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Sensory hypersensitivity predicts enhanced attention capture by faces in the early development of ASD

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ABSTRACT

Sensory sensitivity is prevalent among young children with ASD, but its relation to social communication impairment is unclear. Recently, increased sensory *hyper*sensitivity has been linked to greater activity of the neural salience network (Green et al., 2016). Increased neural sensitivity to stimuli, especially social stimuli, could provide greater opportunity for social learning and improved outcomes. Consistent with this framework, in Experiment 1 we found that parent report of greater sensory hypersensitivity at 2 years in toddlers with ASD (N = 27) was predictive of increased neural responsiveness to social stimuli (larger amplitude event-related potential/ERP responses to faces at P1, P400 and Nc) at 4 years, and this in turn was related to parent report of increased social approach at 4 years. In Experiment 2, parent report of increased perceptual sensitivity at 6 months in infants at low and high familial risk for ASD (N = 35) predicted larger ERP P1 amplitude to faces at 18 months. Increased sensory hypersensitivity in early development thus predicted greater attention capture by faces in later development, and this related to more optimal social behavioral development. Sensory hypersensitivity may index a child's ability to benefit from supportive environments during development. Early sensory symptoms may not always be developmentally problematic for individuals with ASD.

1. Introduction

Autism spectrum disorder (ASD) is characterized by the presence of persistent difficulties in social communication across multiple contexts, and restricted and repetitive patterns of behavior, interests or activities. Although common, the fact that sensory sensitivity symptoms are not always present suggests that they are not necessary causal of ASD (Morton and Frith, 1995). Studying the relationship between individual differences in sensory processing and social communication impairment within groups of children with ASD can inform theoretical models regarding how these domains interrelate. Further, the domains must be studied over developmental time in order to develop causal models of symptom emergence that can then be tested in intervention designs (Karmiloff-Smith, 1998).

The new edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) has incorporated 'hyper- or hypo-reactivity to sensory input or unusual interests in sensory aspects of the environment' as possible ASD symptoms in the category of restricted and repetitive behaviors. Cross-sectional factor analyses confirm that sensory symptoms are most closely associated with this broad category of symptoms (Mandy et al., 2012). Sensory symptoms can be divided into three separable constructs that can be broadly described as hypersensitivity, hyposensitivity, and sensation seeking (Boyd et al., 2010). These symptoms are distinct but may co-occur in individual children, and are often experienced across sensory modalities (Baranek et al., 2006; Liss et al., 2006; Watson et al., 2011). However, their relation to the core socio-communicative symptoms of ASD remains a topic of significant interest. Notably, sensory sensitivities are experienced for both social and nonsocial stimuli in children with ASD at roughly similar levels (Baranek et al., 2006). In older children, significant relations between higher levels of sensory symptoms and poorer socio-communicative functioning have been observed in a number of reports (Hilton et al., 2007; Ausderau et al., 2014). However, other studies suggest that relations may differ between hyposensitivity and sensation-seeking, and

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hypersensitivity. For example, Liss and colleagues found that the presence of hyposensitivity and sensory seeking was associated with more severe social and communication symptoms in both children and adults, whilst more hyper-responsiveness was only weakly related to fewer adaptive social behaviors and more social symptoms; there were no relations with communication symptoms (Liss et al., 2006). In a group of 4.5-year-old children, Watson and colleagues (Watson et al., 2011) also found that hyposensitivity and sensation seeking were related to greater severity of ASD and poorer language and social functioning. However, there was a non-significant trend towards a *negative* relation between greater hyper-responsiveness and fewer social-communicative symptoms. Consistent with this negative relation, in 149 toddlers aged around 2.5 years Green and colleagues (Green et al., 2011) found that lower levels of autism symptoms as measured by the ADOS were associated with *greater* sensory hypersensitivity on a parent-report measure. Thus, hypersensitivity may sometimes be associated with *better* social communicative functioning, particularly in early development. Since it is commonly assumed that sensory sensitivities are problematic for children with ASD, understanding this association is critical.

Sensory sensitivity symptoms are present from the earliest stages of development in ASD, consistent with the possibility that they could affect early social development by altering the child's sensory experience of a wide range of stimuli, including social stimuli. For example, at 6-months of age, infants later diagnosed with ASD show higher levels of perceptual sensitivity (Clifford et al., 2013) and parent concerns about sensory behavior at 6 months predicts later ASD diagnosis (Sacrey et al., 2015). Further, 12-month-old infants later diagnosed with ASD show more frequent and intense distress reactions to a variety of sensory stimuli (Zwaigenbaum et al., 2005). Since sensory symptoms (and particularly hypersensitivity) emerge with or before the emergence of clear social-communication symptoms of ASD in the second year of life (Ozonoff et al., 2010), sensory perturbations could affect *the acquisition* of social and communication skills in children with ASD.

Relations between behavioral measures can be challenging to interpret because of the multiple neurocognitive processes that underlie performance. To move forward, we need to examine how sensory sensitivities impact lower-level neurocognitive processes that shape social learning. A recent neuroimaging study linked sensory hypersensitivities in individuals with ASD to greater attribution of neural salience (i.e. greater attention capture) to low-level sensory events (Green et al., 2016). In a naturalistic environment, people possess many low-level features that typically engage the salience network, such as motion, audiovisual synchrony and unpredictability. People would thus be expected to strongly capture attention in individuals with higher levels of hypersensitivity (Baranek et al., 2006). Since attention capture shapes learning (Dayan et al., 2000; Roelfsema et al., 2010), social development should in some circumstances be *facilitated* by heightened sensory sensitivities. Though initially counterintuitive, this could explain the relations between greater hypersensitivity and better social-communicative development observed within some groups of children with ASDc (Watson et al., 2011; Green et al., 2011).

Testing the effect of sensory hypersensitivities on social development requires longitudinal studies of infants and toddlers with ASD (Jones et al., 2014). Whilst fMRI is limited to sleep within this age range, electrophysiological responses such as the early event-related P1, P400 and Nc components can be successfully collected from awake infants and toddlers and can thus be used to measure attention capture by visual stimuli (Webb et al., 2013; de Haan et al., 2003). The posterior P100 can be localized to extra-striate visual areas, and is modulated by selective attention (Hillyard et al., 1998) and the historical salience level of a stimulus (Taylor, 2002). The posterior P400 and anterior Nc components are prominent in infants and toddlers, can be source-localized to midline frontal and parietal, anterior temporal and posterior temporal and occipital brain areas (including the anterior cingulate, a key component of the salience network), and are again modulated by attention (Guy et al., 2016). Thus, examining early ERP responses can index individual differences in attention capture. If people are typically more salient in the child's environment because they move, talk and are unpredictable, over developmental time, faces would elicit greater early-stage attention capture in children with greater levels of hypersensitivity.

1.1. Present study

In the present study, we tested the hypothesis that sensory over-reactivity in early development would predict later enhanced attention capture by faces within a group of children with ASD, and that this would relate to greater social interest and approach. Our data were taken from large longitudinal studies designed to examine social development at behavioral and neurocognitive levels in infants and children with ASD. Thus, our project represents a secondary analysis of this data. However, we had strong predictions following (Green et al., 2016), who showed that increased sensory hypersensitivity is associated with greater activation of the neural salience network; and following a long theoretical and empirical body of work showing that increased attention to social stimuli is associated with positive social development (Dawson et al., 2012a, 2004; Webb et al., 2011; Jones et al., 2016).

