Association between extreme autistic traits and intellectual disability: insights from a general population twin study

THE ASSOCIATION BETWEEN EXTREME AUTISTIC TRAITS AND INTELLECTUAL DISABILITY: INSIGHTS FROM A GENERAL POPULATION TWIN STUDY

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Abstract

Background: Autism is associated with intellectual disability (ID). The strength and origin of this association is unclear.

Aims: To investigate the association between extreme autistic traits and ID in children from a community-based sample and to examine whether the association can be explained by genetic factors.

Method: Children scoring in the extreme 5% on measures of autistic traits, intelligence and academic achievement were selected from 7,965 7/8-year-old and 3,687 9-year-old twin pairs. Phenotypic associations between extreme autistic traits and ID were compared with associations among the full-range scores. Genetic correlations were estimated using bivariate DeFries-Fulker extremes analyses.

Results: Extreme autistic traits were modestly related to ID; this association was driven by communication problems characteristic of autism. Although this association was largely due to genetic factors, the genetic correlation between autistic traits and ID was only modest.

Conclusions: Extreme autistic traits are substantially genetically independent of ID.

Declaration of interest: None

Intellectual disability (ID; here defined as IQ<70) is common in autism. Historically, the prevalence of ID in autism is estimated at 70%,[1] but recent studies encompassing all autism spectrum conditions (ASC), including Asperger syndrome (AS) and pervasive developmental disorder-not otherwise specified, suggest the prevalence of ID in ASC may be considerably lower.[2,3] It has been suggested that the association between autism and ID may be inflated due to clinical ascertainment bias.[4] If this hypothesis holds true it has implications for studying the causes of ASC. A strong genetic link between ASC and ID would argue for a search for genes influencing both traits. A limited association would argue for separate genetic influences on each trait. A possible ascertainment bias for ID in ASC limits the investigation of this association in clinical samples. Instruments that assess autistic traits on a quantitative scale[5,6] enable studying the relationship in population samples. This study reports on the association between autistic traits, IQ and academic achievement in the extreme 5% scorers of a large community-based twin sample. The genetic informative design allowed for exploration of the genetic and environmental origin of the association.

Methods

Participants

Participants were part of the longitudinal Twins Early Development Study (TEDS), a child twin sample representative for the general population in the UK.[7,8] The sample characteristics of TEDS are described elsewhere.[9] Zygosity in same-sex twins was determined using polymorphic DNA markers (75% of cases) or a parent-report questionnaire which has a reported accuracy of 95%.[10] IQ and academic achievement was assessed at ages 7 and 9. Measures of autistic traits were collected when the twins were nearly 8 (parent-report) and 9 (teacher-report) years.

Exclusion criteria were as follows: no first contact data available (153 families); extreme pregnancy or perinatal difficulties (165 families); unclear twin zygosity (300 families); not having English as the first spoken language (146 families); specific medical syndrome (not including suspected ASC) such as Down syndrome (225 families). After exclusions data were available for 8,104 twin pairs, of which 1,340 were monozygotic male pairs, 1,325 dizygotic males, 1,496 monozygotic females, 1,354 dizygotic females and 2,589 dizygotic twin pairs of opposite sex. At age 9, only twins born between January 1994 and August 1995 were contacted, resulting in a smaller sample size. Data on IQ, academic achievement and/or autistic traits were available for 7,965 7/8-year-old twin pairs and for 3,687 pairs at age 9.

Measures

The Childhood Autism Spectrum Test (CAST)[5] is a 31-item questionnaire asking about behaviours associated with ASC. A CAST score of ≥15 is the cut-off for identifying children at risk for ASC. Items can be divided into three subscales,[11] based on the DSM-IV criteria[12] for autism: Social impairments (SIs, 12 items); communication impairments (CIs, 12 items); and restricted repetitive behaviours and interests (RRBIs, 7 items). The CAST shows good test-retest reliability (r=.83)[13] and satisfactory internal consistency (α=.73 in TEDS) for the full CAST and moderate α-values for the subscales (SIs: α=.57; CIs: α=.66; RRBIs: α=.50). Parents rated the child's autistic traits at age 8. If the families gave consent, teachers were asked to complete an abbreviated version of the CAST (20 items)[8] when the twins were 9 years.

