

Phenotypic and Genetic Overlap Between Autistic Traits at the Extremes of the General Population

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ABSTRACT

Objective: To investigate children selected from a community sample for showing extreme autistic-like traits and to assess the degree to which these individual traits—social impairments (SIs), communication impairments (CIs), and restricted repetitive behaviors and interests (RRBIs)—are caused by genes and environments, whether all of them are caused by the same genes and environments, and how often they occur together (as required by an autism diagnosis).

Method: The most extreme-scoring 5% were selected from 3,419 8-year-old pairs in the Twins Early Development Study assessed on the Childhood Asperger Syndrome Test. Phenotypic associations between extreme traits were compared with associations among the full-scale scores. Genetic associations between extreme traits were quantified using bivariate DeFries-Fulker extremes analysis. **Results:** Phenotypic relationships between extreme SIs, CIs, and RRBIs were modest. There was a degree of genetic overlap between them, but also substantial genetic specificity. **Conclusions:**

This first twin study assessing the links between extreme individual autistic-like traits (SIs, CIs, and RRBIs) found that all are highly heritable but show modest phenotypic and genetic overlap. This finding concurs with that of an earlier study from the same cohort that showed that a total autistic symptoms score at the extreme showed high heritability and that SIs, CIs, and RRBIs show weak links in the general population. This new finding has relevance for both clinical models and future molecular genetic studies. *J. Am. Acad. Child Adolesc. Psychiatry*, 2006;45(10):1206–1214. **Key Words:** twins, genetics, autism, autistic traits.

Autism spectrum disorders (ASDs) are defined by a triad of features: social impairments (SIs), communication impairments (CIs), and restricted repetitive behaviors and interests (RRBIs). Historically, this has also been referred to as the “triad of impairments,” although a more neutral descriptor simply refers to this

as the “triad” because it is not necessarily the case that RRBIs are impairments (e.g., Baron-Cohen and Wheelwright, 1999). A study more than 25 years ago attempted to identify all individuals who met criteria for any part of the triad (Wing and Gould, 1979). The authors report evidence of a “marked tendency for these problems to occur together.” However, it was also reported that some children showed SIs but not RRBIs, and vice versa, suggesting some splintering of the autism phenotype. Since this study, there have been changes in the definition of ASDs, and the sample in the Wing and Gould study was selected from a psychiatric/learning difficulties register, “enriching” it with children with greater severity and comorbidity (Caron and Rutter, 1991).

In terms of causal influences, twin studies have shown that autism and the broader manifestation of the autism phenotype are highly heritable (Bailey et al., 1995; Folstein and Rutter, 1977; Steffenburg et al., 1989). Broader autism phenotype family studies have

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reported that some relatives of individuals with autism show only some of the traits that are characteristic of autism, suggesting segregation of the phenotype among relatives (Bailey et al., 1998; Bishop et al., 2004; Pickles et al., 2000; Piven, 1999; Szatmari et al., 2000). These observations hint that different causal influences may affect the three domains and that it may be fruitful to consider whether there are different genetic influences on the various aspects of the autism phenotype.

Indeed, two recent twin studies have reported only modest genetic overlap between SIs and RRBI measured as traits in the general population, despite the fact that they are both highly heritable individually (Ronald et al., 2005, 2006). These results can be contrasted to a recent family study of autistic traits that reported high “genetic” overlap between social motivation and range of interest/ flexibility (Sung et al., 2005). However, these studies used different samples: more than 3,000 7- and 8-year-old twin pairs in a representative community sample versus 201 nuclear families ascertained through the existence of at least two children affected with an ASD (average IQ 80; mean age 10.0; SD = 5.1 years).

One way to reconcile these findings is to consider the possibility that there may be genetic heterogeneity in the etiology of autistic traits in the general population, but that at the extreme, different autistic traits have common genetic origins. This would explain why the study with a community sample found genetic heterogeneity between SIs and RRBI (Ronald et al., 2005, 2006), but the study with a clinical sample (Sung et al., 2005) did not. The best way to compare the etiology of extreme traits and traits in the general population is to select children who score at the extreme end of the distribution from a general population twin sample. One of the previous twin studies reported high heritability of a total autistic symptoms score at the extreme (Ronald et al., 2006), but this approach has not been used before for individual autistic traits. Selecting the sample in this way provides a large enough extreme-scoring sample to have power to detect effects, as well as the ability to disentangle genetic and shared environmental influences (not possible in family studies). A useful tool for this is DeFries-Fulker (DF) extremes analysis (DeFries and Fulker, 1988), a type of analysis used with twin data. Furthermore, the bivariate extension of DF can reveal the genetic overlap between two different extreme traits by considering the quantitative

“impairment” on one trait of probands selected as behaviorally extreme on a second trait.

