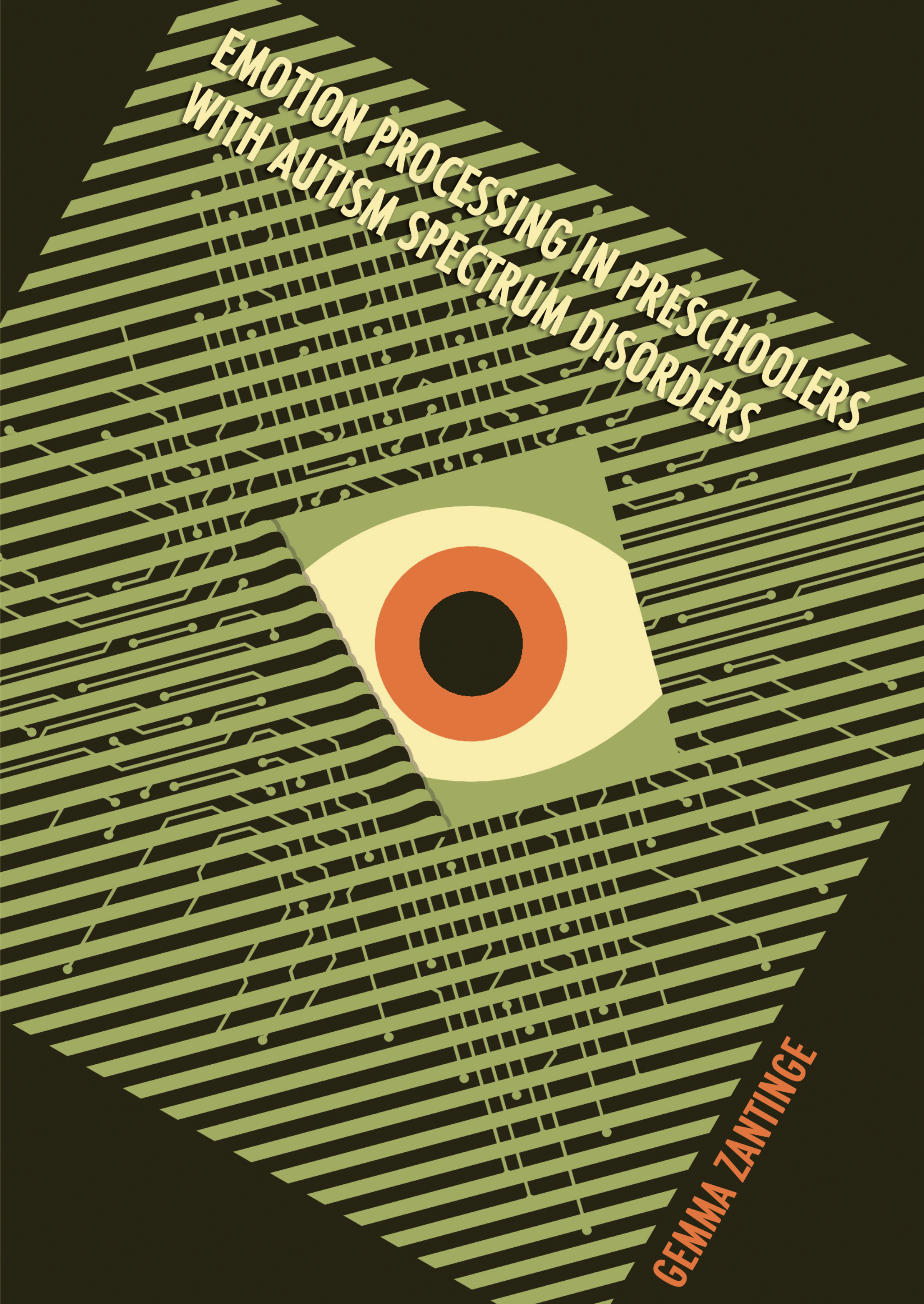
EMOTION PROCESSING IN PRESCHOOLERS
WITH AUTISM SPECTRUM DISORDERS
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Emotion processing in preschoolers with Autism Spectrum Disorders

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Emotion processing in preschoolers with Autism Spectrum Disorders

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Chapter 1

General introduction

Humans spend a great deal of their lives on social interactions, normally within the same species, and usually beneficial to one or more of the individuals. It is believed that social behavior evolved because it is helpful to those who engage in it, which means that these individuals are more likely to survive and reproduce (Brothers, 2002). Social behavior serves many purposes and provides many benefits to those who practice it. Being able to participate in a social environment is a condition for maintaining a successful personal and professional life, such as having friends and a career. But social functioning also determines greater feelings of worthiness, purpose, and experiencing quality of life. In infancy, social behavior is already of vital importance to the development of children, from the first social smile to responding to your own name. These early social interactions thrive the developing brain and are crucial in our early years of life. During childhood, social behavior further evolves and is important for making friends, feeling confident, discovering your own identity but also to adapt in different contexts such as school, social activities, and at home.

The human brain is designed for social interactions to run smoothly. The neuropsychology of social behavior studies these neural networks and related cognitive and emotional systems that enable humans to understand, predict and share feelings, thoughts, desires, and intentions (Van Rijn, Van 't Wout, & Spik, 2012). An important question is to what extend cognitive and emotion processes can be discriminated and how they work together in facilitating social behavior. It is believed that cognition and emotion are two specific, functionally different systems for information processing, that are closely working together to successfully navigate through a complex, dynamic, social, and constantly changing world (Beauchamp & Anderson, 2010).

Cognitive functions can be defined as mental processes involved in social interactions and can be divided into three stages; perception (attending), interpretation, and reaction (Van Rijn et al., 2012). Examples of social cognitive functions are the ability to recognize faces and facial expressions, understanding the feelings and needs of others, and taking part in a conversation. Social cognitive functions can be differentiated from more general cognitive skills that also work in facilitating social behavior, such as attention, inhibitory control, and working memory.

Emotions are a prerequisite for social motivation because emotional incentives, like finding reward or pleasure or successfully avoiding pain or sadness play a major role in facilitating behaviors. Social interactions are full of emotions and vice versa social emotions become meaningful when interacting with others. In social situations, that are often unpredictable and contain incomplete information, emotions can enhance adaptive behavior and can be helpful in making decisions (Izard, 1971). Emotions have a motivational function, and make you pay attention in a fearful situation, but also have a strong communicative function which is necessary for the environment to be able to rapidly understand what is needed (Blair, 2003). Emotions however, can also be hindering when the timing is off, when the intensity does not match the social situation, or when directed towards irrelevant aspects (Lazarus, 1991; Parrott, 2001). Emotion related processes, in contrast to cognitive processes, are physical or bodily reactions that lead to adequate adaptive behavior to the specific situation. Given the complex nature of social functioning, involving not only social cognitive processes but also emotion related processes, social development is vulnerable to developmental disruptions and shows great individual variability. Ranging from children who easily tune in to others, to children who have substantial difficulties navigating their social environment. This vulnerability and the impact of developmental disruptions can be seen in Autism Spectrum Disorders (ASD; Box 1.), a spectrum of pervasive neurodevelopmental disorders which manifest before the age of four and are characterized by persistent deficits in social communication and social interaction, such as social-emotional reciprocity, nonverbal communicative behaviors, and deficits in developing, maintaining and understanding relationships (APA, 2013). The worldwide population prevalence of ASD is about 1% and affects more male than female individuals (Lai, Lombardo, & Baron-Cohen, 2014). Consequences of the social communication problems in ASD on later outcomes can be severe, expressed in a high risk for poor quality of (social) life, even compared to other childhood psychopathology (Barneveld, Swaab, Fagel, van Engeland, & de Sonneville, 2014). The compromised overall quality of life in individuals with ASD stresses the importance of understanding the underlying mechanisms of impaired social behavior. The majority of studies in ASD that aimed at explaining the social behavior problems over the last decades, have had a focus on cognitive functions such as facial recognition and theory of mind. In addition, emotion has mainly been investigated in terms of empathy. Empathy has been defined as 'the capacity to be affected by and share the emotional state of another, to assess the reasons for the other's state, and to identify with the other, adopting his or her perspective' (de Waal, 2008). A distinction is typically made between 'cognitive empathy', i.e. understanding emotions of others (also termed Theory of Mind), and affective empathy, i.e. resonating with others in terms of affective state. Much more research has been done on cognitive empathy (Theory of Mind) than affective empathy, and how affective empathy relates to other aspects of emotion processing remain poorly understood in ASD. There is a need for studies integrating all levels of emotion processing, including how children with ASD perceive, experience, regulate, and express emotions by investigating not only what can be seen on the 'outside' in terms of behavior, but also the processing of emotions on the 'inside' referring to underlying processes.

The central aim of this dissertation was to further explore emotion processing by combining new, sensitive, and direct measures of physiological, cognitive, and behavioral mechanisms that are involved in the development of emotion processing in preschool children with ASD during a critical period of development. Knowledge about the development of early emotion processing that are building blocks of social development is crucial for identifying windows of opportunity to stimulate development. This knowledge could benefit parents and professionals in understanding and supporting children with ASD, optimizing the circumstances in which these children develop and benefitting from brain plasticity during the early preschool years in particular. Eventually this could lead to improvement of interventions that are adapted to the origins and underlying mechanisms of social dysfunction.

Box 1. DSM-5 diagnostic criteria for autism spectrum disorder 299.00 (F84.0)

A) Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive):
   1) Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
   2) Deficits in non-verbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and non-verbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and non-verbal communication.
   3) Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

B) Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive):
   1) Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
   2) Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or non-verbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
   3) Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).

4) Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

C) Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).

D) Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E) These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

From the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (APA, 2013)

What are emotions?

Already 36 years ago, a list was composed of the 92 definitions of emotion (Kleinginna & Kleinginna, 1981). And still, there is debate as to what an emotion actually is considered to be. The first important characteristic of an emotion that is commonly mentioned is *when is occurs*. Generally, an emotion is felt when you direct your attention, which can either be conscious, complicated and enduring (writing a thesis), or less conscious, simple and transient (such as a startle response when the window washer suddenly appears). They may be widely shared in a group, containing complex social interactions (laughing in response to social interactions during coffee with colleagues) or individual (in response to reading an acceptance email from an editor). Emotions can be experienced in response to what others do, but can also be felt intrapersonal. It is the subjective meaning of the particular situation that gives rise to the emotion and these emotions change constantly due to changes in the situation itself or changes in the meaning the situation holds for the individual (Gross, 2013).

Another broadly accepted characteristic of emotions is that they are *multifaceted*. This is described in the definition by Hockenbury & Hockenbury (2010) stating that an emotion is a complex psychological state that involves three distinct components; *a subjective experience (feeling), observable behavior or expression, and physiological activity*. So emotions not only make us feel, but they make us act (Gross, 2013). Examples of these actions are facial and bodily expressions, but also instrumental actions such as staring and cheering and the actions that are initiated by the fight or flight response. These changes that occur in the body and in behavior are closely related to underlying autonomic and neurobiological (physiological) responses, that enable us to achieve our goals that gave rise to the emotion in the first place (Levenson, 2014).

As our environment is largely social, we are able to adapt to changes in our social environment with the help of our emotions. A distinction can be made between perceiving the emotions of others and own experienced emotions. The perception of other people's emotions is necessary to continuously collect information in a social context, to give meaning to this information, and to adjust your behavior and responses accordingly. Besides the emotions of others, it is of equal importance to recognize your own emotions, which also has social consequences. For example, showing sadness results in getting support from others and smiling eases entering into relationships. A crucial prerequisite for recognizing emotions in others but also one's own emotions, is that you have attention for the social information in your environment.

Attention and emotion

Attending to (the emotions of) others is an important part of social information processing and is one of the most valuable sources of social information. It is believed that this capacity is part of an evolutionarily ancient process activating animals to preferentially attend to other animals (Simion, Regolin, & Bulf, 2008). Preferential attention towards biological motion (such as motor movements) and other meaningful social signals in humans is already present from a very early age, even in two-day-old infants (Haith, Bergman, & Moore, 1977; Klein, Shepherd, & Platt, 2009; Salva, Farroni, Regolin, Vallortigara, & Johnson, 2011; Simion et al., 2008) and is referred to as social attention. Social attention is considered an intrinsic capacity of the visual system, triggered by or resulting in an arousal response. Detecting emotions of others, as evident from facial expressions, tone of voice, body postures, and motor movements, is crucial for the development of adaptive social behaviors, such as learning to socialize and tune into the wishes, desires, and intentions of others. Thus, adequate attention to other people's emotions is supposed to be necessary to continuously gather information about the social interaction that is taking place and if necessary to adjust behavior accordingly.

Emotional arousal

Another aspect of social information processing is an arousal response which triggers an emotion and enables the body to respond accordingly. Arousal is driven by the complex and interactive functioning of the autonomic nervous system. Together with other neurophysiological and neuroanatomical processes, reciprocally linked with the central nervous system (the brain and the spinal cord) as part of the nervous system, and is considered a primary behavioral regulator (Porges, 2001). The autonomic nervous system has two branches, the sympathetic nervous system (involved in stress and activity, also referred to as the ‘gas pedal’) and the parasympathetic nervous system (promoting calm, vegetative activities, described as the ‘brake’). For example, the perception of a dangerous situation leads to rapid physiological changes, such as the production of adrenaline, increase in heart rate, and tension of muscles which prepares the body for action. The importance of the autonomic nervous system as regulator, activator, coordinator, and communicator is reflected in the constant monitoring and adjusting of our functioning, enabling the body to respond to internal and external demands (Levenson, 2014).

In daily life, an arousal response is necessary for being able to experience emotions but also has a regulatory function with regard to the response to emotions of others, expressed in behavior. An arousal response, or modulation in arousal is necessary for responding to situational demands, such as emotionally resonating with others but also for example to tone down a behavioral response when others seem to be hurt by your actions or words (Lydon et al., 2016). Vice versa, autonomic rigidity is related to a lessened capacity to generate or alter physiological and emotional responses in synchrony with changes in the environment (Appelhans & Luecken, 2006) and has been identified as risk factor for later development of behavioral and emotional problems (Lydon et al., 2016).

An increase in arousal is thought to improve performance, but only up to a certain level (which is different for every individual), also called the optimum level of arousal (Yerkes & Dodson, 1908). When tipping over the optimum level of arousal (e.g. hyper-arousal), performance begins to suffer and this high level of arousal can lead to stress, panic, anger or even violence. On the contrary, a blunted arousal response is associated with feelings of dullness, under-stimulation, and also interferes with social behavior (Lydon et al., 2016). So, regulation of these arousal responses is necessary for promoting calm behavior or action in order to emotionally resonate with others in the social environment.

Emotion regulation

The ability to regulate emotions is crucial for social interactions and important for achieving long-term goals. An arousal response triggers emotions but then, this emotional arousal response needs to be regulated into goal-directed behavior, in proportion to the situation. For example, imagine a girl taking the ball from a boy, unannounced. This might trigger an arousal response in the boy and an emotional reaction (maybe anger or surprise). Without regulating the emotional response, the boy might burst in to anger or even worse, use violence to get the ball back. Short-term consequences of this outburst could be an affected relationship with that girl, and parents needing to intervene in the situation. In the long-term, not being able to regulate such emotions in an age appropriate way by for example asking the girl to return the ball or even suggest to play together, might eventually lead to social dysfunction

Emotion regulation is defined as "those behaviors, skills, and strategies, whether conscious or unconscious, automatic or effortful, that serve to modulate, inhibit, and enhance emotional experiences and expressions" (Gross & Thompson, 2007, p. 229). Emotion regulation can be achieved through roughly two categories of strategies, antecedent focused and response-focused. Antecedent-focused strategies refer to tactics that are implemented before emotion response tendencies have become fully activated or while they are becoming activated. Examples are situation selection (going to the playground when chances of encountering other children are little), situation modification (bringing more than one toy in case someone takes the ball), attentional deployment (changing your mind and find something else to play with), and cognitive change (reappraisal; recognizing the fun of playing together and joining the girl). Response-focused strategies refer to strategies implemented once an emotion is already under way and the response tendencies have been generated, such as thinking afterwards and revalue that the situation was not that bad. All of these examples of regulatory behavior can be considered more or less adaptive, depending on the situation and the goals that were set.

With regard to emotion regulation, cognitive capacities play an important role, expressed in for example language skills. Language is important for social navigation, including the regulation of emotions that are part of the social interaction, so for example asking the ball back or suggesting to play together with the ball (Beauchamp & Anderson, 2010). Thus, language is a means for influencing the environment, it enables children to communicate about social interactions and to learn about appropriate ways to manage emotions (Eisenberg, Sadovsky, & Spinrad, 2005). (Non-) verbal language evolves in the early years from the first social smile to the emergence of intentional imitative behavior and dyadic interaction with aspects of communication such as joint attention and expressive and receptive communication. Being able to identify and express emotions is a prerequisite for regulating emotions (Eisenberg et al., 2005).

Besides language, executive functioning is also important for emotion regulation. Executive function is an umbrella term for a broad range of higher order cognitive processes that are critical for efficient functioning in everyday life such as attention, problem solving, cognitive flexibility, and inhibitory control. With regard to the example of the ball, this would mean paying attention to what just happened, thinking of different solutions, being able to switch between solutions when they don't work, and preventing yourself from starting to cry, yell or worse. Executive functions develop mostly stepwise through childhood and adolescence, together with the maturation of prefrontal regions of the brain (Anderson, 2008) and thus can be considered an indicator of very early frontal brain development. Together, executive functioning and language reflect the ability to express, control and steer emotions and are important to study as they are related to emotion processing in daily life.

The development of emotion regulation is strongly dependent on the maturation of neural networks in the brain that support these capacities. This refers not only to the development of certain structures and related functions, but also the integration and specialization of these brain regions. Of interest with regard to the study of ASD and emotion regulation are the prefrontal cortex and the amygdala. The amygdala, an almond-shaped structure located deep in the frontal portion of the temporal lobe and is related to emotion and social cognition. Among other functions, it is important in the registration and taxation of for example fearful or threatening situations and connects to the brain functions that initiate physical responses (hypothalamus) expressed in heart rate increases. The amygdala is directly linked to the survival response of fight or flight, but is also active in the process of recognizing facial expressions. The amygdala not only sends information to the frontal cortex, but is also directed by the same frontal areas, which allows for regulation of emotions. The prefrontal cortex is the center for emotional regulation and regulatory functions in general (e.g. executive functioning) and when functioning of the prefrontal cortex is impaired or even damaged, this leads to in control over behavior and emotions.

Emotion expression

Closely related to the regulation of emotion as expressed in observable behavior, is the expression of emotions. Emotional (facial) expressions were a topic of research since Darwin's *The expression of the emotions in man and animals* (Darwin, 1872) and have been of specific interest with regard to the study of ASD. Emotions have an important motivational function which is especially important in a complex, ever changing environment. As our environment is largely social, we are able, through our emotions, to adjust to changes in our social environment and in ourselves. The expression of emotions has important social consequences. Seeing sadness or someone in pain results in being able to support others and eases entering into relationships. Therefore, the behavioral expression and translation into action of what is experienced emotionally on the inside needs to be in tune with each other. This coordination between (behavioral and facial) expression, regulation, and perception is referred to as emotional concordance (Hollenstein & Lanteigne, 2014) Concordance allows parents, caregivers, but also the social environment in general to be able to rely on the emotional expressions of children as a signal that may trigger the need for support, comfort, and help. An impediment in the concordance, or discordance, may disrupt caregiver responses which, over time, may amplify early vulnerability into a developmental trajectory of increasingly dysfunctional emotion regulation, social development, and early language skills (Kasari, Sigman, Mundy, & Yirmiya, 1990; Sullivan & Lewis, 2003; Wan et al., 2012).

Emotion processing in Autism spectrum disorders

Considering the complex picture of social functioning and its components, behavioral disorders such as ASD manifest themselves heterogeneously and clinically divers. The importance of understanding the underlying emotion processes of social behavior and their relationships can give more insight into the origins of the clinical symptoms of ASD.

Attention and emotion

Research in ASD has shown that children with ASD lack early social attention to the emotions of others and it is believed that problems in spontaneous visual orienting toward such social cues might be among the first manifestations of ASD (Ames & Fletcher-Watson, 2010; Falck-Ytter, Bolte, & Gredeback, 2013; Klin, Jones, Schultz, Volkmar, & Cohen, 2002). Behaviors reported in children with ASD in the first year of life include less frequent orienting to their own name, diminished eye-contact, and social aloofness in response to others (Osterling, Dawson, & Munson, 2002). What we do not know however, is how this lack in early social attending to emotions of others is related to the emotional experience (e.g. emotional arousal). How does attending to emotions of others impact one's own emotional arousal system? In addition to this question, it is important to note that the majority of emotion research in ASD has had a focus on perceiving and cognitive appreciation of the emotions of others (empathy). Besides this important question of whether children with ASD have attention for the emotions of others, it is also important to study how children with ASD express and respond to *own* experienced emotions in terms of emotional arousal in response to such social triggers.

Emotional arousal

Measuring the internal states of emotion as expressed in physiological arousal is important because this might help explain the observed behavioral dysregulation in children with ASD. Taking together the research on physiological arousal in ASD during rest, there is evidence for normal resting state heart rate levels (Benevides & Lane, 2015), but lower heart rate variability. Higher heart rate variability enables an individual to select from a larger repertoire of actions to react to environmental demands if needed and vice versa, lower heart rate variability is associated with impaired behavioral repertoires (Guy, Souders, Bradstreet, DeLussey, & Herrington, 2014; Neuhaus, Bernier, & Beauchaine, 2014; Van Hecke et al., 2009). Furthermore, studies indicate overall similar heart rate responses but different arousal patterns in response to a variety of stimuli (for a review see; Benevides & Lane, 2015). These results however, do not explicitly address the role of arousal responses triggered by the emotions of self or others in social situations. Studying emotional arousal in response to emotional expressions of others in ASD may help gain insight in specific and different dysfunctions that may underlie behavioral problems. For example, less engagement in social interactions may arise from high emotional arousal and related social anxiety, or from low emotional arousal related to low social motivation. Thus, it is important to study emotional arousal that accompanies own emotions, for example during frustration or anxiety, as well as arousal triggered by emotions of others.

Emotion regulation

Emotional behavior problems in ASD expressed in tantrums, irritability, aggression, self-injury, and impulsivity are among the most frequently reported behavioral difficulties by parents and professionals (Geller, 2005; Lecavalier, Leone, & Wiltz, 2006). Even though these behavior problems are neither a part of the clinical diagnosis for ASD (Box 1) nor are they exclusive to ASD, recent research stresses the importance to consider emotion dysregulation as potential underlying mechanism of the reported behavior problems in ASD (Mazefsky, Pelphrey, & Dahl, 2012). The consequences of not being able to adequately regulate your emotions is highlighted by related increases in social and behavioral difficulties across time (Berkovits, Eisenhower, & Blacher, 2017). More specifically, emotion dysregulation predicts negative outcomes in school success (Graziano, Reavis, Keane, & Calkins, 2007; Gumora & Arsenio, 2002; Howse, Calkins, Anastopoulos, Keane, & Shelton, 2003), problem behavior, and mental health problems (Eisenberg, Fabes, Guthrie, & Reiser, 2000; Graziano et al., 2007; Silk, Steinberg, & Morris, 2003). The effects of dysregulation are already present at 12 months of age, as is reported by parents of children with ASD (Gomez & Baird, 2005). Studying emotion regulation could potentially contribute to understanding the observed emotional behavior problems in ASD (Mazefsky et al., 2013; Mazefsky et al., 2012). Research has shown that children with ASD less often use adaptive social strategies, use more maladaptive strategies such as venting or avoiding the situation, and resign more quickly from a social situation (Jahromi, Meek, & Ober-Reynolds, 2012; Konstantareas & Stewart, 2006). The question to be answered is whether the observable problems in regulation of behavior correspond to the experienced emotional arousal response. In other words, is the perceived dysregulation of behavior in ASD a consequence of less arousal modulation or caused by over-arousal preventing children from adapting their behavior effectively to the situation.

Emotion expression

Studying emotion expressions may especially be relevant in early childhood when children in general, and children with ASD even more, are dependent on caregivers for their physical and emotional needs and when interaction patterns between the child and caregivers shape the developing brain. The nature and specificity of emotion expression difficulties however, do not seem universal for all individuals with ASD (Nuske, Vivanti, & Dissanayake, 2013) with studies reporting equal levels of emotional expressiveness (Jahromi et al., 2012) and studies reporting less expressivity (Stagg, Slavny, Hand, Cardoso, & Smith, 2013). Studies investigating the correspondence between expressivity and underlying arousal are scarce and have yielded evidence for both discordance (however measured with self-report), and concordance (Stein et al., 2014). A disconnection between expression and experience could serve as explanatory factor for reported behavior problems in ASD. However, more research into the relationship between arousal and expressed behavior, using sensitive and direct measures at a young age during critical periods of development to identify and target the developmental trajectory of ASD, is warranted.

Considering the current knowledge about emotion processing in ASD as just described, studying emotion processing in ASD should have a multi-faceted approach including the attention, arousal, regulation, and expression of emotional functioning. The combination of these components of emotion processes in scientific research is scarce, especially in developmental disorders and even more in early childhood.

The importance of studying early development

Research interest for ASD has shown dramatic increases from 6054 studies between 1940-1999, to 16741 between 2000 and 2012 (Lai et al., 2014). Even though the vast majority of this surge in ASD research has examined individuals from mid-childhood onwards, only over the past two decades there has been a shift to early childhood and even infancy in the study of ASD (Bradshaw, Steiner, Gengoux, & Koegel, 2015; Brian, Bryson, & Zwaigenbaum, 2015; Daniels, Halladay, Shih, Elder, & Dawson, 2014; Zwaigenbaum et al., 2015). And while there is increased consensus for reliable identification of ASD before 24 months, knowledge about the early markers, underlying mechanisms of social dysfunction, and windows of opportunity for positively influencing the developmental trajectory remains challenged. Early identification of ASD is still mainly based on behavioral characteristics, parent concerns, and early markers observed in clinical practice.

Early knowledge about the underlying mechanisms of social development is crucial for identifying windows of opportunity and recognizing the early sings of vulnerability for developmental disruptions. This knowledge could benefit parents and professionals in understanding and supporting children with ASD, optimizing the social circumstances in which these children develop and benefitting from brain plasticity during the early years in particular (Bölte et al., 2016). In addition, new technologies, such as non-invasive eyetracking and heart rate measures, could potentially lead to more objectively measurable, quantifiably, and generalizable phenotypes, especially in young children for whom these measures are non-invasive and provide rich information about underlying mechanisms.

Aims and outline of this dissertation

The central aim of the current thesis is to study emotions in young children with ASD, by focusing on the attention, arousal, regulation, and expression of emotion. The studies presented in this thesis are part of a larger longitudinal study, designed to gain insight into the underlying mechanisms of emotion processes in children with ASD.

Participants in the studies are typically developing children and children with ASD, aged between 3.5 and 6.5 years old. These children and their parents were recruited through two large regional institutions specialized in the diagnosis and treatment of ASD and through daycare centers and elementary schools in the western part of the Netherlands.

The first study (**chapter 2**) addresses the question of whether attention to the emotions of others is different in ASD, compared to typically developing children using eyetracking.

