

Cortical markers of excitation/inhibition balance are associated with sensory responsivity from infancy in longitudinal cohorts enriched for autism and ADHD

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Abstract

Autism and ADHD are characterised by atypical sensory responsivity, and this may be driven by alterations in the balance of cortical excitation to inhibition (E/I). Studies in early development are required to establish the primary of effects. We utilised data from a prospective longitudinal cohort of infants with and without a family history (FH) of autism and/or ADHD (N=151; 55% male, 83% white). We extracted electroencephalography (EEG) metrics of E/I balance at 5, 10 and 14 months; the aperiodic exponent of the slope of the power spectrum ('1/f'). Models estimated correlated latent growth curves of parent-reported hyper and hypo-responsivity between 10 – 36 months. Analyses tested associations between developmental trajectories of sensory responsivity and FH, parent-rated neurodevelopmental traits at 3 years and E/I balance. Results showed that FH-autism was associated with steeper increases in parent-reported hyper-responsivity between 10 to 36 months, whereas FH-ADHD was associated with steeper increases in hypo-responsivity. Higher hypo-responsivity at 10-month baseline was associated with both autistic and ADHD traits at 3 years. A steeper slope of hypo-responsivity predicted ADHD traits at 3 years. Neither the baseline or slope of hyper-responsivity was associated with FH-ADHD, or autistic or ADHD traits at 3 years. Males displayed higher baseline hypo-responsivity. Aperiodic exponent values at 5 and 10, but not 14 months, were associated with hyper-responsivity. Results suggest that hypo-responsivity in infancy may be an indicator of later autism and ADHD outcomes. Alterations in E/I balance may contribute to early differences in sensory responsivity and thus could represent a useful target for intervention development.

Introduction

Although atypical sensory responsivity is traditionally associated with autism¹⁻³ (and included in the diagnostic criteria), recent research has suggested sensory responsivity may also be altered in other neurodevelopmental conditions, such as Attention-Deficit Hyperactivity Disorder (ADHD)⁴, which commonly co-occurs with autism⁵. Despite the wide-ranging negative consequences of atypical sensory responsivity in childhood⁶⁻⁸, and it being a priority area for individuals with lived experience⁹, little is known about how sensory responsivity may develop differently in children with autism and/or ADHD, or the neurobiological factors that may contribute to these individual differences. Better understanding of relevant neurobiological processes that underpin sensory responsivity is required to inform evidence-based intervention.

To detect causal pathways, and understand what is distinct or common between autism and ADHD (e.g., does sensory responsivity represent a shared neuroendophenotype⁵), studies are required that examine sensory differences before symptom emergence, and capture different forms of sensory difference (i.e., hyper and hypo-responsivity). Infant-sibling designs, where infants with a family history of neurodevelopmental conditions are recruited around birth, report infants with a family history of autism (FH-autism) who receive a diagnosis themselves have atypical sensory responsivity from early in development¹⁰⁻¹³. One study found 3 year old children with a family history of ADHD (FH-ADHD) also

score higher on parent-reported hyper and hypo-responsivity¹⁴. To our knowledge, no study has compared FH-autism and FH-ADHD siblings in terms of developmental patterns of sensory responsivity, or examined how these pattern predict emerging traits of these conditions.

One proposed mechanism that underpins differences in sensory processing and responsivity is the relative ratio of cortical excitatory to inhibitory activity (E/I balance), with inhibition in particular thought to govern the processing of sensory inputs through mechanisms such as neuronal tuning¹⁵. This has been a topic of great interest in the autism research field, although methodologies vary considerable, and little consensus has been reached as to the nature of alterations in autistic individuals¹⁶. There is some evidence that alterations in markers of E/I balance are correlated with atypical sensory responsivity in autistic children and adults^{7,17–20}. However, these studies were conducted in older individuals, usually after they have received a diagnosis, limiting inference about directionality of effects. One infant study, in an overlapping cohort to the current analytic sample, reported that although 10-month old FH-autism infants showed altered repetition suppression to tactile stimulation (a marker of GABAergic inhibition), no association was found between tactile suppression index and parent-rated tactile sensory seeking²¹. This may be in part due to difficulties capturing observable individual differences in tactile sensory seeking at such a young age.

