

## BIROn - Birkbeck Institutional Research Online

Narvekar, N. and Carter Leno, V. and Pasco, G. and Begum-Ali, J. and Johnson, Mark H. and Charman, T. and Jones, Emily J.H. (2024) The roles of sensory hyperreactivity and hyporeactivity in understanding infant fearfulness and emerging autistic traits. Journal of Child Psychology and Psychiatry, ISSN 0021-9630.

Downloaded from: https://eprints.bbk.ac.uk/id/eprint/52358/

Usage Guidelines:

Please refer to usage guidelines at https://eprints.bbk.ac.uk/policies.html contact lib-eprints@bbk.ac.uk.

or alternatively

# The roles of sensory hyperreactivity and hyporeactivity in understanding infant fearfulness and emerging autistic traits

Running Head: Paths from sensory reactivity to fearfulness and autistic traits

- N. Narvekar<sup>1\*</sup>, V. Carter Leno<sup>1\*</sup>, G. Pasco<sup>1</sup>, J. Begum Ali<sup>2</sup>, M. H. Johnson<sup>2,3</sup>, T. Charman<sup>1</sup>, E. J. H. Jones<sup>2</sup> & The STAARS Team<sup>+</sup>.
- (1) Institute of Psychiatry, Psychology and Neuroscience, King's College London, United Kingdom
- (2) Centre for Brain and Cognitive Development, Birkbeck, London, United Kingdom
- (3) Department of Psychology, University of Cambridge, United Kingdom.
- \*Joint first author.
- + The members of STAARS Team are listed in the Acknowledgments section.

Word count (Title page, Abstract, Main text) = 6908

#### **Abstract**

**Background**: Existing evidence indicates that atypical sensory reactivity is a core characteristic of autism, and has been linked to both anxiety (and its putative infant precursor of fearfulness) and repetitive behaviours. However, most work has used cross-sectional designs and not considered the differential roles of hyperreactivity and hyporeactivity to sensory inputs, and is thus limited in specificity.

Methods: 161 infants with and without an elevated likelihood of developing autism and attention-deficit hyperactivity disorder (ADHD) were followed from 10-36 months of age. Parents rated an infant precursor of later anxiety (fearfulness) using the Infant Behaviour Questionnaire at 10 and 14 months, and the Early Childhood Behavioural Questionnaire at 24 months, and sensory hyperreactivity and hyporeactivity at 10, 14 and 24 months using the Infant Toddler Sensory Profile. Domains of autistic traits (restrictive and repetitive behaviours; RRB, and social communication interaction, SCI) were assessed using the parent-rated Social Responsiveness Scale at 36 months. Cross-lagged models tested 1) paths between fearfulness and hyperreactivity at 10-24-months, and from fearfulness and hyperreactivity to later autism traits, 2) the specificity of hyperreactivity effects by including hyporeactivity as a correlated predictor.

**Results**: Hyperreactivity at 14 months was positively associated with fearfulness at 24 months, and hyperreactivity at 24 months was positively associated with SCI and RRB at 36 months. When hyporeactivity was included in the model, paths between hyperreactivity and fearfulness remained, but paths between hyperreactivity and autistic traits became non-significant.

*Conclusions:* Our findings indicate that alterations in early sensory reactivity may increase the likelihood of showing fearfulness in infancy, and relate to later social interactions and repetitive behaviours, particularly in individuals with a family history of autism or ADHD.

*Keywords*: autism, hyperreactivity, hyporeactivity, anxiety, early development, elevated likelihood, sensory reactivity.

#### **Abbreviations:**

ADHD - Attention Deficit Hyperactivity Disorder; ADI-R - Autism Diagnostic Interview-Revised; ADOS - Autism Diagnostic Observation Schedule; APA - American Psychological Association; B – Non-standardised Covariant;  $\beta$  – Standardised Covariant; CBCL – Child Behaviour Checklist; DSM - Diagnostic and Statistical Manual; ECBQ - Early Childhood Behaviour Questionnaire; EL - Elevated Likelihood; IBQ-R - Infant Behaviour Questionnaire-Revised; ITSP - Infant Toddler Sensory Profile; MSEL- ELC - Mullen Scales of Early Learning – Early Learning Composite; p – Probability; RRB - Restricted Repetitive Behaviours; SCI - Social Communication Interaction; SEM - Structural Equation Modelling; SRS - Social Responsiveness Scale; STAARS – Studying Autism and ADHD Risks Study; TL - Typical Likelihood; VABS - Vineland Adaptive Behaviour Scale.

#### Introduction

Autism is a neurodevelopmental condition characterised by differences in social communication and the presence of restricted interests and repetitive behaviours. Recent diagnostic frameworks have incorporated sensory atypicalities into the cluster of restricted and repetitive behaviours (RRB) as part of the core autism symptoms (DSM-5; American Psychological Association, APA, 2013). Sensory differences are experienced by almost 74% of autistic children (Kirby et al., 2022). However, sensory differences are not unique to autism and are present in other neurodevelopmental conditions such as Down's Syndrome and Williams Syndrome (Baranek et al., 2013), intellectual disability (Posar & Visconti, 2018), and Attention Deficit Hyperactivity Disorder (ADHD) (Schulz et al., 2023); some report they are present in a significant proportion of typically developing children (Carpenter et al., 2019). Although not all alterations in sensory reactivity are experienced as negative, certain sensory differences can negatively impact daily activities, especially in situations where environments are less controlled (Posar & Visconti, 2018). Sensory challenges continue to present themselves in adulthood, making it an important consideration across the lifespan (Crane, Goddard, & Pring, 2009). Despite this, our knowledge of the developmental manifestation and impact of atypical sensory reactivity early on in life is limited.

#### Characterising Sensory Atypicalities

Progress in understanding the drivers and impact of sensory differences has been complicated by the broad range of terminologies used to describe differences in sensory functioning (e.g., hyper and hypo sensitivity/processing/reactivity/responsiveness, sensation seeking) (see He et al., 2022 for a review of nomenclature and theoretical frameworks) and the different modalities of sensory experience (e.g., visual, auditory, tactile). In this study, we use the terminology of hyperreactivity and hyporeactivity, with hyperreactivity representing greater behavioural reactivity to sensory inputs and hyporeactivity observed as lower behavioural reactivity to

sensory inputs. A significant proportion of autistic children experience both hyperreactivity and hyporeactivity in multiple domains (Marco et al., 2012; Niedźwiecka, Domasiewicz, Kawa, Tomalski, & Pisula, 2019). Although data-driven approaches have had success in differentiating individuals with profiles of high and low sensory atypicalities, they do not find evidence for specificity of sensory reactivity profiles, again suggesting most people with sensory differences experience both hyperreactivity and hyporeactivity (Tillmann et al., 2020).

Developmental Consequences of Early Alterations in Sensory Reactivity

One way to conceptualise the role of early alterations in sensory reactivity is through the developmental cascades framework (Bradshaw, Schwichtenberg, & Iverson, 2022), where early differences in specific domains (e.g., sensory reactivity) can have cascading and farreaching effects on a variety of other, seemingly unrelated domains (e.g., autistic characteristics, mental health difficulties). Focusing early in development is particularly pertinent when thinking about sensory differences, given the early maturation of primary sensory systems in the brain. Indeed, infant-sibling designs (where infants with a family history of autism are recruited to give a sample enriched for neurodevelopmental outcomes, referred to as elevated likelihood; EL) find differences in sensory behaviour and brain function from as early as 6 months in infants who go onto receive an autism diagnosis (Sacrey et al., 2015; Shen & Piven, 2022). In terms of dimensional symptom profiles, RRB have been the primary focus since sensory atypicalities are located within this symptom domain according to DSM-5 criteria. In 14-month-old infants showing early autistic traits (as identified through community screening), parent-rated hyperreactivity, but not hyporeactivity, was associated with higher RRB at 3-5 years of age (Grzadzinski et al., 2020). However, there is evidence for a broader effect of early alterations in sensory differences and responsivity on autistic traits. In an infant-sibling cohort tracked from 10 to 36 months, perceptual sensitivity at 24 months were both positively associated with RRB and social communication and interaction (SCI) traits at age 3 years (Narvekar et al., 2022). Others find using a directly assessed playbased observational measure, hyporeactivity (but not hyperreactivity) at 14 months was associated with later SCI difficulties and RRB. In the same cohort, greater directly-assessed atypical sensory behaviours (a combination of hyporeactivity and sensory seeking) was concurrently associated with lower joint attention at 12 and 22 months, and predictive of greater observer-rated social difficulties at 3 – 5 years (Nowell et al., 2020); hyperreactivity was not included as a predictor of interest. Similarly, studies from prospective infant-sibling cohorts report stronger correlations between RRB and hyperreactivity as compared to hyporeactivity between 12 and 24 months (Wolff et al., 2019). In the study by Wolff and colleagues (2019), although sensory atypicalities were not associated with observer-rated social affect, both hyperreactivity and hyporeactivity were associated with lower parent-rated socialization skills, and only hyporeactivity was associated with lower parent-rated communication skills. Similarly, higher parent-reported hyporeactivity is reported to be associated with lower communication skills in infant-siblings aged 12 to 18 months (Feldman et al., 2021). In autistic toddlers aged 2 years, parent-reported hyperreactivity was found to be a predictor of enhanced neural response to faces and increased social approach at age 4 (Jones, Dawson, & Webb, 2018), again suggesting differential effects for hyperreactivity as compared to hyporeactivity.