The present study used bivariate DF analysis in the first twin study to investigate the links between extreme individual autistic-like traits: SIs, CIs, and RRBI. The extreme-scoring sample was selected from the same community sample used by Ronald et al. (2006). The characteristics of these extreme groups, such as overlap across the triad, sex ratio, and their verbal/nonverbal ability, academic ability, and behavior problems, were also studied.

METHOD

Participants

Participants were a subsample of the Twins Early Development Study (TEDS), a United Kingdom-based community sample of twins contacted from birth records (Trouton et al., 2002). Questionnaires were sent to 7,687 families when the twins were age 8 (mean = 8.09, SD = 0.48). A total of 3,807 families (49.5%) returned completed questionnaires. The questionnaires were sent to all families on whom TEDS had details who had not formally withdrawn from the study, regardless of whether families had provided data at age 7 and earlier. Families were not pushed to respond, and so the 7,687 families include a proportion of inactive families, which accounts in part for the modest response rate.

The TEDS sample that did provide data at age 8 was reasonably representative of the U.K. population. Comparing this sample to data from the General Household Survey (Office for National Statistics, 2005), 94% versus 93% were white, 48% versus 50% were male, 37% versus 32% of mothers had one or more A levels (U.K. advanced educational qualification), and 4% of children had a statement of special educational needs versus 3% of children in England (Department for Education and Skills, 2002). Comparing participating families and families invited to participate but who did not send back data, using data collected when the twins were 12 months old: 94% versus 90% were white, 49% versus 50% were male, and 38% versus 32% of mothers had at least A levels as their highest educational qualification.

Exclusions were made for the following reasons: no consent signature (40 families), unclear zygosity (86 families), less than half of the items completed (13 individuals), specific medical syndrome (not including suspected ASDs) such as Down syndrome or chromosomal anomalies (33 families), extreme pregnancy or perinatal difficulties (60 families), or no first contact data available (73 families).

The final sample with data after exclusions, from which the children in this study were selected, was 3,419 pairs. Children who scored in the top 5% of the distributions of autistic traits were defined as extreme. This cutoff was chosen as a compromise between the need for a sample size large enough to provide adequate power versus the desire to study extreme groups.

Existing information about suspected ASD diagnoses comes from using the Social Communication Questionnaire (Rutter et al., 2003) on children whose parents alerted TEDS that they had an ASD. Thirty-one suspected autism cases (based on Social Communication Questionnaire scores that were above the cutoff) provided Childhood Asperger Syndrome Test (CAST) data at age 8. A full diagnostic study of all children with possible ASDs in TEDS is under way.

Measures

The CAST (Scott et al., 2002) is a 31-item questionnaire designed for parents to complete in nonclinical settings. Items are scored additively and were divided into three subscales, based on DSM-IV criteria (American Psychiatric Association, 1994; Ronald et al., 2006). The SI subscale had 12 items (e.g., *Does s/he join in playing games with other children easily?* [reversed item]), as did the CI subscale (e.g., *Can s/he keep a two-way conversation going?* [reversed item]); the RRBI subscale had seven items (e.g., *Does s/he like to do things over and over again, in the same way all the time?*). Figure 1 shows the distributions for the whole sample, and the cutoff for selecting extreme scorers. Mean scores of children with suspected ASDs in TEDS are also shown in Figure 1.

Analyses

Analyses on Phenotypic Overlap of Extreme Autistic-like Traits. The relationship among the features of the triad was assessed using tetrachoric correlations, odds ratios, and concordances (all of which rely on categorical data), as well as phenotypic group correlations (PGCs) and individual differences correlations. Tetrachoric correlations assume that there is an underlying bivariate normal distribution of liability, whereas PGCs exploit the quantitative information available: PGCs are calculated by dividing the proband's score on the unselected variable by the proband's score on the selected variable. The way in which PGCs are calculated means that the relationships are bidirectional. For example, the PGC between the extreme socially impaired group and their quantitative scores on communication impairments is separate from the PGC between the extreme group defined by CIs and their scores on the SIs scale. If the regression of one variable on another is linear across the full sample, then the PGC is expected to be similar in magnitude to the Pearson's correlation for the entire sample (Plomin et al., 2002). Thus, by comparing PGCs and Pearson's correlations, it is possible to determine whether two traits cluster more at the extreme than throughout the population. Because the scales were skewed, Spearman's rho, which operates on rank rather than linear value, was also used.