In Experiment 1, we tested our hypothesis in a longitudinal study of toddlers with ASD enrolled at 18- to 30-months, and followed up two years later. We used a parental questionnaire measure of sensory sensitivities (the Short Sensory Profile), ERP data (P1, Nc and P400 amplitude) from previously published ERP tasks that involved presentation of pictures of faces and objects (Webb et al., 2011; Dawson et al., 2012b) to assess natural variation in attention capture by passively watched social and nonsocial stimuli, and a parental questionnaire measure of the child's degree of social interest (the Pervasive Developmental Disorders Behavioral Inventory (Cohen et al., 2016)). In Experiment 2, we examined similar data from a prospective longitudinal study of infants with older siblings with ASD ("high familial risk infants") to establish whether sensory hypersensitivities (measured with the perceptual sensitivity scale of the Infant Behavior Questionnaire) were correlated with ERP measures reflecting social attention (P1 amplitude to faces) during symptom emergence.

Because ERP component amplitude is also modulated by general factors such as skull thickness, in control analyses we covaried ERP responses to objects to determine whether effects were specific to face stimuli. Of note, under our hypothesis one would expect some degree of relation between responses to objects and hypersensitivity, but we predicted this relation would be weaker than that with face stimuli and so our primary results would survive covariation. If any results were due to general factors like skull thickness, covarying responses to objects should completely negate them. As an additional control, we examined relations between hypersensitivity and the amplitude of the negative-going N290 component over posterior regions, since this component has been strongly linked to face processing (de Haan et al., 2003) and is not modulated by attention capture in people with ASD (Churches et al., 2010). If our results simply reflect general factors like skull thickness or generalized arousal, there should be equally strong relations between increased N290 negativity and sensory hypersensitivity. If these relations are absent, this would support our hypothesis that our findings are linked to attention engagement (which modulates our three target components).

2. Experiment 1: a longitudinal study of toddlers with ASD

2.1. Participants

Data were taken from larger study of the early development of autism and a randomized control trial of the Early Start Denver Model (ESDM) intervention, which included standardized diagnostic, cognitive, adaptive, and language assessments as well as an experimental battery including social and cognitive tasks (Webb et al., 2011; Dawson et al., 2012b; Jones et al., 2013; Webb et al., 2010). At 18–30 months, both children with ASD (n = 59) and TD (typical development; n = 34) were assessed on a mother vs. stranger face ERP task (Webb et al., 2011) and a parent-report questionnaire (the Short Sensory Profile (Tomchek and Dunn, 2007)) used in the present report. (See S1.1.1 for further details of inclusion/exclusion criteria.) Subsequently, children with ASD were entered into a randomized control trial of an early intervention program such that half received ESDM and half treatment as usual (TAU; see S1.1.2 for details) and underwent follow-up assessments two years after study entry at approximately age 4 years (n = 47 ASD). Full details of the intervention and its effects can be found in Dawson et al. (2010). Assessments at 4 years included a face versus object ERP tas (Dawson et al., 2012b), the Short Sensory Profile, and a questionnaire measure of the child's social functioning (the Pervasive Developmental Disorders Behavioral Inventory (Cohen et al., 2016)). Measures are described in detail below.

2.1.1. Final sample

For cross-sectional analyses at baseline (see Results Section 2.3.1), 18 children with ASD and 16 children with typical development provided both ERP and questionnaire data at 2 years. Because ERP components are not always clear in this age range, 15 of the 18 children with ASD had P1 data, 16 children had P400 and N290 data, and 18 had Nc data. 11 of the 16 children with TD had P1 data, 12 had P400 and N290 data, and 16 had Nc data. For longitudinal analyses (Results Section 2.3.2), 27 children provided valid ERP data across all components at 4 years (12 TAU, 15 ESDM) and had a Short Sensory Profile available from the baseline assessment at age 2 years. Out of the 27, 24 children had available data on social approach from the PDDBI. Out of the 27, 10 children (5 ESDM, 5 TAU) also had 2 year ERP data. To maximize the value of our data, we have included all children with data available for each analysis strategy. Section S1.1.3 gives reasons for data loss. Table 1 provides cognitive and clinical data for participants with valid ERP data and baseline questionnaire data.

2.2. Methods

2.2.1. ERP procedure

At study entrance (18–30 months, referred to as “at 2 years” or “baseline”), children participated in a mother/stranger ERP paradigm (Webb et al., 2011), in which they watched repeated pictures of their mother’s or a stranger’s face while EEG was recorded using a Geodesic sensor net at 250 Hz, with full description of the ERP procedure, extraction of components and initial analysis in the Supplementary Materials (see S1.1.5).

At 4 years (49–77 months), children participated in a face/object ERP paradigm (Dawson et al., 2012b), in which they watched trial-unique pictures of faces vs toys while EEG was recorded using a Geodesic sensor net at 250 Hz, with full description of the ERP procedure, extraction of components and initial analysis in the Supplementary Materials (see Section 1.1.6).

Table 1
Cognitive and clinical data for children included in analyses at the 2- and 4-year age points.

	ASD – 2 years	*TD – 2 years*	*ASD – 4 years*
Age (m)	23.8 (.9)	23.3 (0.8)	23.2 (1.4)
Mullen verbal SS	43.4 (2.6)	107.2 (2.2)	84.3 (3.8)
Mullen nonverbal SS	81.3 (2.9)	99.2 (3.2)	87.5 (3.4)
ADOS Social + Com	16.4 (0.8)	2.7 (0.5)	13.0 (0.9)
ADI Social	17.4 (0.8)	N/A	12.8 (1.4)
ADI Communication	11.8 (0.4)	N/A	6.0 (0.5)
ADI Repetitive Behavior	2.5 (0.4)	N/A	14.5 (0.9)

Key: SS = Standard Score; Com = Communication.

2.2.2. Sensory sensitivity

Parents were asked to complete the Short Sensory Profile (SSP (Tomchek and Dunn, 2007)). The SSP is a 38-item measure that includes items that demonstrate the highest discriminative power for atypical sensory processing from the longer Sensory Profile (Dunn and Westman, 1997). Parents rate their child's response to sensory input on a scale from Always (1) to Never (5). Some questions focus on hypersensitivity, and some ask about hyposensitivity since these are considered separable domains of atypical sensory processing (Boyd et al., 2010). For the present report, we analysed a composite of responses from the visual/auditory, tactile and taste/smell *hyper*sensitivity scales (similar to Green et al. (2016)). Within questions asking about hypersensitivity, *lower* scores represent *higher* hypersensitivity (e.g. the child is ‘Always’ bothered by bright lights after others have adapted to them; see S1.1.4 for further example questions). We tested the specificity of our results to hypersensitivity by examining ‘under-responsivity’, a scale most closely related to hyposensitivity.