Although the extant evidence regarding the specificity of associations between the types of early sensory differences and later clusters of autism characteristics is mixed, likely due in part to variability in measurement of sensory reactivity and sample ascertainment, an emerging theme is that hyperreactivity is more closely related to RRB, whereas hyporeactivity is more closely linked to difficulties in socio-communication skills. With regards to the effect of hyperreactivity on RRB, some posit that RRB might reflect a compensatory strategy to reduce negative affect/arousal (Kapp et al., 2019). Further, research has reported associations

between anxiety, sensory atypicalities and RRB (Gotham et al., 2013; Lidstone et al., 2014; Rodgers, Glod, Connolly, & McConachie, 2012; Williams, Campi, & Baranek, 2021). Some have suggested that hyperreactivity acts upon RRB through anxiety (Wigham, Rodgers, South, McConachie, & Freeston, 2015) in autistic children. Indeed, hyperreactivity is reported to be predictive of longitudinal increases in anxiety in both autistic (Green, Ben-Sasson, Soto, & Carter, 2012) and typically developing (Carpenter et al., 2019; Schwarzlose, Tillman, Hoyniak, Luby, & Barch, 2022) children. In very young infants, anxiety per se is hard to measure and thus typically researchers focus on domains of temperament that are thought to be developmental precursors, namely behavioural inhibition/fearfulness (Gartstein et al., 2010; Shephard et al., 2019; Tonnsen, Malone, Hatton, & Roberts, 2013). Potentially suggestive of bidirectional cascading effects, in one infant sibling study greater fearfulness at 14 months predicts enhanced perceptual sensitivity at 36 months (characterized by enhanced detection of slight, low intensity environmental stimuli, conceptually close to hyperreactivity) (Narvekar et al., 2022). However, the field is limited by the lack of models that include both hyperreactivity and hyporeactivity. As hyporeactivity and hyperreactivity often co-occur in the same individual, studies which only focus on one domain of sensory atypicalities may be attributing phenotypic specificity (e.g., the proposed hyperreactivity to anxiety/RRB pathway) when global sensory alterations could explain the pattern of results.

The present study extends our previous work on infant fearfulness and sensory reactivity (Narvekar et al., 2022), by examining bidirectional associations between hyperreactivity and fearfulness in early infancy, and how these domains relate to later SCI and RRB traits in toddlerhood, using a more precise measure of sensory differences that distinguishes between hyperreactivity and hyporeactivity. Importantly, we examine the effect of including hyporeactivity on our findings to assess the specificity of associations between hyperreactivity and later fearfulness and SCI and RRB traits. We test these associations in a prospective

longitudinal cohort enriched for atypical neurodevelopmental outcomes through a family history design. This includes infants with family history of autism and/or ADHD. Both conditions are associated with early alterations in sensory reactivity (Shephard et al., 2022), have significant symptom overlap (Nijmeijer et al., 2008), and share aetiological underpinnings evidenced by twin studies (Ronald, Larsson, Anckarsäter, & Lichtenstein, 2014; Ronald, Simonoff, Kuntsi, Asherson, & Plomin, 2008). Furthermore, they have a high co-occurrence rate ranging from 40 to 70% (Antshel & Russo, 2019). Hence, we expect shared transdiagnostic pathways from early alterations to developmental outcomes to be common (although some may be distinct) in infants with a family history or autism and/or ADHD, due to common behavioural co-occurrence and moderate cross-condition heritability. We predicted that early hyperreactivity will be associated with infant fearfulness, and that both hyperreactivity and infant fearfulness will be associated with RRB traits. We also predicted that when we included hyporeactivity, effects of hyperreactivity on infant fearfulness and RRB traits would remain, and we would see a specific path from hyporeactivity to SCI traits. To maximise statistical power, and given that our sample is a heterogenous group spanning the clinical and nonclinical range, we focused on autistic traits rather than categorical diagnosis.

#### Methods

#### **Participants**

Participants were recruited for a longitudinal study as part of the Studying Autism and ADHD Risks Study (STAARS); for more details see Begum-Ali et al. (2022). Infants either had an elevated likelihood for autism (EL-autism; n=80; 42 male; 38 female), who had a first degree relative with a community clinical diagnosis of autism; elevated likelihood for ADHD (EL-ADHD; n=31; 19 male; 12 female), who had a first degree relative with a community clinical diagnosis of ADHD or a probable research diagnosis of ADHD, and elevated likelihood for both conditions (EL-autism+ADHD, n=21; 12 male; 9 female), which consisted

of the criteria of the previous two groups and diagnosed with both autism and ADHD; and lastly typical likelihood (TL; n= 29; 18 male; 11 female), who had at least one older sibling with typical development and no known autism or ADHD diagnosis in first-degree family members, which included the child's biological parents and full/half siblings (as confirmed through parent interviews regarding family medical history). Current analyses included infants who had at least one datapoint at the 10, 14, 24 or 36-month assessments, giving a final sample size of 161. See Table 1 for a breakdown of datapoints at each timepoint.

The Mullen Scales of Early Learning (MSEL; (Mullen, 1995)) and Vineland Adaptive Behaviour Scale-II (VABS-II; (Sparrow, Cicchetti, & Balla, 2005)) were administered at each visit. All toddlers were assessed at 24 and 36 months with the Autism Diagnostic Observation Schedule-2 (ADOS-2; (Lord et al., 2012)), and at 36 months parents were interviewed using the Autism Diagnostic Interview-Revised (ADI-R; (Lord, Rutter, & Le Couteur, 1994)). Best estimate DSM-5 clinical diagnosis of autism was made at age three informed by, but not dependent on outcomes from the ADOS-2, the ADI-R, the VABS-II, and MSEL scores by experienced researchers (TC, GP). 12 EL infants met the diagnostic criteria for autism at 36 months (9 in the EL-autism group, 3 in the EL-autism+ADHD group). All parents included in the study completed written informed consent before each visit.

#### Measures

Infant fearfulness was assessed with the fear subscale of the Infant Behaviour Questionnaire – Revised short form (IBQ-R; (Gartstein & Rothbart, 2003); fear subscale = 6 items) at 10 and 14 months and Early Childhood Behavioural Questionnaire – short form (ECBQ; (Putnam, Gartstein, & Rothbart, 2006); fear subscale = 8 items) at 24 months. The fear subscale measures infant/toddler distress or inhibited approach to novel social and non-social stimuli and higher fear scores in infancy are associated with greater child anxiety later in childhood (Gartstein et al., 2010; Shephard et al., 2019). Parents rated their child on how

often they exhibited certain behaviours in the previous 2-weeks. Items are scored on a Likert scale from 1 (Never) to 7 (Always). The IBQ-R is designed for infants aged 3–12 months and the ECBQ for children aged 18 to 36 months. Both measures are reliable and well-validated parent-report questionnaires (Gartstein & Rothbart, 2003; Tomlinson, Harbaugh, & Anderson, 1996). The reliability of the fear subscale of the IBQ-R and ECBQ in our sample was assessed using Cronbach's alpha, which showed good internal consistency ( $\alpha = 0.75 - 0.83$ ).

Infant sensory hyporeactivity and hyperreactivity were measured with the Infant Toddler Sensory Profile (ITSP; Dunn, 2002), a 48-item parent-caregiver questionnaire that measures sensory difficulties in children aged 7–36 months. Parents rate the frequency of their child's behaviour on a 5-point scale from 1 (almost always) to 5 (almost never). The ITSP scores assess sensory differences across five domains; auditory, visual, tactile, vestibular, and oral. Items are also grouped into four quadrants; low registration, sensation seeking, sensory sensitivity, and sensation avoiding. A composite low threshold score can be calculated by combining scores from the sensory sensitivity and sensation avoiding scales. Higher scores indicate the child shows less atypicality as compared to their peers. We used the total scores from the low registration quadrant as our index of hyporeactivity (11 items) and the total scores from the low threshold quadrant as our index of hyperreactivity (25 items) (Germani et al., 2014; Vlaeminck, Vermeirsch, Verhaeghe, Warreyn, & Roeyers, 2020).

The ITSP showed high internal consistence for hyporeactivity ( $\alpha = 0.81$  - 0.88 across 10, 14 and 24 months); and hyperreactivity ( $\alpha = 0.90$  - 0.91 across 10, 14 and 24 months). In the current sample, correlations between the quadrants of sensory sensitivity and sensation avoidance subscales that form the low threshold/hyperreactivity scale were strong at each timepoint (10 months: r = 0.834; 14 months: r = 0.807; 24 months: r = 0.812, all p < .001) (see Table S1).

As analyses focused on traits rather than diagnostic symptoms, we used the preschool version of Social Responsiveness Scale -2 (SRS-2; (Constantino & Gruber, 2012)) at 36 months to capture RRB (12 items) and SCI (53 items) traits. The SRS is a parent-rated questionnaire designed to measure autistic traits, consisting of 65 items, each rated on a 4-point scale ranging from 1 (Not True) to 4 (Almost Always True). In our sample, both subscales of RRB and SCI showed excellent internal consistency ( $\alpha$ =0.90 and  $\alpha$ =0.97 respectively).