Analyses on Genetic and Environmental Overlap of Extreme Autistic-like Traits. DF extremes analysis is a means-based regression analysis of twin data in which a cotwin's score is predicted by two sources of information: their proband's score on a quantitative trait and the twin pair's coefficient of genetic relatedness (DeFries and Fulker, 1988). By comparing the regression to the population mean for the monozygotic (MZ) and dizygotic (DZ) cotwins of the probands, it is possible to infer whether there is genetic influence on extreme traits. DF was carried out on same-sex twins only. The basic multiple regression model for the analysis of selected twin data is as follows: $C = B_1P + B_2R + A$ where C is the cotwin's predicted score, P is the proband's score, R is the coefficient of relationship, and A is the regression constant. B_1 is the partial regression of the cotwin's score on the proband's score and is a measure of twin resemblance independent of zygosity, and B_2 is the partial regression of the cotwin's score on the coefficient of relationship. B_2 equals twice the difference between MZ and DZ cotwin means after covariance adjustment for any differences between MZ and DZ proband scores. By standardizing and transforming the scores (i.e., expressing each score as a deviation from the control mean [standardizing] and then dividing by the difference between the proband and control means before multiple regression [transforming]), B_2 provides a direct estimate of group

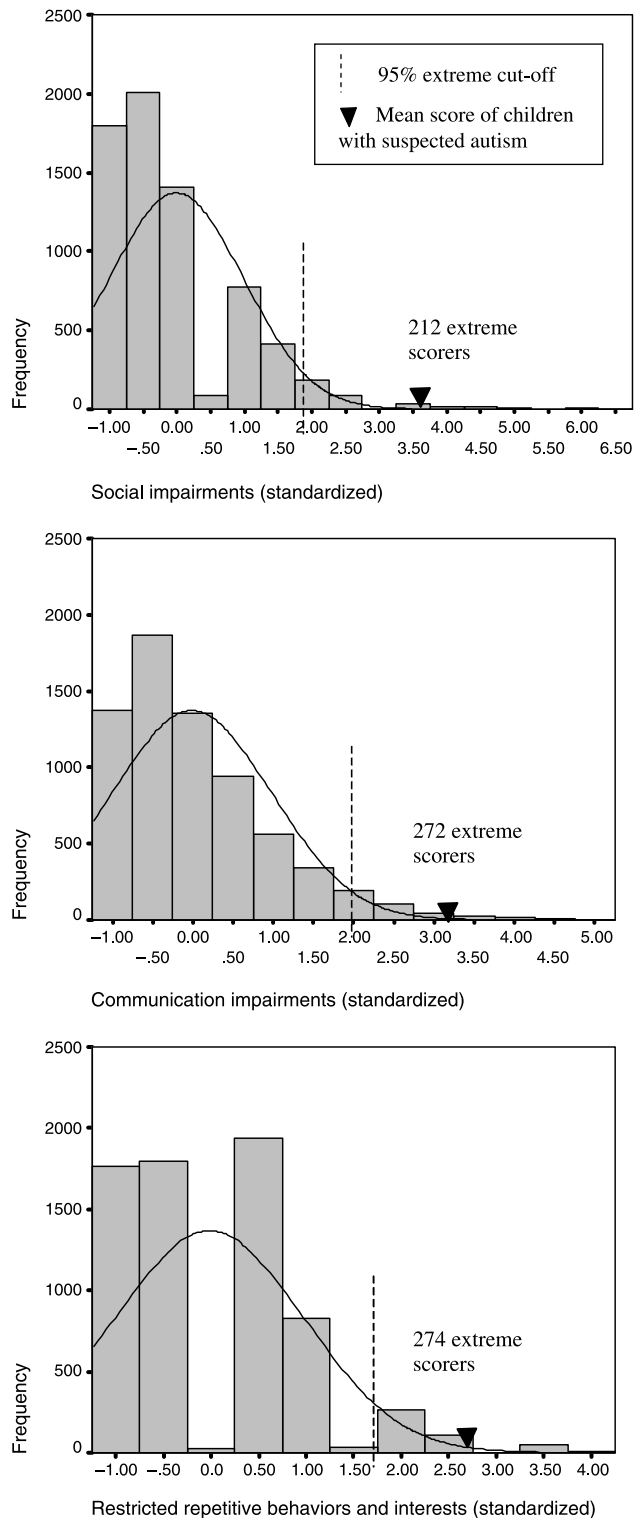


Fig. 1 Histograms of social impairments, communication impairments, and restricted repetitive behaviors and interests standardized scales, showing extreme scorers selected from the Twins Early Development Study (TEDS) community sample.

heritability. Group heritability (h_g^2) refers to the extent to which genetic factors account for the mean difference between probands and the population. Group shared environment (c_g^2) refers to the extent to which the mean difference between the extreme group and the unselected population is caused by shared environmental factors. Hence, the DF method addresses the genetic and environmental origins of the mean difference on the quantitative trait between the probands and the population. Transformed cotwin means, which can be interpreted as twin group correlations comparable to traditional twin correlations, are calculated by dividing the quantitative trait scores of the cotwins by the proband mean, specific to each sex and zygosity group.