Children watch a social-emotional video clip of peers in an argument displaying negative emotions. The eyetracker records the exact location of visual focus, providing information about where children look when confronted with emotions of others. While they watch this clip, electrodes measure the heart rate of children as index of emotionally resonating with their peers. This study aims to gain insight into the experience of emotions while watching other's distress. The results are related to social behavioral problems as expressed in autism symptomatology. **Chapter 3** focuses on the emotions that young children with and without ASD experience. This is done by using a frustration task, which means that they choose a very desirable toy that was placed in a transparent locked box. The task always ends well, by providing the children the right key and letting them play with the toy for a while, which also enables us to measure recovery after frustration. The role of cognitive skills, especially executive functioning and language skills are discussed. In **chapter 4** we evaluate the experienced emotional arousal, but now in response to a frightening situation. The children are confronted with a remote-controlled robot that walks towards them and emits noise. In addition to measuring emotional arousal in response to the robot, facial and bodily expressions of fear were coded in order to assess the level of emotional concordance; how does the 'outside' expression relate to the 'inside' experience. In **chapter 5** results of a longitudinal study are presented to gain insight into the development of social attention towards others and corresponding emotional arousal. The assessment described in chapter 2 was repeated after six months, with a parallel version of the social-emotional video clip. In addition, the role of executive functioning in the development of social attention and arousal is investigated, in the typically developing children only. By studying this we aim to take the first preliminary steps in investigating which mechanisms are of influence on the development of these early processes of social behavior. This knowledge is important with regard to identifying windows of opportunity for children with ASD and possible sensitive periods for the development of social behavior which could lead to specific treatment targets. In **chapter 6** the conclusions and implications of these studies are summarized and directions for future research are provided.

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Chapter 2

Psychophysiological responses to emotions of others in young children with Autism Spectrum Disorders; Correlates of social functioning

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Autism Research.

Abstract

Studying cognitive and affective mechanisms of social behavior could lead to identifying early indicators of derailing social behavior in young children with Autism Spectrum Disorders (ASD). The present study combined sensitive and objective techniques, such as eyetracking and psychophysiology, to provide insight into early neurodevelopmental mechanisms that are more difficult to uncover when relying on behavioral measures. Social attention towards faces and changes in affective arousal were investigated together in 28 young children with ASD (42-75 months) and 45 non-clinical controls (41-81months). Children were shown a social-emotional video clip while eyetracking and heart rate were measured. Children with ASD fixated less on key social-emotional features within the clip as compared to controls, even though both groups attended equally towards the screen. In contrast to the control group, children with ASD did not show an increase or modulation in affective arousal in response to the social-emotional scenes. Severity of ASD symptoms, specifically social problems, was associated with arousal modulation and social attention within the ASD group. Early ASD symptoms are associated with impairments in fundamental building blocks of social behavior as expressed in a lack in spontaneous social attention and affective arousal. Such sensitive and objective measures of underlying mechanisms might serve as indicators for tailored approaches in treatment and may help in evaluating effectiveness of early interventions aimed at positively influencing social development and related quality of life in individuals with ASD.

Introduction

Over the past two decades, research dedicated to the assessment and treatment of Autism Spectrum Disorders (ASD) has made a shift to early childhood and even infancy (Bradshaw, Steiner, Gengoux, & Koegel, 2015; Daniels, Halladay, Shih, Elder, & Dawson, 2014; Dawson & Bernier, 2013; Zwaigenbaum et al., 2015). While there is increased consensus for reliable identification of ASD before 24 months, interventions for infants in this period remain limited (Bradshaw et al., 2015). Early identification of ASD is mainly based on behavioral characteristics, parent concerns, and early markers observed in clinical practice. In addition to these important observations, integrating early biological processes of derailing social behavior is necessary to identify and target the developmental trajectory of ASD, especially considering the large heterogeneity in ASD (Zwaigenbaum et al., 2015). Objectively and sensitively studying mechanisms that are closely related to social functioning during critical periods of development in childhood could not only contribute to the identification of early markers but may also serve as indicators for tailored treatment approaches in these early years (Dawson & Bernier, 2013; Landa, 2008). The relevance for this focus on early identification and related intervention options is strengthened by results demonstrating significant progress and diminished ASD symptoms after intensive early interventions, even though more research is needed to further investigate the mechanisms underlying effectiveness (Bradshaw et al., 2015; Dawson et al., 2012)

Social behavior, from a very early age, requires a child to respond to a fast-paced and ambiguous environment. Social situations can be fraught with challenges and large amounts of information need to be processed simultaneously (Knafo, Zahn-Waxler, Van Hulle, Robinson, & Rhee, 2008). When engaging, both affective and cognitive processes trigger individuals to attend and respond (Baron-Cohen & Wheelwright, 2004; Blair, 2005; Bons et al., 2013). Affective processes facilitate the body to respond to the emotional state of others. Cognitive processes that help to understand social information and guide social responses are described in the Social model by Beauchamp and Anderson (2010) and include the domains of social cognition, executive functioning, and language/ communication.

Fundamental to the cognitive processing of information in a social context, is an automatic and spontaneous visual orientation, also referred to as social attention (Chawarska, Macari, & Shic, 2012; Klein, Shepherd, & Platt, 2009). It is necessary that the observer selects and encodes relevant aspects of other people (Frank, Vul, & Saxe, 2012). This involves attention to faces of others, because faces reveal essential information about a person's emotional state, intentions, and desires. (Birmingham & Kingstone, 2009; Klein et al., 2009). Social attention is present from early infancy; by three months infants have a strong tendency to focus on the face (Haith, Bergman, & Moore, 1977).

For typically developing children, this early social preference towards relevant social stimuli is largely automatic, efficient, and requires little effort (Haith et al., 1977; Salva, Farroni, Regolin, Vallortigara, & Johnson, 2011; Simion, Regolin, & Bulf, 2008). For children with ASD however, social situations can be challenging (Volkmar, Chawarska, & Klin, 2005). Studies have shown that children with ASD lack early social predispositions and it is believed that problems in spontaneous visual orienting towards social cues might be among the earliest symptoms in ASD (Ames & Fletcher-Watson, 2010; Dawson et al., 2004; Falck-Ytter, Bolte, & Gredeback, 2013; Klin, Jones, Schultz, Volkmar, & Cohen, 2002). Indeed, there is evidence that children with ASD have deficits in attending to social cues, orient less towards socially relevant information, show problems in face recognition, and diminished attention toward people versus objects and geometric figures (Chawarska & Shic, 2009; Dawson et al., 2004; Guillon, Hadjikhani, Baduel, & Roge, 2014; Jones & Klin, 2013; Klin, Lin, Gorrindo, Ramsay, & Jones, 2009; Maestro, Muratori, Cavallaro, et al., 2005; Pierce, Conant, Hazin, Stoner, & Desmond, 2011). However, not all studies find social attention deficits in children with ASD which is thought te be in part related to variation in for example stimulus type (static, dynamic, social, non-social, and the presence of facial stimuli) (Pelphrey et al., 2002; van der Geest, Kemner, Verbaten, & van Engeland, 2002) and for face specific features as differences in looking at the mouth yield mixed results (Papagiannopoulou, Chitty, Hermens, Hickie, & Lagopoulos, 2014). These mixed findings stress the relevance of better identifying underlying mechanisms of atypical social attention in early life.

In order to adapt behavior and meet social goals, it is necessary to have and maintain an optimum level of arousal (Chambers, Gullone, & Allen, 2009). An arousal response is crucial for steering and tuning our behavior in social situations. Arousal can be conceptualized as a dimension of emotional responsiveness and is considered a prerequisite for emotionally resonating with others in social context (For reviews on the topic of arousal and emotion see; Kreibig, 2010; Mauss & Robinson, 2009). Therefore, in addition to social attention, it may be of equal importance to address affective arousal in response to such social cues in children with ASD.

The autonomic nervous system (ANS) is thought to contribute to affective, but also cognitive and behavioral responses in children (Benevides & Lane, 2015) expressed in arousal responses. One psychophysiological index of affective arousal is heart rate. Although heart rate is frequently described as a measure of autonomic arousal, it varies due to the influence and interaction between both sympathetic (preparing the body for action) and parasympathetic activity (rest and digest) of the ANS (Benevides & Lane, 2015). The literature about affective arousal and ASD however, primarily focuses on parental interviews, questionnaires, and behavioral observations (Mazefsky, Pelphrey, & Dahl, 2012). It is becoming increasingly recognized that biological parameters of arousal in children with ASD should also be studied because the degree to which social cues of others impact the ANS might be fundamental to the early developmental disruptions (Mazefsky et al., 2012). Research on resting-state arousal in children with and without ASD has shown similar levels (Althaus, Mulder, Mulder, Aarnoudse, & Minderaa, 1999; Nuske, Vivanti, & Dissanayake,

2014). However, in *response* to social cues, there is evidence for abnormal affective arousal in ASD, although some report slower and others report faster heart rate levels (heightened and lowered responsiveness, respectively) (Benevides & Lane, 2015). Unfortunately, studies investigating baseline heart rate and task related changes in response to social-emotional cues in young children with ASD are scarce (Benevides & Lane, 2015; Bons et al., 2013). We therefore aimed to simultaneously investigate social attention and arousal in young children during a critical period in attentional and social development. In order to tap responses with high ecological validity, it is important to rely on dynamic stimuli, with high levels of social interaction, and showing daily-life rather than acted emotions (Chevallier et al., 2015; Chita-Tegmark, 2016; Risko, Laidlaw, Freeth, Foulsham, & Kingstone, 2012; Speer, Cook, McMahon, & Clark, 2007).
Our research questions were if 1) young children with ASD attend less to socially relevant cues when looking at a daily-life social scene, and 2) whether social attention was associated with atypical affective arousal patterns in children with ASD. In order to assess the relevance of these mechanisms, we also investigated if abnormalities in social attention and affective arousal were associated to social behavioral problems as expressed in more severe ASD symptoms.

Methods

Participants

A group of 28 children (26 boys) with ASD aged 42 through 75 months (mean 57.96, *SD* 10.06) were recruited through the Centre for Autism, Rivierduinen in the Netherlands, the Dutch Autism association (NVA), and the Dutch association for Developmental Disorders (Balans). All children with ASD were classified according to the DSM-IV-TR criteria (APA, 1994) and exceeded the diagnostic threshold. Further diagnostic details are provided below. The non-clinical control group consisted of 45 children (37 boys) aged 41 through 81 months (mean 55.22, *SD* 11.31), recruited from daycare centers, elementary schools, and by postings in public area's in The Netherlands. Parental versions of the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005) and the Childhood Behavior Checklist (CBCL 1,5-5; Achenbach & Rescorla, 2000) showed normed sum scores below the clinical cut off in the non-clinical control group. Participants were between 41 and 81 months old, Dutch or English speaking parent(s) and/ or child, had no neurological conditions, previous head injuries with loss of consciousness, and metabolic diseases. Further demographics are presented in Table 1.

Table 1. Demographic characteristics of the ASD group and the non-clinical control group.

	ASD (*N*= 28)	Control (*N*= 45)	
	Mean (*SD*)	**Mean (*SD*)**	**Group differences ***
Age in months	57.96 (10.06)	55.22 (11.31)	$t(71) = -1.05$, $p = .30$
Gender	M= 26, F= 2	M= 37, F= 8	(χ^2 (1)=1.65, p=.20)
FSIQ	83.71 (22.32)	109.96 (14.76)	$t(41.8) = 5.52$, $p < .01$*
PPVT	83.25 (21.42)	110.02 (10.37)	$t(35.0) = 6.18$, $p < .01$*
SES † (ASD *N*26, Control *N*44)	2.30 (0.72)	2.58 (0.48)	$t(38.3) = 1.83$, $p = .08$

* Significant $p < .05$
† SES: 1= low, 2= medium, 3= high

Autism diagnosis

Current diagnosis according to the DSM-IV-TR criteria (APA, 1994) was provided by child psychiatrists and psychologists with extensive clinical experience in a multidisciplinary consensus meeting. Clinical procedures for psychiatric assessment included questionnaires for parents, an interview with parents, developmental history and family history, information from treating physicians, and extensive expert clinical observations. Both the Autism Diagnostic Interview-Revised (ADI-R; Le Couteur, Lord, & Rutter, 2003) and the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) were administered.

ADI-R

The ADI-R (Le Couteur et al., 2003) is a semi-structured parent interview about the child developmental history that assesses autism symptoms across three domains: social relatedness; communication; and repetitive, restricted behaviors. The diagnostic algorithm was used, which is based on the retrospective or current functioning (depending on age) at age four to five years. Scores for the subscales are provided in Table 3.

ADOS

The ADOS (Lord et al., 2000) was used to evaluate current symptoms of autism according to the DSM-IV-TR criteria in social relatedness, communication, play, and repetitive behaviors. Standardized severity scores were calculated according to Gotham and colleagues (2009) in order to compare modules one through three. Severity scores are provided in Table 3.

Intellectual functioning

In the non-clinical control group, all children completed the Dutch Wechsler Nonverbal Scale of Ability (WNV-NL; Wechsler & Naglieri, 2006). The short version consists of two subtests, Matrix Reasoning and Recognizing, providing a standardized full scale IQ score with good validity and reliability (Wechsler & Naglieri, 2006). In the ASD group, intellectual functioning was assessed using the test that matched the child's verbal, motor, and developmental level. 23 children (82%) completed the WNV-NL, one child the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III-NL; Wechsler, 2006), one child the Snijders-Oomen Nonverbal Intelligence Test (SON-R 2.5-7; Tellegen, Winkel, Wijnberg-Williams, & Laros, 1998), and three children the Mullen Scales of Early Learning (MSEL; Mullen, 1995). Appropriate normative standard IQ scores were computed. In case raw scores were outside the standard range for deviation scores, a ratio IQ was computed by taking the average age equivalents across the subtests, divided by the chronological age in months, and multiplied by 100. IQ scores based on age equivalents are similar to the normative standard IQ scores (Bishop, Guthrie, Coffing, & Lord, 2011).

Experimental design

Baseline condition

A three-minute video clip of fish in an aquarium was used to assess baseline arousal levels during rest which has shown to be an adequate measure for resting state (Piferi, Kline, Younger, & Lawler, 2000). The duration of the baseline assessment was based on earlier studies showing age appropriate baseline periods between two and five minutes (Benevides & Lane, 2015). Heart rate over the course of the clip was analyzed in epochs of 20 seconds each, to identify a series of three consecutive epochs (one minute) representing resting state in accordance with the duration of the social-emotional clip. This was done on group level, for the non-clinical control group and the ASD group separately.

Social-emotional clips

In a pilot study with the non-clinical control group (N= 34, aged 41 to 81 months) four different social-emotional video clips were explored to select the clip that best induced affective arousal. The video clips were taken from TV broadcasted home video programs, and were selected based on stimulus characteristics important for studying social attention: dynamic scenes with high social and interactive context and real rather than acted emotions (Chevallier et al., 2015; Chita-Tegmark, 2016; Risko et al., 2012; Speer et al., 2007). Selected clips represented the following emotions; happy, sadness, anger, or fear. The clip that showed the most stable increase in arousal over the course of exposure, resulting in a significant difference in arousal as compared to baseline condition, was the clip displaying anger ($t(45) = -2.73$, $p < .01$). This clip showed two toddlers (around the same age as the participating children) arguing over a toy, pushing, pulling, and showing angry expressions. Children's faces were visible for the full duration of the clip. Sound was on to maximize ecological validity, volume was stable and fixed at an acceptable level. An identical parallel version was selected in order to account for clip specific effects. Children in the non-clinical control group attended towards version one 98.2% and version two 98.1% of the total clip (p= .96). Mean heart rate levels, in beats per minute, was 93.0 for version one and 93.5 for version two ($t(44) = -.15$, p= .89).

Both versions were equal in terms of attracting attention and inducing arousal. In order to validate the target emotion of the clips, participants were asked to identify the primary emotion and to label it as either positive, negative or neutral. The results showed that 91.5% labeled the clips as negative and at most 82.0% reported anger as the primary emotion.

Eyetracking

Gaze data within specific areas of interest (AOIs) were collected using the Tobii T120 eye tracker (Tobii Technology AB, Danderyd, Sweden), which records the X and Y coordinates of the child's eye position at 120 Hz by using corneal reflection techniques. The eye tracker was placed on a table adapted to the height of the seat, 65 centimeters from the child's eyes. After a 5-point infant calibration procedure, the anger clip of approximately 60 seconds was presented (resolution 960x720). Tobii automatically selects only valid data for calculating visit duration (representing the time eyes were on the screen) and fixation duration (total time eyes fixated within an AOI). Gaze data were processed using the Tobii I-VT fixation filter in Tobii Studio (Version 3.2.1). This filter controls for validity of the raw eyetracking data making sure only valid data were used (Olsen, 2012). With the 'Dynamic AOI' tool, face and total screen AOI's were drawn. The AOI's were drawn around the face with a one centimeter margin. Eyes and mouth were included in the face AOI to prevent overlap, in terms of reliably distinguishing the face. In addition, AOIs should be of adequate size, especially for young children with regard to noise-robustness (Hessels, Kemner, van den Boomen, & Hooge, 2015; Hooge & Camps, 2013). A 'relative' total fixation duration was calculated in order to control for any differences in duration of the stimuli. The total fixation duration within the AOI (for example the face or the total screen) was taken from Tobii, and subsequently divided by the total duration of the clip, multiplied by 100. The relative total fixation duration reflects the percentage of time children were attending to the AOI.

Physiological arousal

Data were recorded continuously with AcqKnowledge (Version 4.3.1. BIOPAC Systems Inc.). Electrodes were attached, at the top center of the chest, (10 centimeters below the suprasternal notch) the bottom left, and right of the ribs (10 centimeters above the bottom of the rib cage). Recordings were acquired through an Electrocardiogram amplifier (ECG100C) and a BIOPAC data acquisition system (MP150 Windows) with a sampling rate of 200 Hz. Physiological monitoring equipment was synchronized with Tobii software by event markers representing the start of the social-emotional clip. In AcqKnowledge a 0.5 Hz highpass filter and a 50 Hz notch filter were applied to stabilize the ECG signal. Recorded physiological data was further processed by manually inspecting the detected R peaks and valid interbeat intervals (IBI) in MATLAB Release 2012b (The MathWorks, Inc., Natick, Massachusetts, United States). Motion artifacts were visually identified and excluded from the data.

Procedures

Both the ASD group and non-clinical control group underwent same procedures. Beforehand, children were explicitly prepared with an information brochure and a copy set of the electrodes to familiarize. During assessment, children completed cognitive tasks while parents were in the room next to the children filling out questionnaires. After a break, the session continued in the lab in the presence of the parent (who was out of direct sight). Electrodes were applied after which children played an easy exploration game on a touch screen to familiarize and for the electrodes to adapt to the skin. After 5 to 10 minutes, children sat in an adapted car seat to have a stable position and to minimize distraction with the head protection on the side. After the baseline clip, the anger clip was played. Children were instructed to watch the clips while trying to sit quietly.

Ethics statement

This study was approved by the Ethical Committee of the Leiden University Medical Center, Leiden, the Netherlands. A written informed consent, according to the declaration of Helsinki, was signed by the parents of all participating children. All tests were completed at the Centre for Autism by a certified child psychologist and trained experimenters who used written protocols detailing all procedures and verbal instructions.

Statistical analyses

ECG data were excluded for one control child and seven children in the ASD group, because there was too much noise in the data. For the eyetracking analyses, all children were included. Total visit duration (AOI; total screen) and total fixation duration (AOI; face) between the two groups (ASD, control) were compared using ANOVA. For heart rate, baseline arousal levels were compared between the groups using independent-samples t-tests with baseline heart rate as dependent and the two groups as independent. GLM repeated measures analyses were used to analyze group differences in heart rate over the course of the clip (in 10 sec epochs), with and without total fixation duration (AOI; face) as covariate. For all analyses concerning group comparisons, tests were performed both with and without IQ as covariate considering the significant difference in intellectual functioning between the ASD group and the control group. Post hoc within group paired samples t-tests were used to assess emotional arousal over time for both groups separately. Linear regression analyses (with a backward procedure) were done to study associations between clinical symptoms (ADI-R and ADOS scores separately because of collinearity), heart rate, and total fixation duration. Effect sizes according to Cohen's *d* and partial eta squared. Level of significance was set at $p < .05$ (two-tailed).

Results

Intellectual functioning

Within the ASD group, there was no significant relationship between IQ and total fixation duration towards the face (r= .35, p= .07) nor between IQ and heart rate during the social-emotional clip (r= .09, p= .70). Nonetheless, in further analyses concerning group comparisons, tests were performed both without and with IQ as covariate.

Eyetracking: Attention towards the screen

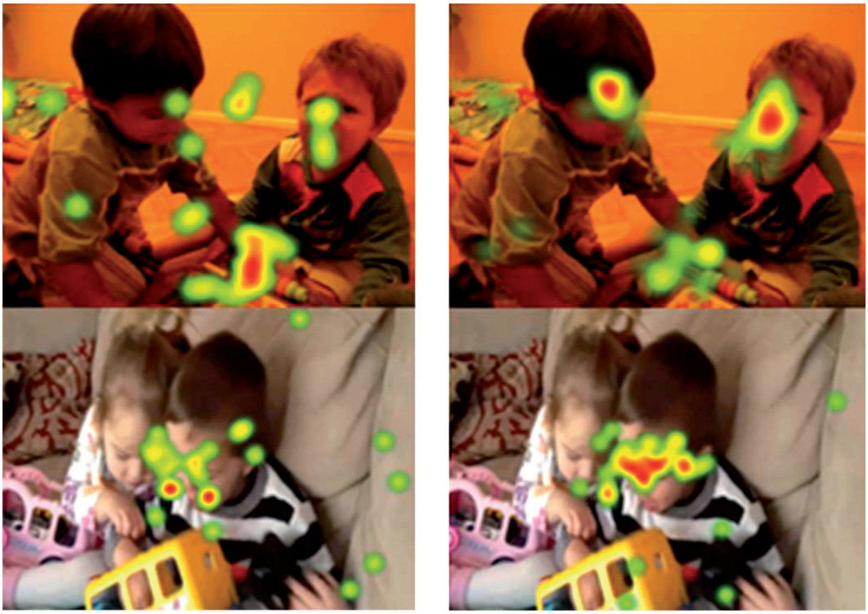
Group differences in overall attention towards the screen were analyzed. This could confound group comparisons of fixation duration towards specific areas of interest. ANOVA with group (ASD, control) as the independent and total visit duration towards the screen as dependent variable indicated no significant group difference (p= .18). The ASD group spent on average 96.5 % (SD= 4.4) and the control group 98.2 % (SD= 4.9) of the time looking at the screen indicating good and equal eyetracking quality. Results remained the same when controlling for IQ, i.e. there were no significant group differences (p= .86). IQ was a significant covariate (p= .02), suggesting that even though IQ mattered in overall attention towards the screen, IQ did not influence group comparisons.

Eyetracking: Attention towards social-emotional information

ANOVA with total fixation duration (AOI face) as dependent and the groups (ASD, control) as independent variable, showed that children with autism (M 27.32, SE 2.68) fixated significantly less on the face compared to children in the control group (M 35.91, SE 1.48), (F(1,72) = 9.283, p< .01). Cohen's d was 0.7, indicating a large effect. This data is illustrated in Figure 1. When controlling for IQ, group differences in total fixation duration were still borderline significant (F(1,72)= 3.294, p= .07, Cohen's d 0.7). IQ was not a significant covariate (p= .26).

Heart rate: arousal in response to social-emotional information

Independent-sample t-test with baseline heart rate levels (in beats per minute) as dependent, and the two groups (ASD, control) as independent variables revealed that the baseline arousal level within the ASD group (M 96.44, SE 2.35) did not significantly differ from the baseline arousal level in the control group (M 92.66, SE 1.84) (t(64) = -1.22, p= .23). Results remained the same when controlling for IQ with no significant group differences (p= .60) and no significant influence of IQ as covariate (p= .39).
Group differences in arousal during the social-emotional clip were analyzed, taking baseline levels into account. GLM repeated measure analysis with the between-subjects factor group (ASD, control) and the within-subjects factor time (baseline heart rate and heart rate during the 6 epochs of the social emotional clip) revealed a significant main effect of time



A B

Figure 1. Heat maps of the ASD group (A) versus the control group (B) reflecting total fixation duration in a scene, illustrating group differences in visual fixation patterns.

(F(6,396) = 3.70, p< .01, η_p^2= .05) and a significant time by group interaction (F(6,396) = 4.36, p< .01, η_p^2= .06). There was no significant main effect of group (p= .20). When controlling for IQ, the interaction effect remained significant (F(6,390) = 2.34, p = .03, η_p^2= .04) and non-significant results did not change. Also, IQ was no significant covariate (p = .35). In sum, the pattern of arousal in response to the social-emotional clip was different in the ASD group as compared the control group. Data are presented in Figure 2.

In order to assess if differential arousal levels in the ASD group were a consequence of looking less at the faces, the analysis was repeated with total fixation duration (AOI face) as covariate. Results remained that there was no significant main effect of time (F(6,378) = 1.39, p= .22) and a significant time by group interaction (F(6,378) = 3.31, p< .01, η_p^2= .05). There was no significant effect of the covariate AOI face (F(6,378) = 1.80, p= .10). When controlling for IQ, the significant time by group interaction remained significant (F(6,372) = 2.23, p = .04, η_p^2= .04) IQ was no significant covariate (p = .52) and non-significant results did not change. In sum, reduced fixation towards faces could not explain deficient arousal modulation in the ASD group.

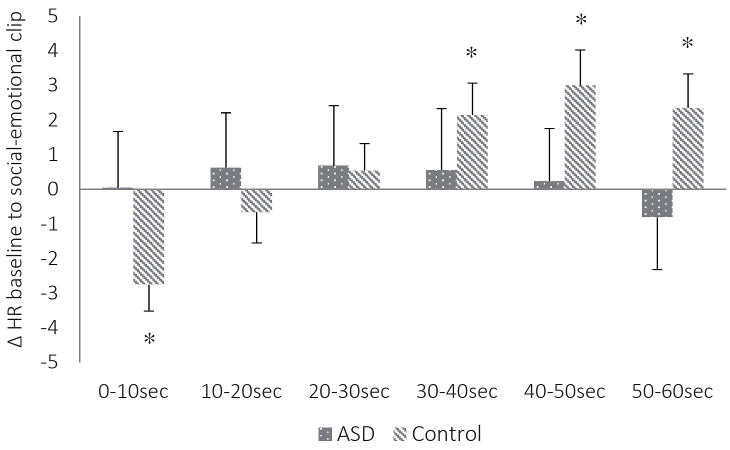


Figure 2. Difference in heart rate from baseline to the social emotional clip in the ASD group and the control group. Error bars displaying *SE*. *significant at $p< .05$.

To further specify the significant group by time interaction, post-hoc within group paired samples *t*-tests (pairing baseline with all the epochs of the social-emotional clip) were done. The ASD group did not show significant differences in heart rate between baseline and any of the epochs of the social-emotional clip. The control group however, showed a significant decrease in arousal from baseline to the first epoch and subsequently, a significant increase in arousal from baseline to epoch four, five and six (see Table 2.).

To assess the difference in arousal from start to end of the clip, irrespective of baseline levels, within-group post-hoc paired samples *t*-tests showed no significant increase in arousal during the clip from the start (*M* 96.5, *SE* 2.3) to end (*M* 95.6, *SE* 2.1), $t(21) = .50$, $p= .62$ in the ASD group. For the control group, there was a significant increase from start (*M* 89.7, *SE* 1.6) to end (*M* 94.8, *SE* 1.8), $t(45) = -5.31$, $p< .001$. Cohen's $d= 0.4$ (medium effect size).

Table 2. Affective arousal from baseline to all epochs of the socio-emotional clip for the ASD group and the control group separately.

	ASD	Control
Baseline to epoch 1	$p= .98$	$t(45) = 3.59$, $p< .05$*, d 0.3
Baseline to epoch 2	$p= .70$	$p= .46$
Baseline to epoch 3	$p= .70$	$p= .49$
Baseline to epoch 4	$p= .76$	$t(45) = -2.34$, $p< .05$*, d 0.2
Baseline to epoch 5	$p= .88$	$t(45) = -2.93$, $p< .05$*, d 0.3
Baseline to epoch 6	$p= .60$	$t(45) = -2.40$, $p< .05$*, d 0.2

* Significant p <.05. Effect sizes displayed in Cohens *d*.

Table 3. ADI and ADOS scores for the ASD group (N=28).