#### Data Analysis

All analyses were run in Stata 16. Due to positive skewed distributions, the RRB and SCI variables were log transformed. For completeness, we present unadjusted correlation coefficients between all variables (see Table S2). To test our predicted hypotheses, 1) hyperreactivity will be associated with infant fearfulness, 2) hyperreactivity and infant fearfulness would be associated with RRB, 3) effects of hyperreactivity on infant fearfulness and RRB would remain with the inclusion of hyporeactivity, and 4) we would see a specific path from hyporeactivity to SCI, two cross-lagged structural equation models were estimated using maximum likelihood to account for missing data, and robust standard errors were used to correct for any residual skew in RRB/SCI scores. Model 1 examined the direction of longitudinal associations between each timepoint of fear, hyperreactivity and later RRB and SCI (Figure 1). To test the specificity of the associations with hyperreactivity we re-ran Model 1, but also included measurement of hyporeactivity at 10, 14, and 24 months (Model 2; Figure 2). All models were adjusted for sex and group. Sex was included to account for actual sexdifferences in reactivity, and potential gender-based differences in how parents rate their children's behaviour. Group status was accounted for by entering two binary variables (EL-Autism present/absent; EL-ADHD present/absent) as predictors of all variables in the model. We also specified an interaction between the two likelihood groups, but all interaction terms

were non-significant and therefore not included in final models. We also ran additional follow-up sensitivity analyses to better understand the role of ADHD family history and co-occurring ADHD traits. This involved 1) excluding EL-ADHD infants and 2) including ADHD traits at 36 months (Child Behaviour Checklist (CBCL) ADHD subscale) as an outcome that correlated with SCI and RRB. We report unstandardised (B) and standardised ( $\beta$ ) coefficients. As an additional robustness check, we used the Wald test to test whether constraining all significant coefficients to zero (i.e., leaving out these predictor variables) significantly reduced the fit of the model (conceptually equivalent to a Likelihood Ratio test for nested models). A significant p value indicates that the selected coefficients are not simultaneously equal to zero, meaning that including these paths create a statistically significant improvement in the fit of the model.

#### **Results**

Sample characteristics and likelihood group comparisons are shown in Table 1.

Model 1: Bidirectional associations between fear and hyperreactivity from 10 to 24 months and later autism traits at 36 months

The model fit was good ( $\chi^2$  = 1.73, p = .422, CFI = 1.00, TLI = 1.01). The Wald test of combined coefficients was significant ( $\chi^2$  = 394.01, p < .001). There was within-domain continuity for both constructs (see Figure 1, Table 2). As predicted, there was a negative association between hyperreactivity at 14 months and fear at 24 months (B = -0.04,  $\beta$  = -0.46, p < 0.001), with the negative scoring of the ITSP indicating that greater hyperreactivity was associated with higher levels of fear. Higher hyperreactivity at 14 months was also associated with higher SCI (B = -0.02,  $\beta$  = -0.33, p = .04) but not RRB (B = -0.02,  $\beta$  = -0.23, p = .14) at 36 months. Higher hyperreactivity at 24 months was significantly associated with higher RRB (B = -0.02,  $\beta$  =

0.30, p = .02) and SCI (B = -0.02,  $\beta = -0.35$ , p < .01) at 36 months. There was a concurrent positive association between RRB and SCI at 36 months (B = 0.16,  $\beta = .52$ , p < .001). All other pathways were non-significant (see Figure 1).

As the association between hyperreactivity and fear was in the opposite direction to our previously published results in an independent infant-sibling cohort (where we found higher infant fear predicted enhanced perceptual sensitivity), to better understand the drivers of opposing results, we ran a comparable model using the same variables as in our previous work in the current sample. Results from modelling perceptual sensitivity (our previous marker of sensory reactivities) and fear/shyness (to mirror our previously used subscales) in the current cohort showed a negative association at the threshold of statistical significance between perceptual sensitivity at 14 months and shyness at 24 months, such that higher perceptual sensitivity at 14 months was associated with lower shyness at 24 months ( $\beta = -.19$ , p = .055). (see Figure S1). However, when we accounted for differences in the presence of ADHD family history between previous and current samples by excluding EL-ADHD infants (the previous cohort only recruited TL and EL-autism infants) this path became non-significant ( $\beta = -.13$ , p = .30) (see Figure S2). We also noted a significant drop in within-domain continuity for perceptual sensitivity between 14 and 24 months, regardless of the inclusion of EL-ADHD infants, which contrasted to the strong within-domain continuity observed for hyperreactivity in the current analyses. Based on these results, we infer that perceptual sensitivity may not be a stable measure across time points or cohorts, or that the transition from the IBQ to the ECBQ at 14 to 24 months impacted our ability to capture the same underlying construct over developmental time.

Given the lack of association between fear and RRB in our primary analysis was also unexpected (and goes against previous reports of associations between infant manifestations of anxiety and autism traits in a comparable developmental period; Ersoy et al., 2021), we ran an

additional supplementary model testing whether fear in isolation (e.g., removing measurements of hyperreactivity from the model) predicted autistic traits (see Figure S3). We found fear at 24 months was positively associated with both RRB (B = 0.41,  $\beta$  = .42, p < .001) and SCI (B = 0.28,  $\beta$  = .43, p < .001) at 36 months, suggesting these associations may be in part driven by unmeasured effects of hyperreactivity.

#### Model 2: Analyses testing specificity of hyperreactivity effects

When we included hyporeactivity measured at 10, 14 and 24 months as an additional variable in the model (see Figure 2), the model fit was good ( $\chi^2 = 7.33$ , p = .292, CFI = .99, TLI = .98). The Wald test of combined coefficients was significant ( $\chi^2 = 536.28$ , p < .001). Cross-lagged paths indicated higher hyperreactivity at 14 months remained associated with higher fear at 24 months (B = -0.04,  $\beta$  = -0.48, p = .002), and higher hyperreactivity at 14 months was also associated with higher hyporeactivity at 24 months (B = 0.16,  $\beta$  = 0.29, p = .01). Higher hyporeactivity at 24 months was significantly associated with higher RRB (B = -0.04,  $\beta$  = -0.30, p = .001) and SCI (B = -0.03,  $\beta = -0.32, p < .001$ ) at 36 months, and the paths from hyperreactivity at 24 months to RRB and SCI at 36 months both became non-significant (B = -0.01,  $\beta = -0.15$ , p = .21; B = 0.00,  $\beta = -0.11$ , p = .37 respectively). Higher hyporeactivity at 14 months was also associated with increased SCI (B = -0.03,  $\beta$  = -0.31, p < .01). The concurrent positive association between RRB and SCI at 36 months remained (B = 0.12,  $\beta$  = .47, p < .001). All other pathways were non-significant (see Figure 2 and Table 3). As an additional check, we excluded the two items from the low registration quadrant (our metric of hyporeactivity) that had clear overlap with autistic traits/symptomatology (Item 13 "It takes a long time for my child to respond to his/her name when it is called", Item 16 "My child avoids eye contact with me") (9 items total using this revised scoring) to prevent contamination when seeking to look at paths from hyporeactivity to later autistic traits. Results from the model using this amended scoring were largely unchanged (see Figure S4).

Sensitivity Analyses Accounting for ADHD Family History and Traits

First, we ran a sensitivity analysis excluding EL-ADHD infants to check that main findings were not only driven by the sub-group of infants with a family likelihood of ADHD (see Models S5 and S6, akin to Model 1 and Model 2). Model S5 largely replicates the paths found in Model 1, in that higher 14-month hyperreactivity is associated with higher 24-month fear ( $\beta$  = -.49, p < .001), and 24-month hyperreactivity remains associated with SCI ( $\beta$  = -.39, p = .001) and RRB with similar coefficient of effect, although at a trend level of significance ( $\beta$  = -.29, p = .06). Model S6, where we include hyporeactivity, again mostly replicates Model 2, in that higher 14-month hyperreactivity is associated with higher 24 months fear ( $\beta$  = -.50, p = .01) and higher 24 months hyporeactivity respectively ( $\beta$  = .31, p = .02), and higher 24-month hyporeactivity is associated with greater 36-month SCI and RRB ( $\beta$  = -.32, p < .001,  $\beta$  = -.24, p = .02 respectively). One new path became statistically significant; higher fear at 14 months was associated with higher SCI at 24 months ( $\beta$  = .28, p = .01), although the standardized coefficient of effect was similar to models run on the full sample ( $\beta$  = .19, p = .07).

Next, in the full sample, we then ran a second sensitivity analysis where we included ADHD traits (CBCL-ADHD subscale) as correlated outcome at 36 months (see Models S7 and S8, again akin to Model 1 and Model 2). When ADHD traits were included as well as autism traits at 36 months, the pattern of associations between 24-month fear, hyporeactivity and hyperreactivity and later SCI and RRB remained unchanged, but additional associations were identified between hyperreactivity at 10 months and hyporreactivity at 10 and 24 months with ADHD traits at 36 months. Thus, we found no clear evidence that unmeasured ADHD was driving observed associations with autistic traits, but it is possible that unmeasured ADHD could be masking some significant pathways that contribute to observed associations.

Finally, we re-ran Model 1 and 2 using a subset of IBQ/ECBQ items from the Fear and Shyness subscales that were more closely matched to check that differences in construct measurement between the two versions of the questionnaire was not driving the pattern of results (see Table S3 for item matching, Figures S9 and S10 for results). Results were unchanged, with a marginal increase in within-domain continuity for Fear/Shyness.