A bivariate extension of the basic multiple regression model for the analysis of selected twin data is also possible (Knopik et al., 1997; Light and DeFries, 1995; Stevenson et al., 1993). In the bivariate extension, the probands are selected on the selection variable x , but the cotwin's score is investigated on the unselected variable y . The bivariate DF regression equation is now: $C_y = B_1P_x + B_2R + A$ where C is the cotwin's predicted score on the unselected variable, P is the proband's score on the selected variable, R is the coefficient of relationship, A is the regression constant. B_1 is the partial regression of the cotwin's unselected variable score on the proband's selected variable score, and B_2 is the partial regression of the cotwin's unselected variable score on the coefficient of relationship. When the data are transformed before the multiple regression analysis, B_2 is an index of the extent to which the proband deficit on x results from genetic factors that also influence y (i.e., bivariate heritability; Light and DeFries, 1995). As explained earlier, the bivariate extension is bidirectional, involving investigating proband scores on x and cotwin scores on y , and vice versa, and from these two analyses, a genetic correlation is derived (Knopik et al., 1997) as: $r_g(xy) = \sqrt{(B_2(xy))(B_2(yx)) / (B_2(x))(B_2(y))}$.

In all DF analyses, probands were selected on the basis of raw scores, and age- and sex-regressed scores were used for the analyses. Group heritability and bivariate heritability estimates should not be

higher than the MZ transformed cotwin mean, but this can sometimes occur when data show a nonadditive genetic pattern of effects (i.e., when DZ transformed cotwin means are less than half the MZ cotwin means). Under these circumstances, h_g^2 and B_2 were constrained to the value of the MZ transformed cotwin mean. Bivariate DF analyses were repeated using a log-transformed scale to determine whether normalizing the data changed the results.

Phenotypic Analyses on Groups with One, Two, and Three Extreme Autistic-like Traits. For the following phenotypic analyses, the total sample was divided into nine groups consisting of individuals who scored in the top 5% of (1) none of the three subscales ("no extreme autism-like traits"), (2) only the SI distribution but not CI or RRBI distributions ("high S only"), (3) only the CI distribution but not the SI or RRBI distributions ("high C only"), (4) only the RRBI distribution but not the SI or CI distributions ("high R only"), (5) the SI and CI distributions but not the RRBI distribution ("high S + C"), (6) the SI and RRBI distributions but not the CI distribution ("high S + R"), (7) the CI and RRBI distributions but not the SI distribution ("high C + R"), (8) in all three distributions ("high S + C + R"). The children with suspected autism were included in a separate "autism" group in these phenotypic analyses.

Mean scores of these groups were compared on each of the CAST subscales as well as on verbal and nonverbal ability, assessed at age 7 using telephone-administered adaptations (for TEDS) of WISC-III Vocabulary, Similarities, and Picture Completion (Wechsler, 1992) and McCarthy Scales of Children's Abilities Conceptual Grouping (McCarthy, 1972). The groups were also compared on academic achievement using teacher assessments on a U.K. National Curriculum measure (Walker et al., 2004) and on behavior problems using teacher ratings on the Strengths and Difficulties Questionnaire (Goodman, 1997). Analyses of variance and the Games-Howell multiple comparison post hoc test were employed (this test was chosen because group sizes differed, and equal variance across groups could not be assumed [Field, 2002]).

TABLE 1

Strength of Phenotypic Association Among the Features of the Autistic Triad Throughout the General Population and at the Extreme, by Sex

Subscales	Sex	Tetrachoric Correlations	Odds Ratios	Concordances	Phenotypic Group		Pearson's r	Spearman's ρ
					Correlations (PGCs)			
SIs-CIs	Male	0.58 (0.52–0.65)	11.50 (7.54–17.54)	34% (SIs) 35% (CIs)	0.51 (SIs) 0.54 (CIs)	0.39 (0.37–0.41) ^a	0.22	
	Female	0.51 (0.39–0.62)	9.17 (4.29–19.60)	26% (SIs) 17% (CIs)	0.44 (SIs) 0.49 (CIs)	0.26 (0.24–0.28) ^a	0.17	
SIs-RRBIs	Male	0.50 (0.42–0.57)	5.76 (3.77–8.80)	31% (SIs) 29% (RRBIs)	0.32 (SIs) 0.46 (RRBIs)	0.27 (0.25–0.29) ^a	0.17	
	Female	0.43 (0.29–0.55)	2.05 (0.62–6.83)	21% (SIs) 13% (RRBIs)	0.26 (SIs) 0.32 (RRBIs)	0.17 (0.15–0.19) ^a	0.14	
CIs-RRBIs	Male	0.60 (0.53–0.66)	10.46 (6.94–15.76)	38% (CIs) 34% (RRBIs)	0.44 (CIs) 0.55 (RRBIs)	0.42 (0.40–0.44) ^b	0.32	
	Female	0.55 (0.45–0.64)	9.00 (4.76–17.03)	26% (CIs) 24% (RRBIs)	0.39 (CIs) 0.43 (RRBIs)	0.34 (0.32–0.36) ^b	0.28	