There is evidence from infant-sibling studies that certain brain and cognitive features are more clearly associated with autism outcomes when measured earlier in development^{22,23}. This may reflect the emerging influence of other modifying domains that come online later in life that obscure brain-behaviour associations (i.e., developmental moderators) or compensatory processes. The idea of developmental specificity is of particular relevance to E/I balance, as it has been proposed that the brain may attempt to compensate for alterations to E/I balance early in the lifespan, which in turn could lead to group effects reversing later in development (as the brain ‘overcorrects’ itself)²⁴. Similar biological compensatory processes are noted elsewhere, for example arterial remodelling in response to atherosclerotic plaques,²⁵ neural reorganization such that non-speech areas predict language outcomes in children with cochlear implants²⁶, and increased levels of obesity in adults exposed to famine in utero²⁷.

To address limitations of current knowledge, we estimate a dual latent growth curve model where trajectories of hyper and hypo-responsivity are predicted by family history, and predictive of childhood neurodevelopmental traits. We estimate developmental change as previous work finds that change rates in sensory responsivity are the most robust predictors of autistic traits²⁸. We predict that infants with FH-autism would show increased hyper- and hypo-responsivity, and increases in both would be associated with higher autistic traits at 36 months. We predict that infants with FH-ADHD would show increased hypo-responsivity, which would in turn predict ADHD traits at 36 months, based on theoretical frameworks that certain attributes of ADHD (e.g., hyperactive behaviour) may represent attempts to increase environmental input to compensate for hypo-sensitivity²⁹. We examine associations between E/I balance (indexed by the aperiodic exponent) and hyper- and hypo-responsivity, as listed in our pre-registered analysis (<https://osf.io/sm4f8>). To explore the idea that there may be specific periods where

E/I balance is the critical determinant of sensory processing, we examined associations at 5, 10, and 14 months of age.

Methods

Infants were recruited as part of a longitudinal prospective study (Studying Autism and ADHD in the early years; STAARS) see³⁰ for more details. Participants were recruited between 2013 to 2019 from a volunteer database, community flyers, internet adverts and clinical networks. Informed written consent was provided by the parent(s). The study was approved by the National Research Ethics Service and the Research Ethics Committees of Birkbeck, University of London and King's College London. 161 infants completed visits at approximately 5, 10, 14, 24 and 36 months of age. Infants were assigned group membership based on information on clinical diagnoses and scores on various screening measures (see Supplement Materials, section SM1 and Table S1). Infants in the FH-autism group had at least one first-degree relative with a community clinical diagnosis of autism, infants in the FH-ADHD group had at least one first-degree relative with a community clinical diagnosis or probable research diagnosis of ADHD, and infants in the FH-typical group had at least one older sibling with typical development and no known autism or ADHD in first-degree family members. Infants with a family history of both autism and ADHD formed the FH-autism + ADHD group. The current sample includes infants who had at least one measurement of sensory responsivity between 10 and 36 months (n = 151).

Sensory Responsivity

Sensory hyper-responsivity and hypo-responsivity were measured at 10, 14, 24 and 36 months with the 48-item Infant Toddler Sensory Profile (ITSP)³¹. A composite low threshold score was calculated by combining the sensory sensitivity and sensation avoiding subscales. We used the total score from the low threshold quadrant as an index of hyper-responsivity (25 items) and scores from the low registration quadrant as an index of hypo-responsivity (11 items). Scores were reverse scored to aid interpretability.

Neurodevelopmental Traits

Autistic traits were measured at 36 months using the Preschool form of the Social Responsiveness Scale – 2³². The SRS consists of 65 items and is designed to measure autistic traits in the general population. ADHD traits were measured at 36 months using the Preschool Child Behavior Checklist DSM Attention Deficit/Hyperactivity Problems subscale³³, which comprises six items that measure inattentive and hyperactive behaviours.

EEG Acquisition and Procedure

EEG was collected at 5, 10 and 14 months. EEG was recorded using an EGI (Philips Neuro, Oregon, USA) 128-electrode Hydrocel Sensor Net, online referenced to Cz. EEG was collected at 500Hz at 5 and 10 months and 1000Hz at 14 months. Infants were seated on their caregiver's lap, 60cm from a screen, in a sound attenuated and electrically-shielded room. Stimuli consisted of naturalistic social (women singing)

or non-social (toys moving) videos designed to produce calm attention. Videos were 1 minute in length and presented up to 3 times, interspersed between other tasks as part of a longer session. EEG was bandpass filtered (0.1-100Hz), and 1-second segmented. Data was manually cleaned in NetStation 4.5; segments with excessive artifact, where infants were not looking at the video, or with > 25 noisy channels were excluded. Infants with < 10 artifact-free trials in either condition were excluded. Noisy channels were interpolated from neighbouring channels using spline interpolation. 1-second non-overlapping segments were referenced to the average reference, imported into Matlab, detrended and subjected to a Fast Fourier Transform (FFT). Power values were calculated and averaged across artefact-free segments in 1Hz bins from all electrodes excluding those on the outer rim of the net.