#### **Discussion**

The current paper examined the developmental correlates of alterations in sensory reactivity on infant fearfulness and autistic traits in the first three years of life. Results showed a pathway from 14-month hyperreactivity to 24-month infant fearfulness, in line with previous research, which found sensory over-responsivity was positively associated with anxiety one year later in a cohort of toddlers with a similar age to our later time points (mean age of 28 months upon study entry) (Green et al., 2012). The anxiety measure used by Green and colleagues (General Anxiety subscale of the ITSEA) includes items that tap fearfulness, similar to the current work, but also items that index more compulsive and ritualistic type behaviours. We also found that greater hyperreactivity at 14 months was associated with higher levels of SCI at 36 months, and greater hyperreactivity at 24 months was longitudinally associated with both more RRB and SCI traits at 36 months. When hyporeactivity was included in the model to assess specificity of effects, pathways between hyperreactivity and fear remained, but paths from hyperreactivity to SCI and RRB became non-significant, suggesting unmeasured hyporeactivity may have been driving observed effects. Thus, to comprehend the developmental pathways to autism and specificity of effects, we need to take into account different types of sensory reactivities.

The relationship between hyperreactivity, infant fearfulness and autistic traits

Our cross-lag models of infant fearfulness and hyperreactivity measured at 10, 14 and 24 months found associations between greater 14-month hyperreactivity and later fearfulness.

This is in contrast to our previous report (Narvekar et al., 2022), where we found a path in the reverse direction between 14-month fearfulness and 24-month perceptual sensitivity (conceptually similar to hyperreactivity). Our additional supplementary analyses, using the same measures as in our previous work (i.e., moving from the ITSP hyperreactivity to the IBQ-R perceptual sensitivity subscale), did not replicate the fearfulness-sensitivity path in this new sample. This lack of replication, and the fact that other studies with overlapping age ranges (Green et al., 2012), including current results, report the opposite direction of effect, indicates that further work is needed to probe generalisability; factors that could have impacted our ability to replicate previously reported effects include moving from pure ELautism cohorts to other groups enriched for other atypical neurodevelopmental outcomes, in addition to unobserved differences in sample ascertainment and possible lack of stability in perceptual sensitivity measure with age. Finally, we note when we re-ran models with a novel fear/shyness subscale based on the subset of items that were more clearly matched between the IBQ and ECBQ, we found a decrease in the standardized coefficient for the association between 14 months hyperreactivity and 24 months fear/shyness (e.g.,  $\beta = -.28$  in item-matched Model S9 vs.  $\beta = -.46$  in original Model 1). This change in coefficient suggests that the large effect may in part reflect incomplete adjustment of early fear/shyness levels due to a change in measure to match developmental level (although the effect remains relatively large in the item-matched models).

Although within diagnostic manuals sensory reactivities are included in the RRB domain, we found pathways from hyperreactivity to RRB *and* SCI. Some report evidence of specific associations between hyperreactivity and RRB (Black et al., 2017; Boyd et al., 2010; Chen, Sideris, Watson, Crais, & Baranek, 2022; Schulz & Stevenson, 2019), others report hyperreactivity also predicts social difficulties (Feldman et al., 2021; Wolff et al., 2019), including our own previous work on perceptual sensitivity (Narvekar et al., 2022). The degree

to which hyperreactivity truly only impacts RRB remains unclear; current diagnostic frameworks may have inadvertently encouraged researchers to primarily consider the mechanisms by which atypical sensory reactivity can lead to RRB, rather than autistic traits more broadly. It is worth noting here the wide range of phenomena that fall under the umbrella term of atypical sensory differences (e.g., sensitivity, reactivity, and/or responsivity) (He et al., 2022). More precise definition of levels of meaning and measurement will support generation of empirical mechanistic hypotheses linking sensory reactivity to different domains of autism characteristics.

One interpretation of the observed path from hyperreactivity to RRB is that RRB represent a coping mechanism to regulate states of high arousal associated with fear and anxiety (Vlaeminck et al., 2020). If this was the case, we might also expect to see associations between infant fearfulness and RRB, such that fearfulness acts as a mediator between hyperreactivity and RRB (as in Wigham et al., 2015). However, in contrast to previous studies (Ersoy et al., 2020; Narvekar et al., 2022; Shephard et al., 2019), we did not find significant paths from infant fearfulness to RRB. One explanation is that these latter studies (Ersoy et al., 2020; Narvekar et al., 2022; Shephard et al., 2019) did not include a specific measure of hyperreactivity, and observed relations between fearfulness and RRB could thus reflect unmeasured hyperreactivity. In support of this hypothesis, our supplementary analyses (Figure S3) showed when we removed hyperreactivity from the model, we recover the association from infant fearfulness to later autism traits. The lack of path from fearfulness to RRB when we include hyperreactivity in the model suggests that at least at this developmental stage, RRB may not function as coping mechanism for high levels of fearfulness. It may be that over time, being more reactive leads to anxiety about encountering situations with aversive sensory stimuli in the future, but also use of RRB to manage in-the-moment arousal. Measures that can separate arousal from anticipatory anxiety and avoidance behaviours, and moment-tomoment dynamic data including direct capture of arousal, are required to test this working hypothesis. These analyses highlight the importance of carefully constructed multivariate analyses that can capture the different aspects of complex developmental systems present in the early infant period.

#### The specificity of hyperreactivity effects

We next examined whether the effects of hyperreactivity on infant fearfulness and autistic traits were specific to this type of sensory atypicality, or whether they were shared with hyporeactivity. As it is known that different types of atypical sensory reactivities are correlated, even within a given individual (Elwin, Ek, Kjellin, & Schröder, 2013; Niedźwiecka et al., 2019; Tillmann et al., 2020), it is important to include multiple types of sensory atypicalities in analytic models. When we also included hyporeactivity in our cross-lag models, we found strong bivariate correlations between hyporeactivity and hyperreactivity, in line with the idea that individuals who experience hyporeactivity are also more likely to experience hyperreactivity. However, the effect of hyperreactivity on fearfulness appeared relatively specific; no paths were seen from hyporeactivity to fearfulness, and hyperreactivity effects remained even in multivariate models. Thus, even though hyporeactivity and hyperreactivity share high variance, there may be specific variation in hyperreactivity that raises the likelihood of fearfulness. Since infant fearfulness has been proposed as an early precursor of child anxiety (Gartstein et al., 2010; Shephard et al., 2019), this is in keeping with recent conceptualisations of 'sensory over responsivity' as a transdiagnostic risk factor for anxiety that is present even in typically developing populations (Carpenter et al., 2019; Schwarzlose et al., 2022). The current results demonstrate this may be true even in the first year of life, and much like the developmental cascade framework (Bradshaw et al., 2022), it is important to better understand the mechanisms by which heightened sensory reactivity increases anxiety, in order to develop targeted (and thus effective) support.

When considering the associations between hyperreactivity and later autism traits, when hyporeactivity was included in the model it was found to be predictive of later RRB and SCI, and associations with hyperreactivity became non-significant. This pattern is different to results from a recent general population study which found even when hyperreactivity and hyporeactivity were both included as predictors of autism traits, hyperreactivity was still predictive of RRB (Chen et al., 2022). There are multiple possible interpretations of these findings. One possible explanation may be that hyporeactivity is on the pathway to autism outcomes, but hyperreactivity is not, and the latter is more relevant for understanding cooccurring features such as anxiety. Alternatively, it could be that the hyporeactivity scale used in the current study is capturing features of early autism, and that is why it 'trumps' the effects of hyperreactivity. Indeed, inspection of the ITSP hyporeactivity subscale suggests some items are very similar to the types of early social communication difficulties that are characteristic of autism. However, when we run the same model with a revised version of the ITSP hyporeactivity subscale, where we remove two items that most clearly overlap with the early autism phenotype ('it takes a long time for my child to respond to his/her name when it is called', 'my child avoids eye contact with me') from the scale to minimize construct overlap. (shown in Supplementary Figure S4), we found most associations remained the same, including those between hyporeactivity and later autistic traits. This question of measurement relates to wider debates about what is a marker or manifestation of autism early in the developmental pathway, and what are factors that are causally involved in the aetiology of autism and associated characteristics. Unpicking these two possibilities is challenging; analytic models that can test directionality of within-person associations between aspects of sensory reactivity and autistic traits (Hamaker, Kuiper, & Grasman, 2015; Mund & Nestler, 2019), or delineate stability and change in statistically-defined classes of symptoms (McCulloch, Lin, Slate, &

Turnbull, 2002), may help. Precise measurement of proposed markers/likelihood factors as compared to clinical outcomes is critical.

Finally, we note that additional supplementary analyses found that when ADHD traits were included as well as autism traits at 36 months, the pattern of associations between 24-month fear, hyporeactivity and hyperreactivity and later SCI and RRB remained unchanged. Thus, we found no clear evidence that co-occurring ADHD traits were driving observed associations with autistic traits, despite the SRS and other autism measures being confounded with other neurodevelopmental traits, including ADHD (as noted by Grzadzinski et al., 2011; Havdahl et al., 2016). One possibility is given the earlier age of autism onset than ADHD, the SRS may be less likely to be confounded at this young age. On the other hand, it appears that certain sensory reactivity measures that predicted autistic traits also predicted ADHD traits i.e., hyperreactivity at 24 months. Interestingly, the fact that when we include hyporeactivity in models with ADHD traits, this also 'overrides' previously observed associations from hyperreactivity, suggests the similar override effect to autistic traits is likely not solely due to our measure of hyporeactivity being contaminated with autism traits. Overall, our additional sensitivity analyses suggest the observed associations with autistic traits are unlikely to be purely due to the presence of unmeasured ADHD, and some associations were shared between autistic and ADHD traits. These findings highlight that sensory differences may function in a transdiagnostic manner and as such may not be specific to autism traits (Scheerer et al., 2022), although we also found some evidence of a limited number of specific associations (e.g., 10month hyperreactivity and hyporeactivity to ADHD only).