	Mean (*SD*)
ADI Social Communication (cut-off=10)	18.82 (5.95)
ADI Verbal Communication (*N*=23, cut-off=8)	14.22 (3.87)
ADI Non-verbal Communication (*N*=5, cut-off=7)	13.20 (0.84)
ADI Repetitive behavior (cut-off=3)	6.21 (3.12)
ADI Developmental deviance (cut-off=1)	4.14 (1.27)
ADOS Severity score (*N*=24)	8.08 (1.69)

Relationship between arousal, social attention and ASD symptomatology

Linear regression analyses (backwards) were done to investigate the relationship between autism symptom severity (Table 3) and abnormalities in affective arousal and social attention within the ASD group. First, with heart rate change (Δ baseline to social-emotional clip) as dependent variable. For the ADI scores, no significant model was found ($R^2 = .03$, $F(3,18) = 0.18$, $p = .91$). Also for the ADOS scores no significant model was found ($R^2 = .07$, $F(1,17) = 1.25$, $p = .28$). Second, we looked at the arousal response during the clip (Δ heart rate between last and first epoch). For the ADI scores, a significant model was found ($R^2 = .22$, $F(1,20) = 5.51$, $p = .03$). The Social scale was a significant predictor ($\beta = -.47$, $p = .03$) indicating that more severe social problems were associated with less modulation in arousal. For ADOS scores, no significant model was found ($R^2 = .12$, $F(1,17) = 2.42$, $p = .14$). Third, we looked at total fixation duration (AOI face). For the ADI scores, a significant model was found ($R^2 = .14$, $F(1,26) = 4.15$, $p = .05$). The Social scale was a significant predictor ($\beta = -.37$, $p = .05$). Finally, for ADOS scores, a significant model was found ($R^2 = .28$, $F(1,22) = 8.41$, $p = .008$). The ADOS severity score was a significant predictor in this model ($\beta = -.53$, $p = .008$). These results indicated that both more severe ASD symptomatology, specifically social problems, were associated with less attention towards socially relevant information.

Discussion

To our knowledge, this is the first study simultaneously addressing social attention and arousal, in response to daily-life social-emotional scenes in young children with autism spectrum disorders (ASD). In answer to our first research question eyetracking analyses revealed that children with ASD looked less at relevant social-emotional information (i.e. the face) compared to typically developing children (large effect size), even though they equally attended to the screen in general and IQ was controlled for. This result is supported by an extensive meta-analysis by Chita-Tegmark (2016) who found an overall effect size of 0.55 over 38 articles indicating that individuals with ASD spend less time than typically developing children attending to social cues.

In answer to our second research question objective measures of affective arousal showed, in correspondence with the literature, that children with ASD did not differ from controls in baseline regardless of intellectual functioning (Benevides & Lane, 2015; Nuske et al., 2014). With respect to arousal *response*, the control group showed a significant heart rate deceleration from baseline to the social-emotional clip. This is in line with the literature on typical development, which suggests that heart rate deceleration is an indication of directing attention towards a stimulus (Van Hulle et al., 2013). Next, the control group showed increasing heart rate while watching the social-emotional clip, indicating a modulation in arousal. In contrast to the control group, children with ASD did not show a difference in heart rate level from baseline to clip, nor during the social-emotional clip.

Such a lack in spontaneous orienting and emotionally resonating with social-emotional cues, at this point in development may have substantial impact on the fundaments of social learning. It may lead to a reduced quantity and quality of social responding, and thus less child-initiated social behavior. Poor social initiative is already reported in children aged 6 to 12 months old who later developed ASD (Maestro, Muratori, Cesari, et al., 2005). Being able to spontaneously orient and resonate in response to others is a crucial prerequisite for the development of joint attention, language, learning to socialize, and is an important target in early treatment and intervention for children with ASD (Bruinsma, Koegel, & Koegel, 2004; Koegel, Koegel, Shoshan, & McNerney, 1999). There are treatment studies that provide evidence for being able to positively influence the quantity and quality of child-initiated social engagement resulting in improving social behavior.

Our results stress the importance studying cognitive and affective processes together. Results from the objective measures of arousal provided evidence that children with ASD have a lack in affective arousal responses and an inability to modulate affective arousal levels over time. This result remained when taking into account intellectual functioning and the amount of time spent looking at relevant social-emotional cues. In contrast to the non-clinical group, there was no initial deceleration in heart rate, which could be a consequence of a failing arousal system that does not trigger children with ASD to attend to the social-emotional cues. However, attending more or less towards the social emotional cues within the clip was not associated to the ability to modulate heart rate levels. This suggests a fundamental disconnection between the arousal system and social attention and an inability to emotionally resonate with others. These findings add to the growing body of research that show intact resting state heart rate levels, but a deviating arousal *response* in children with ASD (Benevides & Lane, 2015). This corresponds with an earlier retrospective observational study on home videos of children who later developed ASD. Behavioral observations showed that poor social initiative, hypoactivity, and lack of emotional modulation often appeared together, with 87.5% of the children displaying symptoms within the first year of life (Maestro, Muratori, Cesari, et al., 2005). The present study provides neurobiological support for these results.

To our knowledge, two other studies have investigated affective responses in relation to social functioning in young children with ASD (Benevides & Lane, 2015). The first study by Patriquin and colleagues (2013) supported our findings that greater heart rate variability was associated with adaptive social behavior. This study however, did not simultaneously assess physiological responses and actual social behavior and there was no control group, so results have to be compared with caution. The second known study by Watson and colleagues (2012) reported non-specific elevated arousal levels, but reduced attention towards child-directed speech compared to aged-matched peers in contrast to our results. However, there were no baseline measures to compare the arousal levels to (Watson et al., 2012).

When focusing on the relevance of underlying mechanisms in understanding the behavioral phenotype of ASD, the present study has shown that more severe ASD symptoms in general and social impairment in particular, are associated to less adaptive arousal levels and more social attention problems. The early social behavioral problems that are reported in children with ASD are associated with problems in social attention and emotion regulation. This combined pattern of an arousal dysfunction, decreased attention to social cues and the relation to symptom severity in children young children with ASD stresses the importance for early behavioral interventions that aim to target these processes that are associated with social adaptation during the early years of childhood.

There are some limitations to this study. First, current findings will need to be replicated in a larger sample in order to strengthen the findings and examine individual differences. Second, children were tested in a clinical setting, which could have had an influence on baseline physiological levels. In order to diminish possible effects, parents and children were carefully instructed about the study using a brochure and mothers were present in the room during measurements. Third, the group of children with ASD was not homogeneous with respect to IQ and differed significantly from the control group in IQ scores. Therefore, it was decided to include the results with and without IQ as covariate. There is a need for research that is more representative of the general ASD population, with one third of children having a co-occurring intellectual disability while the majority of published studies concerns high functioning individuals with ASD (Baio, 2012; Dykens & Lense, 2011). Even though the experiment was designed to suit all children included in the study by demanding little cognitive, verbal and motor effort, and group comparisons were controlled for IQ, we do encourage replication of these results including a lower IQ matched control group. Finally, careful considerations were made to create an ecological valid experiment, yet this was at the expense of experimental control over the stimuli.

Our findings may have relevance for to the identification of early markers of ASD and could serve as indicators for tailored treatment approaches in these early years. Evidence is growing that sensitive and specific detection of early ASD symptoms before the second year of life is possible, however challenged by the large heterogeneity in children in general and children with ASD in particular. Focusing on affective responding during social attention might contribute to the identification of early makers and the degree of impact on development. Because this can be measured using sensitive and objective techniques, suitable for young children, these may also prove to be relevant outcome parameters in early intervention studies.

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Chapter 3

Physiological arousal and emotion regulation strategies in young children with autism spectrum disorders

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Abstract

This study aimed to assess physiological arousal and behavioral regulation of emotion in the context of frustration in 29 children with Autism Spectrum Disorders (ASD) and 45 typically developing children (41-81 months). Heart rate was continuously measured and emotion strategies were coded, during a locked-box task. Results revealed increases in arousal followed by a decline during recovery, significant for both groups indicating that heart rate patterns between groups were identical. The ASD group deployed less constructive and more venting and avoidance strategies, which was related to language impairments. We conclude that rather than abnormal levels of emotional arousal, a key impairment in young children with ASD may be difficulties in behaviorally regulating and expressing experienced emotions to others.

Introduction

Problematic emotional behavior as expressed in tantrums, irritability, aggression, self-injury, anxiety, and impulsivity is often reported by parents of children with Autism Spectrum Disorders (ASD) and professionals (Geller, 2005; Lecavalier, Leone, & Wiltz, 2006). These emotional behavior problems could be the consequence of compromised experience or expression of emotion. Abnormal levels of emotional arousal, deficient emotional control or a failure to adequately cope with emotions might help explain such emotional behavior problems.

Broadly defined, an emotion can be considered a complex psychological state involving a physiological response, a subjective feeling, and a behavioral response (Hockenbury & Hockenbury, 2010). In typical development, adaptively coping with emotions can be helpful for decision making, motivation, and communication (Izard, 1971, 2013) but emotions can also be hindering when the timing is off, when they are directed towards irrelevant aspects, or when the emotional intensity levels are not adapted to the situation (Lazarus, 1991; Parrott, 2001).

Problematic emotional behavior however, is not a diagnostic criterion for ASD, it is not exclusive to ASD, and over the past decades there has been little attention on emotion processing problems related to ASD in comparison to other domains such as social cognition. This has changed in recent years with an increased recognition that studying emotions may contribute substantially to the understanding of observed emotional and behavioral problems in ASD (Mazefsky et al., 2013). The majority of studies however, have focused on the ability of individuals with ASD to recognize emotions in others, rather than the experience and management of own emotions (Mazefsky, Pelphrey, & Dahl, 2012). Also, studies have largely relied on behavioral observations and survey reports (Mazefsky et al., 2012) of emotional behavior. In addition to such behavioral measures of emotions, it is important to also include more sensitive and objective measures of the experienced emotions, such as physiological emotional arousal responses. The present study was designed to provide this.

Emotional arousal originates from the Autonomic Nervous System (ANS). The ANS consists of the parasympathetic nervous system (PNS; promoting calm, vegetative activities) and the sympathetic nervous system (SNS; involved in stress and activity), and is believed to be involved in affective, cognitive and behavioral responses of individuals (Benevides & Lane, 2015). Heart rate is a commonly used measure of autonomic arousal, it varies due to influence and interaction between both the sympathetic (preparing the body for action) and parasympathetic activity (rest and digest) of the ANS (Benevides & Lane, 2015). Arousal is crucial for steering and tuning our emotions and behavior in social situations in order to adapt and meet social goals (Chambers, Gullone, & Allen, 2009).

Research on arousal in children with ASD yielded mixed results (Benevides & Lane, 2015). There seems to be evidence for normative baseline arousal, but deviating arousal levels in response to a variety of tasks and emotions of others (Benevides & Lane, 2015; Rogers & Ozonoff, 2005). However, caution should be taken because of the great variety in child characteristics and task design (Benevides & Lane, 2015; Kreibig, 2010). In addition, there is much less known about how young children with ASD experience emotions.

One way to study experienced emotions in young children is to elicit frustration (Kreibig, 2010), which is a negative affect related to interruption of ongoing tasks or goal blocking (Rothbart, 2007). Especially at this young age, blocking personal goals will inevitably trigger emotional arousal that is not only evident in a physiological response but also expressed in emotional behavior. Previous behavioral studies on emotion regulation in young children with ASD have shown that children with ASD deploy different coping strategies compared to typically developing children in the context of frustration (Jahromi, Meek, & Ober-Reynolds, 2012; Samson, Wells, Phillips, Hardan, & Gross, 2015). Children with ASD used significantly less constructive strategies (such as goal-directed behaviors, social support orienting, and verbal assistance seeking) but more venting (i.e. vocal and physical venting and self-speech) and avoidance (i.e. avoidance, distraction, and alternative behavior) strategies. However, there were no observed differences in facial or bodily negativity. The question is whether these expressed emotional behaviors originate from an inadequate arousal response. In other words, it is important to study both arousal and emotion regulation strategies, as these may be differentially affected in young children with ASD.

This study aims to integrate subjective, objective, and sensitive measures to investigate arousal and regulation of emotion in a sample of very young children with ASD in order to identify and understand possible differential mechanisms. Including physiological arousal measures (i.e. heart rate) in addition to behavioral measures could benefit the current need for knowledge about underlying mechanisms of daily life socio-emotional problems, which could be targeted in early intervention, and accompanying the advances in early detection of ASD (Bradshaw, Steiner, Gengoux, & Koegel, 2015). The relevance of early intervention is further stressed by several studies showing that a vulnerability in emotional behavior has been associated with negative outcomes with respect to social functioning, depression, and anxiety later in life (Mazefsky, 2015; Mazefsky, Borue, Day, & Minshew, 2014; Nader-Grosbois & Mazzone, 2014; Swain, Scarpa, White, & Laugeson, 2015).

We hypothesize that children with ASD have more difficulties deploying adequate emotion coping strategies and show more venting and/ or avoidance strategies. Given the previous literature on physiological arousal in children with ASD we expect a different arousal pattern in response to frustration. We also focus on characteristics of children with ASD, i.e. IQ, language skills, inhibitory control, mental flexibility, and self-control. This is done based on the “Emotion dysregulation in ASD model” by Mazefsky (2013), which highlights ASD related cognitive characteristics that are likely to be of influence on emotion regulation and may contribute to management of emotions (Mazefsky et al., 2013).

Methods

Participants

This study included 27 children with ASD (25 boys) and 44 typically developing children (35 boys), matched on age (M_{ASD}= 59.48, *SD*= 10.45, $M_{control}$= 55.57, *SD*= 11.17, see Table 1). Socio Economic Status (SES) did not differ between groups (Table 1). Children with ASD were recruited through the Autism Center Rivierduinen (the Netherlands), the Dutch Autism Association (NVA), and the Dutch Association for Developmental Disorders (Balans). Children from the non-clinical control group were recruited through daycare centers, elementary schools, and postings in public areas in the Netherlands. Parent report versions of the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005) and the Childhood Behavior Checklist (CBCL 1,5-5; Achenbach & Rescorla, 2000) showed normed sum scores below the clinical cut-off in the non-clinical control group. All parents and/or children were Dutch or English speaking. Children had no neurological conditions, previous head injuries with loss of consciousness, and/or metabolic diseases.

Autism Diagnosis

Diagnosis was provided during a multidisciplinary consensus meeting of child psychiatrists and child psychologists according to the DSM-IV-TR criteria (APA, 1994). The diagnostic algorithm of the Autism Diagnostic Interview-Revised (ADI; Le Couteur, Lord, & Rutter, 2003) was used, which is based on retrospective or current functioning (depending on age) at age four to five years. Current ASD symptoms were evaluated using the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000). Standardized severity scores were calculated according to Gotham and colleagues (2009) to compare the three different modules of the ADOS that were administered. All children exceeded the diagnostic threshold on both the ADI-R and the ADOS (Table 2).

Table 1. Demographic characteristics of the ASD group and the non-clinical control group.

	ASD (*N*= 27)	**Control (*N*= 44)**	
	Mean (*SD*)	**Mean (*SD*)**	**Group differences**
Age range	43-79 months	41-81 months	$t(69) = -1.47$, $p= .15$
Gender	M= 25 , F= 2	M= 35, F= 9	(χ^2 (1)=2.18, p=.19)
FSIQ	86.89 (22.43)	110.27 (14.61)	$t(39.69)= 4.83$, $p <.01$*
SES † (N_{ASD}= 26, $N_{control}$= 42)	2.33 (0.72)	2.61 (0.47)	$t(38.59)= 1.76$, $p= .09$

* Group difference significant at $p <.05$
† SES: 1= low, 2= medium, 3= high

Table 2. ADI and ADOS scores for the ASD group (*N*=27).

Scale		Mean (*SD*)
ADI Social Communication (cut-off=10)		18.93 (5.87)
ADI Communication	Verbal (*N*=24, cut-off=8)	14.58 (4.19)
	Non-verbal (*N*=3, cut-off=7)	13.20 (0.84)
ADI Repetitive behavior (cut-off=3)		6.41 (3.25)
ADI Developmental deviance (cut-off=1)		4.10 (1.26)
ADOS Severity score		8.08 (1.66)

Child characteristics

Intellectual functioning IQ scores of children with ASD were assessed using the test that matched children's verbal, motor, and developmental level. The majority of children with ASD (24) completed the Dutch Wechsler Nonverbal Scale of Ability (WNV-NL; Wechsler & Naglieri, 2006). One child completed the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III-NL; Wechsler, 2006), one child the Snijders-Oomen Nonverbal Intelligence Test (SON-R 2.5-7; Tellegen, Winkel, Wijnberg-Williams, & Laros, 1998), and three children the Mullen Scales of Early Learning (MSEL; Mullen, 1995). A ratio IQ was computed in case raw scores were outside the standard range for deviation scores by taking the average age equivalents across the subtests, divided by the chronological age in months, multiplied by 100 (Bishop, Guthrie, Coffing, & Lord, 2011). The non-clinical control group completed the WNV-NL (Wechsler & Naglieri, 2006).

Inhibition The Inhibition scale of the Behavior Rating Inventory of Executive Function–Preschool version (BRIEF-P; Gioia, Espy, & Isquith, 2001) was used to evaluate inhibitory skills (i.e. the ability to suppress impulses and to stop behavior at the right time). The Dutch translation of this parent report questionnaire showed sufficient to high internal consistency, interrater reliability, construct validity, and test-retest reliability indicating suitability for research purposes. Also, it showed adequate convergent discriminant and predictive validity and (Sherman & Brooks, 2010; Van der Heijden, Suurland, De Sonneville, & Swaab, 2013). The inhibition scale consists of 16 items and higher scores represent lower levels of inhibitory control.

Cognitive flexibility The Flexibility scale of the Dutch BRIEF-P was used (Van der Heijden et al., 2013). This scale consists of 10 items and measures the ability to switch from a situation, activity, perspective, or aspect of a problem to another, if necessary. High scores represent low levels of cognitive flexibility.

Self-control The preschool version of the *Social Skills Rating System* (SSRS; Gresham & Elliott, 1990) was used as a measure of self-control, as reported by the primary teacher or mentor. The Self-control scale measures behaviors that emerge in conflict and non-conflict situations, such as taking turns, adequately responding to provocations, and being able to compromise. The scale consists of 10 questions that were rated on a 3-point scale. High scores represent low levels of self-control. The SSRS has high internal consistency estimates and moderately high validity indices for total scores (Gresham, Elliott, Vance, & Cook, 2011).

Language The Dutch version of the widely used Peabody Picture Vocabulary Test-III-NL (PPVT-III-NL; Schlichting, 2005) was administered to test receptive language skills and vocabulary. Each item of this non-verbal multiple choice test consists of four pictures from which the child is asked to pick the one that corresponds with the examiner's stimulus word.

Emotional expression measures

Locked box task (Goldsmith, Reilly, Lemery, Longley, & Prescott, 1999). This task is part of the preschool Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith et al., 1999). It was designed to evoke frustration by deliberately preventing children from playing with a toy they had chosen for four minutes by handing them a wrong set of keys (see Figure 1 for a timeline). Recovery was measured by allowing children to play with the desired toy for one minute directly after unlocking the box. The episode was recorded with video camera's (JVC Everio GZ-E15) from two angles in order to fully capture the child's entire body, the box, and the keys. Physiological data from the locked box task were analyzed in 30 second epochs. Of the total 240 seconds (four minutes), the first 30 seconds were discarded due to the fact that it takes 30 seconds for the frustration to start (children first need to try the keys to find out that none fit the lock). The majority of children were able to complete the full four minutes (79% of the control children and 67% of ASD children), however some children were not able to finish the four minutes and for example stoop up and tried to walk away from the task, resulting in motion artifacts. In order to prevent bias due to the duration of the task, it was decided to use the epochs that included data from all children, resulting in seconds 30 through 120. The last 120 seconds of the task could be discarded after analyzing these epochs for children who did complete the full 240 seconds, revealing comparable data. The mean duration of the task completed was 230 for the control group and 160 seconds for the ASD group. In total, 90 seconds of data were included in the analyses. ECG data were manually checked in consultation with the lab-technicians at Leiden University who was blind to group membership of the children. Data were excluded due to motion artifacts that could not be corrected using digital filters.

Figure 1. Timeline locked box task (Lab-TAB; Goldsmith et al., 1999)

Observational coding Children's emotional coping strategies were coded and categorized as described in Jahromi et al. (2012). In total 14 emotion coping strategies were coded in 10-second intervals as either present or absent (scored as 1 or 0). These 14 coping strategies were assessed independently which means that more than one strategy can occur in the same 10-second interval. Strategies were grouped into three categories and their average inter-rater reliability (expressed in Cohen's kappa) were (a) constructive strategies (consisting of strategy behaviors such as goal-directed behaviors, orienting to experimenter or parent, and social support seeking); k = .84, (b) venting strategies (i.e. vocal venting, self-soothing, and self-speech); k = .82, and (c) avoidance strategies (avoidance, distraction, and alternate strategies); k = .81. Two independent coders scored all videos. Interrater reliability was monitored continuously in regular consensus meetings. Cohen's kappa reflect reliability between the two independent coders on 20% of the videos, in percentages the coders reached 93%, 96%, and 97% agreement on the categories, respectively. Three strategies (disruptive behavior, physical venting, and other-directed comfort-seeking) occurred too infrequent to be included in subsequent behavioral composites or analyses.

Emotional experience measures

Physiological arousal During the locked box task data were recorded continuously with AcqKnowledge (Version 4.3.1. BIOPAC Systems Inc.). Electrodes were attached, at the top center of the chest, (10 centimeters below the suprasternal notch) the bottom left, and right of the ribs (10 centimeters above the bottom of the rib cage). Recordings were acquired through an Electrocardiogram amplifier (ECG100C) and a BIOPAC data acquisition system (MP150 Windows) with a sampling rate of 200 Hz. In AcqKnowledge a 0.5 Hz highpass filter and a 50 Hz notch filter were applied to stabilize the ECG signal. Recorded physiological data was further processed by inspecting the detected R peaks and valid interbeat intervals (IBI) in MATLAB Release 2012b (The MathWorks, Inc., Natick, Massachusetts, United States). Motion artifacts were visually identified and excluded from the data. Heart rate data were summarized in 30-second epochs, in concordance with the behavioral data.

Procedures

Children attended one research visit accompanied by a parent at the Centre for Autism, Leiden, the Netherlands. Both the ASD group and non-clinical control group underwent the same procedures. Children and parents were prepared with an information brochure and a copy set of the electrodes to familiarize. Before the three electrodes were applied to the chest, the skin was cleaned with alcohol swabs. After attaching the electrodes, children were seated behind a touch screen, which showed a house with objects they could select that moved and played sounds. This was done to familiarize children to the experimental setting and for the electrodes to adapt to the skin. For the locked-box task, children were seated in a high chair behind a table on which four toys were on display. After choosing, the unselected toys were placed out of sight and the chosen toy was directly placed in the box to avoid the child from starting to play. The experimenter explained the task, showed the keys and sat out of direct sight from the child in the back of the room together with the parent who filled out questionnaires and was asked not to respond to the child. If the child asked for help, the experimenter was only allowed to say that the mother was busy. By means of debriefing, the experimenter explained that she had given the wrong set of keys and handed the child the correct key. All elements of the experimental procedure were age appropriate and designed for both verbal and non-verbal children. Finally, teacher report SSRS anonymously numbered questionnaires were given to the parents to hand over to the teachers that best knew their child, which could also be a mentor. A return envelope was included for the teacher to return the questionnaire free of costs.

Statistical analyses

ECG data were excluded for one child from the control group and nine children from the ASD group, due to motion artifacts. No further participants were excluded after normality inspections. The excluded children with ASD did not differ from the included children with ASD in IQ (p=.63), ADI total score (p= .443), or ADOS severity score (p= .30). After checking baseline heart rate levels with independent samples t-tests, a GLM repeated measure analysis was performed with the between-subjects factor group (ASD, control) and the within-subjects factor task (60 seconds baseline heart rate, 90 seconds frustration, and 60 seconds recovery). To further analyze within group differences, paired samples t-tests were done for the ASD and control group separately. Independent samples t-tests were used to assess group differences (ASD, control) in self-control (SSRS) and executive functioning (BRIEF-P). For the three coping strategies (Constructive, Venting, and Avoidance) Multivariate Analysis of Variance (MANOVA) was done with Group (ASD, control) as fixed factor. For the ASD group, Pearson correlation coefficients were chosen to assess correlations between cognitive functioning and coping strategies within the ASD group. Finally, two separate backward regressions were performed for the ASD group with the cognitive variables to identify the prominent predictors for coping strategies. Effect sizes are reported as η_p^2 with .01 being a small, .06 medium, and .14 a large effect (Cohen, 1977). Cohen's d effect sizes were calculated for the paired samples t-tests with .2 being a small, .5 medium, and .8 a large effect.

Ethics statement

This study was approved by the Ethical Committee of the Leiden University Medical Center, Leiden, the Netherlands. A written informed consent, according to the declaration of Helsinki, was signed by the parents of all participating children. All tests were completed at the Centre for Autism by a certified child psychologist and trained experimenters who used written protocols detailing all procedures and verbal instructions.

Results

Emotional arousal: psychophysiological arousal in response to frustration

There was no difference in baseline heart rate between children with ASD (*M* 95.92, *SD* 10.85) as compared to children in the control group (*M* 92.41, *SD* 12.24) ($t(62) = -1.10$, p .28). Next, group differences in arousal during the locked box task were analyzed. GLM repeated measure analysis with the between-subjects factor group (ASD, control) and the within-subjects factor task (60 seconds baseline heart rate, 90 seconds frustration, and 60 seconds recovery) revealed a significant main effect of Task ($F(5,305) = 33.49$, $p < .001$, $\eta_p^2 = .35$), no main effect for Group ($F(1,61) = .16$, $p = .69$, and no interaction effect ($F(5,305) = .93$, $p = .46$) indicating no difference in the pattern of arousal response across groups. Results are presented in Figure 1. To further investigate the arousal responsivity for both groups, within group comparisons revealed similar increases and decreases during the locked box task. In other words, arousal increase in response to frustration and arousal reduction during recovery were similar for both groups separately (Table 3).

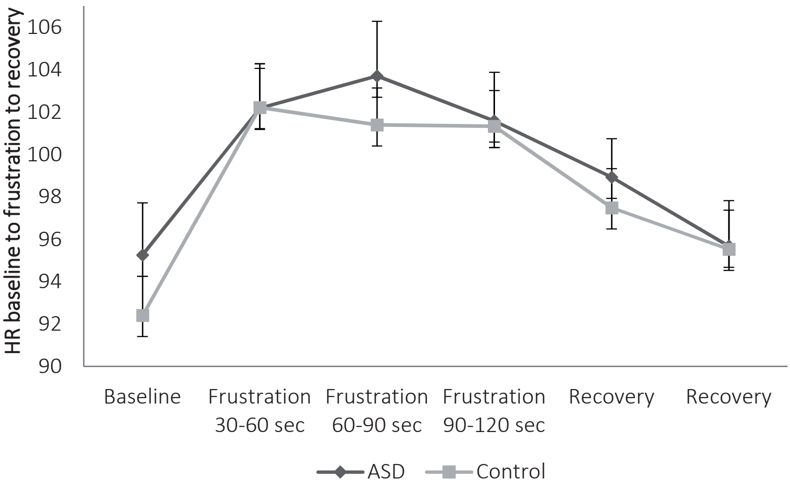

Figure 2. Heart rate (BPM) from baseline to frustration and from frustration to recovery in 30s epochs. Error bars displaying SE. At all individual time points there are no significant differences between groups.

Table 3. Within group increases in emotional arousal (heart rate) during the locked-box task.

	ASD	Control
Baseline to frustration 1	$t(18) = -2.56$, $p = .02$*, d 0.6	$t(43) = 7.49$, $p < .01$*, d 0.6
Baseline to frustration 2	$t(18) = -3.82$, $p < .01$*, d 0.7	$t(43) = -10.95$, $p < .01$*, d 0.8
Baseline to frustration 3	$t(18) = -5.00$, $p < .01$*, d 0.8	$t(43) = -10.40$, $p < .01$*, d 0.8
Recovery 1 to recovery 2	$t(18) = 3.09$, $p < .01$*, d 0.4	$t(43) = 2.28$, $p = .03$*, d 0.2

* Significant at p <.05. Effect sizes displayed in Cohens *d*.