Extraction of E/I Metrics from EEG

The fitting oscillations and one over f (FOOOF) algorithm was used to obtain individual aperiodic exponent values³⁴. When the power spectrum is plotted on a log–log axis (i.e., power on the y axis, frequency on the x axis), the aperiodic exponent is equivalent to the coefficient of the regression line. We parameterized spectra in the 1–20 Hz range, and only exponents from model fits with $R^2 \geq 0.95$ and > 20 trials were retained (see eFigure 1 and eTable 2 in Supplement 1 for a breakdown and analysis of EEG attrition). Other settings were: peak width limits = 2, 8, maximum number of peaks = 4, peak threshold = 0.1, aperiodic mode = 'fixed'. Previous work finds no differences in aperiodic exponent for the social as compared to non-social videos³⁵; therefore, aperiodic exponents were averaged for the social and non-social videos (as outlined in our pre-registered analysis). To minimise the impact of outliers, values were winsorized such that the 5% of the lowest/highest values were recoded to the value of the 5th/95th percentile.

Statistical Analysis

All analyses were conducted in Stata v16. Analyses were largely pre-registered (<https://osf.io/sm4f8>; see Supplementary Materials SM2 for deviations). First, a joint latent growth curve mediation model was estimated, specifying correlated latent factors of intercept (baseline) and slope (change over time) for sensory hyper-responsivity and hypo-responsivity (see Figure S2). Paths were specified from family history and sex to sensory responsivity intercepts, slopes and neurodevelopmental traits, and from sensory responsivity intercepts and slopes to neurodevelopmental traits. In these models, the FH-autism*FH-ADHD interaction was added in a second step to aid interpretation of main effects. Time-varying age effects were accounted for by specifying age at visit as a predictor of observed ITSP scores at each wave. Second, we then re-ran the models with the 5-, 10- and 14-month aperiodic exponents and number of available EEG trials as a predictor of intercept and slope (one model for each EEG timepoint). FH-autism, FH-ADHD, FH-autism*FH-ADHD and sex were included as covariates. All models were estimated with maximum likelihood to account for missing data. We report both unstandardised (b) and standardized (B) coefficients.

Results

Associations between Autism/ADHD Family History, Sensory Responsivity, and Childhood Traits

See Tables 1 and Table S3 for descriptive statistics, and Tables S4 and S5 for full results. FH-autism was associated with a steeper slope of hyper-responsivity ($b = 1.90$, 95% CIs [0.12, 3.67], $p = .036$, $B = .25$). FH-ADHD was associated with a steeper slope of hypo-responsivity ($b = 1.41$, 95% CIs [0.51, 2.30], $p = .002$, $B = .36$). See Fig. 1 for estimated trajectories. Males had higher scores than females for the hypo-responsivity intercept ($b = -2.27$, 95% CIs [-4.18, -0.35], $p = .020$, $B = -.21$). Hyper-responsivity was significantly associated with hypo-responsivity (intercept covariance: $B = .85$, $p < .001$, slope covariance: $B = .71$, $p < .001$). A higher hypo-responsivity intercept was associated with higher autistic traits ($b = 0.06$, 95% CIs [0.01, 0.11], $p = .011$, $B = 0.49$) and ADHD traits at aged 3 ($b = 0.25$, 95% CIs [0.00, 0.49], $p = 0.051$, $B = 0.39$), although the latter was at significance. A steeper slope for hypo-responsivity was associated with higher ADHD traits at aged 3 ($b = 1.40$, 95% CIs [0.58, 2.22], $p = .001$, $B = 0.75$). Neither the intercept or slope of hyper-responsivity was associated with later autistic or ADHD traits (p s $> .10$). Autistic and ADHD traits at 3 years were significantly correlated ($B = .38$, $p = .004$). See Fig. 2 for a summary of significant associations.

