Clinical, socio-demographic, and parental correlates of early autism traits

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Key Points

Question What factors influence autism trait emergence in toddlers?

Findings In this cohort study of 536 toddlers we observed a positive association between exposure to early-life psycho-social adversity and autism traits at age 18 months. Associations were independent of general neurodevelopment. Factors known to increase the likelihood of a childhood autism diagnosis, such as sex, family history of autism or gestational age at birth, were not associated with autism traits at 18 months.

Meaning Psycho-social adversity has a significant influence on early-life autism trait emergence.

Abstract

Importance Autism traits typically emerge between the ages of 1 and 2. It is not known if experiences which increase the likelihood of childhood autism are related to early trait emergence, or if other exposures are more important. Identifying factors linked to toddler autism traits may improve our understanding of the mechanisms underlying atypical neurodevelopment.

Objective To characterise the association between 18-month autism traits and clinical, socio-demographic, and parental factors.

Design This is a cohort study of toddlers (n=536). Clinical, socio-demographic, and parental information was collected at birth (gestational age at birth, sex, maternal body mass index, age, parental education level, parental first language, parental history of neurodevelopmental disorders) and at 18 months (parent cohabiting status, two measures of social deprivation, three measures of maternal parenting style, and a measure of maternal postnatal depression). General neurodevelopment was assessed with the Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III), and autism traits were assessed using the Quantitative Checklist for Autism in Toddlers (Q-CHAT). Multivariable models were used to identify associations between variables and Q-CHAT. A model including BSID-III was used to identify factors associated with Q-CHAT independent of general neurodevelopment. Models were also evaluated addressing variable collinearity with principal component analysis (PCA).

Setting Single centre (London, UK).

Participants Sub-sample from the developing Human Connectome Project (dHCP).

Results A multivariable model explained 20% of Q-CHAT variance, with four individually significant variables (two measures of parenting style and two measures of socio-economic deprivation). After adding general neurodevelopment into the model 37% of Q-CHAT variance was explained, with three individually significant variables (two measures of parenting style and one measure of language development). After addressing variable collinearity with PCA, experience of early life adversity was positively correlated with Q-CHAT score via a single principal component, independently of general neurodevelopment. Neither sex nor family history of autism were associated with Q-CHAT score.

Conclusions and Relevance Our findings question whether potential autism diagnoses are being missed in more socially deprived groups, or if there are unidentified factors influencing the likelihood of transitioning from early traits at age 18 months to a clinical autism diagnosis in childhood.

Introduction

Autism spectrum disorders (ASD) are typically diagnosed between 4 and 7 years of age (Brett et al., 2016; Daniels & Mandell, 2014). The age at symptom onset however is often lower than this, with neurodivergence first being suspected by parents in most instances between 1 and 2 years of age (Crane et al., 2016). Screening tools aiming to quantify autism traits in this age group are well established and have been shown to have high specificity (albeit with low sensitivity) for predicting a future clinical autism diagnosis (Jullien, 2021; Toh et al., 2018). One such tool is the Qualitative Checklist for Autism in Toddlers (Q-CHAT) (Allison et al., 2008). The Q-CHAT is a 25-item questionnaire with each item rated by the parents from 0-4. It has been validated for use in multiple countries (Magiati et al., 2015; Mohammadian et al., 2015; Park et al., 2018; Ruta et al., 2019; Wong et al., 2014), and has been reported to show a positive predictive value of 28% for a future ASD diagnosis (using screening at two timepoints) (Allison et al., 2021).