Note: One twin per pair selected for analyses. $n = 3,419$ (49% males) for whole sample. Numbers of extreme groups are shown in Table 2. The 95% confidence intervals are presented in parentheses, where provided. For phenotypic group correlations (PGCs) and concordances, the selection variable is given in parentheses. SIs = social impairments; CIs = communication impairments; RRBIs = restricted repetitive behaviors and interests.

^a Correlations significantly higher for males than females ($p < .01$).

^b Correlations significantly higher for males than females ($p < .05$).

RESULTS

Figure 1 shows the SI, CI, and RRBI distributions from the original TEDS sample and the cutoffs used to select the extreme scorers. Table 1 presents statistics describing the strength of the phenotypic association among the features of the triad throughout the general population and at the extreme, split by gender. As shown in the table, PGCs and tetrachoric correlations were modest but fell on or above the upper confidence intervals of the Pearson's correlations and above the Spearman's ρ_s , suggesting somewhat greater clustering of autistic traits at the extreme than in the general population. The differences between the Pearson's and Spearman's correlations are thought to be the result of the skew of the distributions.

Comparing the strength of the relationships among the features of the triad, the links between SIs and CIs and between RRBI and CIs tended to be of a similar magnitude and were both stronger than the relationship between SIs and RRBI, which was consistently the weakest according to all of the statistics presented in Table 1. All of the Pearson's r values were significantly higher for males than for females (Cohen, 1988), and for all other statistics, males showed the same pattern of

stronger associations among the features of the triad than females, although confidence intervals overlapped for male and female tetrachoric correlations and odds ratios.

As shown in Table 2, univariate DF analyses showed that all three subscales had high group heritabilities ($h^2_g = 0.71-0.77$). SIs and RRBI but not CIs showed a nonadditive genetic pattern in the transformed cotwin means because the DZ values (0.12 and 0.17, respectively) were less than half the MZ values (0.72 and 0.71, respectively), but nonadditive genetic influences were not found to be significant in the univariate DF model fitting.

In the bivariate models in Table 2, the transformed cotwin means were consistently higher for MZ than DZ twins, suggesting genetic influence across extreme traits. Using the formula provided, the genetic correlation between SIs and CIs was calculated as 0.53, the CI-RRBI genetic correlation as 0.57, and the SI-RRBI genetic correlation as 0.32.

These bivariate DF analyses were repeated using some older data, collected in the same sample at age 7 and reported for the first time here. The autistic trait measures used then assessed SIs and RRBI (Ronald et al., 2005). Similar results were found: high group heritability estimates for both parent- and teacher-rated

TABLE 2
DeFries-Fulker Univariate and Bivariate Extremes Model-Fitting Results

Zygosity	No.	Scores	Univariate			Bivariate (CIs)			Bivariate (RRBI)		
			p	Cotwin	h^2_g	p	Cotwin	B_2	p	Cotwin	B_2
SI probands											
MZ	96	SS	2.70	1.96		1.47	1.35		0.91	0.81	
DZ	116	SS	2.74	0.33		1.17	0.16		0.61	-0.04	
MZ	96	TS	1.00	0.72 ± 0.13		0.54	0.50 ± 0.15		0.34	0.23 ± 0.15	
DZ	116	TS	1.00	0.12 ± 0.08	0.72 ± 0.28	0.43	0.06 ± 0.06	0.50 ± 0.25	0.30	-0.01 ± 0.08	0.23 ± 0.27
CI probands											
MZ	141	SS	2.60	2.01		0.97	0.82		1.06	0.90	
DZ	131	SS	2.52	0.93		1.04	0.08		1.26	0.32	
MZ	141	TS	1.00	0.77 ± 0.10		0.37	0.31 ± 0.13		0.41	0.34 ± 0.10	
DZ	131	TS	1.00	0.37 ± 0.10	0.77 ± 0.26	0.41	0.03 ± 0.07	0.31 ± 0.26	0.50	0.13 ± 0.09	0.34 ± 0.26
RRBI probands											
MZ	120	SS	2.39	1.70		0.78	0.56		1.45	1.26	
DZ	154	SS	2.29	0.38		0.97	0.10		1.29	0.50	
MZ	120	TS	1.00	0.71 ± 0.10		0.33	0.23 ± 0.12		0.61	0.53 ± 0.12	
DZ	154	TS	1.00	0.17 ± 0.09	0.71 ± 0.28	0.43	0.04 ± 0.06	0.23 ± 0.25	0.56	0.22 ± 0.09	0.53 ± 0.25