Table 1
Characteristics of Analytic Sample

Mean (SD) unless otherwise indicated	Total sample (N = 151)	Typical FH (n = 26)	FH-autism (n = 76)	FH-ADHD (n = 29)	FH-autism + ADHD (n = 20)
Gender n (%)					
Male	83 (55%)	15 (58%)	38 (50%)	18 (62%)	12 (60%)
Female	68 (45%)	11 (42%)	38 (50%)	11 (38%)	8 (40%)
Ethnicity n (%)					
White	121 (83%)	23 (92%)	54 (74%)	27 (93%)	17 (89%)
Mixed Race	15 (10%)	1 (4%)	10 (14%)	2 (7%)	2 (11%)
Asian	7 (5%)	1 (4%)	6 (8%)	0	0
Black	2 (1%)	0	2 (3%)	0	0
Other	1 (1%)	0	1 (1%)	0	0
Parent education n (%)					
Primary/Secondary	41 (28%)	2 (8%)	17 (23%)	10 (34%)	12 (63%)
BA/BSc or above	105 (72%)	23 (92%)	56 (77%)	19 (66%)	7 (37%)
Child Assessments					
5m age of assessment	5.32 (0.57)	5.39 (0.50)	5.35 (0.66)	5.15 (0.38)	5.25 (0.45)
5m Mullen ELC	84.48 (10.04)	85.30 (8.71)	83.02 (10.93)	85.54 (9.01)	87.75 (9.72)
10m Age at visit	10.06 (0.62)	10.00 (0.63)	10.03 (0.52)	10.20 (0.91)	10.11 (0.46)
10m Mullen ELC	87.57 (14.90)	89.23 (12.30)	88.49 (15.00)	84.76 (15.86)	85.42 (16.83)
14m Age at visit	14.29 (0.65)	14.23 (0.61)	14.31 (0.64)	14.22 (0.80)	14.37 (0.60)
14m Mullen ELC	77.82 (12.25)	79.50 (11.76)	78.28 (12.00)	79.08 (11.12)	72.53 (14.50)
24m Age at visit	24.75 (1.33)	24.61 (1.16)	24.91 (1.56)	24.68 (1.09)	24.38 (0.72)

CBCL = Child Behavior Checklist; ELC = Early Learning Composite; FH = family history; SRS = Social Responsiveness Scale

Mean (SD) unless otherwise indicated	Total sample (N = 151)	Typical FH (n = 26)	FH-autism (n = 76)	FH-ADHD (n = 29)	FH-autism + ADHD (n = 20)
24m Mullen ELC	104.05 (20.63)	115.30 (15.53)	100.71 (20.92)	106.86 (21.21)	96.94 (17.12)
36m Age at visit	37.18 (1.81)	36.83 (1.82)	37.21 (1.46)	37.35 (2.69)	37.19 (1.52)
36m Mullen ELC	113.25 (19.52)	129.94 (11.41)	108.10 (18.53)	118.39 (18.83)	105.93 (19.90)
36m SRS total	39.95 (31.75)	23.37 (9.46)	42.91 (32.39)	35.55 (24.19)	61.00 (48.52)
36m CBCL ADHD total	4.30 (3.28)	3.05 (2.16)	4.22 (3.28)	4.77 (3.49)	5.79 (3.93)
CBCL = Child Behavior Checklist; ELC = Early Learning Composite; FH = family history; SRS = Social Responsiveness Scale					

Associations between EEG Markers of E/I Balance and Sensory Responsivity

See Table 2 and Fig. 3 for results. 5-month and 10-month aperiodic exponent were positively associated with the intercept of sensory hyper-responsivity (5 months: $b = 22.24$, 95% CIs [1.27, 43.22], $p = .038$, $B = .26$; 10 months: $b = 18.06$, 95% CIs [1.29, 34.83], $p = .035$, $B = .21$). The association between 5-month aperiodic exponent and hypo-responsivity intercept was at significance ($b = 10.59$, 95% CIs [-0.16, 21.35], $p = .054$, $B = .25$). 14-month aperiodic exponent was not associated with sensory responsivity. No associations were observed with number of retained EEG trials, aside from an at-significance association between number of trials at the 14-month assessment and the slope of hypo-responsivity ($b = .01$, 95% CIs [0.00, 0.02], $p = .051$, $B = .26$).