Some factors previously reported to increase the likelihood of an autism diagnosis have also been shown to correlate with autism traits at age 18 months – for example, sex (with males scoring higher than females) (Allison et al., 2008; Auyeung et al., 2012; Guthrie et al., 2019) or preterm birth (Gray et al., 2015; Wong et al., 2014). However, beyond these factors there is a relative lack of research into what else may influence the emergence of autism traits in early life. Evidence suggests that a broader range of exposures may be associated with the emergence of autism traits, including maternal nausea and vomiting during pregnancy (Syn et al., 2021), neonatal illness (Ravi et al., 2016), maternal depression and anxiety (Goh et al., 2018; Kleine et al., 2021) and lower levels of parental education (Goh et al., 2018). Motor and cognitive development are also known to be influenced by a wide range of exposures, including biological or clinical factors such as preterm birth (Spencer-Smith et al., 2015), neonatal illness (Rao et al., 2019), and multiple psychosocial factors (Ferreira et al., 2018; Khowaja et al., 2015; Neamah et al., 2018; Ross & Perlman, 2019). Moreover, Q-CHAT score at 18 months has been shown to be negatively correlated with general language development (Wong et al., 2014). Hence, it is reasonable to expect that the autism trait emergence as captured by the Q-CHAT score may themselves be influenced by general development.

Understanding clinical, socio-demographic, and parental correlates of the Q-CHAT score at 18 months may help us to understand what early life experiences are associated with an increased likelihood of a future autism diagnosis in some individuals. The developing Human Connectome Project (dHCP) has collected Q-CHAT scores, other neurodevelopmental measures and demographic information from a large cohort of 18-month-old toddlers in London, UK. Using this dataset, we aimed to characterise correlates of Q-CHAT score. We hypothesised that, in keeping with the known associations between early life adversity and other measures of neurodevelopment, we would observe a pattern of psychosocial adversity being associated with higher Q-CHAT scores. Relationships between variables and Q-CHAT score are presented in both univariable (in part to inform future studies which may only have some of our variables available) and multivariable models, with scores from the Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III) (Bayley, 2006) additionally included as a covariate to understand whether any relationships between these early life experiences and autism traits are part of a broader pattern of influence on general neurodevelopment.

Methods

Sample

This study is based on a sample of neonates participating in the Developing Human Connectome Project (dHCP, http://www.developingconnectome.org/). Participants were all recruited at St Thomas' Hospital, London, UK. There were no specific inclusion or exclusion criteria for enrolment in this study, and recruitment was primarily from the antenatal clinic with no specific stratification – this is therefore a representative sample of individuals born at a single centre.

Toddlers were invited for neurodevelopmental assessment at 18 months post-expected delivery date; appointments were made according to family availability as close as possible to this time-point. The only inclusion criteria for this manuscript from the overall cohort was completion of the neurodevelopmental assessment. There were no exclusion criteria – we sought to use the most representative sample possible.

This project has received UK NHS research ethics committee approval (14/LO/1169, IRAS 138070), and conducted in accordance with the World Medical Association's Code of Ethics (Declaration of Helsinki). Written informed consent was obtained from parents at recruitment into the study.

Data Collection

Data collection took place either at St Thomas' Hospital, London, UK, or via questionnaires distributed to the participants' parents. At the time of birth, clinical variables, gestational age at birth and sex were extracted from the medical records of participants in the study; and maternal age, maternal pre-pregnancy BMI, and parent ASD/attention deficit hyperactivity disorder (ADHD) history were also collected via a maternal questionnaire. The last of these was asked in the format "Have you or your child's biological father ever been diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) or Autism?" This was a yes/no question.

At the time of birth, the socio-demographic status of participant families was recorded as measured by the Index of Multiple Deprivation Rank (IMD), a postcode-based score assigned to every address in the UK which gives a composite measure of socio-economic disadvantage, based on the mother's address at the time of birth. A lower score corresponds to greater geographical deprivation.

Further socio-demographic information was collected by questionnaire: maternal education ("At what age were you last in full time education?"), maternal 1st language ("Is English your first language"?), and parent cohabiting status. The Cognitively Stimulating Parenting Scale (CSPS), a questionnaire assessing the availability of resources to support cognitively stimulation parenting, associated to both parenting style and socioeconomic deprivation was also collected (Vanes et al., 2021; Wolke et al., 2013). The CSPS was updated to include items relating to access to mobile phones and apps. The Q-CHAT score (a parent reported questionnaire) was collected at the time of 18-month follow-up. The Bayley Scales of Infant and Toddler Development, 3rd edition (BSID-III) (Bayley, 2006), was administered by either a Chartered Psychologist or Pediatrician when the children were 18-month of age. The composite scores (Cognitive, Motor and Language) are used for analysis in this manuscript. Two measures of parenting style were also collected at this time. The first of these, the Parenting Scale (Arnold et al., 1993), is a self-reported tool that reports three different dimensions of parenting: Laxness, the tendency to behave passively and give in to misbehaviour; Overreactivity, which measures anger, meanness and irritability in parenting; and Verbosity, a measure of parental