Intelligence tests were administered by telephone at age 7. Two verbal (Similarities and Vocabulary) and two nonverbal subtests (Picture completion and

Conceptual grouping) from the Wechsler Intelligence Scale for Children-III (WISC-III)[14] and the McCarthy Scales of Children's Abilities[15] were modified for telephone administration. The intelligence composite score derived from the telephone administered test battery correlates 0.72 with the Stanford-Binet Intelligence Scale.[16] At age 9, IQ was assessed using test booklets completed by the twins under parental supervision. A composite score was derived from two verbal (adaptations of the WISC-III Vocabulary and Information subtests) and two nonverbal tests (adaptations of the subtests Figure classification and Figure analogies from the Cognitive Abilities Test: Third Edition[17]).

Teachers were asked to assess the twin's academic achievement using a 5-point rating scale following the UK National Curriculum achievement goals. A composite score was used at both ages, based on achievement in English and Mathematics at age 7 and in English, Mathematics and Science at age 9.

Children with ASC

Children at risk for ASC were identified from parents informing TEDS about their twins' diagnoses or from scores above the cut-off on the CAST at age 8. These children were followed up and were administered the Development and Well-Being Assessment (DAWBA).[18] Based on the data available at the time of the present analyses, 85 were identified with the DAWBA as having autism, 11 children with AS, and 64 children with ASC other than autism or AS. Parent-rated CAST scores were available for 145 of these children (75 with autism; 10 with AS; 60 with other ASC). IQ and academic achievement data were available for respectively 51 and 84 children at age 7. Most children with ASC were not invited to participate at age 9 to avoid over-testing, as these children were enrolled in another project during this time.

Data analyses

Children scoring in the top 5% of the distribution of autistic traits and/or in the bottom 5% of the distribution of IQ and academic achievement scores were defined as extreme cases (probands). This cut-off was chosen as the best balance between the need for a sufficient sample size and the aim of studying extreme groups. All analyses were based on age- and sex-regressed scores.

To examine whether children with extreme autistic traits were at increased risk for ID (as indexed by low IQ/academic achievement), chi-square tests were performed for one randomly selected twin from each pair. The phenotypic correlations across the full-range scores were examined using structural equation modelling in Mx, taking into account the genetic relatedness between the twins.[19] Phenotypic correlations indicate whether variation in trait X covaries with individual differences in trait Y. Phenotypic group correlations (PGCs) examine the extent to which extreme scorers on trait X *as a group* score above or below the population mean on unselected trait Y.[20] PGCs are calculated by dividing the proband's standardised score on the unselected variable Y by the proband's standardised score on the selected variable X. A PGC of 1.0 indicates that the probands' mean score on Y is as extreme as the probands' mean score on X; a PGC of 0.0 means that the probands' score on Y is no different from the population mean. PGCs are bidirectional: selecting probands for extreme autistic traits and examining their IQ score could yield different results from selecting probands for extremely low IQ and examining their CAST scores.

Genetic analyses

DeFries-Fulker (DF) extremes analysis[21] is a regression analysis of twin data in which the co-twin's mean score is predicted by their proband's score, taking into account the genetic relatedness between the twins (1.0 for monozygotic (MZ) twins; on average 0.5 for dizygotic (DZ) twins). Rather than assessing a dichotomy (e.g. ID present or absent), DF extremes analysis assesses the continuous distribution directly and thereby provides a powerful test of the aetiology of extreme scores on a continuous dimension.