Table 2
Associations between Global Metrics of Excitation/Inhibition Balance and Trajectories of Sensory Hyper- and Hypo-Responsivity

Hyper-responsivity										
	Intercept				Slope					
	b	95% CI		p	B	b	95% CI		p	B
5m aperiodic exponent	22.24	1.27	43.22	.038	0.26	0.22	-8.88	9.32	.963	0.01
5m number of trials	0.05	-0.02	0.13	.184	0.16	0.01	-0.02	0.05	.434	0.12
10m aperiodic exponent	18.06	1.29	34.83	.035	0.21	-0.67	-7.82	6.48	.854	-0.02
10m number of trials	-0.03	-0.09	0.03	.286	-0.11	0.00	-0.02	0.03	.819	0.03
14m aperiodic exponent	-0.65	-19.80	18.50	.947	-0.01	-1.34	-8.78	6.09	.723	-0.05
14m number of trials	-0.04	-0.10	0.02	.236	-0.14	0.00	-0.02	0.03	.816	0.03
Hypo-responsivity										
	Intercept				Slope					
	b	95% CI		p	B	b	95% CI		p	B
5m aperiodic exponent	10.59	-0.16	21.35	.054	0.25	-1.54	-5.90	2.81	.488	-0.11
5m number of trials	-0.01	-0.05	0.03	.764	-0.04	0.01	-0.01	0.02	.509	0.10
10m aperiodic exponent	6.47	-1.63	14.58	.118	0.15	-0.32	-3.74	3.10	.855	-0.02
10m number of trials	-0.02	-0.05	0.01	.209	-0.13	0.00	-0.01	0.01	.841	0.02
14m aperiodic exponent	0.21	-8.61	9.03	.962	0.01	0.99	-2.51	4.50	.578	0.07
14m number of trials	-0.02	-0.05	0.01	.196	-0.15	0.01	0.00	0.02	.051	0.26
<p>Note: Although effects for FH-autism, FH-ADHD, FH-autism*FH-ADHD and sex were included as before, they are omitted from the table for brevity. Models for the 5-, 10- and 14-month data were run separately. FH = family history</p>										

Discussion

Disturbances of sensory responsivity are commonly associated with diagnosed autism, and emerging evidence suggests potentially also with ADHD. However, critical questions remain as to whether these differences emerge early in development – suggesting causality – and the neurobiological mechanisms that may drive variation in sensory responsivity. We present analyses of a prospective longitudinal cohort of infants, followed from 10–36 months. Results showed that a family history of autism (FH-autism) was associated with steeper increases in hyper-responsivity. Conversely, a family history of ADHD (FH-ADHD) was associated with increasing hypo-responsivity. A higher intercept (equivalent to estimated level at 10-month baseline) of hypo-responsivity was associated with being male, and having higher later autistic and ADHD traits at age 3 years; a steeper slope of hypo-responsivity was also associated with higher ADHD traits. Alterations in markers of global E/I balance, potentially indicative of enhanced inhibition, were associated with increased hyper-responsivity (and there was evidence to suggest increased hypo-responsivity also).

Our predictions that FH-autism infants would show increased sensory hyper- and hypo-responsivity, and these increases would in turn be associated with increases in emerging autistic traits, was partially supported. FH-autism infants displayed a steeper increase in hyper-responsivity over the first three years of life, however, hyper-responsivity was not associated with later autism traits. These results contrast with meta-analyses reporting that sensory over-responsivity is best able to distinguish autism from other clinical groups³, and reports that FH-autism infants who receive a diagnosis of autism score higher on hyper-responsivity at 12 months of age¹¹. What did predict later autistic (and ADHD) traits was increased hypo-responsivity at 10-month baseline. It is of interest that the form of sensory responsivity associated with a family history of autism (hyper-responsivity) is different to that which relates to later autistic traits (hypo-responsivity), and calls into question the centrality of hyper-responsivity as a mechanism for core autism characteristics. Increased responsivity has been associated with anxiety in both autistic³⁶ and typically developing⁶ children, and thus could in-part explain the increased prevalence of mental health difficulties in autistic populations. The association with hypo-responsivity is consistent with reports that hypo-responsivity is more prevalent in autism in early childhood³⁷, and predicts later autism symptoms in infant-siblings³⁸. Early hypo-responsivity may have knock-on effects on cognitive development; hypo-responsivity is associated with lower levels of joint attention and language³⁹, decreased neural response to social stimuli and fewer social approach behaviours⁴⁰. Notably, in most previous studies, associations with hyper- and hypo-responsivity are tested in separate models and without examining co-occurring conditions, limiting inference about specificity. One prospective community study that included both types of sensory responsivity in the same model reported both hyper- and hypo-responsivity were associated with later autism outcomes²⁸, although this work covered a wider developmental window (6 months – 7 years) and did not assess ADHD traits. Current results suggest that increased hypo-responsivity may not be a specific marker for later autistic characteristics, but also relevant for emerging ADHD behaviours (and thus may function as a shared neuroendophenotype).