2.2.3. Social approach and social interaction

To assess whether P1 amplitude to faces related to greater social interest and approach, we used a scale from the PDDBI (Cohen et al., 2016). The PDDBI is a parent-report questionnaire assessing both problems and skills in the domains of social communication. We selected the ‘social approach’ behaviors subdomains (raw score), for which higher scores are associated with greater levels of social interest and interaction. This measure has been previously related to EEG metrics within this sample (Dawson et al., 2012b); and it is specifically designed to measure variability within groups of children with pervasive developmental disorders, rather than being designed to identify ‘impairments’.

2.2.4. Analysis approach

We used ANCOVAs to explore the relation between attention capture by faces and sensory hypersensitivity both concurrently and over time, including Diagnostic Groups (ASD, TD) or within the ASD Treatment Groups (ESDM, TAU) as between subject factors and in interaction with the predictor variable. This established whether there were group differences in the relations between attention capture and sensory hypersensitivity. Of note, we included treatment group as a factor to control for any effects of intervention (though we did not expect them), since we have previously established that intervention impacted oscillatory responses to faces and social behaviors on the PDDBI in this group (Dawson et al., 2012b). Where significant relations were observed, we examined whether they were specific to faces by covarying attention capture by objects; and we examined whether relations were specific to hypersensitivity by examining relations with under-responsivity. Finally, we used a regression model to examine whether attention capture mediated relations between sensory sensitivity and social approach.

2.3. Results

See S1.2.1 and Fig. S3 for details of group differences in basic variables, including sensory hypersensitivity (Fig. 1D).

2.3.1. Diagnostic groups at baseline

In ANCOVAs on 2-year-old sensory sensitivity by concurrent ERP amplitude to faces and Diagnostic Group (see Fig. 1A–C), sensory sensitivity was not significantly related to amplitude to faces for the P1 ($F(1,25) = 1.25$, $p = 0.22$, $\rho^2 = 0.05$), P400 ($F(1,27) = 0.03$, $p = 0.84$, $\rho^2 = 0.002$), or Nc ($F(1,33) = 0.06$, $p = 0.86$, $\rho^2 = 0.002$); and did not interact with Diagnostic Group (P1: $F(1,25) = 1.66$, $p = 0.21$, $\rho^2 = 0.07$; P400: $F(1,27) = 0.13$, $p = 0.73$, $\rho^2 = 0.005$; Nc: $F(1,33) = 0.03$, p = 0.87, $\rho^2 = 0.001$).

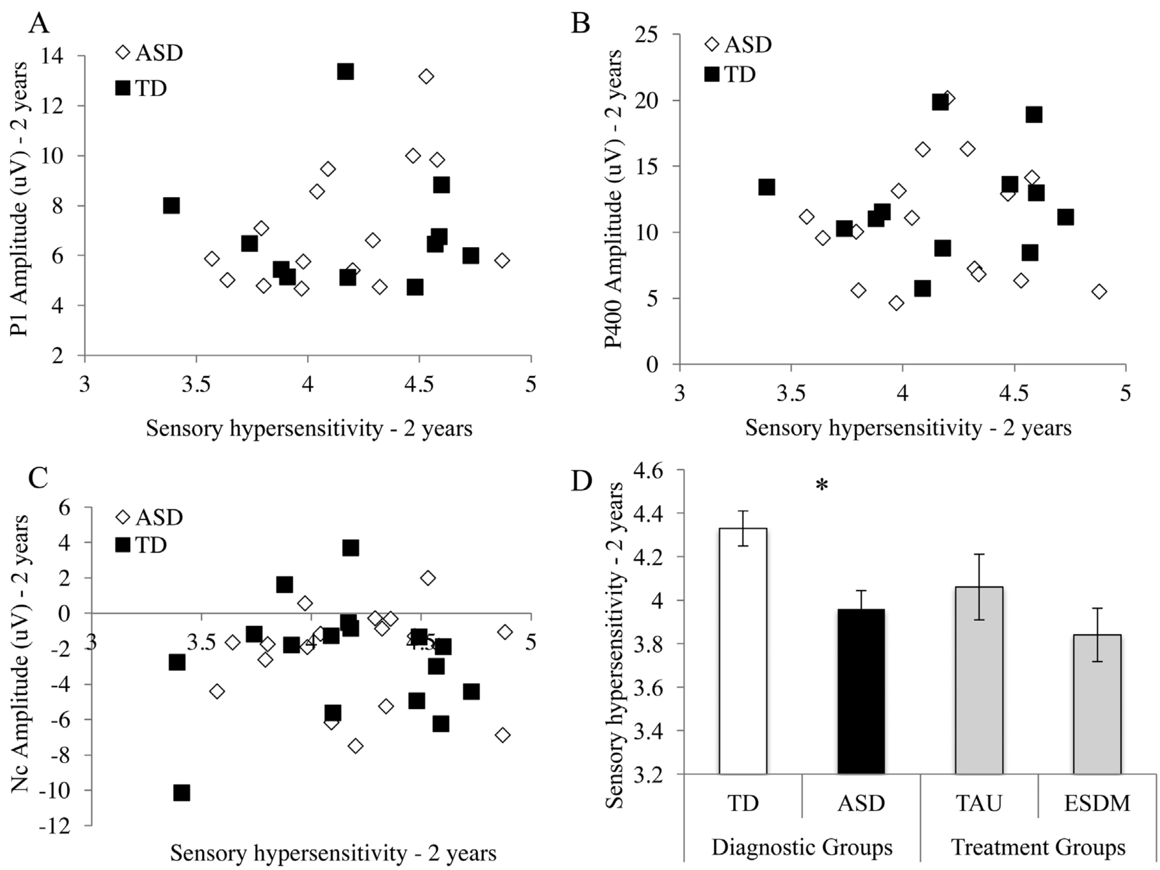

Fig. 1. Relation at 2 years between sensory hypersensitivity and ERP components.Scatter plots of children with ASD (open diamond) and TD (black square) display sensory hypersensitivity at 2 years and relation with (A) concurrent P1 amplitude to faces; (B) P400 amplitude to faces; and (C) Nc amplitude to faces. Note that the Nc is a negative-going deflection, and so greater negativity is associated with greater attention capture. (D) Group differences in sensory hypersensitivity at 2 years. Note that lower scores for sensory hypersensitivity reflect greater sensitivity.

2.3.2. *Longitudinal analysis of hypersensitivity and later ERP responses*

In the main ANCOVA on P1/P400/Nc amplitude to faces at 4 years with sensory hypersensitivity at 2 years as a covariate and intervention group as a factor, greater sensory hypersensitivity at 2 years (lower scores) was related to greater P1 amplitude to faces at 4 years in children with ASD ($F(1,26) = 8.82$, $p = 0.007$, $\rho^2 = 0.28$; Fig. 2A). This effect was also present for P400 amplitude ($F(1,26) = 23.59$, $p < 0.001$, $\rho^2 = 0.51$; Fig. 2C) and Nc amplitude ($F(1,26) = 17.29$, $p < 0.001$, $\rho^2 = 0.43$; Fig. 2D). Effects did not significantly vary between ASD Treatment Groups ($Fs < 1.5$, $ps > 0.2$, $\rho^2 < 0.05$). Analysis of control variables (see S1.2 for additional statistics) indicated that relations between 2-year sensory hypersensitivity and 4-year response to faces remained broadly significant when responses to objects were covaried (P1 $F(1,26) = 3.04$, $p = 0.095$, $\rho^2 = 0.12$; P400 $F(1,27) = 12.73$, $p = 0.002$, $\rho^2 = 037$; Nc $F(1,27) = 10.54$, $p = 0.002$, $\rho^2 = 037$).