Sex differences are reported for autism. To maintain the comparability of the MZ and DZ pairs, DF extremes analyses were carried out on data from same-sex DZ twins only. Prior to the regression analysis all scores were standardised (i.e. expressed as a deviation from the population mean) and then transformed (i.e. divided by the difference between the proband and general population means, specific for each zygosity). Comparing the regression to the population mean for MZ and DZ co-twins of probands gives insight in the genetic influences on extreme traits. If the mean scores of MZ co-twins resemble the proband scores more closely than DZ co-twin scores do there is evidence for genetic effects on the extreme trait.

The following regression equation is used in DF extremes analyses: $C = B_1P + B_2R + A$, in which C is the predicted score for the co-twin, P is the proband score, R is the coefficient of the genetic relatedness between the twins and A is the regression constant. B_1 is the partial regression of the co-twin's score on the proband's score and is an index of average MZ and DZ resemblance independent of zygosity. B_2 is the partial regression of the co-twin's score on R and is equivalent to twice the difference between the standardised transformed means for MZ and DZ co-twins. It provides a direct estimate of group heritability (h^2_g): the extent to which genetic factors account for the mean difference between probands and the population.

The aetiology of the association between extreme autistic traits and low IQ/academic achievement was studied using the bivariate extension of DF analysis.[22] Bivariate DF analysis selects the probands on trait X, but compares the quantitative scores of their co-twins on unselected trait Y. In the bivariate DF regression equation ($C_y = B_1P_x + B_2R + A$), C is the predicted score of the co-twin on unselected variable Y, P is the proband's score on selected variable X, B_1 is the partial regression of the co-twin's Y score on the proband's X score, and B_2 is the partial regression of the co-twin's Y score on the coefficient of the genetic relatedness. B_2 indicates the extent to which the proband's deficit on trait X can be ascribed to genetic factors that also influence trait Y. Dividing B_2 by the corresponding PGC provides a measure of the proportion of the covariance that can be attributed to genetic factors, called bivariate heritability.[23]

Since bivariate DF extreme analyses are bidirectional, the analysis for the opposite direction has to be examined separately. The genetic correlation[24] (the extent to which deficits on trait X and deficits on trait Y are affected by the same set of genes) can be derived as:

$$r_g\,(xy) = \sqrt{(B_{2(xy)})(B_{2\,(yx)})/(B_{2(x)})(B_{2\,(y)})}$$

A genetic correlation of 1.0 suggests complete genetic overlap; a correlation of 0.0 indicates that the traits are affected by two separate sets of genes.

If the DZ transformed co-twin means are less than half the MZ co-twin means, non-additive genetic effects might play a role (although sibling interaction effects could also apply). Because the power in DF analyses is limited to distinguish non-additive from additive genetic influences, only broad heritability is examined in this study. When the data suggested non-additive effects (when the estimate for h^2_g or B_2

exceeded the estimate of the transformed MZ co-twin mean), h^2_g or B_2 were based on the estimated value of the MZ transformed co-twin mean.

Results

The distribution of the IQ and academic achievement scores were approximately normal; the CAST scores were slightly skewed (skewness statistics were 1.00 (parent ratings) and 1.47 (teacher ratings)). The untransformed scores were used in subsequent analyses, since previous DF extremes analyses using the CAST showed that data transformation did not affect the results.[7] The most extreme-scoring 5% on the parent-rated CAST obtained scores ≥1.83s.d. above the population mean, equivalent to CAST scores ≥11.83. The lowest-scoring 5% on the measure of IQ scored ≤1.68s.d. (age 7) and 1.85s.d. (age 9) below the population mean. Mean CAST scores in children with ASC were well above the clinical cut-off (mean=19.17, s.d.=5.11), and CAST total and subscale scores were significantly higher than the population mean (all $P<.001$). IQ (mean=-.69, s.d.=.121) and academic achievement (mean=-1.51, s.d.=1.60) were significantly lower than the population mean ($F(1, 9986)=26.86$, $P<.001$ and $F(1, 11217)=213.80$, $P<.001$), although these descriptive statistics should be interpreted with care since IQ and academic achievement data were only available for respectively 51 and 84 ASC children.