In addition to the aforementioned associations between baseline hypo-reactivity and ADHD traits, a family history of ADHD was associated with steeper slope of hypo-responsivity (greater increase between 10–36 months), which in turn was associated with higher ADHD traits at age 3. This result extends findings from meta-analyses that report broad alterations in sensory processing in the early years are predictive of ADHD outcomes⁴. The lack of association with hyper-responsivity goes against previous reports^{14,41}, although many of these studies did not account for the co-occurrence of ADHD and autism, or were conducted in older samples. One hypothesis is that ADHD traits are a form of compensation for early hypo-responsivity, such that the child learns to sample the environment more rapidly and randomly to overcome for a decreased response to external inputs. However, it could also be that increases in parent-reported hypo-responsivity are a reflection off increasing differences in attention control that are characteristic of ADHD, which in turn lead to an apparent lack of responsivity as cues are ‘missed’. Finally, we found males were rated as more hypo-responsive than females (as found in general population cohorts²⁸), emphasising the need to account for sex in analytic models.

In terms of putative neurobiological mechanisms, our pre-registered hypothesis on the role of E/I balance was supported, such that increased aperiodic exponent values, indicative of enhanced inhibitory activity, were associated with greater hyper-responsivity. However, our pre-registered plan had specified analysis of EEG data at 14 months, whereas we found significant effects at 5- and 10-months only. Thus, current results require replication. Results concur with other infant-sibling studies that find brain or cognitive features are more strongly predictive of later autism outcomes when measured earlier in development^{22,23}, and genetic research which finds critical periods early in development for *SCN2A* mutations to produce an autistic phenotype⁴². Crucially, results demonstrate the role of alterations in E/I balance early in the lifespan, potentially before initial effects become confounded by developmental compensation²⁴ or later emerging moderating factors⁴³. We also note the association between 5-month aperiodic exponent and hypo-responsivity was at significance ($p = .054$), and the standardized coefficients of effect were comparable for hyper and hypo-responsivity ($B = .26$ and $.25$), suggesting enhanced inhibition in early development may alter sensory processing at a system-wide level¹⁵. Possible mechanisms of effect include disruption in evoked gamma oscillatory activity, which in turn alters the temporal sharpening of cortical sensory responses⁴⁴.

One limitation is the reliance on parent ratings for behavioural phenotypes, which could be impacted by rater biases (e.g., sex effects could in part reflect gendered expectations of child behaviour). Future studies with greater diversity of ethnicity and socio-economic status are needed to understand the generalisability of results.

To summarize, increased hypo-responsivity may function as a general marker for later neurodivergence. Early alterations in E/I balance may contribute to differences in childhood sensory responsivity, highlighting a putative neurobiological mechanism that could inform assessment and intervention. Future research should explore how differences in sensory processing may arise from alterations in E/I balance, and in turn how these translate to observable differences in responsivity.