There was a relation at trend level ($F(1,26) = 3.81$, $p = 0.06$, $\rho^2 = 0.14$) between 2-year sensory hypersensitivity and the N290 component at 4 years, but this was in a negative direction such that greater hypersensitivity was associated weakly with a less negative-going N290. This is likely because of residual effects of the more positive P1; when P1 amplitudes were covaried this effect disappeared ($F(1,26) = 0.47$, $p = 0.51$, $\rho^2 = 0.021$), whilst covarying N290 amplitude did not affect the relation between hypersensitivity and P4 amplitude ($F(1,26) = 17.4$, $p < 0.001$, $\rho^2 = 0.44$). Taken together, the N290 analysis indicates that the results do not reflect a generalized effect of factors that may affect ERP amplitude in general (e.g. skull thickness, cortical organization), because this should lead to effects across all components.

Other control analyses showed no relations between ERP components at 4 years and under-sensitivity at 2 years ($Fs <= 0.25$, $ps > 0.63$, $\rho^2 < 0.01$), indicating that our results were specific to hypersensitivity. Further, the observed relations between toddler hypersensitivity and 4-year ERP responses remained when concurrent (4-year) hypersensitivity was covaried (P1 $F(1,24) = 6.27$, $p = 0.021$, $\rho^2 = 0.24$; P400 $F(1,25) = 18.50$, $p < 0.001$, $\rho^2 = 0.48$; Nc $F(1,24) = 14.95$, $p = 0.001$, $\rho^2 = 0.43$), indicating that effects were longitudinal and not mediated through the stability of hypersensitivity over time. Longitudinal relations between 2-year sensory hypersensitivity and 4-year P1 amplitude to faces were even stronger when 2-year P1 amplitude to faces was covaried (P1 $F(1,9) = 14.3$, $p = 0.013$, $\rho^2 = 0.74$ vs 0.28, Fig. 2B), indicating that any residual relation between ERPs and hypersensitivity at baseline does not confound our results. Finally, 2-year responses to faces did not predict later sensory sensitivity (all $Fs < 3.64$, $ps > 0.11$, $\rho^2 < 0.38$), indicating that the direction of the longitudinal effect was specific to sensory sensitivities predicting ERP amplitude.

2.3.3. *Longitudinal relation to social behavior*

To examine whether increased ERP amplitudes were associated with better social behavior, we conducted a regression on 4-year-old social approach behaviors, first entering sensory hypersensitivity as a predictor. This revealed a significant effect such that greater 2-year hypersensitivity predicted 4-year increased social approach ($F(1,23) = 4.49$, $p = 0.046$; $t = -2.2$, $p = 0.046$; Fig. 3D).

Second, we conducted a regression on 4-year-old social approach behaviors, entering P1, P400 and Nc amplitudes as predictors. The model was significant ($F(2,23) = 3.51$, $p = 0.03$), explaining 35% of the variance in social approach (Fig. 3A–C). P1 amplitude was the only significant individual predictor ($t = 2.15$, $p = 0.044$), indicating that

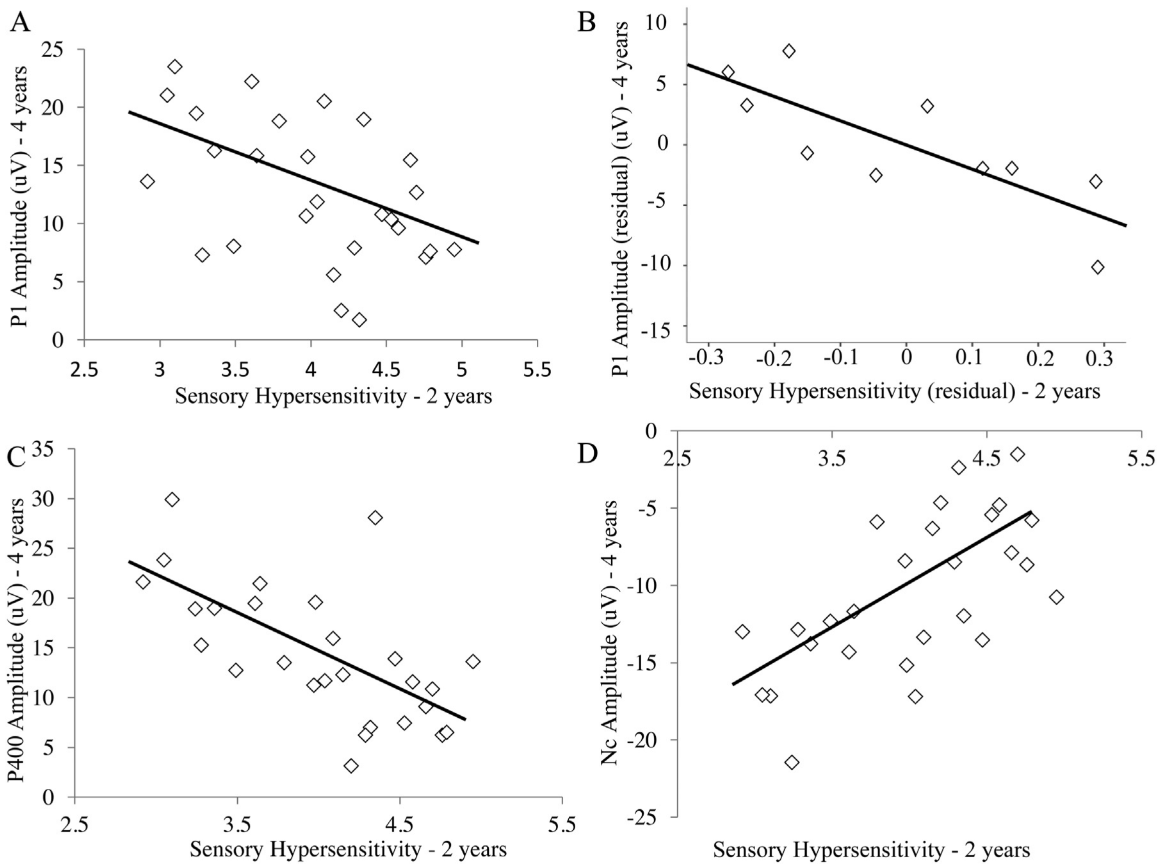

Fig. 2. Relation between sensory hypersensitivity at 2 years and ERP components at 4 years.Scatter plots display data from children with ASD (black diamond) for sensory hypersensitivity at 2 years and relationship to 4-year (A) P1 amplitude to faces, (B) P1 amplitude to faces at 4 years controlling for P1 amplitude to faces at 2 years; (C) P400 amplitude to faces; and (D) Nc amplitude to faces. Note that the Nc is a negative-going deflection, and so greater negativity is associated with greater attention capture, and that lower scores for sensory hypersensitivity reflect greater sensitivity.

effects across all three components are likely related and originate from the effect of early attention allocation on neural responses.