Behavioral regulation: Emotion coping strategies

Multivariate Analyses of Variance (MANOVA) with the three strategies (Constructive, Venting, and Avoidance) as dependent variables and Group (ASD, control) as fixed factor, revealed a main effect for Group during the locked box task ($F(3,67) = 12.19$, $p < .001$; Wilk's $\Lambda = 0.65$, $\eta_p^2 = .35$). Children with ASD engaged significantly less in Constructive strategies as compared to children in the control group. In contrast, children with ASD showed significantly more Venting than controls and Avoidance as compared to children in the control group. Table 4 shows that the group effect is significant for all three strategies.

Table 4. Group comparisons of behavioral emotion coping strategies during the locked-box task.

	ASD (N= 27) Mean (SD)	Control (N= 44) Mean (SD)	p	η_p^2
Constructive strategies	2.29 (*1.06*)	2.72 (*0.55*)	.03*	.07
Venting strategies	1.83 (*1.39*)	0.98 (*1.18*)	<.01*	.10
Avoidance strategies	0.84 (*0.80*)	0.12 (*0.22*)	<.01*	.32

* Group differences significant at p <.05

Self-control

An independent samples t-test with the *Self-control* scale from the SSRS as dependent and the two groups (ASD, control) as independent variables revealed that teachers of children with ASD reported significantly less self-control skills (M 5.52, SD 4.41) than teachers from children in the control group (M 15.39, SD 3.71) ($t(64) = 9.80$, $p < .01$, Cohen's d 2.8, indicating a large effect).

Executive functioning

Independent samples t-tests with Inhibition and Mental flexibility (as measured with the parent reported BRIEF-P questionnaire) as dependent and the two groups (ASD, control) as independent variables revealed that children with ASD had significantly more problems in inhibitory control (M= 35.2, SD= 6.2) and mental flexibility (M= 20.5, SD= 5.4) as compared to children from the control group on inhibitory control (M= 24.3, SD= 4.5) $t(67)$= -8.48, p<.01and cognitive flexibility (M= 13.5, SD= 3.4) $t(67)$= -6.68, p<.01.

Predictors of Coping Strategy

For the ASD group, correlations between the emotion regulation variables (three emotion coping strategies) and child characteristics (IQ, language skills, inhibition, mental flexibility and self-control) were calculated using Pearson correlations. Constructive strategies were positively correlated with IQ (r_s.71, p<.01) and Language skills (r_s.48, p<.01). Indicating that better general cognitive abilities and more specific, better language skills were associated with the use of more constructive emotion regulation skills. The Avoidance strategies were negatively correlated with IQ (r_s -.39, p<.05), Language skills (r_s -.41, p<.05), and self-control (r_s -.39, p<.05) suggesting that weaker IQ, language, and self-control skills were associated with more avoidance. Finally, venting strategies showed no correlations with any of the cognitive functions.

All variables that were significantly correlated with the emotion coping strategies were entered in linear regression analyses, to identify the most prominent predictors. Two separate backward regressions were performed with total score for Constructive strategies (with the dependent variables IQ and language skills) and total score for Avoidance strategies (with the dependent variables IQ, language skills and self-control) as independent variables. For Constructive strategies a significant model was found, $F(1,26) = 25.6$, $p < .001$, with 50.6 % explained variance. This model consisted of one significant predictor, which was IQ ($t = 5.1$, $p < .001$, $\beta = 0.71$). In other words, higher IQ predicted being able to deploy more constructive strategies. Also for Avoidance strategies a significant model was found, $F(1,26) = 5.0$, $p = .03$, with 16.7 % explained variance. This model consisted of one significant predictor, which was Language skills ($t = -2.2$, $p = .03$, $\beta = -0.41$). In other words, more compromised language skills predicted more avoidance strategies. In further support of this finding, significant group differences in language skills between children with ASD (M_{WBQ}= 84, SD= 20) and typically developing children (M_{WBQ}= 110, SD= 10) were found ($t(34)$= 6.13, p<.01).

Discussion

In this study we investigated emotional arousal and emotion regulation strategies in young children with Autism Spectrum Disorders (ASD). We assessed if children with ASD become under-aroused or over-aroused in response to frustration, and how they cope with these emotions in terms of regulation strategies. Core to the study was the inclusion of physiological, i.e. heart rate measures, in parallel to structured behavior observations, which may provide insight in the responsivity of the arousal system in addition to how emotions are regulated.

Measures of emotional arousal revealed that the pattern of emotional responding in children with ASD was similar to that of typically developing children. There was no difference in the arousal response across groups. For both groups separately, there was an increase in arousal from baseline in response to frustration. In addition, both groups showed that heart rate decreased during recovery of frustration, to similar degrees. In other words, children with ASD did not differ in emotional response (from point to point) in the context of frustration as compared to typically developing children.

In contrast, structured behavioral observations of emotion regulation strategies, which were scored parallel to the arousal measures, showed that children with ASD deployed different strategies, specifically increased use of venting and avoidance behavior compared to typically developing children. Children with ASD showed less constructive (i.e. goal directed) strategies compared to typically developing children. These results are in line with other studies using similar groups and measures, i.e. Jahromi et al. (2012). In this study, children with ASD also showed more self-control problems in the daily life school setting as reported by teachers. This is in line with the observed patterns of emotion coping strategies, as self-control plays an important role in order to be able to regulate emotions in daily life, as also shown in this study. Taken together, our data suggest that while children with ASD show similar intensity of emotional arousal responses, they may have difficulties in behavioral regulation of these emotions. In other words, their coping strategies seem different in contrast to an intact emotional response in the context of frustration. This may point to the role of emotion regulation as a mediating factor in this relationship. Behavior, expression, and experience are all part of emotion regulation (Gross & Thompson, 2007), and hence may be differentially affected. Our results suggest dysregulation of behavior in children with ASD (with lowered IQ and language skills) and a lack of self-control in how experienced emotions are expressed to others.

To further investigate the seeming discrepancy between intact emotional responses and the use of different regulation strategies, hypothesized mechanisms that could be of influence on this dysregulation were investigated. These results revealed that being able to deploy constructive strategies, i.e. show goal-directed behaviors, was best explained by one single factor, which was intelligence. In contrast, increased use of less constructive strategies to cope with emotions, i.e. avoidance behavior, was best explained by language ability. Language skills were impaired in children with ASD compared to the typically developing group. Interventions targeting these language impairments should for example include teaching appropriate replacement communicative utterances in particular if a child exhibits excessive tantrums (Koegel, Koegel, Ashbaugh, & Bradshaw, 2014). Interestingly, executive functioning (inhibition and cognitive flexibility) was not related to any of the emotion coping strategies. It could be that that null findings regarding executive functioning in (high functioning) individuals with ASD can be explained by a lack in difference between individuals with ASD and typically developing peers (Brady et al., 2017). Results in the current study however do not support this hypothesis, showing more problems in inhibitory control and cognitive flexibility in children with ASD as compared to typically developing children. For future research concerning executive functioning it is important to study this preschool phase of development, because it is hypothesized that executive functioning during this phase has not yet become fully on-line to support regulation strategies (Best & Miller, 2010), and that regulation strategies are more dependent on language skills. Thus, language impairments at this point may better explain the use of non-constructive emotion coping behavior in children with ASD. However, because of the prolonged development of executive functioning (Best & Miller, 2010), we cannot exclude that these cognitive functions may become increasingly more important for managing experienced emotions over the course of development. Research has shown that executive functions, in particular inhibition, show a first leap in development around age 4 or 5 and continue to improve significantly through the age of 8 years (Best & Miller, 2010; Diamond, 2013). For future research we recommend taking into account these possible age effects which due to the sample size was not part of this study.

This study has limitations that should be addressed. The recovery in arousal was similar between the control group and ASD group, even though coping strategies were different between the groups. This might be explained however by the manipulation that the experimental locked-box task was unsolvable and children eventually all received the correct key in order to open the locked box, after which they were all allowed to play with the favored toy. Thus, recovery in arousal likely resulted from this manipulation, rather than from type of emotion coping strategy. In future research it would be interesting to investigate the effect of different regulation strategies on the levels of emotional arousal and vice versa, how arousal and coping strategies could influence ASD children's negative emotion expressions. Since arousal can be considered not only as the cause, but also as the consequence of emotion regulation, these mechanisms are interacting in a dynamic fashion, and are mutually co-dependent on each other. In order to learn more about this dynamic relationship, we recommend the use of temporal analyses. The behavioral measures (behavior observations) that were used in the current study are too coarse for this approach and are not suited to follow the quick pace of the arousal in such detail which is necessary for temporal analyses in combination with for example measures such as electromyography. With regard to measures of arousal, the current study included a single heart rate measure as indicator of ANS activity. It is recommended for future research to include a larger repertoire such as heart rate variability and skin conductance level (Mauss & Robinson, 2009). Furthermore, even though IQ cannot be separated from the effects of the condition (Dennis et al., 2009), IQ was significantly lower in children with ASD and the current results would be strengthened if this study was replicated in a sample of children without ASD and with matched IQ. Finally, nine children with ASD were excluded due to motion artifacts in the heart rate analyses which could not be filtered from the data. Even though the excluded children did not differ from the other children with ASD on intelligence and symptom severity, the exclusion can be considered a limitation of the study. For future research we recommend the use of wireless heart rate analysis techniques to prevent children to get distracted by the wires that are connected to the electrodes.

In sum, the results of this study show that when it comes to situations that trigger intense/ strong emotions, children with ASD do show emotional arousal responses, but they may rely on less efficient strategies to regulation these emotions (i.e. avoidance), in part driven by lower language abilities. In daily life however, emotional responses are often much less strong. We therefore cannot exclude that an 'atypical' arousal response might be found in children with ASD when situations are more subtle and/or ambiguous. Another factor that may differentially impact the arousal system is the presence of social elements in triggering arousal. A recent study with the same samples of children presented evidence that when it comes to emotional arousal in response to others (so in a social context), that the arousal response of children with ASD is significantly diminished in comparison to typically developing children (Zantinge, van Rijn, Stockmann, & Swaab, 2017). Together, this indicates that the emotional arousal response of children with ASD is intact when it comes to their own emotions (although children may have difficulties behaviorally regulating these emotions), however that emotional arousal responses are deviant when it comes to responding to emotions of others. This hypothesis is further supported by a pilot study from Levine and colleagues (2012) who reported equal ANS activity and no increase in salivary cortisol between children with high functioning autism and a comparison group in response to a social stressor (Trier Social Stress Test). These results highlight the importance of integrating objective and sensitive measures of emotional arousal in addition to the behavior that is observed on the outside or reported/ observed by parents and professionals. Such deficiencies may significantly impact social functioning. Being able to adequately deal with emotions is important for adaptive social responding (Gross, 1999). The preschool phase presents a unique window of development and related opportunities, as strategies to cope with emotions are generally still pre-cognitive at this stage and negative scripts are not yet automated (Greenspan & Shanker, 2004). This allows and advocates for early intervention targeted at the earliest stages of behavioral control during emotionally arousing situations, in which stimulation of language development may play an important role in the prevention of avoidance strategies as suggested by our findings (Koegel et al., 2014; Zwaigenbaum et al., 2015).

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3

Chapter 4

Concordance between physiological arousal and emotion expression during fear in young children with Autism Spectrum Disorders

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Abstract

This study aimed to measure emotional expression and physiological arousal in response to fear in 21 children with Autism Spectrum Disorders (ASD; age range 43-75 months) and 45 typically developing children (TD; age range 41-81 months). Expressions of facial and bodily fear and heart rate arousal were simultaneously measured in response to a remote controlled robot (Lab-TAB; Goldsmith, Reilly, Lemery, Longley, & Prescott, 1999). Heart rate analyses revealed a main effect of task from baseline to fear ($p<.001$), no interaction effect and no effect for group. In other words, the pattern of arousal was similar for both groups. In addition, children with ASD showed intact facial and bodily expressions of fearful affect compared to TD children ($p = .82$). With regard to the relationship between expression and arousal, the results provided evidence for concordance between expression and arousal in TD children, but evidence for discordance in children with ASD. A possible missing link between arousal and expression in response to fear may significantly impact social functioning of children with ASD. In light of both early identification and treatment it is important to be aware that emotional expressions in children with ASD do not necessarily reflect their internal experience.

Introduction

Humans are biologically prepared to express and recognize emotional states, skills that form a crucial component in social behaviour (Cole & Moore, 2015; Darwin, Ekman, & Prodger, 1998; Shariff & Tracy, 2011). The development of children with Autism Spectrum Disorders (ASD) is partly characterized by persistent deficits in social communication and social interaction, such as social-emotional reciprocity, nonverbal communicative behaviors, and deficits in developing, maintaining, and understanding relationships (APA, 2013). The majority of studies in the field of autism research investigated social behaviour and related impairments in social cognition, such as how children with ASD attend to and interpret the emotions of others (Harms, Martin, & Wallace, 2010; Mazefsky, Pelphrey, & Dahl, 2012). Much less is understood about how children with ASD experience and express emotions themselves, which might serve as explanatory construct for behaviour problems frequently reported in ASD (Mazefsky et al., 2012; Samson, Hardan, Podell, Phillips, & Gross, 2015). This imbalance in research focus might in part be explained by the difficulties in measuring emotions and the large phenotypic heterogeneity in early ASD (Benevides & Lane, 2015; Kim, Macari, Koller, & Chawarska, 2016). This study aims to provide this by including both physiological and behavioural components of emotional responding, specifically in a fearful situation.

Emotion is a complex construct and requires the coordination between a physiological response, cognitive appraisal, expression, and a behavioural response (Hockenbury & Hockenbury, 2010), also described as *emotional concordance* (Hollenstein & Lanteigne, 2014). Expressing emotions (for example facial and bodily expression, tone of voice, and gestures) serves a communicatory function which is necessary for the environment to be able to rapidly understand what is needed (Blair, 2003). This may especially be relevant in early childhood, when children are more dependent on caregivers for their physical and emotional needs and when interaction patterns between the child and caregivers shape the developing brain. Emotional (facial) expressions have been the topic of research since Darwin's *The expression of the emotions in man and animals* (Darwin, 1872) and have been of specific interest with regard to the study of ASD. The nature and specificity of emotion expression difficulties however, do not seem universal for all individuals with ASD (Nuske, Vivanti, & Dissanayake, 2013). Jahromi and colleagues (2012) showed that children with ASD express no differences in facial and bodily negativity when confronted with frustrating situations. In a study by Stagg and colleagues (2013), adults blindly rated children with ASD as being less expressive than typically developing children. In addition, children with ASD were rated lower on friendship measures by typically developing peers, suggesting that facial expressivity might influence friendship appraisal (Stagg et al., 2013).

Because of this heterogeneity in emotion expression research, it is of interest to study the degree to which emotion expressions are related to internal states of emotional arousal as expressed in physiological parameters of the autonomic nervous system (ANS). Emotional arousal is driven by the highly complex and interactive functioning of the ANS and the limbic system of which the amygdala is an important area (Yang et al., 2007). Heart rate is considered an indicator of ANS activity, either reflecting reduced parasympathetic activity and/ or increased sympathetic influence (Levenson, 2014). Studies on emotional arousal in typical development have shown arousal responses expressed in heart rate increase, however dependent on type of emotion, induction method, and duration of the physiological variable (for an extensive review see; Kreibig, 2010). For children with ASD there seems to be no evidence for autonomic differences during resting parasympathetic activity, however the literature does support different ANS patterns in *response* to a variety of tasks (Benevides & Lane, 2015). For example, the amount and direction of change during challenging tasks may be different in children with ASD. The majority of studies described in this review however included higher functioning and elementary/ middle school aged children with ASD, which limits generalizability to younger and lower functioning children with ASD.

The importance of the ANS as regulator, activator, coordinator, and communicator is reflected in the constant monitoring and adjusting of our functioning enabling the body to respond to internal and external demands (Levenson, 2014). The concordance between emotional expression and internal emotional states allows parents, caregivers, but also the social environment in general to be able to rely on the emotional expressions of children as a signal that may trigger the need for support, comfort, and help. An impediment in the concordance, or discordance, may disrupt caregiver responses which, over time, may amplify early vulnerability into a developmental trajectory of increasingly dysfunctional emotion regulation, social development, and early language skills (Kasari, Sigman, Mundy, & Yirmiya, 1990; Sullivan & Lewis, 2003; Wan et al., 2012). For example, being able to correctly label a situation as fearful (cognitive appraisal) would lead to an increase in arousal (enabling the body to reach a state of action), facial and/or bodily expression of affect (for the environment to *read* these emotions), and a behavioural response (for example to ask for help or to run away). Understanding the various components of the emotional response is important because specific impairments in emotion would lead to differential interventions to improve emotional behaviour. Simultaneously studying behaviourally expressed emotions and the internal psychophysiological state of arousal might provide us with more insight into the heterogeneous emotion problems reported in ASD as it is important that these channels are in tune with each other.

Even though theoretically assumed, empirical evidence regarding the relationship between internal arousal states and external behavioural expression is mixed due to for example the complexity of operationalizing emotions in research settings (Mauss & Robinson, 2009). Studies investigating these two components in young children with ASD are scarce. A study by Legiša and colleagues (2013) included eight children (8-14 years) with high-functioning ASD and matched controls. They examined the responses to odours using facial expression and arousal which showed relative intact expression and arousal compared to controls

(Legiša et al., 2013). A study by Stein and colleagues (2014) showed that physiological stress (as measured by non-specific skin conductance response frequency during routine dental cleanings) was significantly correlated with overt behavioral distress, indicating that as physiological stress increased so did behavioral distress in children with ASD (mean age 8.2 years). These results stress the importance of studying such sensitive and objective mechanisms of emotional behaviour at a young age during critical periods of development to identify and target the developmental trajectory of ASD (Kim et al., 2016; Zwaigenbaum et al., 2015). These early markers might serve as indicators for tailored treatment development (Dawson & Bernier, 2013; Landa, 2008).

This study aimed to measure emotional expressions and physiological arousal simultaneously in response to a fearful situation in children with ASD compared to typically developing children (TD). The fear paradigm was chosen because this experiment does not require social interaction with others, not to interfere with the social stress of emotion. A strong negative stressor was selected in order to exceed the threshold for an expression, however evidence regarding the relationship between emotion intensity and expression is ambiguous (Reisenzein, Studtmann, & Horstmann, 2013). We hypothesized that children with ASD would show relative intact facial and bodily expressions of negative affect compared to typically developing children based on previous research (e.g., Jahromi et al., 2012). Furthermore, based on the available literature (Benevides & Lane, 2015) we expected that children with ASD would show different ANS patterns (the amount and direction of change in heart rate) in response to the stressor. With regard to concordance, it was hypothesized that the relationship between external expression and internal arousal might be different for children with ASD compared to TD children.

Methods

Ethics statement

The current study is part of a larger longitudinal study which was approved by the Ethical Committee of the Leiden University Medical Center, Leiden, the Netherlands. A written informed consent, according to the declaration of Helsinki, was signed by the legal caretaker(s) of the participants.

Participants

In this study, 21 children with ASD (age range 43-75 months) and 45 TD children (age range 41-81 months) participated (Table 1). Children with ASD were recruited through the Dutch Autism Center (Rivierduinen), the Dutch Autism Association (NVA), and the Dutch Association for Developmental Disorders (Balans). TD children were recruited through day-care centres, elementary schools, and postings in public areas in the Netherlands. Inclusion criteria for all participants were that parents and/or children were Dutch or

English speaking, children had no neurological conditions, previous head injuries with loss of consciousness, and/or metabolic diseases.

Autism diagnosis

Autism diagnosis was provided in a multidisciplinary consensus meeting of child psychiatrists and child psychologists according to the DSM-IV-TR criteria (APA, 1994). Both the Autism Diagnostic Interview-Revised (ADI-R; Le Couteur, Lord, & Rutter, 2003) and the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) were used to evaluate retrospective or current (depending on age) ASD symptoms. For the ADI, the diagnostic algorithm was used and for the ADOS, standardized severity scores were calculated (Gotham, Pickles, & Lord, 2009). All children exceeded the diagnostic threshold on both the ADI-R and the ADOS (Table 2). For the non-clinical control group, parental versions of the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005) and the Childhood Behaviour Checklist (CBCL 1,5-5; Achenbach & Rescorla, 2000) showed normed sum scores below the clinical cut off in the non-clinical control group.

Table 1. Demographic characteristics of the ASD group and TD group.

	ASD (*N*= 21) Mean (*SD*)	**TD (*N*= 45) Mean (*SD*)**	**Group differences**
Age in months	60 (9.33)	56 (11.56)	$t(64) = -1.40$, $p = .17$
Gender	M= 20 , F= 1	M= 35, F= 10	(χ^2 (1)=3.14, p=.08)
FSIQ	86.29 (21.64)	108.31 (14.20)	$t(28.32) = 4.26$, $p < .01$*
SES †	2.26 (0.73)	2.60 (0.48)	(χ^2 (4)=8.11, p=.09)

* Group difference significant at $p < .05$
† SES: 1= low, 2= medium, 3= high (N_{ASD}= 19, $N_{control}$= 43)

Table 2. ADI and ADOS scores for the ASD group (*N*=21).

Scale		**Mean (*SD*)**
ADI Social Communication (cut-off=10)		18.67 (6.10)
ADI Communication	Verbal (*N*=*18*, cut-off=8)	14.11 (3.88)
	Non-verbal (*N*=3, cut-off=7)	13.33 (1.16)
ADI Repetitive behaviour (cut-off=3)		6.10 (3.19)
ADI Developmental deviance (cut-off=1)		4.10 (1.22)
ADOS Severity score (*N*= 18)		7.94 (1.73)

Intellectual functioning

In the ASD group, intellectual functioning was assessed using the test that matched the child's verbal, motor, and developmental level. 13 children (62%) completed the Dutch Wechsler Nonverbal Scale of Ability (WNV-NL; Wechsler & Naglieri, 2006), two children (10%) the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III-NL; Wechsler, 2006), three children (14%) the Snijders-Oomen Nonverbal Intelligence Test (SON-R 2.5-7; Tellegen, Winkel, Wijnberg-Williams, & Laros, 1998), and three children (14%) the Mullen Scales of Early Learning (MSEL; Mullen, 1995). Appropriate normative standard IQ scores were computed. In case raw scores were outside the standard range for deviation scores, a ratio IQ was computed by taking the average age equivalents across the subtests, divided by the chronological age in months, and multiplied by 100. IQ scores based on age equivalents are similar to the normative standard IQ scores (Bishop, Guthrie, Coffing, & Lord, 2011) (see Table 1). In the non-clinical control group, all children completed the WNV-NL.

Procedure of the experimental session

After confirmation of the ASD diagnosis and scores below the clinical cut-off for the TD children, participants were invited to the lab-visit. This visit aimed to assess both intellectual functioning and the fear experiment. Before the visit, participants were explicitly prepared with a visual information brochure and a copy set of the electrodes to adjust. Research took place in a carefully selected room with limited stimuli. Children were given time to familiarize before and after the electrodes were applied by playing an age appropriate game, whilst seated in an adapted car seat to have a stable position suited for physiological measurement.

Baseline

To measure baseline, children watched a 3-minute video of a fish tank, which has been shown to be an adequate measure of resting state (Benevides & Lane, 2015; Piferi, Kline, Younger, & Lawler, 2000). Heart rate over the course of the video was analysed in epochs of 30 sec each, to identify a series of two consecutive epochs (1 min) representing resting state. This was done on group level, for the nonclinical control group and the ASD group separately.

Laboratory Temperament Assessment Battery Fear Paradigm

Fear was induced using the unpredictable mechanical toy task of the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith et al., 1999). For this particular study, a remote-controlled robot was used. Parents were asked to sit in the back of the room out of direct sight, filling out questionnaires. In case parents would judge the situation as too fearful for their child, they would be able to stop the experiment. This did not occur during the 90 seconds of the paradigm that were used for analyses. The procedure of the task was executed according to the Lab-TAB manual, placing the robot 1.5 m away from the child. An experimenter entered the room in a white laboratory coat and protection glasses. The robot made three approaches of 30 seconds each, starting by walking towards the child, stopping 15 cm in front of the child moving its arms and emitting noise. Then, the robot walked backward pausing for 10 s before moving forward again, repeating this sequence three times in total. The unfamiliar experimenter left the room, leaving the robot behind. The procedure was videotaped from two angles. Because the current experiment is part of a larger longitudinal study, the task was counter balanced using two versions of the robot in order to account for familiarity effects; the robot in a white robe and a plain robot. A pilot study revealed that responses between the two versions were equal within the control group and results were therefore taken together in further analyses ($t(43) = 1.24$, p .22).

Observational coding

The 10 s epochs were coded according to Lab-TAB manual (Goldsmith et al., 1999) and the facial indicators of emotion as described in the Fear Action Scale (FACS; Ekman & Friesen, 1976). The peak intensity of the emotion was coded within this 10 s epoch to catch the burst of facial expression during these intervals. Facial and bodily fear were both scored on a four-point scale (0-3): neutral (0; no sign of facial or bodily fear), mild (1; one observable facial or bodily sign of fear), moderate (2; two observable signs of facial or bodily fear), and severe (3; more signs of facial or bodily fear). The scores within both categories were averaged across the epochs. A composite fear score was calculated derived by summing these averages, scores ranged between 0 and 6. Inter-rater reliability (IRR) was assessed using a two-way mixed, absolute agreement intra-class correlation model (Hallgren, 2012). The IRR was substantial for fear (ICC= .71, p <.001). Two trained independent coders scored all videos of which 29% were double coded. Interrater reliability was monitored continuously in regular consensus meetings. Discrepancies were discussed within the team to obtain a final consensus score. Distress vocalizations, as described in the Lab-TAB manual were not included in the analyses since our study focuses on the observable expression of emotion. Furthermore, considering the low level of language functioning in some of the ASD children in this sample, verbal capabilities were not taken into consideration.

Physiological arousal

Electrodes were attached, at the top centre of the chest, (10 centimetres below the suprasternal notch) the bottom left, and right of the ribs (10 centimetres above the bottom of the rib cage). Heart rate was recorded continuously during baseline and the robot approach with AcqKnowledge (Version 4.3.1. BIOPAC Systems Inc.). Recordings were acquired through an Electrocardiogram amplifier (ECG100C) and a BIOPAC data acquisition system (MP150 Windows) with a sampling rate of 200 Hz. In AcqKnowledge a 0.5 Hz highpass filter and a 50 Hz notch filter were applied to stabilize the ECG signal. Recorded physiological data was further processed by inspecting the detected R peaks and valid interbeat intervals (IBI) in MATLAB Release 2012b (The MathWorks, Inc., Natick, Massachusetts, United States). Motion artefacts were visually identified and excluded from the data. Heart rate data were summarized in 30-second epochs, in concordance with the behavioural data.

Data analysis

No children were excluded after inspection for outliers and normality checks regarding the ECG and behavioural data. First, baseline levels between the TD group and the ASD group were analysed. Next, a GLM repeated measures analysis was performed with the between subject factor group (ASD, TD) and the within-subjects factor task (60 seconds baseline, three approaches of 30 seconds fear paradigm). To further analyse the heart rate pattern, paired samples *t*-tests were done. The expression of fear between groups was analysed using an independent samples *t*-test after which the dynamics between expression and arousal were analysed using Pearson correlations, Cohen's *q*, and Analyses of Variance (ANOVA) separately for both groups, with Expression as dependent variable and low versus high heart rate as factor. Effect sizes are reported as η_p^2 with .01 being a small, .06 medium, and .14 a large effect (Cohen, 1977). Cohen's *d* effect sizes were calculated for the paired samples *t*-tests with 0.2 being a small, 0.5 medium, and 0.8 a large effect.

Results

Intellectual functioning

Within both the ASD and the TD group, there was no significant relationship between IQ and heart rate (ASD r= .10, p< .68, TD r= -.17, p= .26) nor between IQ and emotional expression (ASD r= .38, p< .09, TD r= .07, p= .66). Therefore, IQ was not controlled for.