Note: Group heritability (h^2_g) and bivariate heritability (B_2) estimates constrained to be equal or lower than MZ transformed cotwin mean. No. is the number of probands; standardized scores (SS) are expressed as SD units from the mean of whole unselected sample. For transformed scores (TS), see text. The 95% confidence intervals provided, calculated using corrected SEs. In bivariate models, the unselected variable is given in parentheses. PS = proband scores; MZ = monozygotic; DZ = dizygotic; SIs = social impairments; RRBI = restricted repetitive behaviors and interests; CIs = communication impairments.

extreme SIs and RRBI (estimates ranged from 0.57 to 0.72). The genetic correlation between parent-rated extreme SIs and RRBI at age 7 was 0.31, and the genetic correlation between teacher-rated extreme SIs and RRBI at age 7 was 0.35.

These estimates from extremes analyses can be compared to genetic correlations reported in earlier studies on the same cohort for the full community sample. At age 8, genetic correlations, in a model that ignored nonadditive genetic effects, were for males and females, respectively, 0.39 and 0.29 (SIs-CIs), 0.50 and 0.42 (CIs-RRBI), and 0.31 and 0.18 (SIs-RRBI; Ronald et al., 2006). At age 7, the genetic correlations between SIs and RRBI, also derived from individual differences multivariate genetic analyses of the whole sample, were for males and females, respectively, 0.40 and 0.25 for parent data and 0.29 and 0.07 for teacher data (Ronald et al., 2005). Hence, genetic heterogeneity between SIs and RRBI was found to be equivalent at the extreme as in the general population. Genetic overlap between CIs and SIs and between CIs and RRBI, appeared to be somewhat higher at the extreme compared to that in the general population, but there was still evidence of some unique genetic influences for each domain at the extreme. Bivariate DF analyses repeated using log-transformed scales produced similar results: all MZ and DZ cross-trait group correlations fell within ± 0.3 units of the group correlations using untransformed scales, and so the results led to the same conclusions concerning genetic overlap.

As shown in Table 3, there was a significantly larger proportion of males than females for all of the one-, two- and three-autistic-like trait groups compared to the group with no extreme autistic-like traits. The gender difference was greatest for the suspected autism group (87% male) and the groups defined by individuals showing two or more extreme autistic-like characteristics (64%–80% male). In terms of the children with suspected autism, 21 (68%) were eligible for the high S + C + R group, two for the high C + R group, two for the high S + R group, two for the high S only group, three for the high C only group, and one for the group with no extreme autistic-like traits, on the basis of their current behavior at age 8.

The omnibus analysis of variance was significant for all of the variables listed in Table 3, showing that there were some significant differences between children with zero, one, two, or three extreme autistic-like traits.

However, the multiple comparisons in Table 3 show that many groups were not significantly different from each other. For example, the suspected autism group did not differ significantly from the high S + C + R group for any of the CAST scales, and the high S + C + R group did not differ from the two extreme trait groups on the subscales (when one of the two was the subscale being measured; all at $p < .001$). On SIs and CIs, the high S + C + R group did not significantly differ from the high S and high C only groups (all at $p < .001$). RRBI scores were not significantly different between the high R only group and high S + R or high C + R groups, which in turn were not significantly different from the high S + C + R group, although the high R only group had a significantly lower RRBI score than the high S + C + R group (all at $p < .001$). Repeated analyses using only one twin per pair led to the same conclusions.

The majority of the post hoc comparisons between groups for the non-CAST measures showed that there were few significant differences between them (Table 3).

DISCUSSION

The results of this study demonstrate that extreme autistic-like traits are shown together more at the extreme than in the general population, but the strength of the relationship among the features of the triad at the extremes is still modest. All of the features of the triad showed high group heritability, and there was a degree of genetic overlap between the core autistic features but also substantial genetic specificity, with least genetic overlap occurring between SIs and RRBI. The descriptive analyses gave a flavor of the profile of abilities and behaviors of children with extreme autistic-like traits as defined here, and revealed that all of them show a male bias, whether alone or in the full triad.