Finally, we conducted a regression model with 4-year social approach as the dependent variable and 4-year ERP responses to faces and 2-year sensory sensitivities as a predictor. The model was again significant ($F(4,23) = 3.1$, $p = 0.04$) and predicted 39% of the variance in social approach. Critically, only 4-year P1 amplitude remained a significant predictor of 4-year social approach ($t = 2.2$, $p = 0.04$); 2-year sensory sensitivities were no longer significantly related to 4-year social approach ($t = -1.2$, $p = 0.23$). This indicates that increased P1 amplitude to faces might mediate the relation between early sensory sensitivities and later social approach behaviors.

3. Experiment 2: a longitudinal study of infants at high risk for ASD

In Experiment 1, we observed significant relations between 2-year-old sensory hypersensitivity and greater 4-year-old P1 ERP responses to faces in toddlers with ASD. To examine whether these effects are also present prior to ASD diagnosis, we used data from a prospective longitudinal study of infants at low and high familial risk for ASD. Guided by the strongest result in Experiment 1, we specifically focused on P1 amplitude to faces and its relation to early sensory hypersensitivity.

3.1. Participants

Participants were a group of n = 43 high-risk infant siblings of children with ASD (HR) and n = 45 low-risk infants with older siblings with typical development (LR) who were enrolled at 6 or 12 months of age and tested longitudinally at 6, 12 and 18 months on a battery of measures including an event-related potential paradigm identical to that used at 4 years in Experiment 1; see S2.1.1 for inclusion criteria. A proportion of the high-risk infants were randomized to receive a parent-mediated early developmental intervention once a week (Promoting First Relationships/HR_{PFR}; see S2.1.2) or assessment and monitoring only ($HR_{AM,}$). Because intervention did not significantly impact findings in Experiment 1, and we had no specific predictions about the impact of PFR on sensory sensitivities, we only included intervention as a factor in models to control for any group effects; no effects in interaction with intervention were found. To examine whether effects were consistent between infants with and without later ASD, we used information about the child's diagnostic status at 24 months. Briefly, this was based on clinical judgment derived from all available information (including ADOS, ADI-R and interactions with the child and parent) as described in previous reports (Jones et al., 2016) and children were grouped as having behaviors consistent with ASD (HR-ASD) or not (HR-no ASD).

3.1.1. Final sample

Table 2 includes shows sample size (and number of females) for each age point and cognitive and clinical data for the subset of infants included at each time-point. Reasons for data loss can be found in S2.1.3.

3.2. Methods

3.2.1. Event related potential (ERP) task

The task was the same face/object ERP task described for Experiment 1 (Jones et al., 2016); with full description of the ERP procedure, extraction of components and initial analysis in the Supple-

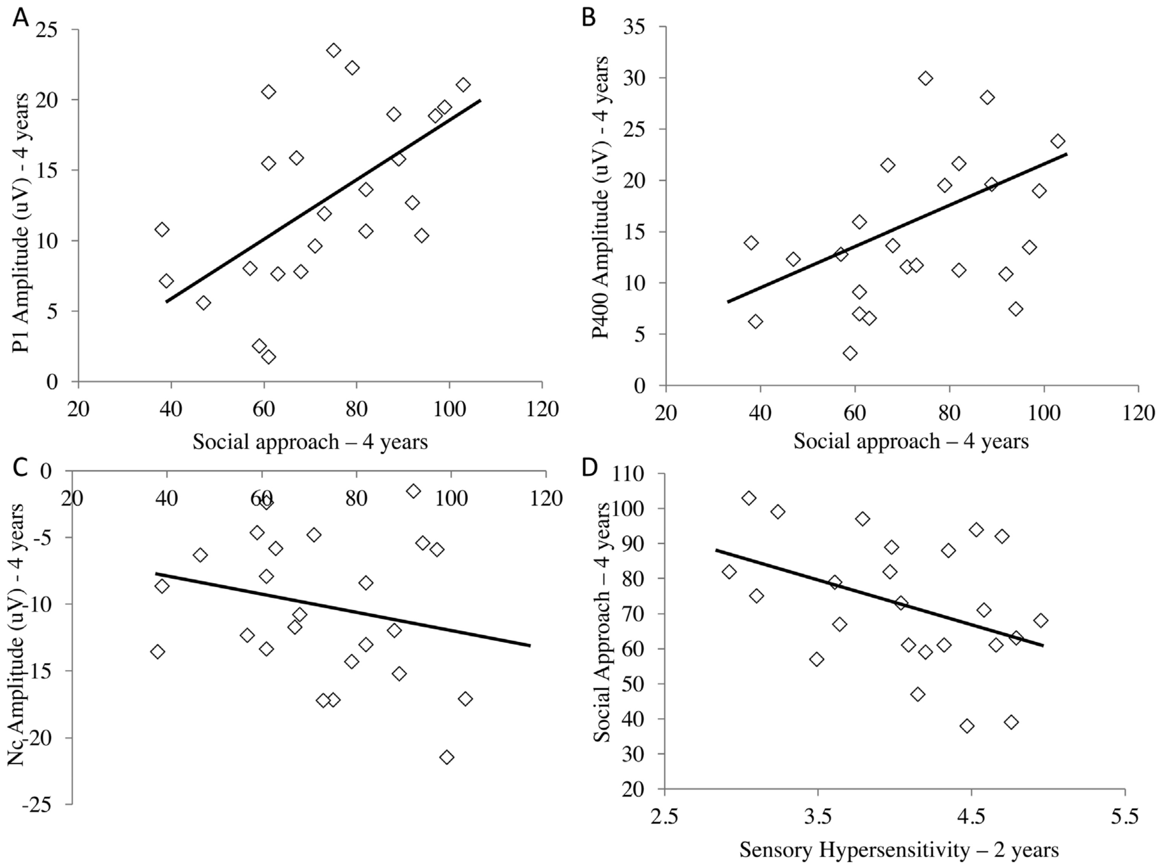

Fig. 3. ERP Response to faces and social approach behaviors.Scatter plots display: (A) Greater P1 amplitude to faces at age 4 related to greater social approach behaviors at age 4. (B) Greater P400 amplitude to faces at age 4 years relates to greater social approach behaviors at age 4 years. (C) More negative Nc amplitude to faces at 4 years relates to greater social approach behaviors at age 4 year. Note that the Nc is a negative-going deflection, and so greater negativity is associated with greater attention capture. (D) Greater sensory hypersensitivity at 2 years (lower scores) relates to better social approach behaviors at age 4 years.

Table 2
Cognitive scores and ASD symptoms for the subset of infants with baseline questionnaire data and good ERP data at 6, 12 and 18 months. Numbers in brackets are number of females for the first part of the table, and standard error for the second part of the table.