Lastly, it is important to consider the implications of these findings for the broader infant population. One interpretation consistent with our findings is that alterations in early sensory reactivity may increase the likelihood of showing fearfulness in infancy, and presage later social interactions and repetitive behaviours, particularly in individuals with a family history of autism or ADHD. Moreover, sensory differences are not exclusive to autism and ADHD; they may be a common feature of the neurodevelopmental pathways to a number of neurodevelopmental conditions (Baranek et. al., 2013; Posar & Visconti, 2018).

#### Strengths and Limitations

This study has several strengths. Although the field of autism research, and psychological research more broadly, often highlights the importance of replication (Asendorpf et al., 2016; Nosek et al., 2022), published examples are relatively lacking. We show here the value in replication and transparency, in terms of gauging the generalisability of past results, and the importance of variation in both measurement and sample design. We also collected detailed and repeated measurement of different aspects of sensory reactivity within a prospective longitudinal design. Most studies examine different aspects of sensory reactivity in isolation; our approach allows us to move towards a more precise mechanistic understanding of how differences in reactivity of incoming sensory input contribute to different types of autistic behaviours and mental health difficulties. However, we also acknowledge important limitations; all data was based on parent report, resulting in the possibility of shared method variance contributing to results. Additionally, even though we removed the two ITSP hyporeactivity items with the clearest overlap with the early autism phenotype, other items may overlap with early autistic social communication features. How we measure sensory differences independently from other autistic characteristics is a challenge for the field more broadly, and may require development of new measures in the future. Observational and experimental measures may be of use here (Baranek et al., 2018; Tavassoli et al., 2019). Additionally, we recognize that the lack of uniform measures across various time periods, even if it is meant to ensure that the questions are suitable for a specific age group, may be considered a limitation. Agreement in the field as to appropriate instruments that capture relevant constructs and can be used in a comparable manner across a broad developmental range is required to support use of more advanced statistical models (e.g., random intercept cross lag panel models) and thus strengthen inference. Regardless of the change in questionnaire, we found within-domain continuity in all our constructs, indicating that the change in measurement scales did not have a large influence on our findings.

#### Conclusions

The results from this study have important methodological and clinical implications. First, hyperreactivity in early infancy may be one of clearest predictors of fearfulness in infancy, and thus may offer a potential target for future interventions. Second, the direction of relation between sensory atypicalities and early fearfulness appeared to vary across cohorts, highlighting the importance of replication studies and the need to carefully consider sample composition in infant-sibling studies. Third, it is crucial to measure independent but correlated aspects of sensory atypicalities, and include them in the same analytic model, to understand shared versus distinct mechanisms. An important goal for future studies is to unpick how these alterations in sensory reactivity translate to challenges in child development, with a focus on later anxiety.

### Key Points

- Most research on sensory reactivity does not account for the fact that different types of sensory atypicality often co-occur.
- We find a specific association between sensory hyperreactivity in early infancy and later fearfulness, even when accounting for the co-occurrence of hyperreactivity and hyporeactivity.
- Although there was some evidence hyperreactivity was associated with later autism traits,
   this appears to be driven by the co-occurrence with hyporeactivity.
- Results suggest alterations in different domains of sensory reactivity may have differential developmental consequences.

Acknowledgments: We gratefully thank all the families who took part in this study, and researchers who helped with data collection and recruitment; Kim Davies, Janice Fernandes, Marian Greensmith, and Natalie Vaz. The authors would also like to thank the placement students Fatima Saleh, Chelsea Nolan, Irina Guliaeva, Zoe Freeman who helped in data collection. The STAARS team consists of: Mary Agyapong, Tessel Bazelmans, Leila Dafner, Mutluhan Ersoy, Teodora Gliga, Amy Goodwin, Rianne Haartsen, Hanna Halkola, Alexandra Hendry, Rebecca Holman, Sarah Kalwarowsky, Anna Kolesnik, Leyan Li, Luke Mason, and Chloë Taylor.

#### **Author Contributions**

N.N., V.C.L., E.J. and T.C. developed the study concept and design. STAARS teams collected the data. N.N., and V.C.L. performed the data analysis and interpretation under the supervision of G.P., J.B.A, T.C., M.H.J. and E.J. N.N. and V.C.L. drafted the manuscript, and all authors provided critical revisions and approved the final version of the manuscript.

Funding: This research was supported by the Medical Research Council (MR/K021389/1, MR/T003057/1) and capital equipment funding from the Maudsley Charity (980) and Guy's and St Thomas' Charity (STR130505). V.C.L. is supported by a Henry Wellcome Postdoctoral Fellowship (213608/Z/18/Z). The results leading to this publication have received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777394 for the project AIMS-2-TRIALS. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA and AUTISM SPEAKS, Autistica, SFARI. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results. Any views expressed are those of the authors and not necessarily those of the funders (IHI-JU2). For the purpose of open access, the author has applied a Creative Commons Attribution (CC BY) licence to any Author Accepted Manuscript version arising.

**Conflicts of Interest:** TC has served as a paid consultant to F. Hoffmann-La Roche Ltd. and Servier; and has received royalties from Sage Publications and Guilford Publications. MHJ has received book royalties from Wiley-Blackwell, Oxford University Press, and MIT Press.

**Ethical Approval and informed consent:** Ethical approval was granted by the National Research Ethics Service (13/LO/0751) and the Research Ethics Committee, Department of Psychological Sciences, Birkbeck, University of London.

Corresponding author: Nisha Narvekar, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London SE5 8AF, UK. Email: Nisha.narvekar@kcl.ac.uk.

#### References

- American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (DSM-5)
- Antshel, K. M., & Russo, N. (2019). Autism Spectrum Disorders and ADHD: Overlapping Phenomenology, Diagnostic Issues, and Treatment Considerations. *Current Psychiatry Reports*, 21(5), 34. doi:10.1007/s11920-019-1020-5
- Asendorpf, J. B., Conner, M., De Fruyt, F., De Houwer, J., Denissen, J. J., Fiedler, K., . . . Nosek, B. A. (2016). Recommendations for increasing replicability in psychology.
- Baranek, G. T., Watson, L. R., Boyd, B. A., Poe, M. D., David, F. J., & McGuire, L. (2013). Hyporesponsiveness to social and nonsocial sensory stimuli in children with autism, children with developmental delays, and typically developing children. *Development and Psychopathology*, 25(2), 307-320.
- Baranek, G. T., Woynaroski, T. G., Nowell, S., Turner-Brown, L., DuBay, M., Crais, E. R., & Watson, L. R. (2018). Cascading effects of attention disengagement and sensory seeking on social symptoms in a community sample of infants at-risk for a future diagnosis of autism spectrum disorder. *Developmental cognitive neuroscience*, 29, 30-40.
- Begum-Ali, J., Goodwin, A., Mason, L., Pasco, G., Charman, T., Johnson, M. H., . . . Team, t. S. (2022). Altered theta—beta ratio in infancy associates with family history of ADHD and later ADHD-relevant temperamental traits. *Journal of Child Psychology and Psychiatry*, 63(9), 1057-1067. doi:https://doi.org/10.1111/jcpp.13563
- Black, K. R., Stevenson, R. A., Segers, M., Ncube, B. L., Sun, S. Z., Philipp-Muller, A., . . . Ferber, S. (2017). Linking Anxiety and Insistence on Sameness in Autistic Children: The Role of Sensory Hypersensitivity. *J Autism Dev Disord*, 47(8), 2459-2470. doi:10.1007/s10803-017-3161-x
- Boyd, B. A., Baranek, G. T., Sideris, J., Poe, M. D., Watson, L. R., Patten, E., & Miller, H. (2010). Sensory features and repetitive behaviors in children with autism and developmental delays. *Autism Research*, *3*(2), 78-87. doi:https://doi.org/10.1002/aur.124
- Bradshaw, J., Schwichtenberg, A. J., & Iverson, J. M. (2022). Capturing the complexity of autism: Applying a developmental cascades framework. *Child Dev Perspect*, 16(1), 18-26. doi:10.1111/cdep.12439
- Carpenter, K. L., Baranek, G. T., Copeland, W. E., Compton, S., Zucker, N., Dawson, G., & Egger, H. L. (2019). Sensory over-responsivity: An early risk factor for anxiety and behavioral challenges in young children. *J Abnorm Child Psychol*, 47(6), 1075-1088.
- Chen, Y. J., Sideris, J., Watson, L. R., Crais, E. R., & Baranek, G. T. (2022). Developmental trajectories of sensory patterns from infancy to school age in a community sample and associations with autistic traits. *Child Dev.* doi:10.1111/cdev.13745
- Constantino, J., & Gruber, C. P. (2012). *Social responsiveness scale: SRS-2*: Western Psychological Services Torrance, CA.
- Crane, L., Goddard, L., & Pring, L. (2009). Sensory processing in adults with autism spectrum disorders. *Autism*, *13*(3), 215-228. doi:10.1177/1362361309103794
- Dunn, W. (2002). The infant toddler sensory profile. San Antonio, TX: Psychological Corporation
- Elwin, M., Ek, L., Kjellin, L., & Schröder, A. (2013). Too much or too little: Hyper-and hypo-reactivity in high-functioning autism spectrum conditions. *Journal of intellectual & developmental disability*, 38(3), 232-241.