dependence on talking even when ineffective as a discipline style. The Edinburgh Postnatal Depression Scale (EPDS) was also completed at followup. This is a well-established self-reported tool for quantifying postnatal depressive symptoms (Cox et al., 1987).

Statistical Analysis

Univariable associations between variables and Q-CHAT score were tested by Pearson's correlation or t-test as appropriate. Associations between variables of interest and Q-CHAT score were assessed by general linear model (GLM). Statistical significance was tested with random permutation tests, using 10,000 permutations. P-values are reported uncorrected, with those surviving multiple comparisons via false discovery rate (FDR) indicated (Benjamini & Hochberg, 1995). Principal component analysis was used to characterize the latent structure of independent variables, and to address collinearity between linear variables. The "elbow method" (Jolliffe & Cadima, 2016) used to determine the optimal number of principal components (PCs) to use in later analyses. Associations between PC scores and the original input variables was determined by Pearson's correlation, with $p<0.05$ after FDR correction considered significant.

Analyses were performed and figures made using Rstudio v4.0.2 (Rstudio, MA, U.S.A). The "FDRestimation", and "corrplot" packages were additionally used (Murray, 2020; Wei, 2021). PCA was performed using the "prcomp" function from base R rather than a dedicated package. Our code to implement random permutation tests for GLMs in R can be downloaded from https://github.com/CoDe-Neuro/ptestR.

Data availability

The dHCP is an open-access project. Data from the project can be downloaded by registering at https://data.developingconnectome.org . Analyses presented here include data to be included in future releases.

Results

Population

At the time of the study commencing, 644 individuals in the dHCP dataset had a Q-CHAT score available. Of these 536 had a complete set of demographic data and were included in the study. A comparison between individuals included and excluded is shown in Supplementary Table S1. There were some small differences, which in general indicate a pattern of more social adversity in individuals who were excluded. The characteristics of the sample used, and the univariate relationships of each variable to Q-CHAT score are shown in Table 1.

Table 1. Sample Characteristics. *Mean, standard deviation, and range displayed for linear variables. Frequency displayed for categorical variables. Correlations to QCHAT calculated by Pearson's r or t-test as appropriate.*

Outcome variable		
Total Q-CHAT Score, *Mean (SD), Range*	30.1 (5.9), 8-70	-
Clinical variables		**r (p)**
Age at follow-up [months], *Mean (SD), Range*	18.8 (1.6), 16-26	0.010 (0.535)
Gestational Age at Birth [weeks], *Mean (SD), Range*	38.1 (3.9), 23.0-43.0	-0.067 (0.120)
BMI [kg/m^2], *Mean (SD), Range*	24.2 (4.4), 15.3-43.4	**0.093 (0.030)**
Mother Age [years], *Mean (SD), Range*	34.3 (4.7), 17-52	**-0.105 (0.014)**
		t (p)
Sex [Male, Female], *N*	278, 258	1.820 (0.068)
Parent ASD/ADHD Diagnosis [Yes, No], *N*	28, 508	-0.4246 (0.674)
Socio-demographic variables		**r (p)**
IMD Rank, *Mean (SD), Range*	14626.2 (7409.2), 2410-32726	**-0.190 (<0.001)**
CSPS, *Mean (SD), Range*	20.5 (3.5), 7-28	**-0.219 (<0.001)**
Mother Education [years], *Mean (SD), Range*	23.6 (4.5), 12-43	0.001 (0.957)
		t (p)
Mother 1st Language [English, Other], *N*	338, 198	**4.518 (<0.001)**
Parents Cohabiting [Yes, No], *N*	520, 16	-1.650 (0.119)
Parental-psychological variables		**r (p)**
Mother Laxness, *Mean (SD), Range*	2.9 (0.8), 1-5.6	**0.286 (<0.001)**
Mother Overreactivity, *Mean (SD), Range*	2.2 (0.7), 1-5.1	**0.180 (<0.001)**
Mother Verbosity, *Mean (SD), Range*	3.4 (0.8), 1-6.4	**0.300 (<0.001)**
Mother EPDS, *Mean (SD), Range*	4.5 (4.2), 0-28	**0.127 (<0.001)**
BSID-III Cognitive Composite, *Mean (SD), Range*	101.0 (11.1), 55-130	**-0.358 (<0.001)**
BSID-III Language Composite, *Mean (SD), Range*	98.2 (15.4), 47-153	**-0.528 (<0.001)**
BSID-III Motor Composite, *Mean (SD), Range*	101.5 (10.2), 52-130	**-0.267 (<0.001)**