Declarations

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Figures

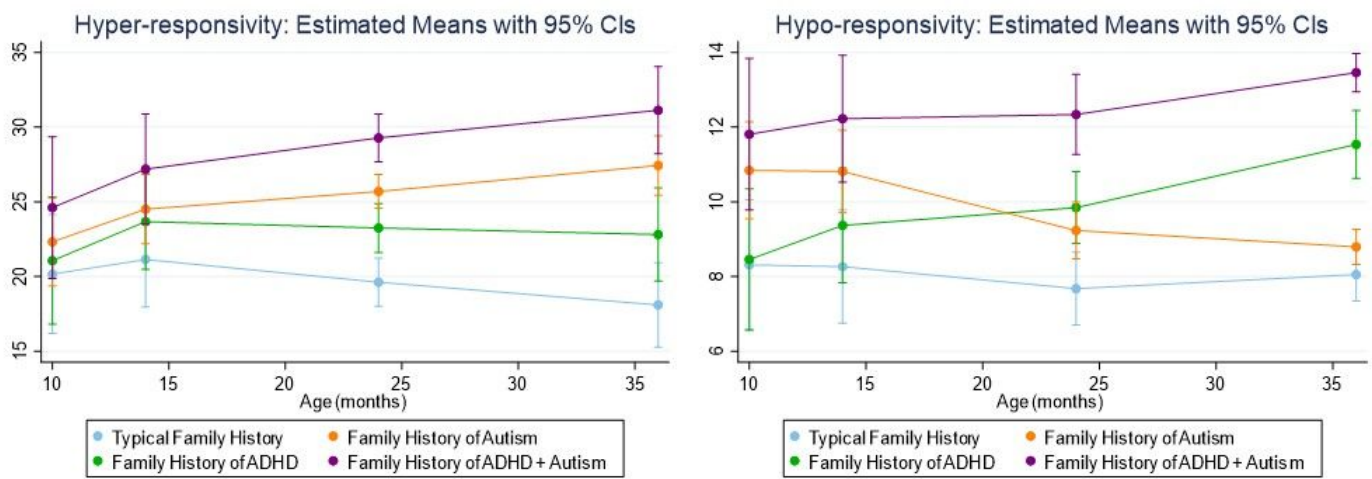


Figure 1

Trajectories of Sensory Hyper-Responsivity and Hypo-Responsivity between 10-36 Months in Infants With and Without Family History of Autism and ADHD