	LR	*HR*	*HR – no ASD*	*HR –ASD*
6 months	N = 17 (6)	N = 18 (8)	n = 12	n = 6
12 months	N = 20 (10)	N = 17 (6)	n = 12	n = 5
18 months	N = 26 (14)	N = 26 (19)	n = 20	n = 6
Autism Symptoms				
6 mo AOSI Total	7.1 (0.6)	9.5 (0.8)	9 (0.9)	10.5 (1.8)
12 mo AOSI Total	4.9 (1.1)	5.5 (1.1)	4.4 (1.1)	8.0 (2.1)
18 mo ADOS T Total	4.1 (0.6)	7.4 (1.0)	5.2 (0.6)	15.0 (1.5)
Mullen Verbal Standard Scores				
6 months	94 (3.0)	89.7 (2.4)	88 (3.5)	93.2 (1.9)
12 months	98.2 (3.1)	92.8 (3.1)	96.7 (5.2)	83.6 (9.0)
18 months	97.7 (3.5)	96.6 (4.7)	103.0 (4.4)	76.2 (10.8)
Mullen Non-Verbal Standard Scores				
6 months	101.4 (3.5)	101.4 (3.0)	102.8 (4.3)	98.8 (2.6)
12 months	123.1 (2.6)	110.9 (2.6)	116.1 (5.3)	98.4 (5.8)
18 months	107.8 (2.3)	105.8 (2.5)	109.6 (2.3)	93.8 (5.1)

mentary materials (S2.1.4).

3.2.2. Perceptual sensitivity

Primary caregivers were asked to complete the Infant Behavior Questionnaire-Revised (IBQ-R (Gartstein and Rothbart, 2003)) at 6 and 12 months, and the Early Childhood Behavior Questionnaire at 18 months. Both measures ask caregivers to report on the frequency of certain behaviors in the past few weeks using a 7-point, Likert-type scale. For the present study, we focused on the 12-item perceptual sensitivity subscale (item list available in Table 2 XI of Gartstein and Rothbart (2003)). This subscale is grouped with the Surgency domain, and is defined by the detection of slight, low intensity environmental stimuli. Higher scores represent greater sensitivity; this is closely related to hypersensitivity as measured by other instruments (see S2.3.). As an additional control to establish whether results were indeed specific to perceptual sensitivity, we examined relations with the overall Surgency domain constructed per previous work (Approach, Vocal Reactivity, High Intensity Pleasure, Smiling and Laughter, Activity Level) but minus perceptual sensitivity. This allowed us to investigate whether other aspects of a child's engagement with their environment were related to social attention, or whether relations are specific to perceptual sensitivity.

3.2.3. Analysis

Analyses followed the broad approach used for Experiment 1.

3.3. Results

See S2.2.1. for group effects on basic ERP and questionnaire variables.

3.3.1. Risk groups

In an ANCOVA including risk group and shown in Fig. 4B, at 6 months there was no concurrent relation between perceptual sensitivity and attention capture by faces ($F(1,34) = 1.21$, $p = 0.28$, $\rho^2 = 0.04$). As well, there was no concurrent relation between perceptual sensitivity and P1 amplitude to faces at 12 months ($F(1,32) = 0.07$, $p = 0.79$, $\rho^2 = 0.003$) or 18 months ($F(1,34) = 1.31$, $p = 0.26$, $\rho^2 = 0.04$).

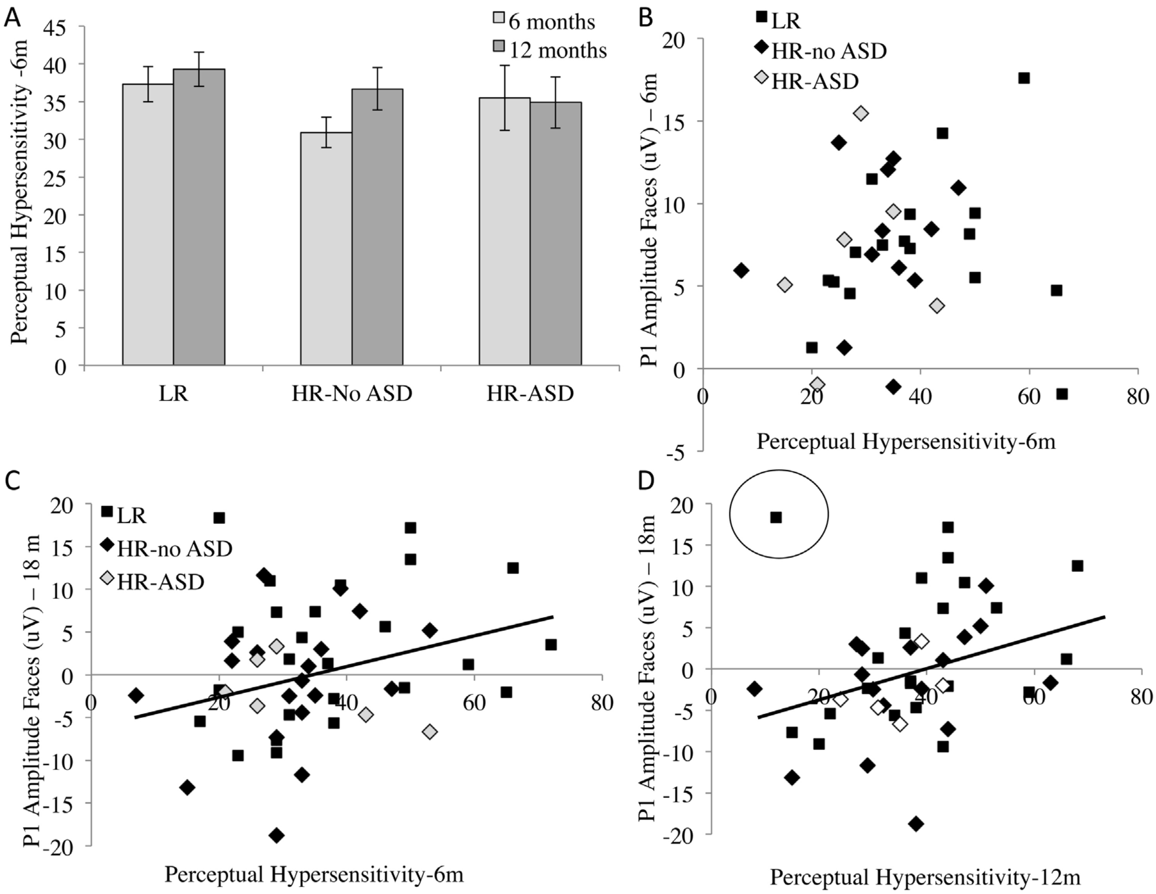

Fig. 4. Exp 2. ERP Response to faces and social approach behaviors.(A) Bar graphs depict perceptual hypersensitivity in LR infants compared to HR infants with (HR-ASD) or without ASD outcomes (HR-No ASD), with higher scores reflecting greater sensitivity. Scatter plots depict the relation between perceptual hypersensitivity at 6 months and (B) 6-month P1 amplitude to faces; and (C) 18-month P1 amplitude to faces. (D) Relation between perceptual hypersensitivity at 12 months and 18-month P1 amplitude to faces.