Nine variables were significantly associated with Q-CHAT score. BMI, EPDS, and three measures of parenting style were positively correlated with Q-CHAT score, and mother's age, IMD rank and CSPS score were negatively correlated with Q-CHAT score. Total Q-CHAT scores were significantly higher in individuals whose mother's spoke a language other than English as their 1st language.

All BSID-III composite scores were negatively associated with Q-CHAT score. The strongest association was with Language Composite Score (r=-0.528, p<0.001).

Multivariable models of Q-CHAT score

We assessed the association of all clinical, demographic, and socioeconomic variables with Q-CHAT score in two separate multivariable models, with or without the addition of BSID-III composite scores to control for the effect of general neurodevelopment and identify specific relationships between demographic variables and Q-CHAT score.

Table 2. *General linear model of the association between clinical, socio-demographic, and parental variables and Q-CHAT with or without the addition of BSID-III Cognitive, Motor and Language Composite Scores to the model.*

	Without BSID-III r^2 *(Adj.* r^2*) = 0.20(0.19),* ***p<0.001***		***With BSID-III*** r^2 *(Adj.* r^2*) = 0.36(0.34),* ***p<0.001***	
	t	**p**	**t**	**p**
Gestational Age at Birth	-1.94	0.052	-0.45	0.646
BMI	0.57	0.567	0.95	0.341
Mother Age	-0.73	0.461	-1.17	0.239
Sex	**-2.32**	**0.020**	-0.83	0.407
Parent ASD/ADHD Diagnosis	0.57	0.567	-0.23	0.813
IMD Rank	**-2.56**	**0.010***	**-2.06**	**0.039**
CSPS	**-3.38**	**<0.001***	-1.17	0.238
Mother Education	-0.08	0.929	0.35	0.719
Mother 1st Language English	-1.58	0.113	-0.01	0.994
Parents Cohabiting	1.74	0.082	1.49	0.135
Mother Laxness	**3.79**	**<0.001***	**2.68**	**0.007***
Mother Overreactivity	1.11	0.269	1.04	0.297
Mother Verbosity	**3.29**	**0.001***	**3.39**	**<0.001***
Mother EPDS	1.72	0.08	1.26	0.206
Cognitive Composite	NA	NA	-0.28	0.779
Language Composite	NA	NA	**-8.32**	**<0.001***
Motor Composite	NA	NA	-0.41	0.677

*Bold indicates p<0.05, * indicates significance after FDR multiple comparison correction ($a<0.05$)*

A multivariable model explained 20% of Q-CHAT variance. After FDR correction four variables were individually associated with Q-CHAT score: IMD Rank (t=-2.56,p=0.10) and CSPS (t=-3.38,p<0.001) were negatively associated and Mother Laxness (t=3.79,p<0.001) and Mother Verbosity (t=3.29,

p=0.001) were positively associated. Adding BSID-III composite scores to the model two of these (Mother Laxness and Mother Verbosity) remained significantly associated with Total Q-CHAT score (t=2.68,p=0.007 and t=3.39,p<0.001 respectively), in addition to BSID-III language composite score (t=-8.32, p<0.001), which was negatively associated with Total Q-CHAT score. Notably sex and parent ASD/ADHD diagnosis status did not correlate individually with Q-CHAT score in either model.

