elke keer als we elkaar spreken. Beste Piet, het is altijd weer inspirerend om samen naar ons vak over de grens heen te kijken. Beste Lidewij, dank voor je steun en interesse en natuurlijk omdat ik als paranimf alvast een voorproefje mocht nemen dat me erg geholpen heeft in de laatste fase. Beste Thomas, dank voor je reflectie en je humor. Wat goed dat we, nu het wat ver is voor koffie tussendoor, een alternatief hebben gevonden.

Lieve papa en mama, de nieuwsgierigheid, de liefde voor taal en het gevoel voor organisatie die jullie aan mij doorgaven is bij dit onderzoek erg van pas gekomen. Steeds meer besef ik wat een rijkdom het is om bij jullie thuis te komen en bij te praten. Wat was en is het goed om af en toe een moment van rust in te bouwen in ons gezin en ons en onze kinderen door jullie te laten verwennen. Beste Hans en Gerda, steeds weer slagen jullie erin om in onze drukke gezinsagenda gaten te vinden om samen te genieten van de goede dingen van het leven en feest, weekendjes of vakantie te vieren. Wat een ongelooflijk goed plan om even een paar dagen uit te waaien zo vlak voor de verdediging van mijn proefschrift. Lieve Zus en Bert, Ruben en Frouke, Lise en Nassim, Maarten en Sophie, wat fijn dat jullie me helpen bij het relativeren van het belang van al dat wetenschappelijk werk.

Lieve Jolien, lieve Anneloes, lieve Pepijn en lieve Floris, ik ben blij en trots dat het boekje nu klaar is, maar nog veel trotser op jullie. In de loop van de bijna 6 jaar dat ik aan dit onderzoek over 6 en 7 jarige kinderen heb gewerkt zijn jullie (bijna) allemaal een keer 6 of 7 geweest. Jullie creativiteit, vrolijkheid en wijsheid hebben me ontzettend geholpen. Ik vind het super om jullie te mogen zien groeien, bij jullie te kunnen zijn, samen te spelen, te knuffelen, te klimmen, muziek te maken en te zwemmen. Laten we naar dat eiland in de zon gaan met de 14 zwembaden en een extra ijsje nemen om te vieren dat het boekje nu echt klaar is.

Lieve, lieve Kaat, de aftiteling van een proefschrift wordt vaker bekeken dan het verhaal gelezen wordt. En de belangrijkste spelers komen pas op het eind. Wat had je veel geduld met dit project waarin ik zo nodig zes jaar lang wilde onderzoeken wat gezond verstand ook aan de keukentafel kan verzinnen. Dankjewel dat ik tijdens het lopen of wandelen met je kan delen wat ik bedenk, ontdek en leer. Zonder jou had ik dit niet voor elkaar kunnen krijgen. Alleen samen met jou zou ik het zo nog een keer over kunnen doen. Dankjewel.

Abstracts and publications

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Empathy in 6-7 year old children with ADHD: A facial electromyography approach.
P.K.H. Deschamps, I. Schutte, L. Kenemans, D.J.L.G. Schutter, & W. Matthys
Eunethydis 1st international ADHD conference: from data to best clinical practice
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European Child and Adolescent Psychiatry (2010) 19 (Suppl 1):S1

Responses to emotional facial expressions in 6-7 year olds with ADHD: A facial electromyography approach.
P.K.H. Deschamps, L. Coppes, L. Kenemans, D.J.L.G. Schutter, & W. Matthys
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Empathy deficits in 6–7 year olds with DBD and ADHD: a computer game based interpersonal response task.
P.K.H. Deschamps, L. Kenemans, D.J.L.G. Schutter, & W. Matthys
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Facial electomyographic responses to emotional facial expressions in 6-7 year olds with autism spectrum disorder.
P.K.H. Deschamps, L. Coppes, L. Kenemans, D.J.L.G. Schutter, & W. Matthys
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P.K.H. Deschamps, L. Kenemans, D.J.L.G. Schutter, & W. Matthys
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P.K.H. Deschamps, N. Munsters, L. Kenemans, D.J.L.G. Schutter, & W. Matthys
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Influence of empathy on the development of proactive aggressive behavior in early school-aged children.
P. Deschamps, E. E. Verhulp, D.J.L.G. Schutter, B. Orobio de Castro, W. Matthys
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European Child & Adolescent Psychiatry (2013) 22 (Suppl 2):S2 p.182-3

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