3.3.2. ASD outcome

Including outcome (ASD versus no ASD) revealed no significant group difference in relations between perceptual sensitivity at 6 months and attention capture by faces at 6 months ($F(2,34) = 0.001, p = 0.99, \rho^2 = 0.00$).

3.3.3. Longitudinal analysis of perceptual sensitivity and later ERP responses

Perceptual sensitivity at 6 months did not predict P1 amplitude to faces at 12 months ($F(1,34) = 0.81, p = 0.38, \rho^2 = 0.03$). However, as seen in Fig. 4C, perceptual sensitivity at 6 months predicted P1 amplitude to faces at 18 months with marginal significance ($F(1,49) = 3.61, p = 0.06, \rho^2 = 0.08$). This did not interact with ASD outcome group ($F(2,49) = 0.88, p = 0.42, \rho^2 = 0.04$), remained marginally significant if responses to objects were covaried ($F(1,49) = 3.44, p = 0.07, \rho^2 = 0.07$), and was not present for other components of Surgency (S2.2.2).

As seen in Fig. 4D, perceptual sensitivity at 12 months significantly predicted P1 amplitude to faces at 18 months ($F(1,43) = 4.95, p = 0.032, \rho^2 = 0.12$) and removal of the outlier circled in Fig. 4D renders this relation highly significant ($F(1,42) = 9.14, p = 0.005, \rho^2 = 0.20$). This did not interact with ASD outcome group ($F(2,43) = 0.03, p = 0.97, \rho^2 = 0.002$), remained if responses to objects were covaried ($F(1,43) = 4.29, p = 0.045, \rho^2 = 0.10$), and was not present for other components of Surgency (S1.4.2). Thus, early perceptual sensitivity predicted greater early attention capture by faces across both low and high-risk infants.

4. Discussion

Sensory hypersensitivities reflect increased responsivity to sensory input across multiple modalities. It is often assumed that sensory hypersensitivity will negatively impact social development in ASD. However, greater responsivity to social stimuli could have positive effects in promoting social learning by promoting early-stage attention capture by social stimuli. We tested this hypothesis in two longitudinal samples, using ERP measures of attention capture by social stimuli and questionnaire measures of hypersensitivity. We found that in toddlers with ASD, higher levels of sensory hypersensitivity at age 2 years were associated with a more positive P1/P400 response and a more negative Nc response to faces at age 4 years. This is consistent with higher levels of sensory sensitivity in toddlerhood relating to greater levels of attention capture by faces in preschoolers. Further, sensory hypersensitivity at 2 years was also correlated with higher levels of social approach at age 4 years, and this relation was mediated by ERP responses to faces at age 4. This suggests that early levels of sensory sensitivity may be associated with later attention capture by social stimuli, which in turns relates to better social interaction skills. Effects were found at the early latency P1 component, consistent with evidence that selective attention capture modulates neural processing in early visual areas (Taylor, 2002). Effects survived covarying responses to objects, and were not observed over the N290 component, indicating that our results do not reflect individual differences in general factors that affect all ERP amplitudes like skull thickness or generalized arousal. Similar effects were observed in a sample of infants at high and low familial risk for ASD. Specifically, higher perceptual sensitivity in infancy predicted a larger P1 response to faces in toddlerhood. Taken together, these findings confirm the hypothesis that sensory hypersensitivities may influence the development of attention capture by social stimuli, and that in some circumstances this may be positive for social development in a child with ASD.

4.1. The development of ERP responses to faces

In the present study, we examined ERP responses to static pictures of faces and objects. The stimuli were all designed to be comfortable for the child to watch, and thus were not designed to elicit hypersensitive responses per se; indeed, there was no correlation between concurrent hypersensitivity and ERP responses to faces. Rather, we contend that children with hypersensitivities are more reactive to people in their natural environment (because of lower-level sensory features) and that over time this leads to larger P1 amplitude to cues associated with people, such as pictures of faces. Specifically, social stimuli often possess more salient low-level features than nonsocial stimuli in a typical naturalistic environment. For example, two of the most significant salience cues that contribute to orienting (particularly in the peripheral visual field) are motion and audiovisual synchrony. Motion is particularly important in controlling orienting in young infants (Valenza et al., 2015; Macfarlane et al., 1976; Regal, 1981). In a typical home environment, the most common source of motion is likely people. Further, as people move around they make noises (opening doors, putting down objects, talking), which is synchronous with their movements. Audiovisual synchrony is a critical determinant of attention in young infants (Bahrick and Lickliter, 2000) and may have a greater effect on attention in children with autism (Klin et al., 2009), though see (Falck-Ytter et al., 2013).

In the present study, the ERP paradigm involved viewing of pictures of people's faces, which were contrasted with pictures of familiar toys. The toys chosen were all selected because they were the favorite toy of a child with ASD who was participating in a previous study (e.g windmill, toy dog, bow and arrow, toy steering wheel, shape sorter, toy car). This approach was selected because we wanted to ensure that the nonsocial control stimuli had similar affective value to the social stimuli. However, in a naturalistic environment, the stimulation provided by these toys is more under the child's control than the stimulation provided by people. Unpredictability of sensory input is also a key determinant of salience attribution in the brain, and difficulties in forming or applying predictions may contribute to sensory sensitivities in ASD (Pellicano and Burr, 2012; Lawson et al., 2014; Sinha et al., 2014). Since uncertainty is thought to be a critical determinant of sensitivity in ASD (Neil et al., 2016), this may explain why hypersensitivities were linked more strongly to ERP responses to faces than toys in this study. Whilst this explanation is relatively speculative, using head-mounted cameras to measure the predictability structure of the child's early environment and how this affects attention capture by different stimuli over developmental time could distinguish between a salience-related explanation and other possible mechanisms.

4.2. Social attention in ASD

A range of evidence indicates that other aspects of social attention are impaired in ASD, and predict poorer social communication functioning (Dawson et al., 2012a; Klin et al., 2015). Behaviorally, 6-month-old infants with later ASD are less likely to look at speaking faces (Shic et al., 2014), show reduced attention to an actress in a naturalistic scene (Chawarska et al., 2013), and show declining interest in the eye region in a naturalistic video (Jones and Klin, 2013). Toddlers with ASD are less likely to response to their name or other naturalistic social stimuli (Dawson et al., 2004), and show robust differences in visual attention to naturalistic videos of people (Chawarska and Shic, 2009; Chawarska et al., 2010). Alterations in social attention can also been seen in ERP studies. For example, groups of infants, children and adults with ASD sometimes show altered responses over the N170 ERP component, which reflects structural aspects of face processing (Webb et al., 2006; McPartland et al., 2004). Alterations have also been observed in the modulation of components like the Nc and P400 by facial familiarity (Webb et al., 2010; Dawson et al., 2002). In response to face stimuli, groups of infants with later ASD show shorter P400 latencies (Jones et al., 2016; Elsabbagh et al., 2012), 2and infants and children with ASD show altered Nc latency and duration (Jones et al., 2016; Dawson et al., 2012b). Young children with ASD show altered theta/alpha power responses to faces versus objects (Dawson et al., 2012b). Such effects have been related to variation in socio-communicative symptoms in some cases, and have been interpreted to reflect alterations in deeper levels of attention engagement to social stimuli (Jones et al., 2016; Klin et al., 2015).