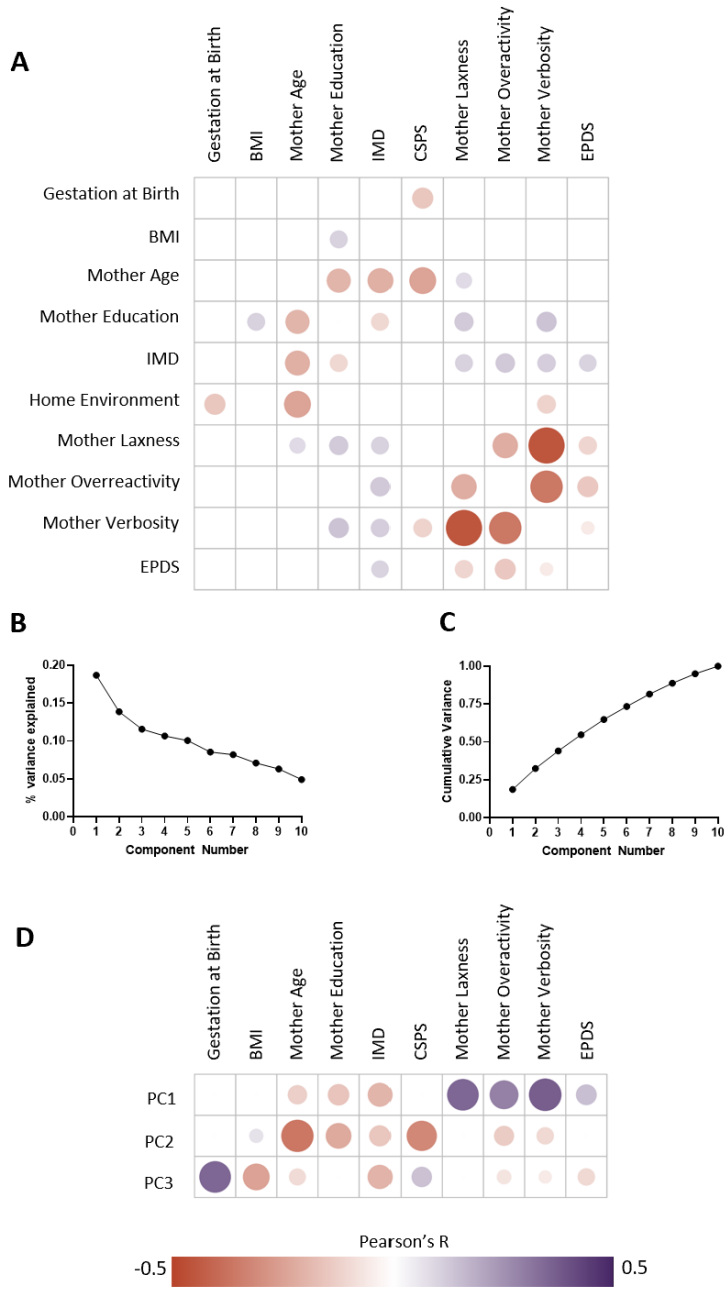

Figure 1 *– Principal Component Analysis of linear variables.* ***A*** *Correlogram of associations between linear variables. Pearson's r indicated for correlations with p<0.05.* ***B*** *Scree plot of PCA components* ***C*** *Cumulative variance plot of PCA components* ***D*** *Correlations of original linear variables to principal components. Correlation indicated by size and colour of circle. Only correlations remaining significant (p<0.05) after FDR correction are shown. Values of each correlation are shown in Supplementary Table S2.*

A limitation of interpreting these models is the collinearity between demographic variables (Figure 1A). In order to address this, we performed a PCA of the linear variables to obtain orthogonal components, which we then used in a general linear model in place of the original linear variables. We determined the optimal number of principal components (PCs) to be 3 (as determined by the elbow on the scree plot, Figure 1B). The multivariable models associating demographic variables and BSID-III composite scores with Q-CHAT score (Table 2) were subsequently repeated, with linear variables being replaced by PCA components 1-3 (Table 3). Details of variable correlations with each PC are shown in Figure 1D.