Psychophysiological arousal during baseline

Baseline heart rate levels did not differ between children with ASD (*M* 97.37, *SD* 12.50) compared to TD children (*M* 92.27, *SD* 12.21) (t(64) = -1.57, p= .12).

Psychophysiological arousal in response to fear

GLM repeated measure analysis with the between-subjects factor group (ASD, TD) and the within-subjects factor Task (one baseline epoch and three fear approaches) revealed a significant main effect of Task (F(3,192) = 21.01, p< .001, η_p^2= .25), no significant effect of group (F(1,64) = 3.01, p= .09), and no interaction effect (F(3,192) = .72, p= .54). Within group comparisons showed a similar increase from baseline to each fear approach for both children with ASD and TD group. In other words, there was an increase in arousal in response to fear, and this increase was similar for both groups (Figure 1).

Table 3. Within group increases in arousal (heart rate) in response to fear

	ASD	TD
Baseline to approach 1	$t(20) = -2.99$, $p< .01$*, d 0.6	$t(44) = -3.38$, $p< .01$*, d 0.3
Baseline to approach 2	$t(20) = -2.94$, $p< .01$*, d 0.6	$t(44) = -4.31$, $p< .01$*, d 0.5
Baseline to approach 3	$t(20) = -3.83$, $p< .01$*, d 0.8	$t(44) = -4.55$, $p< .01$*, d 0.6

* Significant at p <.05. Effect sizes displayed in Cohens d.

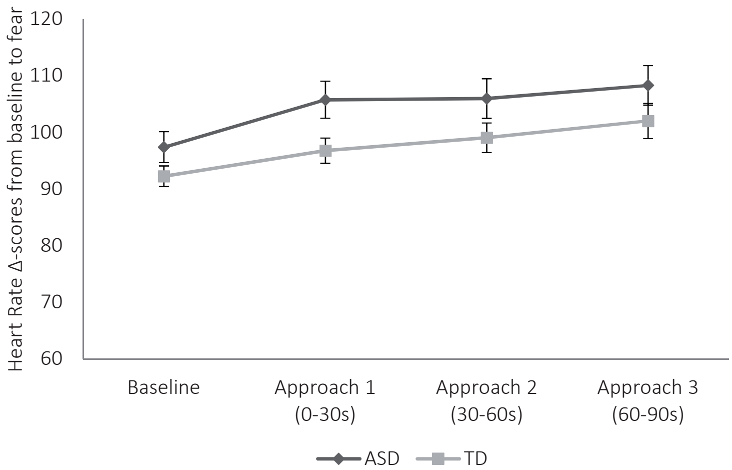

Figure 1. Heart rate at baseline and in response to fear. Error bars displaying *SE*.

Emotional expression of fear

Independent samples *t*-tests showed that children with ASD expressed equal levels of overall emotional fear compared to TD children as reflected in average expression across the total duration of the fear exposure ($t(64) = -.23$, $p = .82$). In other words, the expression of negative emotions in facial expression and body posture in response to fear was equal between children with ASD and TD children (see Figure 2).

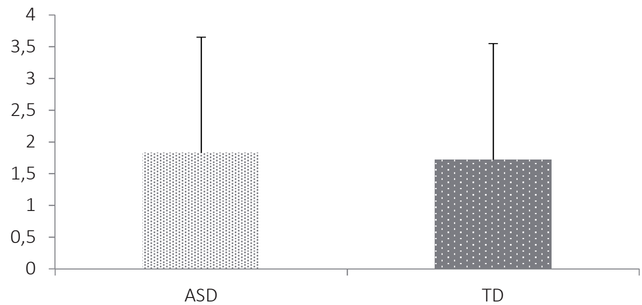

Figure 2. Absolute levels of expression in response to fear for ASD (N=21) and TD children (N=45)

Concordance between arousal and expression

To investigate the concordance between heart rate and the expression of fear, Pearson correlations were calculated within each group. Arousal response during the fear paradigm (as expressed in average heart rate during fear exposure) showed a positive correlation with expression of fear in the control group (r= .45, n= 45, p< .01), with 19.9% explained variance. In contrast to this result, there was no correlation between the arousal response and expression of fear in the ASD group (r= .20, n= 21, p= .38), To check whether any differences in sample sizes between the groups may account for the differences in significance of the correlations, we used the SPSS *select random sample of cases* function to randomly form subsamples of the TD group of equal size as the ASD group. Results showed that correlations remained significant in different subsamples (see Table 4).

To investigate the significance between the Pearson correlations in the TD group and ASD group, Cohen's q was calculated (Cohen, 1977). Correlations were transformed to Fisher's Z, after which the difference was calculated. Cohen's q was .32, indicating that group differences were of a medium effect size. In other words, the TD children who showed an increase in arousal were also the children who showed higher level of expression, in contrast to the ASD children.

Table 4. Multiple random sub-samples within the TD group (N= 45)

n	Pearson r	Significance
22	.41	.05*
22	.75	<.01*
22	.52	.01*

* Significant at p <.05.

To further investigate group differences in the concordance between arousal and expression, both the ASD group and the TD group were divided into a low- and high-arousal group using a median split. The median heart rate in the TD group was 96 BPM. The low-arousal group consisted of 22 children and the high arousal group of 23. The same was done for children in the ASD group, for which the median heart rate was 101 BPM, with 11 children in the low arousal group and 10 children in the high arousal group. ANOVA analyses, separate for the ASD and the TD group, with Expression as dependent variable and low versus high arousal as factor were conducted to determine if the level of facial and bodily expressions was different for groups with either high or low arousal. Results revealed that, within the TD group, the level of expression in response to fear was significantly different for high versus low aroused children (F(1, 43)= 10.61, p< .01), with significantly higher expression in high aroused children. Within the ASD group, expression in response to fear was not different between high versus low aroused children (F(1, 19)= .52, p= .48). This is illustrated in Figure 3.

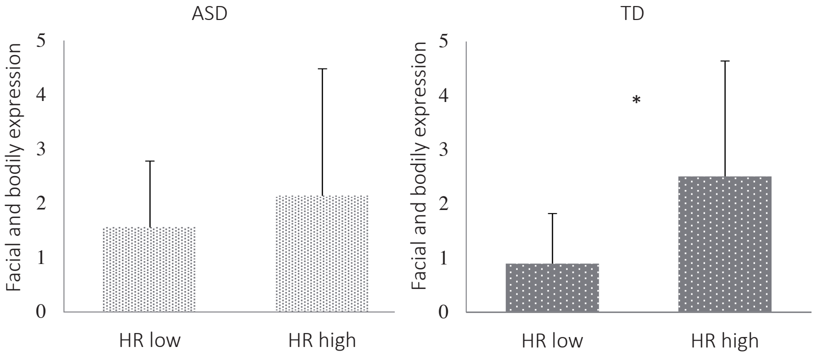

Figure 3. Facial and bodily expression of fear for low versus high arousal.
ASD group left (*N*= 21) and TD group right (*N*= 45). Error bars displaying *SD*.

Discussion

The present study examined physiological arousal and emotional expression in response to fear in young children with Autism Spectrum Disorders (ASD) compared to typically developing children (TD). By simultaneously addressing external components of emotion as expressed in facial and bodily expressions and internal components of emotion as expressed in emotional arousal parameters of the Autonomic Nervous System (ANS), we aimed to provide more insight into possible differential deficits and concordance between these two layers of the complex construct of emotion.

Baseline measures of heart rate revealed no differences in resting state arousal between the ASD group and TD children, which is in line with previous studies (for a review see; Benevides & Lane, 2015). In response to fear, both heart rate patterns and levels of children with ASD revealed increased arousal to the same extend and pattern as TD children. This indicates that children with ASD have autonomic responses when their own emotions are triggered in a fearful situation, similar to TD children. These results provide evidence for an intact emotional arousal in response to fear in children with ASD. Previous studies, mainly concerning older individuals and dominantly high functioning, yielded mixed results regarding cardiac arousal in children with ASD possibly due to the varying nature of the measures that complicated comparisons (Benevides & Lane, 2015). The current study was designed to measure arousal without the possible interference of social interaction aspects, by introducing a stressor that did not require interaction from the children. Another study also reported significant changes in heart rate from baseline to a non-social stimulus (Stroop task) in children with ASD equal to TD children aged 8-15 years (Kushki et al., 2013). This might indicate that the emotional arousal response of children with ASD is intact when it comes to their own emotions, however deviant when it comes to responding to emotions of others. In support of this, a pilot study from Levine and colleagues (2012) showed equal ANS activity as measured with skin conductance between children (8-12 years old) with high functioning autism and a comparison group in response to a social stressor (Trier Social Stress Test). However, cortisol measures during this task showed significant increases in cortisol response in the TD group, and a blunted or even decreased cortisol response in the ASD group. The authors are cautious with interpreting this result, since important factors such as age (8-12 years old), gender, and pubertal level could be of influence on the cortisol results and replication is needed. A recent eyetracking study in young children with ASD showed diminished arousal (heart rate) in response to the emotions of others in comparison to typically developing children (Zantinge, van Rijn, Stockmann, & Swaab, 2017). The either social- or non-social nature of the stimulus should be further investigated to better understand mixed results regarding arousal in children with ASD.

In addition to emotional arousal, we also examined facial and bodily expressions in response to fear. Structured behavioural observations revealed no differences in the intensity of fear expressions between the two groups. However, high amounts of individual variability were noted. Earlier studies also reported relatively intact expression of emotions in children with ASD in response to a negative stimulus, although both of these studies included children with high functioning ASD and the study by Legiša included older children (Jahromi et al., 2012; Legiša et al., 2013). With respect to expressivity, a study by Stagg and colleagues (2013) used videos of children with ASD being interviewed about their daily lives, families, and interests which were rated as being less expressive than TD children. These contradicting results regarding facial and bodily expressivity of children with ASD might be caused by the large individual variability and/or the intensity of the experienced emotion. It could be that subtle or ambiguous expressions are more impaired in children with ASD than unambiguous elicited negative emotions in response to a strong stressor. In daily life, especially in situations with a social nature, interactions are packed with subtle and ambiguous expressions that require the other to encode and respond in a prompt and appropriate manner. In sum, our study shows that with regard to own experienced emotions without social context, children with ASD do show appropriate levels of negative expressions that can clearly be observed on the outside.

Since average levels of arousal response and the accompanying expressions were intact in children with ASD, individual differences gave insight into the variance in both groups and the concordance between expression and arousal. These results revealed that emotional arousal and expression were significantly related within the TD group, but not within the ASD group. TD children who showed an increase in arousal were also the children with higher levels of fear expressions and vice versa. The results remained even after randomly reducing the sample size to match the sample size of ASD group to rule out that this was due to power. Further analyses revealed that the level of expression was different for TD children that were low versus high aroused. In contrast, children with ASD who were highly aroused, did not show increased intensity of expression compared to low aroused children with ASD. This indicates that children with ASD who experience an increase in heart rate, do not necessarily show an increase in expressiveness and vice versa, in contrast to TD children. The difference concordance between children with ASD and TD children represented a medium effect size.

The importance of concordance is illustrated by a study from Mauss and colleagues (2011) who found that discordance was associated with later increased depressive symptoms, lower well-being, and over time undermined psychological functioning in undergraduate female students. Research also showed that discordance can confuse others about actual internal states and could lead to behaviour being interpreted as not trustworthy (Mauss et al., 2011). However, greater concordance does not automatically mean better emotional behaviour (Butler, Gross, & Barnard, 2014), so considering the context of the emotion involved is important. As some have suggested, different components of emotions in circumstances that have little emotional relevance are only loosely connected (Bulteel et al., 2014) and that the appearance of concordance is only associated to relatively strong emotions (Russell, 2003). Even though this last notion has also been debated (Reisenzein et al., 2013), our study provides evidence for the existence of concordance in a sample of TD children which stresses the need for future studies on this topic in young children since the majority of studies has been conducted in adults.

The seemingly absent relationship between expression and arousal in children with ASD might provide evidence that interacting systems are less dependent on each other or at least represent abnormalities in the automatic connections between brain systems responsible for generating behavioural *expression* and brain systems responsible for *experienced* arousal. Two main brain regions (among others) involved in the experience and expression of emotions are the amygdala and the insula. The amygdala plays a critical role in the processing emotional information and, as part of the social brain, has been linked to social-emotional problems in individuals with ASD (Baron-Cohen et al., 2000). In the normal population, amygdala activity has been related to heart rate in healthy adolescents (Yang et al., 2007) and to high intensity facial expressions compared to low intensity and neutral facial expressions (Lin et al., 2016). The insula is important for the sensory perception of emotions, but is also involved in generating emotional and communicative facial expression (Jezzini et al., 2015). In other words, the insula enables the translation of an observed or imitated facial emotional expression into its internally felt emotional significance (Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003; Dapretto et al., 2006). A study by Giuliani and colleagues (2011), showed that anterior insula volume was positively correlated to expressive suppression (Giuliani et al., 2011). The anterior insula (together with motor as well as somato- and limbic-sensory processing) has also been related to the expression of pleasant facial affect (Hennenlotter et al., 2005). Down-regulation of negative emotions reflected in reduced activation of emotional arousal-related brain structures like the amygdala and the insula have also been found (Ochsner & Gross, 2005). There is evidence for abnormalities of the limbic system, in particular the amygdala and the insula, that may be responsible for social-emotional characteristics of ASD (Gaigg & Bowler, 2007). The current study at least provides evidence for poor connectivity between emotional arousal and emotional expression, and might fit with the idea that ASD symptoms may arise as a consequence of disconnection between various functional brain systems, rather than impairments in one single area.

There are some limitations and related suggestions for future research in light of this study. The sample sizes did not allow for more complex statistics to consider patterns of changes in real-time in response to the task. For future studies it is recommended to look at these (individual) patterns of concordance in more detail (for recommendations see; Bulteel et al., 2014; Hollenstein & Lanteigne, 2014). The current sample included a limited amount of girls with ASD which limited comparability between genders. Also, our study included no other indices of arousal than heart rate and expressive behaviour in response to fear. It would be recommended for future studies to also include measures of emotion regulation, cognitive measures, self-report, a broader range of emotions, and other indices of ANS functioning to gain a more complete picture on the different levels of emotion. As heart rate is modulated by both sympathetic and parasympathetic branches of the ANS, measures of ANS activity should be explored further (Benevides & Lane, 2015). In line with this, the current results must be seen in light of a fear-specific response. Different responses might be observed in response to other emotions. Considering the limited amount of comparative studies on this topic in young children with ASD, there is need for caution as well as more research to further explore the results described in the current study. Finally, the results of the current study and the methods used could have important implications to the literature regarding anxiety in children with ASD. The prevalence of anxiety disorders in children with ASD is thought to be as high as 30% however the underlying mechanisms and risk factors for these comorbid problems remain unclear (Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Simonoff et al., 2008; White, Oswald, Ollendick, & Scahill, 2009).

A missing link between arousal and expression in response to emotions (in this case fear) may impact social functioning of children with ASD. The ability to interpret children's expressive signals is essential to promote mutually satisfying interactions (Sullivan & Lewis, 2003). Better understanding emotional responding in children with ASD is important, and awareness of discordance between expression and arousal may be meaningful in psychoeducation and intervention strategies. Considering the increasingly young age at which interventions are implemented (Kim et al., 2016), this could be achieved by raising awareness in the social environment of the children that emotional expressions in children with ASD do not necessarily reflect their internal experience. When children are (mentally) old enough, these interventions could include new techniques that enable children to practice expressive behaviours with techniques such as portable video modelling, which have yielded positive results, especially with regard to generalizability of the learned behaviours (Macpherson, Charlop, & Miltenberger, 2015).

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Chapter 5

Development of social attention and arousal: evidence from eyetracking and heart-rate in typically developing children and children with Autism Spectrum Disorders

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Under review.

Abstract

Studying individual differences in underlying mechanisms of social behavior has substantial implications for understanding both typical development and developmental disorders that are characterized by social challenges such as Autism Spectrum Disorders (ASD). The present study aimed to gain insight into the development of emotional arousal and social attention during a critical period in child development. The role of cognitive development in areas of executive functioning and language, over a period of six months were explored in TD children. Participants included 45 typically developing children (TD; 41-75 months) and 15 children with ASD (43-71 months). Eyetracking and heart rate in response to a social-emotional clip were monitored simultaneously and measurements were repeated six months later. Results revealed stability of arousal in both TD and ASD children in contrast to significant increases in social attention for both TD and ASD children. In TD children, improvements in cognitive flexibility and inhibition, but not language were associated with being more socially attentive. We conclude that even in young children with ASD, fundamental mechanisms of social behavior that are known to be compromised show substantial development in early childhood. In TD children, this improvement was related to maturational changes in higher order cognitive functioning.

Introduction

Being able to show adaptive social behaviors already from an early age requires a child to respond to a fast-paced and ambiguous environment. Understanding social situations and adequate responding to others represent complex behaviors that heavily rely on efficient and effective information processing. As a consequence, social development is vulnerable to developmental disruptions and shows great individual variability, ranging from children who easily 'tune in' to others, to children who have substantial difficulties navigating their social environment. From a developmental perspective, studying underlying mechanisms that are closely related to social behavior during critical periods in childhood could contribute to better understanding the emergence of social behavior in children. Especially since similar social behavioral difficulties may arise from different underlying impairments. To illustrate, less engagement in social interactions may arise from high emotional arousal and related social anxiety or from low emotional arousal and related low social motivation (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012; Corbett et al., 2014; White et al., 2014). Studying individual differences in underlying mechanisms of social behavior has substantial implications for the understanding of developmental disorders that are characterized by social challenges such as Autism Spectrum Disorders (ASD). Core symptoms of this developmental disorder encompass persistent deficits in social communication, social interaction, and restricted, repetitive patterns of behavior, interests, or activities (APA, 2013).

From the literature we know that underlying mechanisms of social behavior such as attending to faces and eyes of others (social attention) and adequate emotional arousal responses to others are affected in children with ASD (e.g.; Benevides & Lane, 2015; Guillon, Hadjikhani, Baduel, & Roge, 2014; Papagiannopoulou, Chitty, Hermens, Hickie, & Lagopoulos, 2014; Zantinge, van Rijn, Stockmann, & Swaab, 2017b). Instead of merely focusing on group differences at a single time point, the present longitudinal study was designed to 1) gain insight into the development of social attention and emotional arousal in both TD and ASD children, and 2) to address the role of cognitive development in areas of executive functioning (EF) and language in TD development in order to take the first steps in exploring mechanisms of developmental trajectories.

From infancy, typically developing children attend preferentially towards social information such as their caregivers, faces, and biological motion also referred to as social attention (Gliga & Csibra, 2007; Haith, Bergman, & Moore, 1977; Simion, Regolin, & Bulf, 2008; Vuilleumier, Armony, Driver, & Dolan, 2003). An early social preference is believed to be largely automatic, efficient, and requires little effort (Chawarska, Macari, & Shic, 2012; Salva, Farroni, Regolin, Vallortigara, & Johnson, 2011) and is considered a crucial prerequisite for the development of social behaviors such as learning to socialize and recognizing emotions of others. As children interact in reciprocal relationships, their experience with faces and voices grows which in turn enhances cortical specialization and the fine-tuning of perceptual systems (Johnson et al., 2005; Webb, Jones, Kelly, & Dawson, 2014). As a result, social brain circuitries specialize and mature, supporting more complex behaviors such as joint attention, intentional communication, and imitation (Dawson, Webb, & McPartland, 2005).

With the emergence of new techniques such as eye tracking, objective and direct measurements have provided insight into preferential attention to social information (Jones & Klin, 2013; Klin, Lin, Gorrindo, Ramsay, & Jones, 2009). Social attention in early childhood has been investigated, however longitudinal studies are scarce. Knowledge about developmental aspects is important particularly with regard to identifying opportunities to positively influence maturation in vulnerable children. Children (later diagnosed) with ASD have shown an initial intact attention towards the eyes in the first months of life, and an average decline in eye fixation from two to six months of age (Jones & Klin, 2013). While another study of infants with and without a family history of ASD showed intact gaze following behavior at both seven and 13 months (Bedford et al., 2012). These studies stress the importance of learning more about the developmental trajectory of this precursor for social development.

Crucial for understanding the dynamics of social attention is to integrate measures of underlying processes, in particular the emotional arousal response. Arousal can be conceptualized as a dimension of emotional responsiveness and is considered a prerequisite for emotionally resonating with others in a social context (Kreibig, 2010; Mauss & Robinson, 2009). An arousal response is generated by the autonomic nervous system (ANS) and causes an individual to attend and respond towards social information (Baron-Cohen & Wheelwright, 2004; Bons et al., 2013). Heart rate is an index of the ANS and varies due to the influence and interaction between both the sympathetic and parasympathetic nervous system. In children with ASD, there is evidence for normative resting state arousal but mixed results regarding arousal patterns in response to stimuli (Benevides & Lane, 2015) showing less modulation in response to social stimuli (Levine et al., 2012; Zantinge et al., 2017b) and intact modulation when it comes to their own emotions (Zantinge, van Rijn, Stockmann, & Swaab, 2017a). From a developmental perspective, there are indications that arousal patterns in typically developing children show maturational changes between 4 months and 4 years, but relative stability in middle to late childhood (Bar-Haim, Marshall, & Fox, 2000; Benevides & Lane, 2015). Studying arousal parallel to social attention, from a developmental perspective, might provide important information about which aspects of social-emotional mechanisms show continued development in early childhood as leads for possible intervention and treatment.

The way children direct their attention to others and how their arousal system responds to this social information may depend on the development of specific cognitive functions. It is therefore important to study cognitive processes such as executive functions and language, which are core to the regulation of behavior, thought, and emotion with regard to the

development of social behavior (Chita-Tegmark, 2016; Hill, 2004a; Moriguchi, 2014).
Executive function is an umbrella term for a broad range of higher order cognitive processes that are critical for efficient functioning in everyday life such as attention, cognitive flexibility, goal setting, and inhibitory control. Executive functions develop mostly stepwise through childhood and adolescence, together with the maturation of prefrontal regions of the brain (Anderson, 2008) and thus can be considered an early indicator of very early frontal brain development. Together with executive functions, communication is important to the successful establishment of relationships and peer acceptance (Beauchamp & Anderson, 2010). More specifically, the development of language is among the most complex neurocognitive functions of humans and are a result of brain development in interaction with the social environment. (Non-) verbal language evolves in the early years from the first social smile to the emergence of intentional imitative behavior and dyadic interaction with aspects of communication such as joint attention and expressive and receptive communication. Both functions are known to be vulnerable in children with ASD compared to typically developing children (APA, 2013; Groen, Zwiers, van der Gaag, & Buitelaar, 2008; Hill, 2004b; O'Hearn, Asato, Ordaz, & Luna, 2008). Together, executive functioning and language/communication reflect the ability to express, control and steer thoughts, behaviors and emotions and are important to study as they might be related to being able to attend to social cues in the environment. Studying the typical development of executive functions and language in relation to social attention and emotional arousal is a prerequisite for understanding the dynamics of these characteristics in children with ASD.
In sum, knowledge is growing about the early symptoms of ASD, indicating that both social attention (Chita-Tegmark, 2016; Frazier et al., 2017; Zantinge et al., 2017b) and emotional arousal response patterns (Benevides & Lane, 2015; Zantinge et al., 2017a) might be different in children with ASD. However, the developmental dynamics in early childhood are less clear. Early interventions could have a significant impact on daily life functioning and later quality of life. For interventions to have optimal effects on the developing brain, we need to have knowledge about the developmental aspects of social attention and emotional arousal, as this may help to identify windows of opportunity. Finally, the present study aimed to take the first steps in understanding the influence of language and executive functioning on the development of social attention and emotional arousal, in typical development only. These exploratory results might prove to be valuable leads for further studying this relationship in the development of young children with ASD.

Methods

Participants

Participants included 45 typically developing children (TD) and a matched group of 15 children with ASD. Children with ASD were recruited through the Dutch Autism Center

(Rivierduinen), the Dutch Autism Association (NVA), and the Dutch Association for Developmental Disorders (Balans). The TD group was recruited through daycare centers, elementary schools, and postings in public areas in the Netherlands. All children were invited to the lab twice. The mean duration between T0 and T1 was 6.42 months (*SD*= .87). For children with ASD, the first visit (T0) was planned as soon as possible after clinical diagnosis (mean duration between T0 and T1= 7.07 months, *SD*= .88). Children were matched on age (M_{TD}= 55.22, SD= 10.79, M_{ASD}= 56.27, *SD*= 9.57) and gender (see Table 1). Parental versions of the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005) and the Childhood Behavior Checklist (CBCL; Achenbach & Rescorla, 2000) showed normed sum scores below the clinical cut off in the TD group. Inclusion criteria for all participants were that parents and/or children were Dutch or English speaking, children had no neurological conditions, previous head injuries with loss of consciousness, and/or metabolic diseases.

Table 1. Demographic characteristics of the TD group and the ASD group at T0.

	TD (*N*= 45) Mean (*SD*)	ASD (*N*= 15) Mean (*SD*)	Group differences
Age range	41-75 months	43-71 months	$t(58)= -.33$, $p= .74$
Gender	M= 37, F= 8	M= 13 , F= 2	$\chi^2(1)= .16$, $p= .69$
FSIQ	110.62 (14.44)	86.80 (21.55)	$t(58)= 4.86$, $p< .01$*
PPVT-III-NL Language	110.89 (10.78)	84.07 (21.02)	$t(16.52)= 4.74$, $p <.01$*
SES †	2.60 (0.48)	2.33 (0.75)	$\chi^2(4)= 9.96$, $p= .04$*

* Group difference significant at $p <.05$
† SES: 1= low, 2= medium, 3= high

Measures

Autism diagnosis

Current symptoms of ASD according to the DSM-IV-TR criteria (APA, 1994) were evaluated using the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000). Standardized severity scores were calculated according to Gotham, Pickles, & Lord (2009) to compare the three different modules of the ADOS that were administered. The diagnostic algorithm of the Autism Diagnostic Interview-Revised (ADI; Le Couteur, Lord, & Rutter, 2003) was used to assess retrospective or current functioning (depending on age) at age four to five years. All children exceeded the diagnostic threshold on both the ADI-R and the ADOS (Table 2). The diagnosis was provided by child psychiatrists and psychologists with extensive clinical experience during a multidisciplinary meeting.

Table 2. ADI and ADOS scores for the ASD group (*N*=15)

Scale		Mean *(SD)*
ADI social communication (cut-off= 10)		19.00 (6.15)
ADI communication	Verbal (*N*= 14, cut-off= 8)	14.64 (3.84)
	Non-verbal (*N*= 1, cut-off= 7)	14.00
ADI repetitive behavior (cut-off= 3)		6.07 (3.13)
ADI developmental deviance (cut-off= 1)		4.00 (1.25)
ADOS severity score		8.33 (1.67)

Intellectual functioning

Children from the TD group completed the Wechsler Non-Verbal (WNV-NL; Wechsler & Naglieri, 2006). Intellectual functioning of children with ASD was assessed using the test that matched children's verbal, motor, and developmental level. 11 children (73%) completed the WNV-NL (Wechsler & Naglieri, 2006), one child the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III-NL; Wechsler, 2006), one child the Snijders-Oomen Nonverbal Intelligence Test (SON-R 2.5-7; Tellegen, Winkel, Wijnberg-Williams, & Laros, 1998), and two children (13%) the Mullen Scales of Early Learning (MSEL; Mullen, 1995). A ratio IQ was computed in case raw scores were outside the standard range for deviation scores by taking the average age equivalents across the subtests, divided by the chronological age in months, multiplied by 100 (Bishop, Guthrie, Coffing, & Lord, 2011).