- Ersoy, M., Charman, T., Pasco, G., Carr, E., Johnson, M. H., & Jones, E. J. (2020). Developmental paths to anxiety in an Autism-enriched infant cohort: the role of temperamental reactivity and regulation. *J Autism Dev Disord*, 1-15.
- Feldman, J. I., Raj, S., Bowman, S. M., Santapuram, P., Golden, A. J., Daly, C., . . . Woynaroski, T. G. (2021). Sensory Responsiveness Is Linked With Communication in Infant Siblings of Children With and Without Autism. *J Speech Lang Hear Res*, 64(6), 1964-1976. doi:10.1044/2021 JSLHR-20-00196
- Gartstein, M., Bridgett, D. J., Rothbart, M. K., Robertson, C., Iddins, E., Ramsay, K., & Schlect, S. (2010). A latent growth examination of fear development in infancy: Contributions of maternal depression and the risk for toddler anxiety. *Developmental Psychology*, 46(3), 651.
- Gartstein, M., & Rothbart, M. K. (2003). Studying infant temperament via the revised infant behavior questionnaire. *Infant Behavior and Development*, 26(1), 64-86.
- Germani, T., Zwaigenbaum, L., Bryson, S., Brian, J., Smith, I., Roberts, W., . . . Vaillancourt, T. (2014). Brief report: assessment of early sensory processing in infants at high-risk of autism spectrum disorder. *J Autism Dev Disord*, *44*(12), 3264-3270. doi:10.1007/s10803-014-2175-x
- Gotham, K., Bishop, S. L., Hus, V., Huerta, M., Lund, S., Buja, A., . . . Lord, C. (2013). Exploring the relationship between anxiety and insistence on sameness in autism spectrum disorders. *Autism Research*, 6(1), 33-41.
- Green, S. A., Ben-Sasson, A., Soto, T. W., & Carter, A. S. (2012). Anxiety and sensory over-responsivity in toddlers with autism spectrum disorders: bidirectional effects across time. *J Autism Dev Disord*, 42(6), 1112-1119. doi:10.1007/s10803-011-1361-3
- Grzadzinski, R., Di Martino, A., Brady, E., Mairena, M. A., O'Neale, M., Petkova, E., . . . Castellanos, F. X. (2011). Examining autistic traits in children with ADHD: does the autism spectrum extend to ADHD? *J Autism Dev Disord*, 41(9), 1178-1191. doi:10.1007/s10803-010-1135-3
- Grzadzinski, R., Donovan, K., Truong, K., Nowell, S., Lee, H., Sideris, J., . . . Watson, L. R. (2020). Sensory Reactivity at 1 and 2 Years Old is Associated with ASD Severity During the Preschool Years. *J Autism Dev Disord*, 1-10.
- Hamaker, E. L., Kuiper, R. M., & Grasman, R. P. (2015). A critique of the cross-lagged panel model. *Psychological Methods*, 20(1), 102.
- Havdahl, K. A., Hus Bal, V., Huerta, M., Pickles, A., Øyen, A.-S., Stoltenberg, C., . . . Bishop, S. L. (2016). Multidimensional Influences on Autism Symptom Measures: Implications for Use in Etiological Research. *Journal of the American Academy of Child & Adolescent Psychiatry*, 55(12), 1054-1063.e1053. doi:10.1016/j.jaac.2016.09.490
- He, J., Williams, Z., Harris, A., Powell, H., Schaaf, R., Tavassoli, T., & Puts, N. (2022). Working Taxonomy for Describing the Sensory Differences of Autism. *PsyArXiv*. doi:https://doi.org/10.31234/osf.io/jmv6k
- Jones, E. J., Dawson, G., & Webb, S. (2018). Sensory hypersensitivity predicts enhanced attention capture by faces in the early development of ASD. *Developmental cognitive neuroscience*, 29, 11-20.
- Kapp, S. K., Steward, R., Crane, L., Elliott, D., Elphick, C., Pellicano, E., & Russell, G. (2019). 'People should be allowed to do what they like': Autistic adults' views and experiences of stimming. *Autism*, 23(7), 1782-1792.
- Kirby, A. V., Bilder, D. A., Wiggins, L. D., Hughes, M. M., Davis, J., Hall-Lande, J. A., . . . Bakian, A. V. (2022). Sensory features in autism: Findings from a large population-based surveillance system. *Autism Res, 15*(4), 751-760. doi:10.1002/aur.2670

- Lidstone, J., Uljarevic, M., Sullivan, J., Rodgers, J., McConachie, H., Freeston, M., . . . Leekam, S. (2014). Relations among restricted and repetitive behaviors, anxiety and sensory features in children with autism spectrum disorders. *Research in Autism Spectrum Disorders*, 8(2), 82-92. doi:10.1016/j.rasd.2013.10.001
- Lord, C., Rutter, M., DiLavore, P., Risi, S., Gotham, K., & Bishop, S. (2012). (ADOS®-2) autism diagnostic observation schedule<sup>TM</sup> Second edition. (ADOS®-2) Autism Diagnostic Observation Schedule.
- Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev Disord*, 24(5), 659-685.
- Marco, E. J., Khatibi, K., Hill, S. S., Siegel, B., Arroyo, M. S., Dowling, A. F., . . . Nagarajan, S. S. (2012). Children with autism show reduced somatosensory response: an MEG study. *Autism Research*, *5*(5), 340-351.
- McCulloch, C. E., Lin, H., Slate, E. H., & Turnbull, B. W. (2002). Discovering subpopulation structure with latent class mixed models. *Statistics in Medicine*, *21*(3), 417-429. doi:https://doi.org/10.1002/sim.1027
- Mullen, E. M. (1995). Mullen scales of early learning: AGS Circle Pines, MN.
- Mund, M., & Nestler, S. (2019). Beyond the cross-lagged panel model: Next-generation statistical tools for analyzing interdependencies across the life course. *Advances in Life Course Research*, 41, 100249.
- Narvekar, N., Carter Leno, V., Pasco, G., Johnson, M. H., Jones, E. J., & Charman, T. (2022). A prospective study of associations between early fearfulness and perceptual sensitivity and later restricted and repetitive behaviours in infants with typical and elevated likelihood of autism. *Autism*, 13623613211068932. doi:10.1177/13623613211068932
- Niedźwiecka, A., Domasiewicz, Z., Kawa, R., Tomalski, P., & Pisula, E. (2019). Sensory Processing in toddlers with autism spectrum disorders. *European Journal of Developmental Psychology*.
- Nijmeijer, J. S., Minderaa, R. B., Buitelaar, J. K., Mulligan, A., Hartman, C. A., & Hoekstra, P. J. (2008). Attention-deficit/hyperactivity disorder and social dysfunctioning. *Clin Psychol Rev*, 28(4), 692-708. doi:10.1016/j.cpr.2007.10.003
- Nosek, B. A., Hardwicke, T. E., Moshontz, H., Allard, A., Corker, K. S., Dreber, A., . . . Nuijten, M. B. (2022). Replicability, robustness, and reproducibility in psychological science. *Annual review of psychology*, 73, 719-748.
- Nowell, S. W., Watson, L. R., Crais, E. R., Baranek, G. T., Faldowski, R. A., & Turner-Brown, L. (2020). Joint Attention and Sensory-Regulatory Features at 13 and 22 Months as Predictors of Preschool Language and Social-Communication Outcomes. *J Speech Lang Hear Res*, 63(9), 3100-3116. doi:10.1044/2020\_JSLHR-20-00036
- Posar, A., & Visconti, P. (2018). Sensory abnormalities in children with autism spectrum disorder. *Jornal de pediatria*, *94*, 342-350.
- Putnam, S. P., Gartstein, M., & Rothbart, M. K. (2006). Measurement of fine-grained aspects of toddler temperament: The Early Childhood Behavior Questionnaire. *Infant Behavior and Development*, 29(3), 386-401.
- Rodgers, J., Glod, M., Connolly, B., & McConachie, H. (2012). The relationship between anxiety and repetitive behaviours in autism spectrum disorder. *J Autism Dev Disord*, 42(11), 2404-2409.
- Ronald, A., Larsson, H., Anckarsäter, H., & Lichtenstein, P. (2014). Symptoms of autism and ADHD: A Swedish twin study examining their overlap. *Journal of abnormal psychology*, 123, 440-451. doi:10.1037/a0036088