PC1 captures variable associations which are associated with early life adversity, PC2 is associated with socioeconomic deprivation and a less stimulating home environment, and PC3 is associated with low clinical adversity.

17% of Q-CHAT variance was explained, with only PC1 remaining statistically significant in the model after FDR correction (t=-8.17, p<0.001, Table 3). 35% of Q-CHAT variance was explained by the model including BSID-III scores to account for general neurodevelopment, with PC1 and BSID-III language composite scores statistically significant (t=-6.59 and t=-8.96 respectively, p<0.001, Table 3).

***Table 3**. General linear model of the association between demographic variables, BSID-III composite scores and Q-CHAT. Linear variables were first transformed into orthogonal components via PCA. PC1 captures variable associations which are associated with low socioeconomic deprivation and non-expressive parenting styles, PC2 is associated with low socioeconomic deprivation and expressive parenting styles, and PC3 is associated with variables describing clinical adversity.*

	Without BSID-III		***With BSID-III***	
	*r^2 (Adj. r^2) = 0.17(0.16), **p<0.001***		*r^2 (Adj. r^2) = 0.35(0.33), **p<0.001***	
	t	**p**	**t**	**p**
PC1	**-8.17**	**<0.001***	**-6.59**	**<0.001***
PC2	-1.86	0.062	-0.70	0.480
PC3	1.29	0.194	0.10	0.913
Sex	-2.02	0.043	-0.48	0.630
Parent ASD/ADHD Diagnosis	0.59	0.550	-0.26	0.790
Mother 1st Language English	-1.86	0.063	-0.06	0.948
Parents Cohabiting	2.04	0.041	1.51	0.129
Cognitive Composite	NA	NA	-0.55	0.577
Language Composite	NA	NA	**-8.96**	**<0.001***
Motor Composite	NA	NA	-0.15	0.880

*Bold indicates p<0.05, * indicates significance after FDR multiple comparison correction ($a<0.05$)*

PC1 (early life adversity) is negatively correlated with Q-CHAT score (ie, individuals with more adversity have lower Q-CHAT scores). Via this PC we can see that maternal age at last full-time education, three measures of parenting style and EPDS are positively associated with Q-CHAT score; whereas maternal age, IMD rank, and CSPS are negatively associated with Q-CHAT score). Once again it is worth noting that sex and parent ASD/ADHD diagnosis status did not correlate with Q-CHAT score in either model.

Discussion

Early life autism trait emergence is influenced by several clinical, socio-demographic, and parental variables. In our study we observed that multiple measures of psychosocial adversity are positively associated with Q-CHAT score. Conversely, some variables known to increase the likelihood of an autism diagnosis in later childhood, such as male sex (Werling & Geschwind, 2013), a family history of autism (Miller et al., 2019) and gestational age at birth (Agrawal et al., 2018) were not associated with higher Q-CHAT scores.

A multivariable model of demographic variables explained 20% of Q-CHAT variance. In this model four variables (two measures of social deprivation and two measures of parenting style) were individually significantly associated with Q-CHAT score. Adding measures of general neurodevelopment to this model increased the explained variance to 36%, however this also resulted in two variables, IMD Rank and CSPS (measures of social deprivation) no longer being individually significantly associated with Q-CHAT score. Taken together this suggests that maternal parenting style is specifically associated with Q-CHAT score, whereas that the association of social deprivation with Q-CHAT is partially explained by general neurodevelopment.