The highest-scoring 5% on the parent-reported CAST were more likely to perform in the bottom 5% on the IQ test ($\chi^2(1)=42.985$, $P<.001$, odds ratio (OR)=4.32) and to show low academic achievement ($\chi^2(1)=60.876$, $P<.001$, OR=4.44). These odds ratio's increased to respectively 6.32 and 7.51 in children who scored at or above the CAST cut-off. Extreme scorers on the teacher-reported CAST were not significantly more likely to have low IQ scores ($\chi^2(1)=1.718$, $P=.083$,

OR=1.76) but did show an increased risk for poor academic achievement ($\chi^2(1)=78.979$, $P<.001$, OR=6.76).

The phenotypic correlations between parent and teacher-rated autistic traits and IQ and academic achievement were all negative and ranged between -.07 to -.24 for the full-range scores and between -.01 and -.40 for the PGCs in the 5% extremes, suggesting that the association between number of autistic traits and ID (as indexed by low IQ/academic achievement) was modest. Both the full-range correlations and the PGCs were similar in boys and girls (difference in $r \leq .05$, see supplementary Table S1), yielding no evidence for a sex effect on the association. To maximize power, all subsequent analyses were conducted for both sexes combined. PGCs were also calculated for 15%, 2% and 1% cut-offs (see Table S1). All associations between autistic traits and IQ were similar, suggesting that the magnitude of the relationship was linear across the sample. For academic achievement, there was a trend in which the PGCs were somewhat stronger with more extreme cut-offs for academic achievement.

Insert Table 1 here

Univariate DF analyses (see Table 1) showed high group heritability for parent and teacher-rated CAST scores (h^2_g=.71 and .65 respectively) and academic achievement (h^2_g=.85 at both ages), and moderate group heritability for IQ (h^2_g=.31 (age 7) and .44 (age 9)). Univariate DF analyses have been reported previously[7,25] and are therefore not discussed in detail here. In the bivariate models, transformed DZ co-twin scores consistently showed a stronger regression to the population mean than MZ co-twin scores, suggesting genetic effects on the overlap between extreme traits. B_2

estimates were negligible for the association between IQ and teacher-rated CAST and modest for all other associations. Dividing each B_2 estimate by the corresponding PGC (bivariate heritability) showed that the modest phenotypic association between extreme autistic traits and ID was mainly accounted for by genetic effects. For example, in the group selected for extremely low IQ, 86% of the association with parent-reported CAST scores was explained by genetic factors (-.19/-.22=0.86). The bivariate heritability estimates were high for all measures, apart from the analyses between extremely low IQ and teacher-rated autistic traits. However, the genetic correlations were only modest. The genetic correlations between extreme parent-rated autistic traits and low IQ or poor academic achievement were .44 and .31. The genetic correlations using teacher-rated CAST scores were .04 and .38. What these results mean is that although genetic factors are largely responsible for the phenotypic association between autistic traits and low IQ/academic achievement, most of the genetic effects on autistic traits and on IQ/academic achievement are *independent*.

Next we explored whether the relation between extreme autistic traits and ID varied for the different features of the autism triad. Both the full-range phenotypic correlations and the PGCs indicated that the association between extreme autistic traits and ID is mainly explained by CAST items assessing communication difficulties (see supplementary Table S2). Examination of the CIs items suggested that the observed association was not simply due to overlapping item content. The CIs items primarily assess difficulties with pragmatic communication (e.g. “Does s/he tend to take things literally?”) and do not directly assess (verbal) intelligence. Repeating the DF extremes analyses using just the CIs subscale yielded similar results to the CAST-total analyses (supplementary Table S3). The genetic correlation between parent-rated CIs and ID was .48 when assessed using IQ scores and .33 using academic

achievement scores. The genetic correlations between these measures and teacher-rated CIs were .22 and .50, respectively.