- Ronald, A., Simonoff, E., Kuntsi, J., Asherson, P., & Plomin, R. (2008). Evidence for overlapping genetic influences on autistic and ADHD behaviours in a community twin sample. *Journal of Child Psychology and Psychiatry*, 49(5), 535-542.
- Sacrey, L.-A. R., Zwaigenbaum, L., Bryson, S., Brian, J., Smith, I. M., Roberts, W., . . . Novak, C. (2015). Can parents' concerns predict autism spectrum disorder? A prospective study of high-risk siblings from 6 to 36 months of age. *Journal of the American Academy of Child & Adolescent Psychiatry*, 54(6), 470-478.
- Scheerer, N. E., Pourtousi, A., Yang, C., Ding, Z., Stojanoski, B., Anagnostou, E., . . . Stevenson, R. A. (2022). Transdiagnostic Patterns of Sensory Processing in Autism and ADHD. *J Autism Dev Disord*. doi:10.1007/s10803-022-05798-3
- Schulz, S., Kelley, E., Anagnostou, E., Nicolson, R., Georgiades, S., Crosbie, J., . . . Stevenson, R. A. (2023). Sensory Processing Patterns Predict Problem Behaviours in Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder. *Advances in Neurodevelopmental Disorders*, 7(1), 46-58. doi:10.1007/s41252-022-00269-3
- Schulz, S., & Stevenson, R. A. (2019). Differentiating between sensory sensitivity and sensory reactivity in relation to restricted interests and repetitive behaviours. *Autism*, 1362361319850402. doi:10.1177/1362361319850402
- Schwarzlose, R. F., Tillman, R., Hoyniak, C. P., Luby, J. L., & Barch, D. M. (2022). Sensory Over-responsivity: A Feature of Childhood Psychiatric Illness Associated With Altered Functional Connectivity of Sensory Networks. *Biological psychiatry*.
- Shen, M. D., & Piven, J. (2022). Brain and behavior development in autism from birth through infancy. *Dialogues in clinical neuroscience*.
- Shephard, E., Bedford, R., Milosavljevic, B., Gliga, T., Jones, E. J. H., Pickles, A., . . . Charman, T. (2019). Early developmental pathways to childhood symptoms of attention-deficit hyperactivity disorder, anxiety and autism spectrum disorder. *J Child Psychol Psychiatry*, 60(9), 963-974. doi:10.1111/jcpp.12947
- Shephard, E., Zuccolo, P. F., Idrees, I., Godoy, P. B. G., Salomone, E., Ferrante, C., . . . Polanczyk, G. V. (2022). Systematic Review and Meta-analysis: The Science of Early-Life Precursors and Interventions for Attention-Deficit/Hyperactivity Disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, 61(2), 187-226. doi:10.1016/j.jaac.2021.03.016
- Sparrow, S., Cicchetti, D., & Balla, D. A. (2005). Vineland adaptive behavior scales second edition survey forms manual. *Circle Pines, MN: America Guidance Service*.
- Tavassoli, T., Brandes-Aitken, A., Chu, R., Porter, L., Schoen, S., Miller, L. J., . . . Marco, E. J. (2019). Sensory over-responsivity: parent report, direct assessment measures, and neural architecture. *Mol Autism*, 10(1), 1-10.
- Tillmann, J., Uljarevic, M., Crawley, D., Dumas, G., Loth, E., Murphy, D., . . . Charman, T. (2020). Dissecting the phenotypic heterogeneity in sensory features in autism spectrum disorder: a factor mixture modelling approach. *Mol Autism*, 11(1), 67. doi:10.1186/s13229-020-00367-w
- Tomlinson, P. S., Harbaugh, B. L., & Anderson, K. (1996). Children's temperament at 3 months and 6 years old: stability, reliability, and measurement issues. *Issues in Comprehensive Pediatric Nursing*, 19(1), 33-47.
- Tonnsen, B. L., Malone, P. S., Hatton, D. D., & Roberts, J. E. (2013). Early Negative Affect Predicts Anxiety, not Autism, in Preschool Boys with Fragile X Syndrome. *Journal of Abnormal Child Psychology*, 41(2), 267-280. doi:10.1007/s10802-012-9671-2
- Vlaeminck, F., Vermeirsch, J., Verhaeghe, L., Warreyn, P., & Roeyers, H. (2020). Predicting cognitive development and early symptoms of autism spectrum disorder in preterm children: The value of temperament and sensory processing. *Infant Behav Dev*, 59, 101442. doi:10.1016/j.infbeh.2020.101442

- Wigham, S., Rodgers, J., South, M., McConachie, H., & Freeston, M. (2015). The interplay between sensory processing abnormalities, intolerance of uncertainty, anxiety and restricted and repetitive behaviours in autism spectrum disorder. *J Autism Dev Disord*, 45(4), 943-952. doi:10.1007/s10803-014-2248-x
- Williams, K. L., Campi, E., & Baranek, G. T. (2021). Associations among sensory hyperresponsiveness, restricted and repetitive behaviors, and anxiety in autism: An integrated systematic review. *Research in Autism Spectrum Disorders*, 83, 101763.
- Wolff, J. J., Dimian, A. F., Botteron, K. N., Dager, S. R., Elison, J. T., Estes, A. M., . . . Network, I. (2019). A longitudinal study of parent-reported sensory responsiveness in toddlers at-risk for autism. *J Child Psychol Psychiatry*. doi:10.1111/jcpp.12978

**Table 1. Sample Characteristics** 

Mean (SD)	N	EL-autism	EL-	EL-	TL	Group	Direction of Effect
		N. 00	ADHD	autism+ADHD	<b>N. 0</b> 0	differences	
		N=80	N=31	N=21	N=29		
10 months							
Sex (n	149	38:38	12:14	8:12	11:16	p = .783	-
female:male)							
Age in months	149	10.03	10.23	10.15	10.00	p = .422	-
		(0.52)	(0.91)	(0.49)	(0.62)		
MSEL ELC	149	88.03	85.04	84.90	88.89	p = .660	-
		(15.09)	(15.61)	(16.55)	(12.19)		
IBQ-R Fear	123	3.67	3.03	3.77	3.14	p = .091	-
		(1.43)	(1.14)	(1.39)	(0.84)		
ITSP	127	44.98	48.13	45.24	46.18	p = .213	-
Hyporeactivity		(7.19)	(3.72)	(7.09)	(4.83)	_	
ITSP	128	93.75	95.65	93.57	95.98	p = .863	-
Hyperreactivity		(15.29)	(7.46)	(13.93)	(8.40)	-	
14 months							
Sex (n	138	35:38	7:16	7:12	10:13	p = .474	-
female: male)						•	
Age in months	138	14.30	14.22	14.37	14.26	p = .893	-
C		(0.64)	(0.80)	(0.60)	(0.62)	1	
MSEL ELC	139	78.2 <del>5</del>	79.08	72.53	78.78	p = .259	-
		(11.92)	(11.12)	(14.50)	(11.99)	-	
IBQ-R Fear	127	3.87	3.83	4.07	3.42	p = .485	-
~		(1.29)	(1.56)	(1.30)	(0.87)	•	
ITSP	129	45.35	45.50	43.74	47.87	p = .294	-
Hyporeactivity		(6.96)	(6.05)	(6.70)	(4.54)	-	
ITSP	129	92.41	93.56	89.28	94.82	p = .617	-
Hyperreactivity		(14.82)	(9.82)	(13.23)	(7.99)	•	

Sex (n female:male)	128	33:33	9:13	5:11	11:13	p = .565	-
Age in months	128	24.92 (1.55)	24.68 (1.09)	24.38 (0.72)	24.58 (1.14)	p = .420	-
MSEL ELC	125	100.63 (20.76)	106.86 (21.21)	96.94 (17.12)	114.25 (17.91)	p = .017	EL-autism, EL-autism+ADHD <tl< td=""></tl<>
ECBQ Fear	115	2.36 (1.11)	2.19 (0.78)	2.41 (1.15)	2.04 (0.59)	p = .570	-
ITSP Hyporeactivity	118	47.53 (7.12)	45.18 (6.86)	44.47 (8.40)	48.95 (3.15)	p = .140	-
ITSP Hyperreactivity	118	92.07 (14.83)	90.42 (14.33)	88.67 (18.57)	97.64 (8.63)	p = .251	-
ADOS CSS SA	127	3.32 (1.95)	2.95 (2.01)	4.13 (2.19)	2.29 (1.00)	p = .019	TL< EL-autism, EL-autism+ADHD
ADOS CSS RRB	127	3.53 (2.54)	4.05 (2.48)	2.88 (2.36)	2.79 (2.19)	p = .279	-
36 months		,			,		
Sex (n female:male)	119	33:28	11:12	5:11	7:12	p = .306	-
Age in months	119	37.21 (1.46)	37.35 (2.69)	37.19 (1.52)	36.79 (1.78)	p = .779	-
MSEL ELC	117	108.10 (18.53)	118.39 (18.83)	105.93 (19.90)	129.05 (11.75)	p < .001	EL-autism, EL-autism+ADHD < TL; EL-autism, EL-autism+ADHD
SRS RRB	107	5.48 (6.38)	4.05 (5.22)	9.00 (9.53)	1.16 (1.61)	p = .005	< EL-ADHD TL <el-autism, EL-autism+ADHD; EL-ADHD<el-autism+adhd< td=""></el-autism+adhd<></el-autism, 
SRS SCI	107	37.43 (26.66)	31.50 (19.41)	52.00 (40.10)	22.21 (8.78)	p = .013	TL <el-autism, el-adhd<el-autism+adhd<="" el-autism+adhd;="" td=""></el-autism,>
ADOS CSS SA	123	2.62 (1.90)	2.27 (1.58)	2.93 (1.44)	3.15 (1.98)	p = .425	-

ADOS CSS RRB	123	3.53 (2.46)	3.00 (2.58)	4.00 (2.67)	3.30 (2.41)	p = .666	-
ADI-R Social	122	3.89	2.55	5.69	0.94	p = .046	TL <el-autism+adhd< td=""></el-autism+adhd<>
ADI-R	122	(5.33) 3.53	(4.04) 1.55	(8.15) 3.38	(1.00) 0.67	p = .021	TL <el-autism,< td=""></el-autism,<>
Communication		(4.65)	(2.69)	(4.10)	(0.97)		EL-autism+ADHD; EL-ADHD <el-autism< td=""></el-autism<>
ADI-R RRB	122	1.42	0.73	1.69	0.39	p = .070	<u>-</u>
	<b>-</b>	(2.03)	(1.49)	(2.12)	(0.61)	F,	

34

ADI-R = Autism Diagnostic Interview-Revised; ADOS = Autism Diagnostic Observation Schedule; CSS = Composite Standard Score; ECBQ = Early Childhood Behavioural Questionnaire; IBQ-R = Infant Behavioural Questionnaire-Revised; ITSP= Infant Toddler Sensory Profile; MSEL ELC= Mullen Scales of Early Learning Early Learning; RRB = Restrictive and Repetitive Behaviours; SA = Social Affect; SCI = Social Communication Interactions; Difficulties; SD = Standard Deviation; SRS = Social Responsiveness Scale. Note: Group differences were tested using one-way ANOVAs with group as a between-subject factor, followed by uncorrected post-hoc pairwise comparisons of means.