Social attention

Detailed information about the pilot study that was conducted to select the baseline and social-emotional video clip, has been reported elsewhere (Zantinge et al., 2017b). Two identical video's, that significantly elicited an arousal response displaying an angry emotion were played using the Tobii T120 eye tracker (Tobii Technology AB, Danderyd Sweden). Videos were counter balanced between T0 and T1 to account for clip-specific effects. Gaze data within specific areas of interest (AOIs) was collected at 120 Hz by using corneal reflection techniques and were processed using the Tobii I-VT fixation filter in Tobii Studio (Version 3.2.1). This filter controls for validity of the raw eyetracking data making sure only valid data was used (Olsen, 2012). With the "Dynamic AOI" tool, face and total screen AOIs were drawn, taking into account the size and the margins around the AOIs (Hessels, Kemner, van den Boomen, & Hooge, 2015; Hooge & Camps, 2013). A "relative" total fixation duration was calculated by taking the total fixation duration within the AOI, divided by the total duration of the clip, multiplied by 100 (Zantinge et al., 2017b). The relative total fixation duration reflected the percentage of time children were attending to the AOI. In the present study, the development of social attention was operationalized in terms of the difference between relative fixation duration towards the face at T1 minus T0, expressed in Δ-scores.

Executive functioning

The Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P; Gioia, Espy, & Isquith, 2001) was used to evaluate executive functioning. This parent report questionnaire consists of 5 scales; inhibition, cognitive flexibility, emotion regulation, working memory, and planning and organizing. The Dutch translation showed sufficient to high internal consistency, interrater reliability, construct validity, and test-retest reliability indicating suitability for research purposes (Van der Heijden, Suurland, De Sonneville, & Swaab, 2013). High scores represented lower levels of executive functioning. In the present study, Δ-scores represented the development over a period of six months, calculated by subtracting the scores at T0 from the scores at T1.

The Amsterdam Neuropsychological Tasks (ANT; De Sonneville, 2014) were used to assess inhibition and attention in the TD group. This computerized test battery has demonstrated satisfactory validity and test-retest reliability (De Sonneville, 2005) and has been used in a variety of clinical and non-clinical samples with young children (e.g.; Rommelse et al., 2008; Swaab et al., 2000; van Rijn & Swaab, 2015). After instructions and a practice trial, children were instructed to work as quickly and accurately as possible by clicking the mouse button with their index finger.

ANT: Inhibition was measured with the Go/NoGo subtest (De Sonneville, 2014). Each of the 48 trials (24 Go- and 24 NoGo) began with a fixation period (500 ms) and was followed by the presentation of the target stimulus, either the Go-stimulus (a green walking man) or the NoGo-stimulus (a red standing man). A higher amount of false alarms (pressing the mouse key on a NoGo stimulus) indicated problems with inhibition. The development of inhibition was expressed in Δ-scores which represented the number of false alarms at T1 minus T0.

ANT: Attentional control was measured with the Sustained Attention subtest (De Sonneville, 2014) operationalized in terms of stability in attentional control over a longer period of time. In this task, a house was continuously presented on the screen in which one animal randomly appeared in one of the three windows. During the 20 series of 12 trials children were instructed only to press the key in case they saw that target animal (a mouse) and to wait in case another animal was presented. A higher standard deviation in response time indicated problems with attentional control. Development in attention was expressed in Δ-scores which represented the difference score between T1 minus T0.

Language

Receptive language was measured with the Dutch version of the widely used Peabody Picture Vocabulary Test-III-NL (PPVT-III-NL; Schlichting, 2005). Each item of this non-verbal multiple choice test consists of four pictures from which the child is asked to pick the one that corresponds with the examiner's stimulus word. Delta (Δ) scores represented the development of receptive language from T0 through T1.

Expressive language was assessed with body part naming subtest of the NEPSY-II-NL (Korkman, Kirk, & Kemp, 2007. Dutch translation by; Zijlstra, Kingma, Swaab, & Brouwer, 2010). A comprehensive child neuropsychological assessment for ages 3–12 years. This task required the child to identify different body parts on a stimulus card that were read aloud by the experimenter. Delta (Δ) scores represented the development of expressive language.

Physiologic measurement

Data were recorded continuously with AcqKnowledge (Version 4.3.1 BIOPAC Systems Inc.). Electrodes were attached at the top center of the chest, (10 cm below the suprasternal notch) the bottom left, and right of the ribs (10 cm above the bottom of the rib cage). Recordings were acquired through an Electrocardiogram amplifier (ECG100C) and BIOPAC data acquisition system (MP150 Windows) with a sampling rate of 200 Hz. Physiological monitoring equipment was synchronized with Tobii software by event markers representing the start of the social-emotional clip. In AcqKnowledge a 0.5 Hz high pass filter and a 50 Hz notch filter were applied to stabilize the ECG signal. Recorded physiological data was further processed by manually inspecting the detected R peaks and valid interbeat intervals in MATLAB Release 2012b (The MathWorks, Inc., Natick, Massachusetts, United States). Motion artifacts were visually identified and excluded from the data.

Procedures

Both the TD group and ASD group followed same procedures. Preparations for the lab visit included an information brochure and a copy set of the electrodes to practice at home. During assessment, children completed cognitive tasks while the parent was in the room next to the child filling out questionnaires. After a break, the session continued in the lab in the presence of the parent (who was out of direct sight). Electrodes were applied after which children played an easy exploration game on a touch screen to familiarize and for the electrodes to adjust to the skin. After 10 minutes, children sat in an adapted car seat to have a stable position and to minimize distraction with the head protection on the side. After baseline, the anger clip was played. Children were instructed to watch the clips while trying to sit quietly (Zantinge et al., 2017b). Tests were completed at the Center for Autism by a certified child psychologist and trained experimenters who used written protocols detailing all procedures and verbal instructions.

Statistical analyses

After a missing data inspection, data was checked for normality. For both groups separately, the development of arousal and social attention was analyzed using paired samples *t*-tests including T0 and T1. Linear regression analyses (with a backward procedure) were done to study associations between executive functioning, language, and social attention. Finally, group comparisons using independent samples *t*-test were performed to investigate whether developmental effects were different between groups. Effect sizes were calculated according to Cohen's *d* with 0.2 being a small, 0.5 medium, and 0.8 a large effect.

Ethics statement

This study was approved by the Ethical Committee of the Department of Education and Child Studies at the Faculty of Social and Behavioral Sciences, Leiden University, and by the Medical Research Ethics Committee at Leiden University Medical Center. A written informed consent according to the declaration of Helsinki was signed by parents/ legal caretakers.

Results

Intellectual functioning

Within the TD group there was no significant relationship between IQ and Δ heart rate (r= -.21, p= .17) nor between IQ and Δ social attention (r= -.05, p= .77). Within the ASD group, there were also no significant relationships between IQ and the outcome measures (IQ and Δ heart rate r= -.02, p= .95, IQ and Δ social attention r= .02, p= .96).

Developmental trajectory in TD children

Development of arousal response in TD children

A paired samples t-test revealed that heart rate, as expressed in peak arousal during video clips, was not significantly different between T0 (M= 3,25, SD= 7,02) and T1 (M= 2,84, SD= 6,50) ($t(44)$= .29, p= .78). In other words, for TD children, peak in arousal while watching a social-emotional clip was stable over a period of 6 months (see Figure 1).

Development of social attention in TD children

A paired samples t-test showed that social attention, as expressed in percentage of fixation duration towards the face including the eyes, increased significantly between T0 (M= 34,56, SD= 9,54) and T1 (M= 45.66, SD= 15,23) ($t(39)$= -3.77, p< .01). Cohen's d was 0.9, indicating a large effect size (see Figure 1). Within the TD group, 72,5% of the children showed higher scores at T1 as compared to T0 in attention towards the face. The other 27,5% of the children attended towards the face equally or less. The percentage total visit duration total screen was 98% at both T0 and T1 indicating that children looked at the screen equally at both time points so increases in social attention were not a consequence of looking more at the screen in general.

Predictors of social attention in TD children

A linear regression analysis with a backwards procedure was done to investigate the relationship between the increase in social attention and executive functioning within the TD group. The increase in social attention (Δ T0 and T1) was entered as dependent variable. IQ and Age were entered in block one, the five Δ BRIEF-P scales and the two Δ ANT measures of executive functioning were entered in block two as independent variables. This resulted in a significant model (R^2= .21, F(2, 29)= 3,90, p< .05) with the combination of the Cognitive flexibility scale of the BRIEF-P (β= -3.20, p= .03) and Inhibition (β= -1.36, p= .08) as measured with the ANT as significant predictors. This indicated that the increase in social attention within the TD group was best predicted by increases in Cognitive flexibility and Inhibitory control. Both IQ and Age were no significant predictors within this model. Next, the Δ PPVT-III-NL (receptive language), Δ NEPSY body part naming (expressive language) were entered as independent variables, in addition to IQ and Age, to investigate the relationship between the increase in social attention and language within the TD group, controlled for intellectual functioning and age. No significant model was found (R^2= .02, F(1, 34)= .56, p= .46).

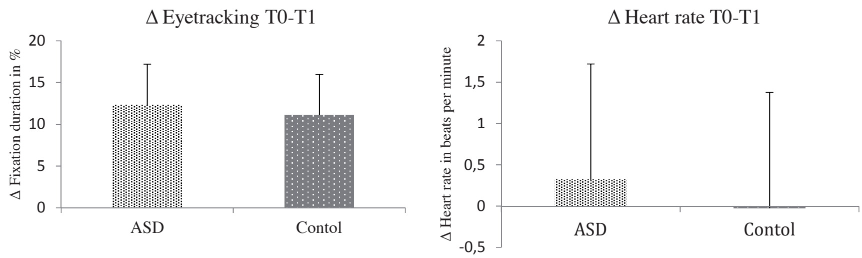

Figure 1. Developmental difference of social attention (left) and arousal response (right) in ASD and TD children between T0 and T1expressed in Delta (Δ) scores.

Developmental trajectory in ASD children

Development of arousal response in ASD children

A paired samples *t*-test revealed that the peak in arousal response did not change between T0 (M= 1,08, SD= 8,46) and T1 (M= 1,40, SD= 6,59) (t(10)= -.088, p= .93). In other words, for children with ASD, emotional arousal in response to a social-emotional clip was stable over a period of 6 months (see Figure 1).

Development of social attention in ASD children

A paired samples *t*-test showed that social attention increased significantly between T0 (M= 28,18, SD= 13,80) and T1 (M= 40.51, SD= 19,22) (t(15)= -2.53, p= .024). Cohen's d was 0.7, indicating a medium effect size (see Figure 1). Within the ASD group, 80% of the children showed an increase in attention towards the face from T0 to T1, and 20% of the children attended equally or less at the face. The percentage total visit duration total screen was 97% at T0 and 96% at T1, which indicated that children attended to the screen equally at both time points and results were not due to looking more at the screen in general.

Group comparisons of social attention development

Both TD and ASD children showed significant increases in social attention over a period of six months. An independent samples *t*-test was performed to investigate whether the increase in social attention was different between groups. Results showed that Δ social attention between TD children (*M*= 11,10, *SD*= 18,60) and children with ASD (*M*= 12,33, *SD*= 18,85) was not significantly different ($t(53)= -.217$, $p=.83$). In other words, the increase in attention towards the face over a period of six months was equal.

Discussion

The present study investigated developmental changes in social attention and emotional arousal in typically developing children (TD) and children with Autism Spectrum Disorders (ASD). The role of cognitive development in areas of executive functioning and language, over a period of six months was explored in TD children.

Measures of the development of emotional arousal in response to a social-emotional stimuli revealed stable heart rate responses over a period of six months in both TD children and children with ASD. Longitudinal measurements of emotional responding to social stimuli in young children with ASD, to our knowledge, has not been investigated before so the present results have to be seen in light of the available literature in TD children and older children with ASD. In the TD population, there is evidence that heart rate is indeed a relatively stable measure during middle to late childhood (For a review see; Benevides & Lane, 2015), also in response to behavioral stress between childhood and adolescence (Matthews, Woodall, & Stoney, 1990). The results regarding developmental stability in heart rate from the present study, together with previous studies, suggest that maturation of the parasympathetic nervous system may contribute to children's increasing ability to self-regulate (Bar-Haim et al., 2000). This is an important concept in the study of autism (Benevides & Lane, 2015). With regard to the development of arousal states (measured with heart rate) during rest, daily life activities, and sleep in children between 3 and 15 years, research shows age related changes, with a slow decline over time (Alkon et al., 2003; El-Sheikh & Buckhalt, 2005; Fleming et al., 2011; Hinnant, Elmore-Staton, & El-Sheikh, 2011). However, results reported in the present study showed that age was not of influence on the development of arousal in the current sample. In sum, our data shows that during this developmental stage there are no *changes* in arousal response over time.

In contrast to the stability in arousal response, social attention improved in both TD children and children with ASD. Previous research has revealed that initial social attention towards social cues (mainly the face, specifically the eyes) in children with ASD is not different from that of TD children before six months, but starts to shows a decline at six to twelve months (Bedford et al., 2012; Jones & Klin, 2013). In sum, our results show that there is substantial development in social attention to the same extend as TD children within a relatively short period of six months.

The results of the present study suggest that even though arousal levels in response to social-emotional information remain very similar over time, social attention can become more coordinated towards the relevant social-emotional cues. From an evolutionary perspective, an affective arousal response can be considered a primitive and fundamental predisposition of the human body which responds to complex triggers already at an early age. Arousal is a reflection of the autonomic nervous system in interaction with the subcortical and limbic brain processes. With regard to development, it is hypothesized that such primary processes are quite innate and possibly less prone to developmental changes over relatively short periods of time (Calkins & Keane, 2004; Jemerin & Boyce, 1990). Higher order cognitive processes however, show continued and rapid development during early childhood as a consequence of brain maturation and environmental influences.

Studying the influence of language (both expressive and receptive) and executive functioning on the improvement of this social attention in TD children revealed that a combination of inhibitory control and cognitive flexibility were the most important predictors of improvement in social attention. This suggests that the development of being able to socially attend to others is associated with higher order cognitive functioning. At this age, rapid maturations of frontal brain regions drive the increases in being able to socially orient toward others, even in a relatively short period of six months. Executive functioning in young children is an essential precursor for the development of social skills such as theory of mind (Hughes & Leekam, 2004; Perner & Lang, 2000). Being able to resonate with other persons and to understand their thoughts, feelings, and emotions is an essential aspect of brain maturation. The current study was limited to investigating these mechanisms in TD children only, but the results provide interesting leads for further research and possible interventions into these relating mechanisms in children with ASD. Existing research suggests that differences in the autonomic nervous system (both sympathetic and parasympathetic) are observed among individuals with ASD during social interaction, which correlates with severity of social difficulties (e.g.; Benevides & Lane, 2015; Neuhaus, Bernier, & Beauchaine, 2016; Zantinge et al., 2017b).

The present study has limitations that are important to address. The role of cognitive development in areas of executive functioning and language could only be explored in the typically developing children. Related to this was the sample size of the ASD group, causing restrictions with regard to the complexity and comprehensiveness of the analyses that could be done. However, we were able to study development by operationalizing development in difference (Δ)-scores as a pure measure of development. The results of the present study need to be replicated, preferably in a larger sample, including a condition with intellectually matched children without ASD considering the difference in IQ between TD and ASD children in the current sample. Heart rate was analyzed in beats per minute as indicator of both the sympatric as the parasympathetic response. Using a larger repertoire of ANS indices is recommended, as studies including indices such as PEP and HRV have yielded complementary results. Even though IQ cannot be separated from the effects of the condition (Dennis et al., 2009), IQ was significantly lower in children with ASD, therefore we decided to investigate the role of IQ in the relationship between cognitive functioning and social attention.

In conclusion, the present study revealed that in young children with ASD, fundamental mechanisms of social behavior develop in early childhood during a relatively short period. In TD children, this improvement is related to maturational changes in behavioral and cognitive repertoires of understanding more and being able to show adaptive social behavior. Even though it is hypothesized that early ASD symptoms might represent a vulnerability in the development social brain systems that fail to become specialized and functionally integrated (Johnson et al., 2005; Webb et al., 2014), the present study highlights that even in six months there certainly is evidence for improvements and that intervening at this age might be warranted. Studying sensitive and direct indices of social-emotional mechanisms, such as eyetracking and heart rate, are anticipated to fuel ASD screening, diagnosis, and treatment (Bölte et al., 2016). With this knowledge, early experiences in this sensitive period can be targeted which could have a long-term impact on development and potentially improve developmental trajectories (Bradshaw, Steiner, Gengoux, & Koegel, 2015).

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Chapter 6

Summary and general discussion

The environment into which children are born and grow up is predominantly social. The ability to participate in this social environment is an important condition for being successful and to experience quality of life on many levels, throughout a lifespan. In social situations, both cognitive and emotional processes work together to enable successful navigation through a complex world that constantly changes and requires behavior to be adaptive. Children are able to adapt to changes in their social environment with the help of emotions. Social situations are filled with emotional messages and experienced emotions become more meaningful when interacting with others. For example, when a child really likes a toy and wants to play with it, being upset when it is out of reach, a parent may notice the distress and provides the toy, followed by a shared smile. Thus, emotions can enhance adaptive behavior, are important for decision making, have a motivational function and inform other individuals what is desired or needed. However, emotions can also interfere with social behavior, for example when the timing or the intensity of the emotion is off or when the emotion is directed towards irrelevant aspects.

Understanding the emotion processes that shape adequate social behavior and communication is important, not only in typical development, but especially in children that show developmental vulnerability with regard to social communication and social interactions, such as Autism Spectrum Disorders (ASD; Box 1). ASD refers to a group of pervasive neurodevelopmental disorders that manifest before the age of four, characterized by impaired social interaction and communication skills. With a focus in the literature on the cognitive processes related to social behavior such as theory of mind and executive functioning, the emotional or affective processes underlying the behavior problems in ASD remain poorly understood. The studies presented in this thesis aimed to provide in better understanding emotion processing in preschoolers with ASD by using a comprehensive approach. This approach included integrating not only behavioral and cognitive but also the affective component of emotion processing in young children with ASD. More specifically, these studies together aimed to investigate how children with ASD perceive, experience, regulate, and express emotions in response to different social and non-social contexts during a critical period of development. Sensitive and direct measures of emotion processing were used, including not only what can be seen on the 'outside' in terms of behavior, but also including processes on the 'inside' referring to more fundamental information processes such as physiological mechanisms that embody the experience of emotions. The studies were conducted in preschool children with and without ASD. This early developmental approach is crucial for better understanding of social difficulties in young children in terms of how they process emotions, and for identifying windows of opportunity to stimulate development and recognize specific targets for intervention.

Together, the results in this thesis revealed that the majority of children with ASD experienced difficulties in emotionally resonating to the emotions of others, expressed in a blunted emotional arousal response and less social attention towards emotional distress of others (**chapter 2**). In contrast, children with ASD did show emotional arousal modulation in response to *own* experienced emotions accompanied with intact facial expressions of the experienced emotions (**chapter 3 and 4**). However, on a behavioral level, children with ASD deployed less constructive and more maladaptive emotion regulation strategies, which was related to language impairments (**chapter 3**). **Chapter 4** provided evidence for a disconnection between what is experienced on the inside, in terms of emotional arousal, versus what is expressed on the outside, in terms of behavioral expression, in children with ASD. From a developmental perspective, the results in **chapter 5** presented stability of emotional arousal, but developmental improvements in social attention over a period of six months, providing promising evidence for a window of opportunity in early childhood to positively influence social development.

Below, the results of the four studies are summarized in more detail, followed by a general discussion of the main conclusions, implications, directions for future research, and in conclusion a summary of the main findings.

Summary

Social attention and emotional arousal in response to the emotions of others

The study presented in **chapter 2** addressed social attention and emotional arousal, in response to daily-life social-emotional scenes in young children with ASD. Eyetracking analyses revealed that children with ASD looked less at relevant social-emotional information (i.e., the face) compared to typically developing children, even though they equally attended to the screen in general. This part of the results adds to the growing body of research indicating that individuals with ASD spend less time than typically developing children attending to social cues with an overall effect size of 0.55 over 38 articles (Chita-Tegmark, 2016). The current study confirmed these earlier findings, in a very young sample of children with ASD in response to a dynamic daily-life social scene that showed peers in emotional distress.

In addition to social attention, we measured emotional arousal while children were attending to the emotional distress of others. The results in the typically developing children revealed a significant heart rate deceleration from baseline to the social-emotional clip which is an indication of directing attention towards a stimulus (Van Hulle et al., 2013). Next, the typically developing children showed increasing heart rate while watching the social-emotional clip, indicating that they emotionally resonated with the social-emotional information presented to them.

In contrast to the typically developing children, children with ASD did not show arousal modulation during the clip. In other words, they did not emotionally resonate to the distress of others on the level of arousal. Also in contrast to typically developing children, children with ASD did not show an initial deceleration in emotional arousal. The absent deceleration in heart rate could be explained as a result from a failing emotional arousal system that does not trigger children with ASD to have attention for the social-emotional cues. However, the lack of emotional arousal was not only seen in children that looked at the socio-emotional cues for shorter durations, but also in children who looked longer.

When focusing on the relevance of underlying mechanisms in understanding the behavioral phenotype of ASD, the present study showed that more severe ASD symptoms in general and social impairment in particular, were associated to less adaptive emotional arousal and more social attention problems.

Together, these results suggest a possible fundamental disconnection between two important systems that work together in emotionally resonating and attending to the distress of others, related to symptom severity. In daily life social interactions, looking at the face of the other person is essential for understanding the other person's emotions and to adapt one's own behavior responses accordingly. It is also important that emotions of others impact your own emotion system; this emotional resonation is embodied in responses of the arousal system. Therefore, when there is no automatic visual orientation that senses the emotions of others, this might make it harder for children with ASD to respond to these social emotional cues resulting in problems in social communication.

An important question is to what degree such deficiencies in the emotional arousal system can (or cannot) be targeted through intervention in children with ASD. Is it possible to influence the emotional arousal system so that children with ASD do orient towards the emotional expression of someone else and thus show emotional (or affective) empathy? The current study showed that looking either longer or shorter at the emotional distress of others did not differentially influence the emotional arousal system. Therefore, it is suggested that interventions should not just focus on social orientation, but also target the child's capacity to understand another's perspective or mental state, also referred to as cognitive empathy. Especially for children during their early preschool years who are not yet able to put their emotions into words (Lewis, Haviland-Jones, & Barrett, 2010), it is important that adults that act in the social environment to be aware that social cues are not automatically picked-up by children with ASD. By putting emotions into words for them and providing subtitles in social interactions, the difficulties that children with ASD experience in emotionally resonating with others might be compensated. When these children are older, these strategies might internalize and generalize to multiple contexts providing them tools for attending to and processing of the emotions of others.

Finally, the findings of the current study help to understand why children with ASD may not always show socially adaptive behavior, explained by a reduced social attention and lack of emotional resonance (also when they do attend). When parents and practitioners are aware that the social inadequate behaviors originate from an inability instead of unwillingness, this could lead to less frustration and miscommunication and eventually might improve overall family functioning.

Emotion regulation strategies and emotional arousal in response to frustration

The study reported in **Chapter 3** is focused on the *own* experienced emotions of young children with and without ASD in addition to the response to the emotions of others that was reported in chapter 2. We investigated emotional arousal levels in response to frustration, and how children cope with the experienced emotional arousal in terms of emotion regulation strategies.

Results revealed that the pattern of emotional arousal responding in children with ASD was similar to that of typically developing children, when the emotion system was triggered by internal cues (frustration). For both groups separately, there was an increase in arousal from baseline in response to frustration and heart rate deceleration during recovery. In other words, with regard to their own emotions, children with ASD do show adequate modulation of emotional arousal in the context of frustration as compared to typically developing children. In contrast, structured behavioral observations of emotion regulation strategies, which were scored parallel to the emotional arousal measures, showed that children with ASD deployed different strategies, expressed in more venting and avoidance behaviors and less constructive (i.e. goal directed) strategies, in coping with these emotions. The behavioral results replicate a previous study that also reported more maladaptive and less adaptive strategies in young children with ASD (Jahromi, Meek, & Ober-Reynolds, 2012). The current study adds to the literature that there is no emotional arousal dysfunction when it concerns own experienced emotions, but that coping with the experienced emotional arousal is more difficult for children with ASD resulting in less adaptive behavior.

Further analyses revealed that increased use of less constructive strategies to cope with emotions, was best explained by language impairments. Executive functioning was not related to any of the emotion coping strategies. Thus, at this age, language impairments may better explain the use of non-constructive emotion coping behavior in children with ASD. However, because of the prolonged development of executive functioning (Best and Miller 2010), we cannot exclude that these cognitive functions may become increasingly important for managing experienced emotions over the course of development.

We conclude that with respect to the experience of own emotions, children with ASD do show emotional arousal responses, but they may rely on less efficient strategies to cope with these emotions, in part explained by lower language abilities.

When translating these conclusions to everyday life situations, they imply that children with ASD may need help in dissecting emotional situations and need tools to cope with these emotions in promoting goal-directed behavior. The parents and caretakers can help children with ASD by giving words to the situation, identifying the emotion, and providing solutions or cognitive-verbal and behavioral tools for dealing with the situation. For example, a parent might define the situation verbally and provide suggestions for how to respond ("I can see that you are angry because the other children are doing something that is not allowed, you could solve this by asking me for help"). In this way, the felt anger or frustration can be managed by recognizing the emotion and providing a solution which in this case is to ask for social support, thus also improving social language skills. When an adult provides subtitles for a situation, the child will likely be better able to understand the experienced emotion and how to cope with the emotion. Providing children with ASD with different roadmaps might eventually lead to internalizing these scenarios and generalizing them to a variety of situations. In early childhood, children with ASD are thus even more dependent on their parents and caretakers than typically developing children when it comes to managing emotions.

Concordance between emotion expression and emotional arousal in response to fear

In **chapter 4** the own experienced emotional arousal in response to a fearful situation is measured. Instead of focusing on how children cope with the experienced emotions in terms of regulation, this study focused on the related facial and bodily expressions in order to assess emotional concordance between experienced and expressed emotions.

Results revealed similar heart rate increases in children with ASD as compared to typically developing children in response to own experienced emotions. This indicates, in correspondence with the results presented in chapter 3, that children with ASD have adequate emotional arousal responses when their own emotions are triggered. The results of the structured behavioral observations revealed no differences between the intensity of fear expressions between the two groups. In other words, the facial and bodily expressions of fear in the ASD group were on average similar to typically developing children.

Next, looking at individual differences gave insight into the variance in both groups and the concordance between emotional experience and the expression. These results revealed that the experience and expression were significantly correlated within the typically developing group, but not within the ASD group. This lack of concordance indicates that children with ASD who were highly aroused, did not necessarily show increased intensity of expressions compared to low aroused children with ASD, and vice versa.

In the literature, there is an ongoing discussion whether concordance between different levels of emotion processing exists in typical development, because this is theoretically assumed, but empirical evidence is lacking. The results of the present study however, do provide evidence for correspondence between expression and emotional arousal in typically developing preschoolers. With regard to ASD, we conclude that the results suggest poor connectivity between the areas that are important for emotional arousal and emotional expression. This might fit with the idea that ASD symptoms arise as a consequence of disconnection between various functional brain systems, rather than impairments in one single area.

In daily life, the awareness that there can be a mismatch between the expression and the experience of emotions in children with ASD is important. If you want to interpret or evaluate how a child with ASD is feeling, it may be difficult to deduce this based on what you can observe on the "outside", i.e. in how the child behaves, in contrast to typically developing children. So, when interacting with children with ASD, it is important to first address whether the emotion that is expressed, corresponds to how they are feeling ("I can see that you are hesitant to go to the birthday party, are you afraid of going inside?"). Checking the emotion is the first step because a possible mismatch between what is felt and what is expressed, makes it difficult for the parents and caretakers in the social environment to provide what is needed: caregivers may not pick up on the actual experienced emotions, or may think that the child is very upset when experienced emotions may actually be much milder. Eventually, when the learned strategies become part of the behavioral repertoire, children with ASD might learn to give words to their emotions themselves ("I feel scared, can you go inside with me?").