In terms of previous literature and expectations about the results, the degree of genetic heterogeneity between SIs and RRBI was found to be equivalent at the extreme as in the general population, with more than half of the genes influencing extreme SIs and RRBI being nonoverlapping. Thus, the results do not agree with data reported by Sung and colleagues (2005) that showed high genetic overlap between certain aspects of SIs and RRBI. Genetic overlap between CIs and SIs, and between CIs and RRBI, appeared to be somewhat higher at the extreme compared to the findings for traits in the general population from the same cohort, but there

TABLE 3

Mean Comparisons of Children With One, Two, and Three Extreme Autistic-like Traits

	Suspected Autism	High S + C + R	High S + C	High S + R	High C + R	High S	High C	High R	No Extreme Traits		
No. (%)	31 (0.4)	48 (0.7)	44 (0.6)	30 (0.6)	61 (0.9)	204 (3.0)	210 (3.1)	266 (3.9)	5,944 (86.9)		
% Male	87%**	79%**	77%**	80%**	64%*	73%**	59%*	62%*	46%		
Scale (M[SD])										ANOVA	Multiple comparisons
Total CAST	21.61 (5.93)	18.84 (3.17)	15.90 (2.73)	14.44 (2.19)	14.10 (2.32)	9.63 (2.27)	10.52 (2.12)	9.07 (2.03)	4.31 (2.37)	$F_{8, 6,829} = 1,067.56,$ $p < .001$	Aut, S + C + R > S + C, S + R, C + R > C, S, R > "no extreme traits"
SIs	0.66 (0.25)	0.54 (0.14)	0.54 (0.12)	0.48 (0.11)	0.20 (0.10)	0.46 (0.07)	0.16 (0.11)	0.16 (0.10)	0.11 (0.10)	$F_{8, 6,829} = 665.46,$ $p < .001$	Aut, S + C + R, S + C, S + R, S > C + R, C, R > "no extreme traits"
CIIs	0.70 (0.21)	0.62 (0.13)	0.62 (0.12)	0.33 (0.11)	0.59 (0.11)	0.22 (0.13)	0.56 (0.08)	0.24 (0.12)	0.14 (0.12)	$F_{8, 6,829} = 691.73,$ $p < .001$	Aut, S + C + R, S + C, C + R, C > S + R, R, S ^a > "no extreme traits"
RRBIs	0.75 (0.25)	0.70 (0.11)	0.29 (0.13)	0.67 (0.12)	0.67 (0.11)	0.22 (0.16)	0.27 (0.14)	0.61 (0.08)	0.18 (0.14)	$F_{8, 6,808} = 544.04,$ $p < .001$	Aut, S + C + R, S + R, C + R, R ^b > S + C, C, S, "no extreme traits" ^c
Verbal	—	-0.55 (1.15)	-0.44 (1.01)	-.33 (1.56)	-0.26 (1.04)	-0.04 (1.06)	-0.55 (0.88)	-0.13 (1.00)	0.11 (0.97)	$F_{7, 5,776} = 15.69,$ $p < .001$	All NS except C > "no extreme traits," and C > S
Nonverbal	—	-0.55 (1.09)	-0.36 (0.96)	0.09 (1.25)	0.25 (1.05)	-0.13 (1.09)	-0.34 (1.02)	-0.10 (0.99)	0.07 (0.97)	$F_{7, 5,817} = 8.10,$ $p < .001$	All NS except C > "no extreme traits"
Academic achievement (standardized)	—	-1.37 (1.42)	-0.55 (1.01)	-0.34 (1.19)	-0.62 (1.24)	-0.09 (1.06)	-0.63 (1.10)	-0.06 (0.97)	0.13 (0.92)	$F_{7, 4,833} = 28.88,$ $p < .001$	All NS except S + C + R > "no extreme traits," and C > "no extreme traits," and C > R
SDQ	—	13.89 (6.41)	12.03 (5.42)	9.61 (6.16)	9.96 (6.79)	8.45 (6.50)	10.71 (6.80)	7.90 (6.85)	5.65 (4.78)	$F_{7, 5,068} = 49.15,$ $p < .001$	All NS except S + C + R, S + C, S, C > "no extreme traits"

Note: Sex bias assessed by mean comparisons, testing whether proportion of males significantly differed from 0.46. In terms of effect sizes, proportions >0.65 are considered medium effect size in departure from 0.50 (Cohen, 1988). Multiple comparisons carried out using Games-Howell. For the multiple comparisons, > indicates significant differences ($p < .001$) between scores, groups that are not significantly different are separated by a comma. Non-CAST measures were collected at age 7; thus, sample size was reduced because of missing data. Suspected autism (Aut) group was excluded from the group comparisons of non-CAST measures because so few had provided 7-year data that the sample was too small ($n < 11$) to consider reliable. CAST = Childhood Asperger Syndrome Test; SIs = social impairments; CIIs = communication impairments; RRBIs = restricted repetitive behaviors and interests; Verbal = standardized verbal ability; Nonverbal = standardized nonverbal ability; NS = not significant; SDQ = teacher-rated Strengths and Difficulties Questionnaire total scale, rated in terms of impairment from 0 to 40. Total CAST: range, 0–31; CAST subscales (SIs, CIIs, RRBIs): range, 0–1. See text for full details of measures.