Lastly, we explored whether a discrepancy between IQ scores and academic achievement is related to number of autistic traits. Difference scores between IQ and academic achievement were correlated to parent and teacher CAST scores. Higher IQ scores relative to academic achievement correlated significantly with parent-reported CIs (r=.06, *P*<.01) and teacher-reported CAST-total (r=.14, *P*<.01), SIs (r=.13, *P*<.01) and CIs scores (r=.17, *P*<.01).

Discussion

Modest genetic correlation between extreme autistic traits and ID

This paper reports the first population-based study testing the association between extreme autistic traits and ID (defined in terms of low IQ/academic achievement). Although the risk of showing poor performance on tests of IQ and academic achievement was significantly increased in children with extreme autistic traits, our results suggest that the association between extreme autistic traits and ID is only modest. There was a degree of genetic overlap between extreme autistic traits and ID, as indicated by modest genetic correlations. Since autistic traits are highly heritable[7,26] there is also substantial genetic specificity for autistic traits.

These results are in agreement with findings from family studies indicating that (severe) ID is not part of the broader autism phenotype observed in relatives of autistic probands. Whilst high intraclass correlations are observed between intelligence scores in affected children from the same family,[27,28] there is no evidence for a familial loading for ID in unaffected family members of autism probands, and the correlation between IQs of affected and unaffected family members is low.[29,30,31]

Also, in ASC, unlike most severe developmental disorders (e.g. Williams Syndrome, Down Syndrome), there is no 'capping' of IQ, and measured IQ can be extremely high.[32, 33]

Clinical studies of the phenotypic association between autism symptom severity, as indexed by ADOS and ADI-R scores, and intellectual functioning generally found modest to moderate correlations between SIs and CIs and measures of IQ.[34, 35, 36] Results for RRBIs symptoms varied, depending on the sample under investigation and the type of RRBIs studied.[34, 35, 36] Several family studies indicated an increased rate of social and communication deficits in relatives of autistic individuals.[37] There is evidence to suggest that relatives who show communication difficulties also tend to have lower IQs.[29,30,38] These studies are in line with our finding that the association between autistic traits and ID was mainly driven by communication difficulties.

Academic achievement vs. IQ in children with extreme autistic traits

Our phenotypic analyses suggested that the association between poor academic achievement and autistic traits became stronger the more stringently the cut-off for extreme groups was set. This trend was not observed in the analyses between autistic traits and IQ, for which the magnitude of the full-range phenotypic correlations and PGCs was similar regardless of the cut-off. Analyses exploring discrepancies between IQ scores and teacher-rated academic achievement suggested that teachers may underestimate the academic abilities of children with social and communication difficulties. Children with such problems may struggle to show their full cognitive potential in the classroom. These results mirror findings from clinical

studies that report attenuated academic achievement relative to IQ in individuals with ASC.[2]

Methodological considerations

The current study defined extreme autistic traits as the highest-scoring 5% of a large community sample assessed on a continuous measure of autistic traits. This selection included children scoring ≥11.83 on the parent-reported CAST. Children with an ASC diagnosis typically obtain parental CAST scores ≥15[5] and our extreme group is therefore likely to include less extreme cases than a clinical ASC sample. Similarly, the lowest-scoring 5% on a measure of IQ and academic achievement were selected. Although the IQ and academic achievement scores in these extreme groups were markedly low (mean academic achievement scores were 2.20-2.60s.d. below the population mean; IQ scores were 2.12-2.26s.d. below the population mean, corresponding to standardised IQs of approximately 67), it should be acknowledged that this sample included few children with severe learning disabilities. Our results cannot, therefore, be generalised to individuals with severe or profound ID, in whom the aetiology of autism may be different.[4] Ten to 20% of ASC cases are caused by known medical conditions, defined mutations or gross chromosomal abnormalities[39] and these cases are likely also to have ID. Our results are only informative for idiopathic ASC cases (accounting for the remaining 80-90%) in which the ASC risk may be influenced by common genetic variants.