Furthermore, this knowledge is important to parents and professionals with regard to psychoeducation. If parents better understand why their child responds differently, this might have a positive influence on their attitude towards the child. This might lead to less frustration, stress, and feelings of inadequacy. Eventually, parenting skills will be better adapted to the needs, possibilities and impossibilities of their child.

Social attention and emotional arousal from a developmental perspective

The study presented in **Chapter 5** addressed the developmental trajectory of emotional arousal and social attention during the preschool years in typically developing children and children with ASD. In the literature, there is a shortage of studies including longitudinal measurements of emotion processes in young children in general, and in children with ASD specifically. The role of cognitive development in areas of executive functioning and language, over a period of six months were explored in typically developing children.

Measures of the development of emotional arousal revealed stable heart rate responses over a period of six months in response to social-emotional stimuli in both typically developing children and children with ASD. In contrast to the stability in emotional arousal response, social attention improved in both typically developing children and children with ASD with a large effect size of 0.9 (Cohen's *d*). The results of the present study suggest that even though emotional arousal levels in response to social-emotional information remain similar over time, social attention can become more coordinated towards the relevant social-emotional cues. Studying the influence of language (both expressive and receptive) and executive functioning on the improvement of social attention in typically developing children revealed that a combination of inhibitory control and cognitive flexibility were the most important predictors of increased social attention. This suggests that the development of being able to socially attend to others is associated with higher order cognitive functioning.

We conclude that, in young children with ASD, fundamental mechanisms of social behavior that are affected, do develop, even during a relatively short period. This is important information with regard to interventions and treatment that can benefit from this possible window of opportunity. Within the clinical practice, the development of social attention could be monitored as treatment outcome but also as starting point for interventions because this provides insight into the extent to which children need support in understanding their social environment. In addition, in typical development, the improvement in social attention was related to maturational changes in higher order cognitive functioning as expressed in inhibition and cognitive flexibility. With regard to emotion regulation, chapter 3 revealed that executive functioning did not play a role in showing adaptive social behavior (yet). These mixed results with regard to the role of executive functioning during these early preschool years needs to be studied, also considering the prolonged development of executive functioning (Best and Miller 2010).

In social interactions, being able to inhibit a primary response and to be mentally flexible can be helpful tools. When confronted with the emotions of someone else and when attending to these emotions, it can be helpful to inhibit the primary response (which could be turning away or start laughing when someone falls and cries), and to be flexible in the available behavior repertoire (considering the options, by for example asking if someone needs help or even just making eye contact). Internalizing these skills and the generalization to other contexts is known to be a challenge in ASD, however, results can be maximized when intervening as early as possible (Dawson & Bernier, 2013; Dawson, Bernier, & Ring, 2012; Webb, Jones, Kelly, & Dawson, 2014).

Conclusions

The studies presented in this thesis aimed to gain insight into emotion processing in preschool children with ASD on the level of attention, arousal, regulation, and expression. From these studies four main conclusions can be drawn.

First, children with ASD show on average impaired visual social attention and a lack of emotionally resonating with the emotions of *others* (chapter 2). This impairment may have substantial impact on the fundaments of social learning. It may lead to a reduced quantity and quality of social responding, and thus less social interactions. Poor social initiative is already reported in children aged 6 to 12 months old who later develop ASD (Maestro et al., 2005). Being able to spontaneously orient and resonate in response to others is a crucial prerequisite for the development of joint attention, language, learning to socialize, and is an important target in early treatment and intervention for children with ASD (Bruinsma, Koegel, & Koegel, 2004; Koegel, Koegel, Shoshan, & McNerney, 1999).

Focusing on affective responding may help in better understanding social behavioral problems in young children with ASD, because emotions are crucial and fundamental driving forces of social interactions. Because this can be measured using sensitive and direct techniques, suitable for young children, these may also prove to be relevant outcome parameters in early intervention studies. With regard to the difficulties that children with ASD experience in attending to the emotions of others, it is important for the social environment to be aware of this challenge. Children with ASD can be supported by translating the emotions that are felt into words. For example, when a sad expression is accompanied by the explanation that you are feeling sad and why, children with ASD will be able to have attention for this emotion and will eventually make the connection between the emotion expression and the behavioral response. So, by targeting the awareness and identification of emotions as intervention goal, this might increase the attention towards the emotions of others.

Second, with regard to *own* experienced emotional situations (chapter 3 & 4), the emotional arousal of children with ASD increased to the same degree as typically developing children. However, our findings also suggest that children with ASD may have more problems in coping with the emotional arousal. They show more inadequate coping strategies such as venting behaviors and avoidance, which play a role in the observed behavior problems in ASD. Being able to adequately deal with your own emotions is important for adaptive social responding (Gross, 1999). The preschool phase presents a unique window of development and related opportunities, as strategies to cope with emotions are generally still pre-cognitive at this stage and negative scripts are not yet automated (Greenspan & Shanker, 2009). This allows and advocates for early intervention targeted at the earliest stages of behavioral control during emotionally arousing situations, in which stimulation of language development may play an important role in the prevention of avoidance strategies as suggested by our findings (Koegel, Koegel, Ashbaugh, & Bradshaw, 2014; Zwaigenbaum et al., 2015). Targeting dysregulation of emotions through treatment could be aimed at improving language skills, among other skills, such as executive functioning. For example, teaching children with ASD appropriate replacement communicative utterances in particular if a child exhibits excessive tantrums (Koegel et al., 2014).

Third, there is evidence for a seemingly discordance between expression of emotions and internal emotional arousal in preschool children with ASD. This might mean that interacting systems are less dependent on each other or at least represent abnormalities in the automatic connections between brain systems responsible for generating behavioral expression and brain systems responsible for experienced emotional arousal. The importance of concordance is illustrated by a study from Mauss and colleagues (2011) who found that discordance was associated with increased depressive symptoms, lower well-being, and over time undermined psychological functioning in young adults. This research also showed that discordance can confuse others about actual internal states and could lead to behavior being wrongly interpreted (Mauss et al., 2011). The ability to interpret children's expressive signals is therefore essential to successful social interactions (Sullivan & Lewis, 2003), as this allows others to adaptively respond to the needs of children. Better understanding emotional experiences in children with ASD is important, and awareness of discordance between expression and emotional arousal may be meaningful in psychoeducation and intervention strategies. Considering the increasingly young age at which interventions are implemented (Kim, Macari, Koller, & Chawarska, 2016), this could be achieved by raising awareness in the social environment of the children that emotional expressions in children with ASD do not necessarily reflect their internal experience. When children are (mentally) old enough, these interventions could include new techniques that enable children to practice expressive behaviors with techniques such as portable video modelling, which have yielded positive results, especially with regard to generalizability of the learned behaviors (Macpherson, Charlop, & Miltenberger, 2015).

Fourth, even though children with ASD show less attention towards emotions of others, which is considered core challenge in the development of ASD, this ability does develop even in a relatively short period of six months during the preschool years while measures of heart rate were stable. In typical development, this increased social attention was related to higher order cognitive processes, expressed in cognitive flexibility and inhibition, which show continued and rapid development during early childhood as a consequence of brain maturation and environmental influences. These executive functions in young children are an essential precursor for the development of social skills such as theory of mind (Hughes & Leekam, 2004; Perner & Lang, 2000), which is also affected in ASD. It enables children to resonate with other persons and to understand their thoughts, feelings, and emotions. The results of this study warrants the investigation of the role of executive functioning in the development of social attention in children with ASD as these might prove to be useful targets for intervention.

Implications

In scientific research over the last decades, the study of social behavior in ASD was largely dominated by cognitive theories such as the central coherence theory (Frith, 1989) and theory of mind (Baron-Cohen, Leslie, & Frith, 1985). More recently, the role of emotions in the development of social behavior has gained more attention aimed at for example cognitive and affective empathy. The focus of the current thesis was to gain more insight into the underlying processes of emotion, such as emotion perception, experience, and emotion regulation using sensitive and direct measures. In other words, the studies presented in the current thesis reveal the importance of not only taking into account how children with ASD cognitively process social information, but also how they process emotions of others, experience emotions themselves, how they regulate emotions, and express them to others. Implementing this multifaceted approach could benefit our understanding of the different pathways and underlying mechanisms of the heterogeneous phenotype of ASD. In addition, it might be easier to apply techniques such as eyetracking to the broad ASD population, not just to those participants who are old enough or mentally able to participate in methods like cognitive neuropsychological testing (Bölte et al., 2016).

In clinical practice, current diagnosis of ASD is mainly based on behavioral characteristics, parent reports, and observations by professionals. Considering the increased focus on early identification, the need to gain insight in underlying processes driving these behaviors is warranted, which also requires the previously mentioned sensitive and direct techniques that help in identifying why these behavioral difficulties and symptoms emerge. The implementation of these techniques for individual purposes in clinical practice is not yet applicable due to the absence of norms (how would norms be defined?), costs, and the expertise that is needed to conduct and interpret these kinds of methods. For example, the use of heart rate analyses as a means of identifying ASD symptoms however, is not suitable. For example, this thesis has shown that children with ASD experience difficulties in emotionally resonating with others (expressed in low heart rate levels), but this does not automatically mean that all children who show no modulation in heart rate in response to others are at risk for developing ASD. The use of eyetracking in identifying early social attention problems as possible early marker for ASD is however anticipated to fuel ASD screening, diagnosis, and eventually treatment (Bölte et al., 2016) for which this thesis provides support. With regard to treatment, there are studies providing evidence for neurobiological changes in response to two-year behavioral intervention in 18 to 30-month old children with ASD, which was associated with improvements in social behavior (Dawson, Jones, et al., 2012). Thus, heart-rate analyses as potential measure of treatment effects should be considered.

It is important to study whether the different levels of emotion can be positively influenced by treatment and how plastic these processes are. The results of the present thesis, provide some important insights that can be translated into treatment implications.

It is believed that the motivation to communicate and engage with others, responding to environmental social stimuli, and to learn new skills and behaviors is challenging for children with ASD (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012; Koegel, Ashbaugh, & Koegel, 2016). However, the results from chapter 3 and 4 show that emotional arousal response in children with ASD is intact when it comes to *own* experienced emotions. In other words, the own emotional motivation of children with ASD can be used to evoke motivation for interaction with *others*. A treatment program that is designed to enhance the motivation for social interaction is Pivotal Response Treatment (PRT©; Koegel et al., 2016). PRT was developed to specifically emphasize response-reinforce contingencies in order to improve social motivation, which has been shown to produce widespread and generalized gains in many other areas such as social responsiveness, language, academic, and social functioning, while simultaneously decreasing disruptive behaviors (Koegel, Koegel, & McNerney, 2001). The techniques that are used to achieve this are child choice (following what is interesting to the child), direct and natural reinforcements (the reward is the same as what the child desires), and incorporating task variation (on order to maintain attention). For example, when a child really likes to be tickled, the only way to achieve this, is to say the word 'tickle' to the parent, who reinforces this social initiative by tickling the child. This situation is further expanded by requesting for example eye contact and the use of multiple words. In sum, the results of the present thesis provide support for the use of motivation

based behavior therapies in provoking social interactions in children with ASD.
Another important practical implication is the discrepancy that was found between experienced emotions and how children with ASD express these emotions. Based on the findings presented in this thesis, emotional expressions in children with ASD might not always be correct representations of what they are feeling. Improving their language skills is an important target in this respect. When children are better able to give words to their emotions, this might help their social environment to meet their needs. In working with parents and caretakers of these children, in for example psychoeducation, the disconnection to what is felt and what is shown could provide as explanation for possible miscommunications. Related to this are the problems children with ASD experience with attending to the relevant information in their social environment. We know that this is difficult for many children with ASD, but this skill does develop over time, possibly related to skills such as inhibition and being mentally flexible. This means that stimulating these behaviors in clinical practice through executive function training might improve the ability to direct attention towards the information that is needed for successful interactions, however further research is needed. In general, the goal of treatment should be that children with ASD are not fully dependent on external structures and adjustments, but that they have a set of tools they can use for influencing and steering their own emotion processes that shape adaptive social behavior.

Directions for future research

Based on current findings, there are several directions that we recommend for future research. With regard to the measures of emotional arousal, the studies in the present thesis used heart rate as index of autonomic functioning. Fur future research it is recommended to include a larger repertoire of indices. Evidence suggests that different measures of emotion appear sensitive to different dimensional aspects of state, so including measures such as skin conductance and heart rate variability might be valuable to gain a more complete view of the complex functioning of the interacting sympathetic and parasympathetic nervous system (Benevides & Lane, 2015; Mauss & Robinson, 2009). Related to this is the use of new techniques in heart rate analyses such as wireless instruments that limit the possibilities for movement artefacts interfering with the data.
The behavioral observations of emotion regulation strategies and the design of the experiment did not allow us to gain insight into the effect of different regulation strategies on the emotional arousal levels directly. Since emotional arousal can be considered not only as the cause, but also as the consequence of emotion regulation, these mechanisms are interacting in a dynamic fashion, and are mutually co-dependent on each other. In order to learn more about this dynamic relationship, we recommend the use of temporal analyses. The behavioral measures (behavior observations) that were used in the current study are too coarse for this approach and are not suited to follow the quick pace of the emotional arousal

in such detail. Thus, we recommend to investigate the effect of different regulation and coping strategies on the levels of emotional arousal and how emotional arousal and coping strategies could influence ASD children's negative emotion expressions. This temporal design could also be implicated when studying social attention and emotional arousal. Even though the current results do not provide evidence for the hypothesis that children with ASD look away from social-emotional information because they get over-aroused, future research should investigate 'live' interactions between emotional arousal levels and social attention towards social-emotional stimuli. Furthermore, the role of cognitive development in areas of executive functioning and language in chapter 5 could only be explored in typically developing children. These results however, warrant the investigation of these mechanisms in relation to development of social attention in children with ASD. Finally, the findings presented in the current thesis were conducted in a sample of 15 to 29 children with ASD. For the results to be translated to clinical practice, replication in a larger sample is recommended.

Summary of the main findings

- Simultaneously combining measures of emotion processing on multiple levels, including the attention, experience, regulation, and expression, is necessary for a better understanding of the ASD phenotype. This allows for improved and tailored support for the development of children with ASD.
- Studying ASD during early development showed that social attention, even though impaired in preschoolers with ASD, does develop, even during a relatively short period of six months. This sensitive period might be related to emerging skills in mental flexibility and inhibitory control.
- Emotional behavior problems as observed in children with ASD, may arise as a consequence of atypical coping with emotions, rather than experience of these emotions, with regulation problems in part due to language impairments.
- Children with ASD experience emotional arousal when it comes to own experienced emotions. The intact *own* emotional motivation of children with ASD can be used to evoke motivation for interaction with *others*.
- It is important for parents and professionals working with children with ASD to be aware that the behavior that is observed on the outside does not always correspond to the emotion experience. Related to this is the notion that when children with ASD respond to others with less emotional expressiveness, this does not mean that they do not experience emotions. Consequently, children with ASD showing extreme emotional expression may have more mild emotion experiences, a discordance that fits with difficulties in coping with experienced emotions.

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Nederlandse samenvatting
(Summary in Dutch)

Nederlandse samenvatting

De omgeving waarin kinderen geboren worden en opgroeien is overwegend sociaal. Vanuit een evolutionair perspectief wordt aangenomen dat sociaal gedrag door de eeuwen heen is geëvolueerd omdat het nuttig is voor degenen die eraan deelnemen, wat betekent dat deze personen meer kans hebben om te overleven en zich te reproduceren (Brothers, 2002). In het huidige dagelijks leven is deel kunnen nemen aan de sociale omgeving een voorwaarde voor een succesvol persoonlijk en professioneel leven, zoals vriendschappen onderhouden en een carrière nastreven. Maar sociaal functioneren bepaalt ook de ervaring van kwaliteit van leven in het algemeen. Vroege sociale interacties zijn van groot belang voor de sociale ontwikkeling van jonge kinderen, van de eerste glimlach tot het reageren op de eigen naam. Gedurende de kindertijd verandert het sociale gedrag. Het is bijvoorbeeld belangrijk om vriendschappen te sluiten en te onderhouden, zelfverzekerd te zijn, je eigen identiteit te ontdekken, maar je ook soepel te kunnen bewegen in verschillende en aan verandering onderhevige contexten zoals op school, bij sociale activiteiten en thuis.

Het menselijk brein is gericht op het soepel laten verlopen van sociaal gedrag. De neuropsychologie van sociaal gedrag bestudeert de onderliggende neurale netwerken en aanverwante *cognitieve* en *emotionele* processen die mensen in staat stellen om gevoelens, gedachten, verlangens en intenties te begrijpen, te voorspellen en te delen (Van Rijn, Van ‘t Wout, & Spik, 2012). Er wordt aangenomen dat deze cognitieve en emotieprocessen twee specifieke, functioneel verschillende systemen zijn voor informatieverwerking in het brein, die nauw samenwerken om succesvol door een complexe, dynamische, sociale en voortdurend veranderende wereld te navigeren (Beauchamp & Anderson, 2010).

Cognitieve functies kunnen worden gedefinieerd als mentale processen die betrokken zijn bij sociale interacties en kunnen in drie fasen worden verdeeld; perceptie (aandacht), interpretatie en reactie (Van Rijn et al., 2012). Voorbeelden van sociaal cognitieve functies zijn gezichten en gezichtsuitdrukkingen kunnen herkennen, de gevoelens en behoeftes van anderen begrijpen en aan een gesprek deel kunnen nemen. Sociaal cognitieve functies kunnen worden onderscheiden van meer algemene cognitieve vaardigheden die ook bijdragen aan het vergemakkelijken van sociaal gedrag, zoals aandacht, gedragsinhibitie en werkgeheugen.

Emoties zijn een belangrijke voorwaarde voor de motivatie tot sociaal gedrag. Emotionele prikkels, zoals het delen van blijdschap of bijvoorbeeld het willen voorkomen van teleurstelling of verdriet bij jezelf of een ander, kunnen aanleiding zijn tot (succesvolle) sociale interacties. Sociale interacties zitten vol met emoties en emoties krijgen betekenis in sociale interacties. In sociale situaties die vaak onvoorspelbaar zijn en onvolledige informatie bevatten, kunnen emoties helpen flexibel te reageren of van nut zijn bij het nemen van beslissingen (Izard, 1971). Emoties hebben dus een motivatie functie en helpen ons op vele fronten; ze zorgen ervoor dat je alert bent in een angstige situatie, maar hebben ook een sterke communicatieve functie die nodig is voor de omgeving om snel in te kunnen schatten wat nodig is (Blair, 2003). Emoties kunnen echter ook belemmeren, wanneer de timing van een emotie onhandig is, de intensiteit niet passend is bij de situatie, of wanneer de emotie gericht is op irrelevante aspecten (Lazarus, 1991; Parrott, 2001). Emotie gerelateerde processen, in tegenstelling tot cognitieve processen, kunnen daarnaast gezien worden als een fysieke of lichamelijke reactie, die leidt tot adequaat adaptief gedrag. Gezien dit geschetste complexe karakter van sociaal functioneren, waarbij dus niet alleen sociaal cognitieve, maar ook aan emotie gerelateerde fysieke reacties betrokken zijn, is de sociale ontwikkeling kwetsbaar voor ontwikkelingsstoornissen en onderhevig aan een grote individuele variabiliteit. Enerzijds zijn er kinderen die makkelijk afstemmen op anderen, anderzijds zijn er kinderen die grote moeilijkheden ervaren met het navigeren door de sociale omgeving.

Het begrijpen van de emotieprocessen die adequaat sociaal gedrag en communicatie vormen is belangrijk, niet alleen binnen de normale ontwikkeling maar vooral ook bij kinderen die ontwikkelingsproblemen hebben met betrekking tot sociale communicatie en sociale interacties, zoals het geval is bij kinderen met Autismespectrumstoornissen (ASS; Box 1). ASS verwijzen naar een spectrum van pervasieve neurobiologische aandoeningen die zich voor het vierde levensjaar manifesteren. ASS worden gekenmerkt door verminderde of afwijkende sociale interacties en problemen met de communicatieve vaardigheden. Met een focus in de literatuur op de cognitieve processen die verband houden met sociaal gedrag zoals *theory of mind* en executief functioneren, blijven de emotionele of affectieve processen minder goed begrepen. De studies die in dit proefschrift worden beschreven, hebben als doel om beter inzicht te krijgen in de processen die onderliggend zijn aan emotieverwerking bij kinderen met ASS in de voorschoolse leeftijd. Dit is niet alleen gedaan door de integratie van gedragsmatige en cognitieve processen, maar juist ook de affectieve componenten van de verwerking van emoties te onderzoeken. De vraagstelling was hoe kinderen met ASS, in een kritieke ontwikkelingsperiode van de voorschoolse leeftijd, emoties waarnemen, ervaren, reguleren en zich uitdrukken in reactie op verschillende sociale en niet-sociale contexten. Sensitieve en directe maten van emotieverwerking werden hiervoor gebruikt, zowel wat je van 'buiten' kunt zien in termen van gedrag, maar ook de processen die zich van 'binnen' afspelen en die betrekking hebben op meer fundamentele informatieprocessen, zoals fysiologische mechanismen. De studies werden uitgevoerd bij kinderen met en zonder ASS in de voorschoolse leeftijd. Deze vroege ontwikkelingsbenadering is van cruciaal belang om beter inzicht te krijgen in sociale moeilijkheden bij jonge kinderen; wij willen beter begrijpen hoe zij emoties verwerken om specifieke momenten in de ontwikkeling te kunnen identificeren waarop deze vaardigheden mogelijk extra vatbaar zijn voor interventie.

Kort samengevat lieten de resultaten beschreven in dit proefschrift zien dat de meerderheid van kinderen met ASS problemen ervaren met het emotioneel afstemmen op de emoties van anderen. Dit uit zich in een afgevlakte emotionele arousal respons en verminderde aandacht voor de emotionele uitingen van anderen (**hoofdstuk 2**). Wanneer de ervaring van de *eigen* emoties onderzocht werd, bleek dat kinderen met ASS wel degelijk een emotionele arousal reactie lieten zien. Dit ging tevens samen met intacte gezichtsexpressies van de ervaren emotie bij kinderen met ASS (**hoofdstuk 3** en **4**). Echter, op gedragsniveau, maakten kinderen met ASS in mindere mate gebruik van constructieve emotieregulatie strategieën en meer maladaptieve strategieën dan normaal ontwikkelende kinderen. Dit bleek gerelateerd aan taalproblemen (**hoofdstuk 3**). **Hoofdstuk 4** leverde bewijs voor een mogelijke disconnectie tussen wat ervaren wordt aan de binnenkant, in termen van emotionele arousal, en wat je kunt zien aan de buitenkant, in termen van gedragsexpressie, bij kinderen met ASS. Vanuit een ontwikkelingsperspectief lieten de resultaten gepresenteerd in **hoofdstuk 5** stabiliteit van emotionele arousal zien, maar verbeteringen in sociale aandacht over een periode van zes maanden. Hieronder worden de resultaten van de vier hoofdstukken uitgebreider besproken, gevolgd door een algemene bespreking van de implicaties, aanwijzingen voor toekomstig onderzoek en een puntsgewijze samenvatting van de belangrijkste bevindingen.

Samenvatting

Sociale aandacht en emotionele arousal in reactie op de emoties van anderen

De studie in **hoofdstuk 2** beschrijft een onderzoek naar sociale aandacht en emotionele arousal van kinderen met en zonder ASS, in reactie op sociaal-emotionele videoclips uit een alledaagse situatie. Eyetracking analyses toonden aan dat kinderen met ASS minder keken naar relevante sociaal-emotionele informatie (het gezicht) in vergelijking met zich normaal ontwikkelende kinderen, hoewel ze over het geheel even lang naar het scherm keken. Dit deel van de resultaten draagt bij aan de groeiende hoeveelheid onderzoek waaruit blijkt dat mensen met ASS minder kijken naar relevante sociale signalen met een totale effect grootte van 0.55 over meer dan 38 studies (Chita-Tegmark, 2016). De huidige studie bevestigt deze eerdere bevindingen, in een zeer jonge steekproef van kinderen met ASS.

Naast sociale aandacht is de emotionele arousal gemeten terwijl de kinderen naar de emotionele clip keken. Uit de resultaten in de controlegroep bleek dat er aanvankelijk een vertraging in hartslag van baseline tot de sociaal-emotionele clip zichtbaar was, wat een indicatie is voor het richten van de aandacht in de richting van een stimulus (Van Hulle et al., 2013). Vervolgens vertoonde deze groep een verhoging in hartslag terwijl ze naar de sociaal-emotionele clip keken, wat impliceert dat zij op adequate wijze emotioneel afstemden met de emoties die te zien waren in de clip.

In tegenstelling tot de controlegroep, vertoonden kinderen met ASS geen modulatie in hartslag tijdens de clip. Met andere woorden, ze reageerden niet emotioneel op de emoties van anderen op het niveau van arousal. Ook in tegenstelling tot de controlegroep, vertoonden kinderen met ASS geen initiële vertraging in emotionele arousal. De afwezige vertraging van de hartfrequentie kan worden uitgelegd als een gevolg van een falend emotioneel arousal systeem, waardoor kinderen met ASS dus niet getriggerd worden om aandacht te hebben voor belangrijke sociaal-emotionele informatie die te vinden is in het gezicht van anderen. Echter, het gebrek aan emotionele arousal werd niet alleen gezien bij kinderen die voor kortere tijd, maar ook bij kinderen die voor langere tijd keken naar de sociaal-emotionele signalen. Kijken naar het belang van de onderliggende mechanismen om het gedragsfenotype van ASS te begrijpen, bleek uit de huidige studie dat meer ernstige ASS-symptomen in het algemeen en sociale problemen in het bijzonder, werden geassocieerd met minder adaptieve emotionele arousal en meer sociale aandachtsproblemen.

Samengenomen wijzen deze resultaten op een mogelijke fundamentele disconnectie tussen twee belangrijke systemen die samenwerken bij het emotioneel afstemmen en het hebben van aandacht voor de emoties van anderen, gerelateerd aan de ernst van de ASS-symptomen. Aandacht hebben voor de gezichtsexpressie van anderen in het dagelijks leven is van essentieel belang voor het begrip van de emoties van een ander om je eigen gedrag daar vervolgens op af te kunnen stemmen. Het is daarnaast ook van belang dat de emoties van anderen impact kunnen hebben op jouw eigen emotie-systeem. Bij het minder goed functioneren van een automatische visuele oriëntatie op de emoties van anderen, kan dit het moeilijker maken voor kinderen met ASS om adequaat te reageren op deze sociale en emotionele aanwijzingen, wat kan resulteren in problemen in de sociale communicatie.

Een belangrijke vraag is in hoeverre dergelijke tekortkomingen in het emotionele arousal systeem wel of niet kunnen worden verbeterd door middel van interventie. Is het mogelijk om het emotionele arousal-systeem te beïnvloeden, zodat kinderen met ASS zich wel oriënteren op de emotionele expressie van iemand anders en daarmee emotionele (of affectieve) empathie tonen? De huidige studie toonde aan dat korter of langer kijken naar de emoties van anderen geen verschillende relatie had met het arousal-systeem. Daarom wordt gesuggereerd dat interventies zich niet alleen moeten richten op sociale aandacht, maar juist ook op het begrip van iemand anders perspectief of mentale staat, ook wel aangeduid als cognitieve empathie. In het bijzonder voor kinderen in de voorschoolse leeftijd, die nog niet in staat zijn om hun emoties onder woorden te brengen (Lewis, Haviland-Jones, & Barrett, 2010), is het belangrijk dat volwassenen in de sociale omgeving zich beseffen dat sociale signalen niet automatisch opgepikt worden door kinderen met ASS. Door emoties voor deze kinderen onder woorden te brengen en ondertiteling te geven in sociale interacties, kunnen de problemen die kinderen met ASS ervaren in het emotioneel afstemmen met anderen gecompenseerd worden. Wanneer deze kinderen ouder zijn, kunnen deze strategieën geïnternaliseerd worden en zich generaliseren naar verschillende contexten.