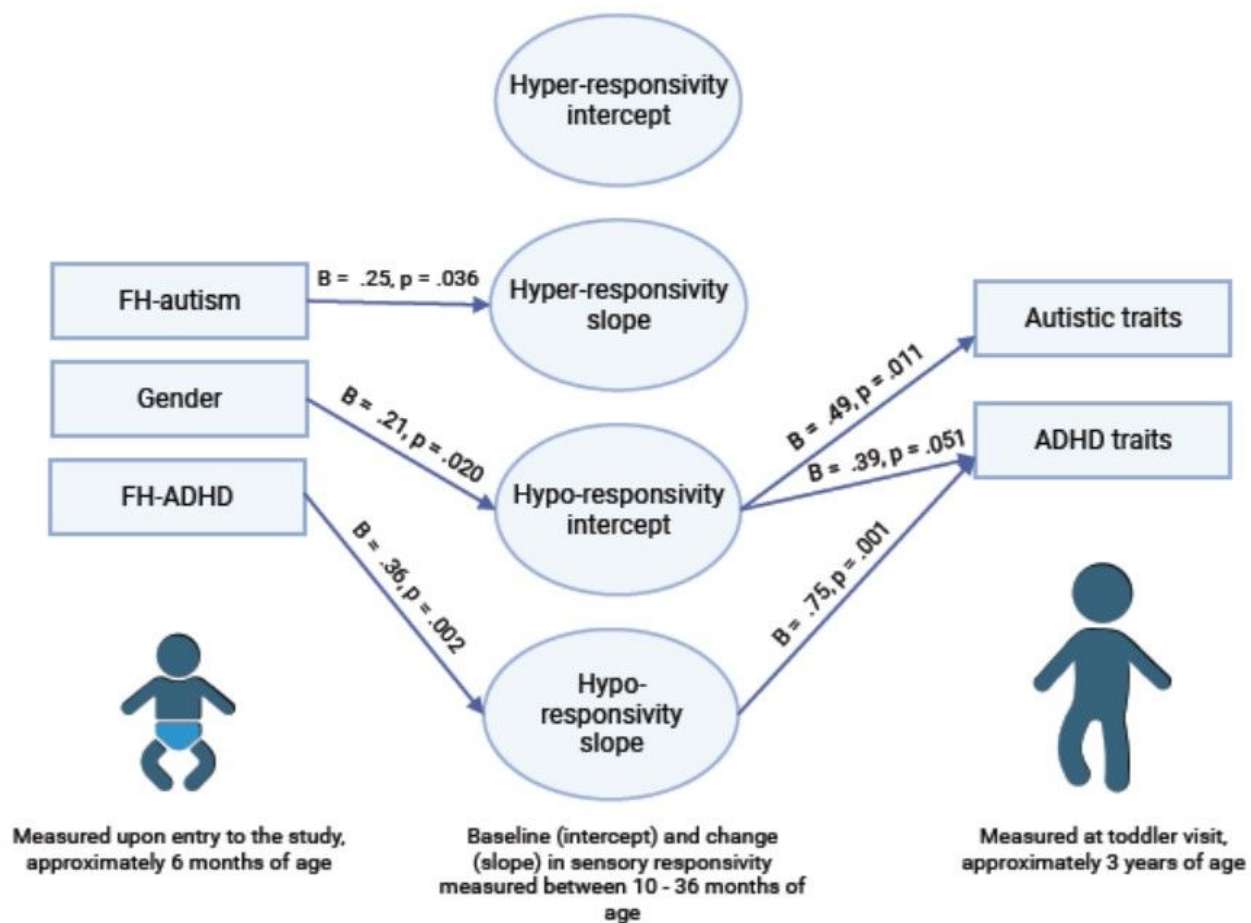


Figure 2

Significant Associations between Autism Family History (FH), ADHD Family History, Gender, Trajectories of Sensory Responsivity and Toddler Neurodevelopmental Traits. Standardised estimates are displayed. Created with BioRender.com

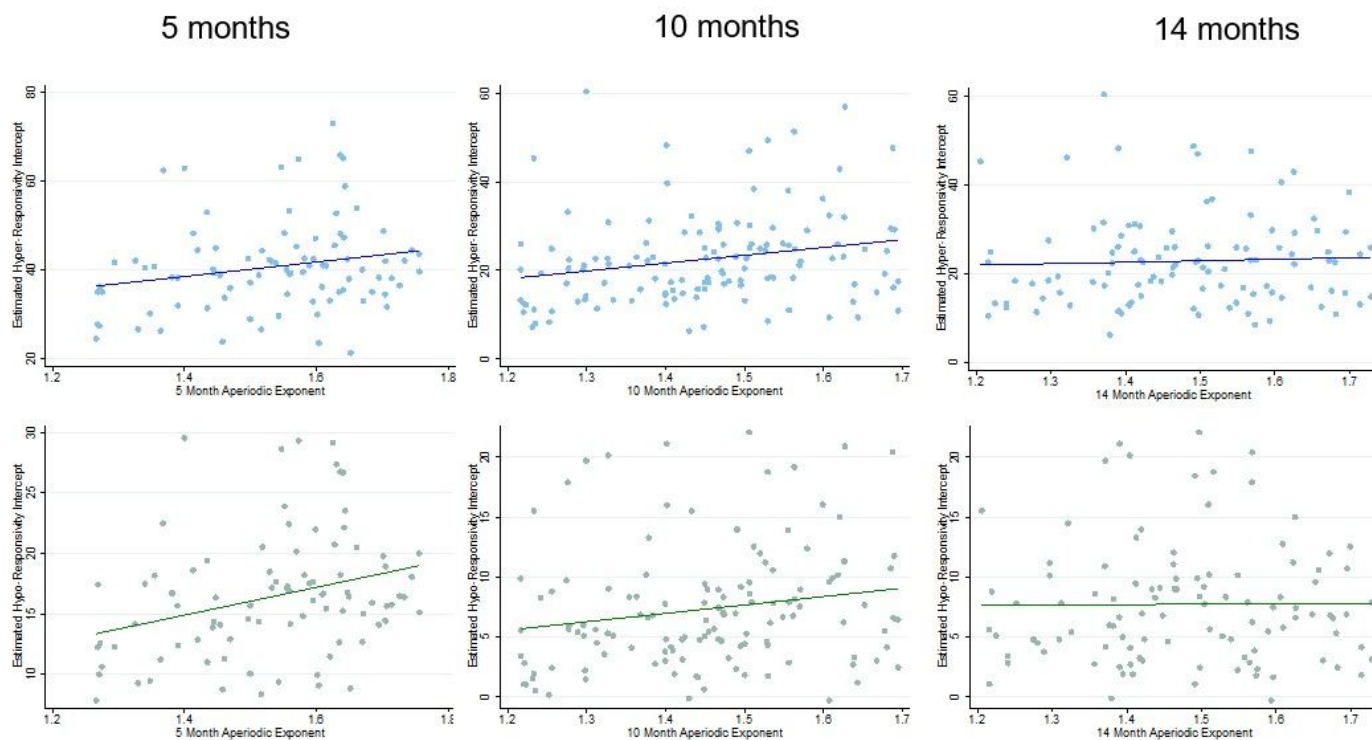


Figure 3

Developmentally Specific Associations between Metrics of Global E/I Balance (Aperiodic Exponent) and Hyper- (top blue panels) and Hypo-Responsivity (bottom green panels)

Supplementary Files

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- [AperiodicexponentSMsTransPsych.docx](#)