Maternal verbosity had the strongest association with Q-CHAT score of any variable tested, remaining significantly associated with Q-CHAT score in multivariable models with and without general neurodevelopment. The mechanism via which this association occurs is unknown, but several pathways are plausible. Previous studies have suggested that parenting styles directly influence childhood behaviour, as children learn by repetition (Johnston et al., 2002; Miller-Lewis et al., 2006). Parent-child relationships of children with childhood autism diagnoses are more likely to be discordant than those of neurotypical offspring (Crowell et al., 2019). This discordance is thought to be both a cause and consequence of difficulties in social understanding (Gau et al., 2010; Ventola et al., 2017), and it is possible that even at 18 months toddlers displaying more autism traits have greater difficulty relating to their parents, leading to greater discordance (Craig et al., 2016; Wan et al., 2019). However, parenting styles are at least partly heritable (Oliver et al., 2014), hence it is also possible that the offspring of parents who naturally display more verbose and less collaborative parenting styles are less able to develop social relationship abilities, and thus score more highly on the Q-CHAT. A final possibility is that maternal verbosity is in part a proxy measure of stress – it has been previously shown to correlate with multiple measures of maternal stress (McQuillan et al., 2019), which in turn has previously been reported to correlate with a higher likelihood of offspring autism (Khambadkone et al., 2020). A more deeply phenotyped sample would be required to investigate how and if these different factors influence the relationship between maternal verbosity and Q-CHAT score.

Based on previous literature, some of our results are expected, while others are unexpected. For instance, we showed that multiple measures of psychosocial disadvantage correlate with higher Q-CHAT scores. There is a significant body of evidence demonstrating that early life adversity affects several domains of early childhood behaviour, including cognitive (Ross & Perlman, 2019), motor (Ferreira et al., 2018), and language (Wild et al., 2013) development, as well as emerging psychopathologies (de Laat et al., 2018; Kleine et al., 2021). It is known that lower socioeconomic status correlates with higher scores on the precursor to the Q-CHAT, the M-CHAT (Khowaja et al., 2015). Also, one previous study has specifically reported higher Q-CHAT scores in the offspring of depressed mothers (Goh et al., 2018). Therefore, our finding that maternal depressive symptom burden, measured using EPDS, correlates with offspring Q-CHAT score is not unexpected. In keeping with existing knowledge about neurodevelopment is our finding that two measures of social adversity correlate with higher Q-CHAT score.

In contrast unexpectedly, we found no association between sex and Q-CHAT score in any analysis performed. A handful of previous studies have demonstrated higher Q-CHAT scores in male toddlers, with small but significant average score differences reported: 3.1 (Kung et al., 2016), 3.1 (Auyeung et al., 2010) and 1.9 (Allison et al., 2008). It is not immediately obvious why we do not see the same difference in our data, although it may be that in a larger sample this difference would have been apparent. Males in our cohort did in fact score 1.4 Q-CHAT points higher than females on average (Cohen's d = 0.16), but the difference is not statistically significant. Similarly in a multivariable model the individual correlation between sex and Q-CHAT score is apparent (t=-2.32, p=0.020, Table 2) but did not survive FDR correction. It would be more appropriate to say that there is a trend towards males having higher Q-CHAT scores in our data than that there is no association at all.

We also found no association between parental history of ASD and Q-CHAT score in any analysis performed. A difference may reasonably have been expected based on the known familial increased likelihood of autism and ADHD diagnoses (Miller et al., 2019; Sandin et al., 2014). To date, one study has directly reported on the association between parental history of ASD and Q-CHAT score and found a large group difference, with the familial ASD history group having higher Q-CHAT scores at age 16-30 months (Ben-Sasson et al., 2018). One other study has specifically examined the difference between Q-CHAT scores in individuals with and without an older sibling with autism, and also found significant group differences (Pasco et al., 2021). It is not clear why we do not see the same effect here, although it is possible that the method in which we recorded family history (the mother was asked only if she or her partner had ever been diagnosed with autism) was too narrow a definition, or alternatively it may be the case that we lacked sufficient positive cases (28 parents reported an ASD or ADHD diagnosis compared to 506 with no diagnosis) to have determinative power.

Preterm birth confers an increasing likelihood of both childhood autism diagnosis and greater early autism trait emergence (Crump et al., 2021; Guy et al., 2015). One previous study reports Q-CHAT scores in a cohort of toddlers born before 30 weeks of gestation, who scored a mean of 33.7 (Wong et al., 2014), although to our knowledge no direct comparison of Q-CHAT scores in individuals born term and preterm has yet been presented. In our cohort we find no association between gestational age at birth and Q-CHAT score directly through univariable or multivariable associations, or indirectly via PCA latent components. One possibility is that early life autism trait emergence is less readily detected by screening tools in some preterm children (Gray, 2017; Moore et al., 2012). A second possible explanation for this difference is that here we consider gestational age at birth as a linear variable across the term and preterm range – the mean of Q-CHAT scores in individuals born before 30 weeks gestation in our sample (n=36) is 34.6, which is in fact in keeping with the 33.7 average score reported by Wong et al. (2014) using the same criteria.

