Emotion processing in preschoolers with autism spectrum disorders

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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

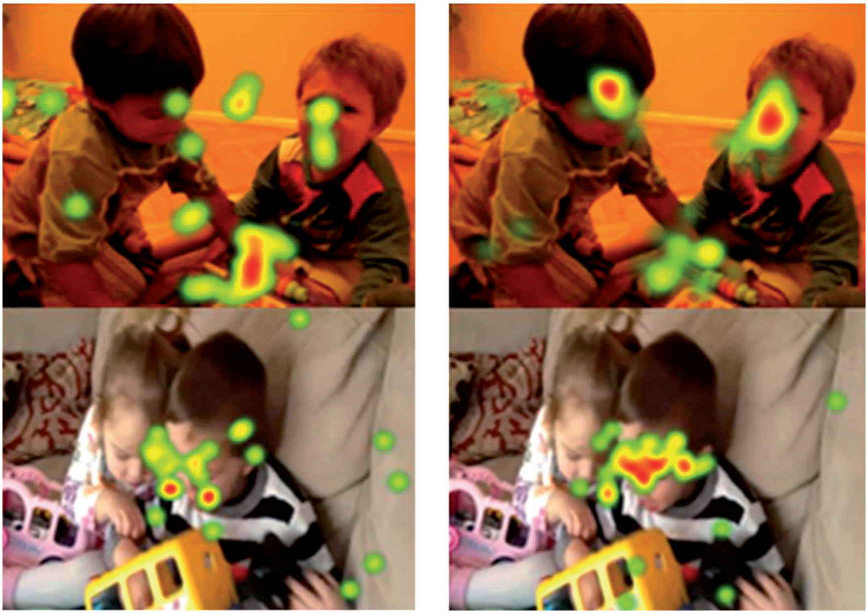

Figure 1. Heat maps of the ASD group (A) versus the control group (B) reflecting total fixation duration in a scene, illustrating group differences in visual fixation patterns.

($F(6,396) = 3.70$, $p < .01$, $\eta_p^2 = .05$) and a significant time by group interaction ($F(6,396) = 4.36$, $p < .01$, $\eta_p^2 = .06$). There was no significant main effect of group ($p = .20$). When controlling for IQ, the interaction effect remained significant ($F(6,390) = 2.34$, $p = .03$, $\eta_p^2 = .04$) 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 ($F(6,378) = 3.31$, $p < .01$, $\eta_p^2 = .05$). 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 ($F(6,372) = 2.23$, $p = .04$, $\eta_p^2 = .04$) 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.

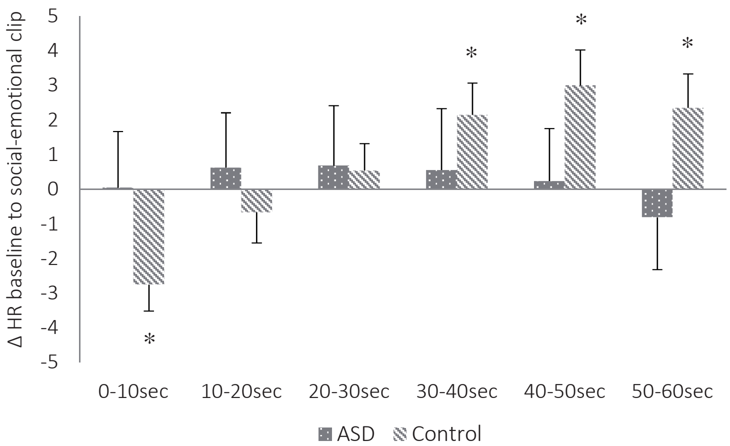

Figure 2. Difference in heart rate from baseline to the social emotional clip in the ASD group and the control group. Error bars displaying *SE*. *significant at $p< .05$.

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 (β= -.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 (β= -.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 (β= -.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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