The large scale of this study did not permit detailed investigation of the relative strengths and weaknesses in cognitive functioning. IQ tests were administered by telephone at age 7. Children with many autistic traits, particularly children with communication difficulties, may find it hard to perform well using this assessment

procedure. However, similar correlations were found using the academic achievement data and at age 9 (when test booklets were used), strengthening our confidence in the validity of the IQ measure at age 7. At age 9 data were available for a smaller number of twins, and most children with ASC were excluded at this age to avoid over-testing. We feel these data are still valuable as the results show remarkable consistency between raters and across age, indicating that these findings are neither rater- nor age-specific.

Implications

This study has implications for future genetic studies of autism. Our results indicate that in a community-based sample the liability to extreme autistic traits is substantially genetically independent of the vulnerability to impaired intellectual functioning. In so far as there is genetic overlap, this link is likely to be found in genes affecting communication abilities. Genes involved in neurodevelopment are probably important in certain forms of ASC,[40] particularly in individuals with severe ID. However, these genes are unlikely to be the sole explanation of the complex aetiology of autism. Our study suggests that genetic variants that do not affect general intellectual abilities also play a role.

Our finding of a limited association between autistic traits and ID contrasts with clinical studies reporting a high prevalence of ID in autism.[1] This discrepancy may be explained, in part, by clinical ascertainment bias.[4] Individuals with extreme autistic traits *and* ID may be more likely to be referred to the clinic. The number of individuals with ASC with normal intelligence may thus be under-reported. Health and education professionals may need to be made more aware that ASC can occur without ID to ensure that all individuals warranting a diagnosis are detected.

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Table 1. Results for DeFries-Fulker Univariate and Bivariate Extremes Analyses

			Univariate			Bivariate (IQ/ac)				Bivariate (CAST)			
zyg	N	scores	proband	Co-twin	h^2_g	Proband	Co-twin	B_2	biv h^2_g	Proband	Co-twin	B_2	biv h^2_g
Parent CAST Total age 8													
MZ	201	Stand	2.79	1.99									
DZ	208	Stand	2.79	.51									
MZ	201	Trans	1.00	.71									
DZ	208	Trans	1.00	.18	.71 ± .09								
IQ age 7													
MZ	174	Stand	-2.12	-1.39		.42	.41			-.58	-.53		
DZ	172	Stand	-2.16	-1.08		.43	.09			-.31	-.02		
MZ	174	Trans	1.00	.66		-.20	-.19			-.24	-.22		
DZ	172	Trans	1.00	.50	.31 ± .20	-.20	-.04	-.19 ± .10	.86	-.12	-.01	- .22 ± .11	1.00
Academic achievement age 7													
MZ	218	Stand	-2.60	-2.21		.58	.48			-.91	-.87		
DZ	157	Stand	-2.58	-1.08		.65	.30			-.68	-.26		
MZ	218	Trans	1.00	.85		-.23	-.19			-.36	-.35		
DZ	157	Trans	1.00	.42	.85 ± .07	-.25	-.12	-.17 ± .21	.68	-.26	-.10	-.35 ± .12	1.00
Teacher CAST Total age 9													
MZ	90	Stand	2.91	2.03									
DZ	90	Stand	2.90	1.07									
MZ	90	Trans	1.00	.70									
DZ	90	Trans	1.00	.37	65 ± .33	.							
IQ age 9													
MZ	110	Stand	-2.26	-1.62		.12	.01			-.09	-.10		
DZ	113	Stand	-2.26	-1.12		.27	-.02			-.07	.09		
MZ	110	Trans	1.00	.72		-.06	-.01			-.03	-.04		
DZ	113	Trans	1.00	.49	.44 ± .21	-.12	.01	-.01 ± .12	.08	-.02	.03	-.04 ± .11	.80