A finding of particular interest is how associations between demographic variables and Q-CHAT score were influenced by general neurodevelopment, which in our study is represented by BSID-III. All BSID-III composite scores correlated individually to the Q-CHAT score (Table 1). In a multivariable model without BSID-III scores four variables (two socio-demographic measures, and two measures of parenting style) were significantly associated with Q-CHAT score (Table 2). With BSID-III composite scores added to the model the two socio-demographic associations were no longer significant, although the BSID-III language composite score association was. This is possibly in part due to co-linearity of the input variables (Figure 1A). After transforming linear variables into latent orthogonal components with PCA, one PC, associated with early life adversity, was significantly negatively associated with Q-CHAT score with or without BSID-III scores as a confounder – ie more early life adversity was associated with more autism traits (Table 3). As this PC was significantly associated with Q-CHAT score in both models suggests that socio-demographic and parental factors are specifically

influencing autism trait development as opposed to solely having a general effect on neurodevelopment. Using this latent component, we can see how our original variables contribute to Q-CHAT score (Figure 1D). Some of the variables contributing to this PC are expected based on our univariable results and previous literature; via this PC, early life adversity is associated with more autism traits, and maternal depression and expressive parenting style is associated with more autism traits. Two variables however correlate in a less intuitive fashion. Firstly, maternal age is positively contributing to the association with Q-CHAT score (Figure 1D). This is not in keeping with a significant body of literature that suggests that the offspring of older parents have a higher likelihood of autism (Parner et al., 2012). One possible explanation is that there are aspects of social deprivation that we are not capturing with our variables, for example income or wider availability of family support, which may be related to both parental age and autism trait development. Secondly, maternal age at leaving full time education is positively contributing to the association with Q-CHAT score via the 1st PC (associated relative social advantage). Given that greater social deprivation in our sample is in general associated with higher Q-CHAT scores this is somewhat counter-intuitive and is not in keeping with the one previous exploratory study to report on this association (Goh et al., 2018). There is a larger body of work regarding associations of parental education and childhood autism diagnoses, with at least some research suggesting that autism is more commonly diagnosed in the offspring of highly educated parents (King & Bearman, 2011), so the same may be true of early life autism trait development.

There are some limitations to our findings. Firstly, the Q-CHAT is parent rated, and therefore is indicative of the parent's subjective assessment of their child, rather than an objective test (Ravi et al., 2016); it is thus possible that reporting bias with common method variance could have altered our results. Secondly although emerging traits at age 18 months increase the likelihood of a future diagnosis of autism, the positive predictive value of a high Q-CHAT score (or indeed a high score on any early autism screening tool) is low (Thabtah & Peebles, 2019). The prevalence of childhood autism in the UK is approximately 1.8% (Roman-Urrestarazu et al., 2021) - if this prevalence is seen in our cohort then approximately 10 individuals may be expected to receive an autism diagnosis, meaning that what we are largely studying here are variations in the spectrum of typical development. Some believe that these variations in the typical spectrum are not necessarily related to the clinical autism phenotype (Mottron, 2021), although this is an ongoing debate (Constantino, 2021).

Our results are of potential interest from two perspectives. Firstly, future authors investigating the Q-CHAT score and other measures of early autism traits should be aware of our findings as potential confounders or limiting factors in their work. Secondly our results merit consideration from a clinical perspective. From our data, it would be reasonable to expect a greater rate of diagnoses in more socioeconomically deprived children, which does not currently occur. This raises two questions: are potential autism diagnoses being missed in more socially deprived groups, or are there a separate set of as yet unidentified factors influencing the likelihood of transitioning from early traits at age 18 months to a clinical autism diagnosis in childhood?

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