Table 2 Model 1 with standardized coefficients

		b	p	[95% Confid	ence Interval	β
Fear 14m	Fear 10m	0.67	0.000	0.51	0.83	0.68
	Hyperreactivity 10m	0.00	0.799	-0.01	0.02	0.02
Fear 24m	Fear 14m	0.25	0.001	0.10	0.39	0.32
	Fear 10m	-0.05	0.534	-0.22	0.12	-0.07
	Hyperreactivity 14m	-0.04	0.000	-0.05	-0.02	-0.46
Hyperreactivity 14m	Fear 10m	-0.72	0.268	-2.00	0.56	-0.07
	Hyperreactivity 10m	0.76	0.000	0.64	0.88	0.77
Hyperreactivity 24m	Fear 14m	0.31	0.737	-1.50	2.13	0.03
	Hyperreactivity 10m	0.07	0.566	-0.16	0.29	0.06
	Hyperreactivity 14m	0.74	0.000	0.50	0.99	0.65
RRB 36m	Fear 14m	0.06	0.446	-0.10	0.22	0.08
	Fear 10m	-0.08	0.379	-0.25	0.10	-0.10
	Hyperreactivity 10m	0.00	0.633	-0.02	0.01	-0.06
	Fear 24m	0.12	0.209	-0.07	0.32	0.13
	Hyperreactivity 14m	-0.02	0.143	-0.04	0.01	-0.23
	Hyperreactivity 24m	-0.02	0.018	-0.04	0.00	-0.30
SCI 36m	Fear 14m	0.08	0.161	-0.03	0.18	0.15
	Fear 10m	-0.08	0.146	-0.19	0.03	-0.16
	Hyperreactivity 10m	0.00	0.910	-0.02	0.01	-0.02
	Fear 24m	0.04	0.504	-0.08	0.17	0.06
	Hyperreactivity 14m	-0.02	0.040	-0.03	0.00	-0.33
	Hyperreactivity 24m	-0.02	0.003	-0.03	-0.01	-0.35
Covariance Fear 14m - Hyperreactivity 14m		-1.61	0.037	-3.12	-0.10	-0.23
Covariance Fear 10m	- Hyperreactivity 10m	-7.34	0.000	-11.05	-3.63	-0.45
Covariance Fear 24m	- Hyperreactivity 24m	-3.43	0.000	-5.17	-1.70	-0.43
Covariance SCI	36m – RRB 36m	0.16	0.000	0.10	0.23	0.52

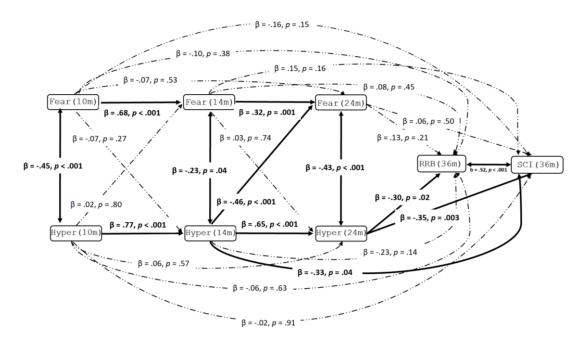
SCI = social communication interaction; RRB = restrictive and repetitive behaviours

**Table 3** Model 2 with standardized coefficients

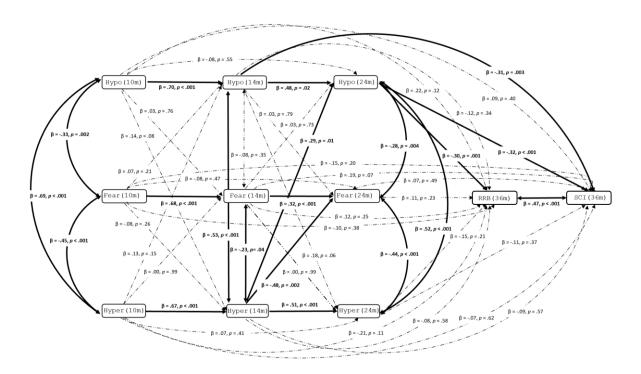
		b	р	[95% Confider	nce Interval]	β
Fear 14m	Fear 10m	0.67	0.000	0.51	0.83	0.68
	Hyporeactivity 10m	0.01	0.756	-0.03	0.04	0.03
	Hyperreactivity 10m	0.00	0.987	-0.02	0.02	0.00
Fear 24m	Fear 14m	0.25	0.000	0.11	0.38	0.32
	Fear 10m	-0.06	0.467	-0.23	0.11	-0.08
	Hyporeactivity 14m	0.00	0.791	-0.03	0.04	0.03
	Hyperreactivity 14m	-0.04	0.002	-0.06	-0.01	-0.48
Hyporeactivity 14m	Fear 10m	0.33	0.210	-0.18	0.84	0.07
	Hyporeactivity 10m	0.70	0.000	0.56	0.83	0.70
	Hyperreactivity 10m	0.06	0.151	-0.02	0.15	0.13
Hyperreactivity 14m	Fear 10m	-0.74	0.262	-2.02	0.55	-0.08
	Hyporeactivity 10m	0.28	0.079	-0.03	0.59	0.14
	Hyperreactivity 10m	0.66	0.000	0.52	0.81	0.67
Hyporeactivity 24m	Fear 14m	0.14	0.732	-0.65	0.92	0.03
	Hyporeactivity 10m	-0.09	0.551	-0.39	0.21	-0.08
	Hyporeactivity 14	0.52	0.017	0.10	0.95	0.48
	Hyperreactivity 14m	0.16	0.006	0.04	0.27	0.29
Hyperreactivity 24m	Fear 14m	0.01	0.992	-1.79	1.81	0.00
	Hyperreactivity 10m	0.08	0.413	-0.11	0.26	0.07
	Hyporeactivity 14m	0.41	0.061	-0.02	0.84	0.18
	Hyperreactivity 14m	0.59	0.000	0.29	0.88	0.51
RRB 36m	Fear 14m	0.09	0.258	-0.07	0.26	0.12
	Fear 10m	-0.08	0.377	-0.25	0.09	-0.10
	Hyporeactivity 10m	0.03	0.119	-0.01	0.08	0.22
	Hyperreactivity 10m	-0.02	0.113	-0.04	0.00	-0.21
	Fear 24m	0.11	0.233	-0.07	0.30	0.11
	Hyporeactivity 14m	-0.02	0.340	-0.06	0.02	-0.12
	Hyperreactivity 14m	-0.01	0.576	-0.03	0.02	-0.08
	Hyporeactivity 24m	-0.04	0.001	-0.07	-0.02	-0.30
	Hyperreactivity 24m	-0.01	0.206	-0.03	0.01	-0.15
SCI 36m	Fear 14m	0.10	0.070	-0.01	0.20	0.19
	Fear 10m	-0.07	0.197	-0.18	0.04	-0.15
	Hyporeactivity 10m	0.01	0.400	-0.01	0.03	0.09
	Hyperreactivity 10m	0.00	0.619	-0.02	0.01	-0.07
	Fear 24m	0.05	0.488	-0.09	0.19	0.07
	Hyporeactivity 14m	-0.03	0.003	-0.05	-0.01	-0.31
	Hyperreactivity 14m	0.00	0.570	-0.02	0.01	-0.09
	Hyporeactivity 24m	-0.03	0.000	-0.05	-0.01	-0.32
	Hyperreactivity 24m	0.00	0.369	-0.02	0.01	-0.11
Covariance Fear 14r	m - Hyporeactivity 14m	-0.29	0.345	-0.89	0.31	-0.08
Covariance Fear 14n	n - Hyperreactivity 14m	-1.60	0.035	-3.09	-0.11	-0.23
Covariance Fear 10m - Hyporeactivity 10m		-2.63	0.002	-4.29	-0.96	-0.33

Covariance Fear 10m - Hyperreactivity 10m	-7.36	0.000	-11.07	-3.64	-0.45
Covariance Hyporeactivity 10m - Hyperreactivity 10m	55.27	0.000	37.71	72.83	0.69
Covariance Fear 24m - Hyporeactivity 24m	-1.07	0.004	-1.79	-0.34	-0.28
Covariance Fear 24m - Hyperreactivity 24m	-3.49	0.000	-5.16	-1.83	-0.44
Covariance Hyporeactivity 14m - Hyperreactivity 14m	15.20	0.000	8.04	22.36	0.53
Covariance Hyporeactivity 24m - Hyperreactivity 24m	25.97	0.000	14.37	37.57	0.52
Covariance RRB 36m - SCI 36m	0.12	0.000	0.06	0.19	0.47

SCI = social communication interaction; RRB = restrictive and repetitive behaviours



**Figure. 1** Cross-lagged associations between Fear, Hyperreactivity, Restricted and Repetitive Behaviours (RRB) and Social Communication Interactions (SCI) at 10 - 36 months of age. Bold indicates significant at p < .05.



**Figure 2.** Cross-lagged associations between Fear, Hyperreactivity, Hyporeactivity, Restricted and Repetitive Behaviours (RRB) and Social Communication Interactions (SCI) at 10-36 months of age. Bold indicates significant at p < .05.