How can evidence of impaired social attention in groups of children with ASD be reconciled with the present data? The most critical factors are that social attention is not a unitary construct; and that conclusions drawn from group differences do not necessarily translate into relations with symptoms within groups of children with ASD. First, frameworks describing general attention typically divide attention into subprocesses such as orienting, feature attention, spatial attention and endogenous attention (Colombo, 2001). These subprocesses rely on different neural networks and develop over different developmental time courses. Recent reviews, as well as earlier reports (Dawson et al., 2000), propose that very early in infancy visual social orienting is intact in ASD (Jones et al., 2014; Johnson, 2014; Gliga et al., 2014). Later in infancy, there exist well-documented impairments in visual social orienting that persist into childhood (Werner et al., 2000; Dawson et al., 1998, 2004; Campbell et al., 2016). Furthermore, deeper levels of attention (such as feature attention, attention engagement or endogenous attention) and attention disengagement (Elsabbagh et al., 2013) may also be altered. The distinction between innate reflexive social orienting and impairments in volitional social orienting, as well as impairments in deeper levels of attention engagement, may reflect a differentiation between bottom-up attention capture by the sensory features of social stimuli, and 'top-down' engagement of attention related to the motivational value of people versus objects. Indeed, in previous ERP studies measures more closely related to early-stage attention capture such as P1, Nc and P400 *amplitude* in response to a face *category* (rather than differences between types of face, like mother and stranger) are not typically altered (Webb et al., 2011; Jones et al., 2016; Dawson et al., 2002; Webb et al., 2012; Hileman et al., 2011). Thus, at the group level there is little evidence of deficits in early-stage attention capture by faces in ASD.

Further, most previous work has not considered the effect of variation in sensory sensitivities on heterogeneity in social attention, in part because of its recent addition to DSM-5. Where this has been explored, there are some intriguing results that are consistent with the idea that stronger attention capture by faces may relate to better social communicative skills within groups of individuals with ASD. In Webb et al. (2012), within the ASD group a relatively greater amplitude P1 response to upright vs inverted faces was associated with *better* face memory, consistent with the possibility that attention capture by upright faces covaried with better face memory performance. Faster P1 responses to upright vs inverted faces were also related to less social anxiety and distress, more self-reported social competence and fewer social ASD symptoms. One intriguing possibility is that heightened sensory hypersensitivities buffer reflexive social attention such that deficits are not observed at a group level (unlike those seen for more 'motivational' aspects of social attention); future work should explore this possibility. In addition, the interaction between greater attention capture and alterations in later components of attention (such as slowed attention disengagement (Elsabbagh et al., 2013) or reduced sustained attention engagement (Jones et al., 2016)) in shaping social communication development should be explored.

4.3. Differential susceptibility

Our results may fit into differential susceptibility and biological susceptibility to context frameworks (Belsky and Pluess, 2009; Boyce and Ellis, 2005; Ellis and Boyce, 2008). A number of longitudinal studies have shown that children with difficult temperaments or generally higher levels of negativity can flourish and do better than their peers if they experience a positive nurturing environment (Kim and Kochanska, 2012; Spinrad and Stifter, 2006). Early negativity or difficult temperament is thought to be marker of the child's reactivity to environmental stimuli and affordances. Early sensory hypersensitivities are often included in the definition of difficult temperament (Rothbart and Bates, 2016; Bradley and Corwyn, 2008) and thus may contribute to susceptibility to rearing experience. In Experiment 1 of the present study, all toddlers with ASD experienced relatively high levels of intervention. Specifically, the ESDM group received about 20.4 h/week of professional-delivered intervention, and the Assessment and Monitoring group received 18.4 h per week (Dawson et al., 2010). Early sensory hypersensitivities may enable children to positively benefit from these highly enriched environments including working with families to ensure that stimuli the children experienced were within their range of tolerance. In less supportive environments this may not be the case, and hypersensitivities may compromise development because the child withdraws from interaction in general. Thus, examining such relations across children with a range of developmental experiences will be important before concluding that hypersensitivities are necessarily positive for some aspects of social development.

4.4. Limitations

The present study has several limitations. Because we leveraged existing data from longitudinal cohorts to address our hypotheses, our ERP task differed at the 2-year and 4-year time-points for Experiment 1. The 4-year ERP task involved trial-unique pictures of female faces and toys, whilst the 2-year ERP task involved repeated pictures of the child's mother and one female stranger. This makes it difficult to determine whether concurrent associations between sensory processing and ERP responses were absent because of our hypothesized developmental model, or because variable face stimuli elicit different responses to repeated face stimuli. However, the infant study used the same ERP task (that used with the 4-year-olds in Experiment 1) at every time-point, and again the relation between sensory sensitivity and ERP responses confirmed our longitudinal predictions. Further, it is always difficult to directly index processes like attentional capture. We have interpreted our results in terms of attention because they are consistent across three ERP components that are most associated with attention capture (P1, P400, Nc). Relations were not observed for the N290 component. The N290 is thought to be an early precursor of the N170 (de Haan et al., 2003), a component associated with structural aspects of face processing. Importantly, the N170 is insensitive to attentional modulation in participants with ASD (Churches et al., 2010). Thus, the fact that our findings don't extend to the N290 is supportive of an attentional interpretation. Of note, other recent studies have also found relations between hypersensitivity and greater early ERP responses to auditory stimuli in participants with ASD, and interpreted this in an attentional context (Karhson and Golob, 2016). However, it remains possible that there are other processes that could account for the observed effects; these would need to be cognitive factors that influence the P1, P4 and Nc but not the N290 to be consistent with our findings.

Further, we did not have a group of longitudinally assessed control participants in Experiment 1, and are thus unable to say whether associations between sensory sensitivity and ERP responses to faces are unique to ASD. Indeed, results from Experiment 2 suggest that they are not, and there is no reason why they would be under our theoretical model. However, further work within normative populations and those with sensory processing disorder (without ASD) would establish the generality of these effects. Finally, our sample of infants with later ASD was relatively small and we only measured hypersensitivity; these results should provide impetus for infant sibling studies to more deeply probe sensory sensitivity within their samples.

4.5. General conclusion

In this study, we provide the first demonstration that early sensory sensitivities predict greater attention capture by faces, and this mediates improved social approach behaviors in the early development of ASD. Although they require further replication, our findings are consistent with a theoretical model in which early hypersensitivities are associated with increased attention capture by stimuli with salient sensory features; and that because people tend to have salient sensory features in naturalistic environments (e.g. motion, audiovisual synchrony and unpredictability) attention capture to faces becomes stronger. In the context of a supportive environment, heightened sensory hypersensitivity may support social development for children with ASD. This information may be critical to consider when designing therapeutic strategies or trying to predict individual outcomes for children with ASD.

Conflicts of interest

Geraldine Dawson receives authorship royalties from Guilford Publications and Oxford University Press and is on the scientific advisory boards of Janssen Research and Development, Roche Pharmaceuticals, Akili, Inc., and Progenity, Inc., for which she receives travel reimbursement and honoraria.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dcn.2017.04.001.

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