^a High S + R significantly higher than high S group.

^b High S + C + R significantly higher than high R group.

^c High C and high S + C groups both significantly higher than the group with no extreme traits.

* $p < .05$; ** $p < .001$.

was still evidence of some unique genetic influences on each domain. Just as high heritability was reported for a total autistic symptoms score at the extreme (Ronald et al., 2006), individual autistic traits (SIs, CIs, and RRBI) showed high heritability at the extreme. Phenotypic links between SIs and CIs were expected to be strongest, given that they involve interlinked processes, such as language and mentalizing ability. However, in these data, CIs and RRBI showed equivalent associations with SIs and CIs, which was a surprising finding, although previous factor analytic studies have reported an association between these domains (Tadevosyan-Leyfer et al., 2003; Wadden et al., 1991).

Limitations

Extreme autistic-like traits were defined here as the most extreme-scoring 5% of a large community sample assessed on the CAST, and this is likely to include children with less severe problems than those seen in diagnosed ASDs (the prevalence of ASDs is currently estimated at 1% [Office for National Statistics, 2005]). Short behavior questionnaires were used to define the groups because in-person assessments of autistic traits in more than 3,000 twin pairs was not feasible. Bivariate DF analyses should be interpreted with some caution because of the large confidence intervals of the resulting estimates. The positive skew of the CAST distributions may have affected the results, for example, by inflating the Pearson's correlations. However, results of the bivariate DF analyses did not change when using log-transformed scales, suggesting that the skewed distributions did not significantly affect the DF results (Bishop, 2005). Another consideration is that the children with ASDs in this sample have not all yet been identified; this work is in progress. Only 68% of the children with suspected ASDs showed all three extreme autistic-like traits, which may be explained by the type of questions that the CAST instrument includes, which tend to reflect Asperger-like behaviors. There is no assessment of language delay and, furthermore, because autism is usually diagnosed in early childhood, lower than expected scores may reflect a tendency in some parents to rate their child relative to the child's past behavior, leading to low (relative) ratings of problems where there has been improvement. It is important to collect information from multiple raters because different raters provide different information (Achenbach et al., 1987). Analyses are planned that will investigate autistic traits in TEDS at age 9 years using

parent, teacher, and child self-reports. The descriptive analyses gave a flavor of the characteristics of children with one, two, or all three extreme autism-like traits, but they should be viewed with caution because of the small sizes of the groups. Finally, the conclusions from the present data should be viewed in light of the developmental status of the sample: a twin study in early childhood is needed to chart the developmental course of the phenotypic and genetic associations among the features of the triad.

Implications

These results on the autistic triad at the extreme mirror previous findings from research on the same cohort on autistic traits in the general population in suggesting that a degree of genetic heterogeneity exists, most notably between SIs and RRBI. This modest phenotypic and genetic overlap between core autistic features defined as extreme in a community sample should be considered in future clinical models of autism spectrum disorders. Molecular genetic studies should expect to find somewhat distinct subsets of genes influencing the different features of the autistic triad.

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There Is No Meaningful Relationship Between Television Exposure and Symptoms of Attention-Deficit/Hyperactivity Disorder

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Objective: The recent but methodologically limited longitudinal study of the adverse attentional effects of television viewing in early childhood suggests a possible association. The purpose of the present study was to extend this investigation to a more current sample of kindergarten students using structural equation modeling, which allows for the simultaneous evaluation of predictors. **Methods:** Two samples were randomly selected from nationally representative data collected from the Early Childhood Longitudinal Study. A structural equation model was developed positing a relationship between kindergartners' television exposure and subsequent first-grade symptoms of attention-deficit/hyperactivity disorder (ADHD) while controlling for variables related to socioeconomic status and parent involvement. Variables were selected rather than developed and do not include an acceptable measure of ADHD, which limited the scope of the measures used. The model was tested by using the first sample and then cross-validated to the second sample. **Results:** Although the adequate fit of the model to the data suggests that children's television exposure during kindergarten was related to symptoms of ADHD during the first grade, the amount of variance accounted for in the ADHD-symptoms variable revealed television exposure as a weak predictor of later ADHD symptoms. Effect sizes for the relationship between television exposure and symptoms of ADHD were close to zero and not statistically significant. **Conclusions:** Methodologic issues, including participant age, the measurement of ADHD symptoms, and evaluation of the importance of variables, may explain the differences between the present study and the results of others who have found television exposure to be related to attention problems. The measurement of ADHD symptoms through the use of longitudinal databases is an important limitation, because only a small number of items can be selected to represent symptoms. Future research is necessary to address these issues. *Pediatrics* 2006;117:665–672.