Academic achievement age 9													
MZ	85	Stand	-2.20	-1.86		.95	.86			-.61	-.59		
DZ	72	Stand	-2.22	-.88		.88	.20			-.54	-.14		
MZ	85	Trans	1.00	.85		-.43	-.40			-.21	-.20		
DZ	72	Trans	1.00	.40	.85 ± .10	-.40	-.09	-.40 ± .15	1.00	-.19	-.05	-.20 ± .11	1.00

Note: Group heritability (h^2g) estimates were constrained to be equal or lower than the MZ transformed co-twin mean. 95% confidence intervals are provided for the h^2_g and B_2 estimates, calculated using corrected standard errors. In bivariate analyses the selected variable is given in parentheses. ac = academic achievement; CAST = Childhood Autism Spectrum Test; N = number of probands; B_2 = bivariate genetic DF estimate; biv h^2g = bivariate group heritability; Stand = standardised scores; Trans = transformed scores; MZ/DZ = monozygotic/dizygotic twin.

Supplementary material

Table DS1. Phenotypic correlations for entire sample ('full-range scores') and phenotypic 'group' correlations ('PGC') between autistic traits and IQ and academic achievement (Ac) with cut-offs of 15%, 5%, 2% and 1%.

		Full-range scores		PGC Extreme 15%		PGC Extreme 5%		PGC Extreme 2%	PGC Extreme 1%
		boys	girls	boys	girls	boys	girls		
Age 7/8 (Parent CAST)	IQ	-.18	-.21	-.16/-.13[a]	-.15/-.21[a]	-.24/-.12[a]	-.19/-.18[a]	-.20/-.14[a]	-.25/-.14[a]
	Ac	-.22	-.23	-.23/-.18[b]	-.21/-.20[b]	-.24/-.23[b]	-.26/-.26[b]	-.32/-.30[b]	-.35/-.32[b]
Age 9 (Teacher CAST)	IQ	-12	-.07	-.09/-.08[a]	-.03/-.07[a]	-.18/-.07[a]	-06/-.01[a]	-.14/-.05[a]	-.13/-.04[a]
	Ac	-.24	-.24	-.31/-.24[b]	-.28/-.29[b]	-.40/-.17[b]	-.39/-.29[b]	-.45/-.19[b]	-.49/-.21[b]

Note: Associations given separately for boys and girls in the full-range scores and the extreme 15% and 5%. Limited sample size did not allow separate associations per sex in the 2% and 1% extreme groups.

[a/b] For the PGCs, the first PGC is for IQ/academic achievement as the selected variables, the second PGC is for CAST as the selected variable. CAST = Childhood Autism Spectrum Test.

Table DS2. Phenotypic correlations for entire sample ('full-range scores') and phenotypic group correlations ('PGC') between the triad of autistic traits and IQ and academic achievement (Ac).

		CAST SIs	CAST RRBIs	CAST CIs
		Full-Range Scores		
Age 7/8 (Parent-report)	IQ	-.10 (-.13 to -.10)	-.07 (-.09 to -.04)	-.24 (-.26 to -.21)
	Ac	-.07 (-.09 to -.05)	-.09 (-.12 to -.06)	-.29 (-.30 to -.26)
Age 9 (Teacher-report)	IQ	-.06 (-.09 to -.02)	.09 (06 to .13)	-.20 (-.23 to -.20)
	Ac	-.18 -.21 to -.15)	.09 (.06 to .12)	-.37 (-.37 to -.34)
		PGC Extreme 5%		
Age 7/8 (Parent-report)	IQ	-.11/-.10[a]	-.09/-.06[a]	-.27/-.21[a]
	Ac	-.12/-.08[b]	-.12/-.16[b]	-.29/-.26[b]
Age 9 (Teacher-report)	IQ	-.08/-.04[a]	.05/.07[a]	-.20/-.13[a]
	Ac	-.30/-.19[b]	-.05/.03[b]	-.50/-.35[b]