Tenslotte helpen deze bevindingen in het begrijpen waarom kinderen met ASS niet altijd sociaal adaptief gedrag kunnen laten zien, verklaard door verminderde sociale aandacht en gebrek aan emotionele resonantie. Als ouders en professionals zich ervan bewust zijn dat sociaal inadequaat gedrag afkomstig is van een onvermogen in plaats van onwilligheid, kan dit leiden tot minder frustratie en miscommunicatie en uiteindelijk het algemene functioneren van de sociale omgeving verbeteren.

Emotieregulatie strategieën en emotionele arousal in reactie op frustratie

De studie beschreven in **Hoofdstuk 3** was gericht op de *eigen* ervaren emoties van jonge kinderen met en zonder ASS in aanvulling op hoofdstuk 2 waarin de eigen reactie op de emoties van *anderen* werd beschreven. Meer specifiek was deze studie gericht op de emotionele arousal in reactie op frustratie, en hoe kinderen omgaan met de ervaren emotionele arousal in termen van emotieregulatie strategieën.

De resultaten lieten zien dat het patroon van emotionele arousal in reactie op frustratie bij kinderen met ASS vergelijkbaar was met die van de controlegroep. Beide groepen lieten een verhoging in hartslag zien van baseline naar frustratie en een afname in hartslag gedurende de herstelperiode. Met andere woorden, wanneer het gaat om de eigen ervaren emoties, tonen kinderen met ASS een adequate modulatie in emotionele arousal in de context van frustratie, in vergelijking met normaal ontwikkelende kinderen. De gestructureerde gedragsobservaties daarentegen, lieten zien dat kinderen met ASS andere emotieregulatie strategieën inzetten dan de controlegroep. Kinderen met ASS leunden sterker op niet-helpende strategieën zoals vermijding en het ventileren van emoties en deze groep lieten minder constructieve (ofwel doelgerichte) strategieën zien. Deze gedragsobservaties repliceren een eerdere studie bij jonge kinderen met ASS (Jahromi, Meek, & Ober-Reynolds, 2012). De huidige studie voegt hieraan toe dat er geen emotionele arousal dysfunctie is wanneer het betrekking heeft op eigen ervaren emoties, maar dat het reguleren van de ervaren emotionele arousal moeilijker is voor kinderen met ASS, met minder adaptief gedrag tot gevolg.

Verdere analyses lieten zien dat het inzetten van minder constructieve strategieën om de emoties te reguleren, het best verklaard werd door problemen in de taalontwikkeling. Executief functioneren bleek niet gerelateerd aan een van de emotieregulatie strategieën. Dus, op deze voorschoolse leeftijd, lijken taalproblemen het gebruik van niet helpende emotieregulatie strategieën bij kinderen met ASS beter te verklaren. Echter, gezien de voortdurende ontwikkeling van executief functioneren (Best & Miller, 2010) kunnen we niet uitsluiten dat deze cognitieve functies wel steeds belangrijker worden om de ervaren emoties in de loop van de ontwikkeling van kinderen beter te beheersen.

We concluderen dat, met betrekking tot de ervaring van eigen emoties, kinderen met ASS emotionele arousal tonen, maar dat ze gebruik maken van minder efficiënte strategieën om deze emoties te reguleren, gedeeltelijk verklaard door beperkte taalvaardigheden. Wanneer de conclusies worden vertaald naar het dagelijks leven van kinderen met ASS, lijkt het dus van belang dat deze kinderen hulp nodig hebben bij het ontrafelen van emotioneel beladen situaties en dat zij hulpmiddelen nodig hebben bij het hanteren van deze situaties. Ouders, verzorgers en professionals kunnen kinderen met ASS helpen door woorden te geven aan een situatie, de emotie te identificeren of bijvoorbeeld cognitieve en verbale oplossingen aan te reiken om de situatie aan te pakken. Bijvoorbeeld, een ouder kan de situatie benoemen en suggesties geven voor hoe te reageren ('Ik kan aan je zien dat je boos bent omdat de andere kinderen iets doen wat niet mag, je kunt dit oplossen door mij te roepen en hulp te vragen'). Op deze manier kan de ervaren woede of frustratie worden gereguleerd door het erkennen van de emotie en het verstrekken van een oplossing, in dit geval het vragen om sociale steun en daarmee ook het verbeteren van de taalvaardigheid. Het verschaffen van verschillende 'routekaarten' voor sociale of emotionele situaties kan uiteindelijk leiden tot het internaliseren van deze scenario's en het generaliseren ervan in een verscheidenheid aan situaties. In de vroege kindertijd zijn kinderen met ASS dus nog meer afhankelijk van hun ouders en verzorgers als het gaat om het reguleren van emoties, dan kinderen zonder ASS. Het is dan ook een taak van professionals in de klinische praktijk dat ouders en verzorgers hiervan bewust worden gemaakt.

Concordantie tussen emotie expressie en emotionele arousal in reactie op angst

In **hoofdstuk 4** werd de eigen ervaren emotionele arousal in reactie op een angstige situatie onderzocht. In aanvulling op het vorige onderzoek dat gericht was op de regulatie van emoties, richtte deze studie zich op hoe kinderen met en zonder ASS de ervaren emoties uitten in termen van gezichts- en lichaamsuitdrukkingen. Oftewel, de emotionele expressie die zichtbaar is in het gezicht en het lichaam. Het doel was, om de samenhang tussen deze expressie en de 'intern' ervaren emotionele arousal te begrijpen, ook wel de concordantie genoemd.

Resultaten onthulde vergelijkbare toenames in hartslag bij kinderen met ASS in vergelijking met de controlegroep in reactie op eigen ervaren emoties. Dit geeft aan, in overeenstemming met de resultaten beschreven in hoofdstuk 3, dat kinderen met ASS emotionele arousal lieten zien wanneer hun eigen emotionele ervaringen werden geactiveerd. De resultaten van de gestructureerde gedragsobservaties lieten geen verschillen zien tussen de intensiteit van angstuitdrukkingen tussen de twee groepen. Met andere woorden, de gezichts- en lichaamsuitdrukkingen van angst in de ASS-groep waren vergelijkbaar met de controlegroep. Het kijken naar individuele verschillen gaf inzicht in de variantie in beide groepen en de concordantie tussen emotionele ervaring en de expressie van de ervaren emotie. Uit deze resultaten bleek dat de arousal overeenstemde met de expressie binnen de controlegroep, maar niet binnen de ASS-groep. Dit ogenschijnlijke gebrek aan concordantie wijst erop dat kinderen met ASS die sterke arousal ervoeren, niet noodzakelijkerwijs een verhoogde intensiteit van expressies vertoonden in vergelijking met kinderen die lage arousal ervoeren, en vice versa.

In de literatuur over concordantie is een discussie gaande over het bestaan van concordantie binnen verschillende lagen van emotie processen in de normale populatie, omdat dit weliswaar theoretisch wordt verondersteld, maar empirisch bewijs veelal nog ontbreekt. De resultaten van de huidige studie verschaffen bewijs voor het bestaan van concordantie tussen expressie en emotionele arousal bij normaal ontwikkelende kinderen in de voorschoolse leeftijd. Met betrekking tot de kinderen met ASS, impliceren de resultaten een zwakke connectiviteit tussen verschillende hersengebieden die belangrijk zijn voor emotionele arousal en de bijbehorende expressie. Dit zou kunnen passen bij de hypothese dat ASS-symptomen ontstaan als gevolg van een disconnectie tussen verschillende functionele systemen, in plaats van gebreken in een enkel functiedomein in het brein.

In het dagelijks leven is het bewustzijn dat er een mogelijke mismatch is tussen de expressie en de ervaring van emoties bij kinderen met ASS van belang. Wanneer je een inschatting wilt maken van hoe een kind met ASS zich voelt (dat wil zeggen, hoe het zich gedraagt), kan het moeilijker zijn om dit af te leiden op basis van wat je kunt zien aan de buitenkant dan bij kinderen zonder ASS. In de interactie met kinderen met ASS kan het dus van belang zijn om eerst te bespreken of de emotie die ogenschijnlijk uitgedrukt wordt, overeenkomt met de emotie die ervaren wordt ('Ik zie dat je twijfelt of je naar het verjaardagsfeestje wilt gaan, ben je bang om naar binnen te gaan?'). Het checken van de emotie is van groot belang, omdat een mogelijke mismatch tussen wat er wordt gevoeld en wat er wordt uitgedrukt door het kind, het de ouders en verzorgers moeilijk kan maken om te voorzien in wat nodig is: de sociale omgeving kan bijvoorbeeld denken dat een kind heel angstig is, terwijl de ervaren emotie in werkelijkheid veel milder blijkt te zijn. Uiteindelijk, als de geleerde strategieën deel gaan uitmaken van het gedragsrepertoire, kunnen kinderen met ASS zelf leren om woorden te geven aan hun emoties ("Ik voel me bang, wil jij eerst naar binnen gaan?").

Bij de behandeling van sociale problemen van kinderen is deze kennis van groot belang voor ouders en professionals met betrekking tot psycho-educatie. Als ouders beter begrijpen waarom hun kind anders of onverwacht reageert, kan dit een positieve invloed hebben op de houding ten opzichte van het kind. Dit kan leiden tot minder frustratie, stress en gevoelens van ontoereikendheid. Uiteindelijk zullen ouderlijke vaardigheden beter aangepast worden aan de behoeften, mogelijkheden en moeilijkheden van hun kind.

Sociale aandacht en emotionele arousal vanuit een ontwikkelingsperspectief

De studie gepresenteerd in **hoofdstuk 5** heeft als doel de ontwikkeling van emotionele arousal en sociale aandacht bij kinderen met en zonder ASS in de voorschoolse leeftijd in kaart te brengen. In de huidige literatuur bestaat een gebrek aan longitudinale studies die zich richten op de processen van emoties bij jonge kinderen in het algemeen, en kinderen met ASS in het bijzonder. De rol van de cognitieve ontwikkeling op het gebied van executieve functies en taal, over een periode van zes maanden werden onderzocht in normaal ontwikkelende kinderen.

Maten van emotionele arousal lieten stabiele hartslagreacties zien over een periode van zes maanden in reactie op de sociaal-emotionele videoclip die eveneens wordt beschreven in hoofdstuk 2, voor zowel kinderen met als zonder ASS. In tegenstelling tot deze stabiliteit in emotionele arousal, laat de ontwikkeling van sociale aandacht een verbetering zien over dezelfde periode van zes maanden, met een effect grootte van 0.9 (Cohen's *d*) binnen de ASS-groep. Deze resultaten suggereren dat hoewel de emotionele arousal in reactie op sociaal-emotionele informatie hetzelfde blijft, de sociale aandacht in dezelfde periode verbetert in de richting van de relevantie sociaal-emotionele signalen. Kijkend naar de invloed van taal (zowel expressief als receptief) en executief functioneren op de verbetering in sociale aandacht in de controlegroep, liet de resultaten zien dat een combinatie van inhibitie en cognitieve flexibiliteit de voornaamste voorspellers waren van een toename in sociale aandacht. Dit resultaat suggereert dat de ontwikkeling van de vaardigheid om sociale aandacht te hebben voor anderen wordt geassocieerd met hogere orde cognitieve functies.

We concluderen dat, fundamentele mechanismen van sociaal gedrag die zijn aangedaan bij kinderen met ASS, zich weldegelijk kunnen ontwikkelen, zelfs gedurende een relatief korte periode in de voorschoolse leeftijd. Dit is belangrijke informatie met betrekking tot interventies en behandelingen waarbij geprofiteerd kan worden van deze mogelijke periode van ontwikkeling.

In de klinische praktijk, kan de ontwikkeling van sociale aandacht bijvoorbeeld gemonitord worden als uitkomstmaat van behandeling. Sociale aandacht kan ook dienen als startpunt voor interventies omdat dit inzicht geeft in de mate van zorg die nodig is voor het kunnen begrijpen van de sociale omgeving. Bovendien werden in de controlegroep aanwijzingen gevonden dat de verbetering van de sociale aandacht gerelateerd was aan rijping van de hoger orde cognitieve functies zoals inhibitie en cognitieve flexibiliteit. Met betrekking tot de regulatie van emoties, liet hoofdstuk 3 zien dat executieve functies (nog) geen rol spelen in het tonen van adaptief sociaal gedrag. Deze tegengestelde resultaten met betrekking tot de rol van het executief functioneren tijdens deze vroege voorschoolse jaar moeten verder worden onderzocht, ook gezien de langdurige ontwikkeling van executieve functies gedurende de kinderjaren die doorgaat tot in de adolescentie en jong volwassenheid (Best & Miller, 2010).

Vaardigheden zoals je gedrag kunnen inhiberen of je gedrag flexibel kunnen aanpassen aan situaties zijn van belang in sociale interacties. Bij behandeling kan alternatief worden aangereikt voor onaangepast sociaal gedrag zoals werfkijken of zelfs gaan lachen als iemand zich pijn doet en huilt. Als je ziet dat iemand hulp nodig heeft, kan je sociaal adaptief reageren door te vragen hoe het gaat of alleen maar oogcontact te maken. Het is bekend dat het internaliseren van zulke vaardigheden en de generalisatie ervan naar andere contexten een uitdaging is voor kinderen met ASS. Voor optimale verbeteringen is het daarom ook van groot belang dat interventies op een vroege leeftijd ingezet kunnen worden (Dawson & Bernier, 2013; Dawson, Bernier, & Ring, 2012; Webb, Jones, Kelly, & Dawson, 2014).

Implicaties

In het wetenschappelijk onderzoek van de laatste decennia, werd de studie van sociaal gedrag in ASS grotendeels gedomineerd door cognitieve theorieën, zoals de centrale coherentie theorie (Frith, 1989) en *theory of mind* (Baron-Cohen, Leslie, & Frith, 1985). Meer recentelijk hebben de rol van emoties in de ontwikkeling van sociaal gedrag meer aandacht gekregen, bijvoorbeeld verklaringen van sociaal gedrag gericht op cognitieve en affectieve empathie. De focus van het huidige proefschrift was om meer inzicht te krijgen in de onderliggende processen van emotie, zoals emotie perceptie, de beleving van emotie en de regulatie, met behulp van sensitieve en directe maten, in aanvulling op het cognitief verwerken van sociale informatie. Deze veelzijdige aanpak is gekozen om meer inzicht te verkrijgen in de verschillende wegen en onderliggende mechanismen van het heterogene fenotype van ASS. Bovendien is het inzetten van technieken zoals eyetracking en fysiologie vernieuwend en heeft als voordeel dat de te onderzoeken populatie breder is doordat deze technieken niet alleen geschikt zijn voor kinderen die oud genoeg zijn of mentaal in staat zijn om deel te nemen aan methoden zoals cognitieve neuropsychologische tests (Bölte et al., 2016).

In de klinische praktijk wordt de huidige diagnose van ASS voornamelijk gebaseerd op gedragskenmerken middels ouder-rapportage over het gedrag van hun kind en gedragsobservaties door professionals. Gezien de toegenomen aandacht voor vroege signalering, wordt de noodzaak om inzicht te krijgen in de onderliggende processen van emoties steeds duidelijker, waarvoor ook de eerdergenoemde sensitieve en directe technieken die helpen bij het identificeren van deze processen van belang zijn. De implementatie van deze technieken voor individuele doeleinden in de klinische praktijk is echter nog niet van toepassing wegens het ontbreken van normen (hoe zouden deze normen kunnen worden gedefinieerd?), de bijkomende kosten en de expertise die nodig is bij het uitvoeren en interpreteren van deze maten. Het gebruik van hartslaganalyses als een middel om vroege ASS-symptomen te identificeren zou bijvoorbeeld ongeschikt zijn. Dit proefschrift heeft aangetoond dat kinderen met ASS, problemen hebben met emotioneel resoneren met anderen (uitgedrukt in lage hartslagniveaus), maar dit betekent niet dat alle kinderen die een verminderde modulatie in hartslag tonen in reactie op anderen risico lopen op het ontwikkelen van autisme symptomen. Daarentegen kan het gebruik van eyetracking bij het identificeren van sociale aandachtsproblemen als vroege indicator voor ASS naar verwachting de screening en diagnose van ASS wel kunnen verbeteren (Bölte et al., 2016) als objectieve maat voor sociale aandacht. De resultaten van dit proefschrift ondersteunen deze gedachte.

Met betrekking tot de behandeling van ASS, zijn er studies die bewijs leveren voor neurobiologische veranderingen in reactie op twee jaar durende gedragsinterventie in 18 tot 30 maanden oude kinderen, wat werd geassocieerd met verbeteringen in sociaal gedrag (Dawson, Jones, et al., 2012). Dus, hartslag analyses als mogelijke maat van effectiviteit van de behandeling lijkt in de toekomst wel overwogen te moeten worden. Het is belangrijk om verder te bestuderen of de verschillende niveaus van emotie processen positief beïnvloed kunnen worden door behandeling, hoe plastisch deze processen zijn en wat een verbetering in hartslagmodulatie in de praktijk betekent.

De motivatie om te communiceren, het interacteren met anderen, het reageren op sociale informatie en het aanleren van nieuwe vaardigheden is een complexe uitdaging voor kinderen met ASS (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012; Koegel, Ashbaugh, & Koegel, 2016). De resultaten van hoofdstuk 3 en 4 tonen echter aan dat emotionele arousal respons bij kinderen met ASS intact is als het gaat om de *eigen* ervaren emoties. Met andere woorden, de eigen emotionele motivatie van kinderen met ASS kan worden gebruikt als ingang om de motivatie voor de interactie met *anderen* te stimuleren en te verbeteren. Een behandeling die ontworpen is met als doel om de motivatie voor sociale interactie te verbeteren is Pivotal Response Treatment (PRT©; Koegel et al., 2016). PRT is specifiek ontwikkeld om de sociale motivatie te vergroten, waarvan is aangetoond dat dit positieve gevolgen heeft op vele andere gebieden in de ontwikkeling zoals sociale responsiviteit, taal, academisch en sociaal functioneren en tegelijkertijd ongewenst gedrag vermindert (Koegel, Koegel, & McNerney, 2001). De technieken die worden gebruikt om dit te bereiken zijn bijvoorbeeld de keuze bij het kind laten (de interesse van het kind volgen), directe en natuurlijke bekrachtigers (de beloning is gelijk aan wat de interesse van het kind had) en taakvariatie (met als doel de aandacht vast te houden). Bijvoorbeeld, wanneer een kind veel plezier heeft aan bellen blazen, is het zeggen van het woord 'bellen' de manier om dit voor elkaar te krijgen. Wanneer het kind een poging doet tot het zeggen van het woord, wordt dit direct bekrachtigt door het blazen van de bellen. Deze situatie wordt vervolgens verder uitgebreid door het verzoeken van bijvoorbeeld oogcontact en het gebruik van meerdere woorden ('Wil je bellenblazen?'). De resultaten van dit proefschrift ondersteunen het gebruik van motivatie gerichte gedragstherapieën voor het uitlokken van sociaal gedrag bij kinderen met ASS.

Een andere belangrijke praktische implicatie is het verschil dat werd gevonden tussen de ervaren emoties en hoe kinderen met ASS deze emoties uitdrukken. Op basis van de in dit proefschrift beschreven bevindingen, kan het zo zijn dat de emotionele expressies van kinderen met ASS niet altijd juiste representaties zijn van wat zij daadwerkelijk voelen, meer nog dan bij normaal ontwikkelende kinderen. Het verbeteren van de taalvaardigheden is een belangrijke doelstelling in dit opzicht. Als kinderen beter in staat zijn om woorden te geven aan hun emoties, kan dit de sociale omgeving helpen om beter in hun behoeftes te voorzien. Voor ouders en professionals is het belangrijk om op de hoogte te zijn van deze mogelijke mismatch tussen de expressie en de beleving in het kader van bijvoorbeeld psycho-educatie, waarbij het bestaan van een talige ontwikkeling een voorwaarde is.

De problemen die kinderen met ASS ervaren met de aandacht voor sociaal-emotioneel relevantie informatie zijn hieraan verbonden. We weten dat dit moeilijk is voor veel kinderen met ASS, maar deze vaardigheid lijkt zich wel te ontwikkelen in de tijd, mogelijk gerelateerd aan vaardigheden zoals inhibitie van gedrag en mentale flexibiliteit. Dit betekent dat het stimuleren van deze executieve vaardigheden in de klinische praktijk door middel van training, het kunnen richten van je aandacht op de sociaal relevantie informatie die zo cruciaal zijn in sociale interacties kan verbeteren. Verder onderzoek op dit gebied is nodig om hier meer over te kunnen zeggen, gezien het feit dat dit alleen onderzocht kon worden in de controlegroep.

In het algemeen zou het doel van de behandeling moeten zijn dat kinderen met ASS niet meer volledig afhankelijk zijn van extern opgelegde structuren en aanpassingen, maar dat zij een set van tools tot hun beschikking hebben die ze kunnen gebruiken voor het beïnvloeden en sturen hun eigen emotie processen die adaptief sociaal gedrag vormgeven.

Aanwijzingen voor toekomstig onderzoek

Op basis van de huidige bevindingen, zijn er verschillende aanwijzingen voor toekomstig onderzoek.

Met betrekking tot de maat van emotionele arousal, is voor de studies beschreven in dit proefschrift gebruik gemaakt van hartslag als afgeleide van het autonome zenuwstelsel. Voor toekomstig onderzoek wordt aanbevolen om een groter repertoire van fysiologische maten in te zetten. Er zijn aanwijzingen dat de verschillende maten van psychofysiologisch functioneren gevoelig zijn voor verschillende dimensionale aspecten emoties, dus het includeren van maten zoals huidgeleiding en hartslagvariabiliteit kunnen waardevol zijn om een meer compleet beeld te krijgen van de complexe interactie tussen het sympathische en parasympatische zenuwstelsel (Benevides & Lane, 2015; Mauss & Robinson, 2009). Hiermee in verband staat het gebruik van nieuwste technieken zoals draadloze instrumenten die de hartslag meten en daarmee mogelijke invloed van bewegingsartefacten beperken.

De gedragsobservaties van de emotieregulatie strategieën en het ontwerp van het experiment lieten het niet toe om het directe effect van specifieke strategieën op de emotionele arousal te onderzoeken. Aangezien emotionele arousal kan worden beschouwd als zowel de oorzaak als het gevolg van emotieregulatie, interacteren deze mechanismen onderling en zijn ze dus ook afhankelijk van elkaar. Om meer te leren over de dynamische relatie, zou toekomstig onderzoek gebruik kunnen maken van analyses waarin deze relatie parallel aan elkaar wordt onderzocht zodat de directe invloed van reguleren op de emotionele arousal (en vice versa) beter begrepen kan worden. De maten van gedragsobservaties die werden gebruikt in de huidige studies zijn te grof voor deze aanpak en zijn niet geschikt om het tempo van de emotionele arousal in detail te volgen. Deze suggestie is eveneens van toepassing op het bestuderen van de sociale aandacht en de daaraan gerelateerde emotionele arousal. Hoewel de huidige resultaten geen bewijs leveren voor de hypothese dat kinderen met ASS door over-arousal wegkijken van de sociaal-emotionele informatie, is het van belang dat toekomstig onderzoek de *live* interactie tussen emotionele arousal en de sociale aandacht in meer detail bekijkt. Een ander aspect is het feit dat de rol van cognitieve ontwikkeling op het gebied van executieve functies en taal in hoofdstuk 5 slechts kon worden onderzocht in de controlegroep. Deze resultaten geven echter aanleiding voor verder onderzoek naar de ontwikkeling van sociale aandacht in relatie tot executief functioneren en taalvaardigheden bij kinderen met ASS. Ten slotte betreft de populatie beschreven in dit proefschrift een groep van 15 tot 29 kinderen met ASS. Om de resultaten te kunnen vertalen naar de klinische praktijk, is replicatie in een grotere onderzoeksgroep van belang.

Samenvatting van de belangrijkste bevindingen

- Het onderzoeken van emotieprocessen op meerdere niveaus door het combineren van verschillende onderzoeksinstrumenten is nodig voor een beter begrip van het ASS-fenotype op het niveau van aandacht, beleving, regulatie en expressie van emoties.
- Onderzoek naar de ontwikkeling van sociale aandacht tijdens op jonge leeftijd heeft aangetoond dat, ook al is de sociale aandacht verminderd, er weldegelijk sprake is van ontwikkeling, zelfs over een relatief korte periode. Deze sensitieve periode is mogelijk gerelateerd aan op dat moment in ontwikkeling zijnde vaardigheden zoals inhibitie en mentale flexibiliteit.
- Emotionele gedragsproblemen zoals waargenomen bij kinderen met ASS, zijn mogelijk het gevolg van problemen in de regulatie van deze emoties, in plaats van de beleving van deze emoties, wat voor een deel te wijten is aan problemen in de taalontwikkeling.
- Kinderen met ASS ervaren emotionele arousal als het gaat om eigen ervaren emoties. De intacte *eigen* emotionele motivatie van kinderen met ASS kan gebruikt worden als ingang om de motivatie voor interactie met *anderen* uit te lokken.
- Het is belangrijk voor ouders en professionals die werken met kinderen met ASS zich ervan bewust te zijn dat het gedrag dat wordt waargenomen aan de buitenkant niet altijd overeenkomt met de emotie zoals deze beleefd wordt. Hieraan gerelateerd is de bevinding dat wanneer kinderen met ASS op anderen reageren met een verminderde emotionele expressiviteit, dit niet direct betekent dat ze geen emoties te ervaren. Andersom, is het dus zo dat kinderen met ASS die emoties in meerdere maten laten zien, de emotie misschien niet als zodanig intens beleven. Deze mogelijke discrepantie past bij het beeld dat kinderen met ASS, moeite hebben met het omgaan met de ervaren emoties.

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List of publications

Zantinge, G., van Rijn, S., Stockmann, L., & Swaab, H. (2017). Psychophysiological responses to emotions of others in young children with Autism Spectrum Disorders: Correlates of social functioning. Autism Research.

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Abstracts

Zantinge, G., van Rijn, S., Stockmann, L., & Swaab, H. (September 17-19, 2015). Social attention and affective arousal in response to emotion evoking video clips in young children with autism spectrum disorders. Flux conference, Leiden, Netherlands.

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Curriculum Vitae

Gemma Zantinge werd geboren op 10 september 1986 te Alphen aan den Rijn. Na het behalen van haar havodiploma aan het Ashram college in 2002, heeft zij in 2007 de opleiding tot Leraar Basisonderwijs aan de Hogeschool Leiden afgerond. In 2008 begon zijn aan de bachelor Pedagogische Wetenschappen aan de Universiteit Leiden waarna zij aansluitend de tweejarige Research Master 'Developmental Psychopathology in Education and Child Studies' (track: Clinical Practice and Research) afrondde bij de afdeling Orthopedagogiek in 2011. Gedurende de Research Master heeft Gemma een klinische stage doorlopen op het Ambulatorium, verbonden aan de Universiteit Leiden, waar zij haar Basisaantekening Diagnostiek behaalde. Na het afronden van deze stage is Gemma als basis orthopedagoog werkzaam geweest binnen de patiëntenzorg van het Ambulatorium, totdat zij in 2012 begon aan haar promotieonderzoek aan de Universiteit Leiden, onder begeleiding van prof. dr. Hanna Swaab en dr. Sophie van Rijn. Het centrale thema van dit onderzoek was om meer inzicht te krijgen in de processen die betrokken zijn bij het verwerken van emoties in kinderen met autismespectrumstoornissen in de voorschoolse leeftijd. De resultaten van dit onderzoek staan beschreven in dit proefschrift. Naast haar aanstelling als promovendus werkte zij gedurende dit gehele traject als docent binnen het masteronderwijs aan de afdeling Orthopedagogiek en verzorgde zij klinisch onderwijs. Daarnaast was zij actief als lid van de personeelsgeleding van de Faculteitsraad. Na de afronding van haar proefschrift heeft Gemma bij de Nederlandse Organisatie voor Wetenschappelijk Onderzoek gewerkt. Per januari 2018 zal zij terugkeren bij de programmagroep Neuropedagogiek en Ontwikkelingsstoornissen van de Universiteit Leiden als Universitair Docent.