Note: [a/b] For the PGCs, the first PGC is for IQ/academic achievement as the selected variable, the second PGC is for CAST as the selected variable. 95% confidence intervals in parentheses for the full-range phenotypic correlations. CAST = Childhood Autism Spectrum Test; SIs = social impairments; RRBIs = restricted repetitive behaviours and interests; CIs = communication impairments.

Table DS3. Results for DeFries-Fulker Univariate and Bivariate Extremes Analyses for Autistic-like Communication Impairments (CAST CIs)

			Univariate			Bivariate (IQ/ac)				Bivariate (CAST CIs)			
zyg	N	scores	proband	Co-twin	h^2_g	Proband	Co-twin	B_2	biv h^2_g	Proband	Co-twin	B_2	biv h^2_g
Parent CAST CIs age 8													
MZ	227	Stand	2.71	2.13									
DZ	206	Stand	2.66	.80									
MZ	227	Trans	1.00	.79									
DZ	206	Trans	1.00	.30	.79 ± .07								
IQ age 7													
MZ	174	Stand	-2.12	-1.39		.50	.52			-.69	-.61		
DZ	172	Stand	-2.16	-1.08		.54	.11			-.34	-.13		
MZ	174	Trans	1.00	.66		-.24	-.25			-.27	-.24		
DZ	172	Trans	1.00	.50	.31 ± .20	-.25	-.05	-.25 ± .10	.93	-.14	-.05	-.23 ± .22	1.00
Academic achievement age 7													
MZ	218	Stand	-2.60	-2.21		.76	.63			-.83	-.79		
DZ	157	Stand	-2.58	-1.08		.63	.25			-.72	-.18		
MZ	218	Trans	1.00	.85		-.29	-.25			-.33	-.31		
DZ	157	Trans	1.00	.42	.85 ± .07	-.25	-.10	-.24 ± .20	.92	-.28	-.07	-.31 ± .11	1.00
Teacher CAST CIs age 9													
MZ	90	Stand	2.72	1.73									
DZ	98	Stand	2.73	.91									
MZ	90	Trans	1.00	.63									
DZ	98	Trans	1.00	.33	.60 ± .31								
IQ age 9													
MZ	110	Stand	-2.26	-1.62		.39	.21			-.49	-.41		
DZ	113	Stand	-2.26	-1.12		.43	-.01			-.05	.06		
MZ	110	Trans	1.00	.72		-.18	-.10			-.19	-.16		
DZ	113	Trans	1.00	.49	.44 ± .21	-.19	.00	-.10 ± .14	.50	-.02	.02	-.13 ± .22	1.00

Academic achievement age 9													
MZ	85	Stand	-2.20	-1.86		1.16	.97			-.88	-.80		
DZ	72	Stand	-2.22	-.88		1.03	.32			-.77	-.36		
MZ	85	Trans	1.00	.85		-.53	-.44			-.33	-.29		
DZ	72	Trans	1.00	.40	.85 ± .10	-.47	-.14	-.44 ± .15	.83	-.29	-.13	-.29 ± .22	.88

Note: Group heritability (h^2g) estimates were constrained to be equal or lower than the MZ transformed co-twin mean. 95% confidence intervals are provided for the h^2_g and B_2 estimates, calculated using corrected standard errors In bivariate analyses the selected variable is given in parentheses. ac = academic achievement; CAST CIs= Communication impairments as assessed by the Childhood Autism Spectrum Test; N = number of probands; B_2 = bivariate genetic DF estimate; biv h^2g = bivariate group heritability; Stand = standardised scores; Trans = transformed scores; MZ/DZ = monozygotic/dizygotic twin