Characteristics of the Broader Phenotype in Autism:
A Study of Siblings Using the Children's Communication Checklist-2

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Non-autistic relatives of people with autistic disorder have an increased risk of social and communicative difficulties: this is known as the "broad phenotype." Better methods for characterizing the broad phenotype are needed to facilitate identification of risk genes for autism. 29 siblings of 20 children with autistic disorder, 13 siblings of 9 children with PDDNOS, and 46 typically developing control children from 26 families were assessed by parental report using the Children's Communication Checklist-2 (CCC-2). Groups were matched on age and IQ and siblings with autism were excluded. Group mean scores on the CCC-2 differed on only one subscale, syntax. However, siblings of children with autism or PDDNOS were over-represented in the tails of the distributions of several scales, and 10 (24%) scored more than 2 SD below the control mean on a total score based on all 10 subscales. Only two of these 10 children scored above threshold on one or more scales of the Autism Diagnostic Interview—Revised (ADI-R). Children with abnormal scores on the CCC-2 total were characterized by low-verbal IQ and their fathers tended to score high on the social and communication scales of the Autism Quotient, a measure of the broad phenotype in adults. The CCC-2 shows promise as a quick screening device for the broad phenotype in non-autistic siblings of children with autism. © 2006 Wiley-Liss, Inc.

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INTRODUCTION

Traditionally, autistic disorder has been regarded as a syndrome that is clearly distinct from typical development. However, both comparative and genetic studies have led to a reconceptualization of autistic disorder as an extreme point on a behavioral continuum that encompasses children who show qualitatively similar characteristics to autism in milder forms [Bishop, 2003a].

Family studies provide one source of evidence for this view of autistic disorder. Although it is uncommon to find more than one person in a family affected by autistic disorder [recurrence risk for siblings is estimated around 2%–6%; Newschaffer et al., 2002] there is an excess of cases who fall short of meeting full diagnostic criteria, but who nevertheless show developmental abnormalities that are qualitatively similar to those seen in autism. Around 12%–20% of siblings are affected with this "broad phenotype," depending on how stringently it is defined [Bolton et al., 1994]. Some of the earliest studies documenting the broad phenotype were based on information garnered from diagnostic interviews [Bolton et al., 1994]. Others have relied on clinical diagnosis: for example, Auranen et al. [2002] studied 19 families who were selected for having more than one child with autism or a related disorder, and found that in 5 of them 1 child had a diagnosis of developmental dysphasia. More recently, a self-report scale, the Autism Quotient [Baron-Cohen et al., 2001], was shown to be effective as a potential indicator of the broad phenotype, insofar as it discriminated between parents of children with autism and a control group of parents who were matched on verbal IQ [Bishop et al., 2004a]. Direct behavioral measurement of cognitive features related to autism has also been used to study the broad phenotype in relatives of those with autism, but findings have not always been consistent from one study to another [see Bailey et al., 1998, for review]. Although it has been postulated that there are etiological overlaps between specific language impairment (SLI) and autistic disorder [Tager-Flusberg and Joseph, 2003], there has been remarkably little evidence from psychometric tests of linguistic impairments in relatives of people with autism [Fombonne et al., 1997; Pilowsky et al., 2003; Bishop et al., 2004b].

The current study aimed to consider why poor language test scores are found only rarely in relatives of people with autism, even though communication deficits have been described as part of the broad phenotype. One possibility is that the focus has been too much on structural language skills, with insufficient emphasis on the communicative use of language. Although pragmatic deficits are a core feature of autism, there is a dearth of clinical instruments suitable for assessing this aspect of communication. Bishop [1998] suggested that one reason may be that the language behaviors that are noted in clinical accounts of autistic disorder are difficult to elicit in the context of a standardized assessment, and proposed that a checklist approach may be more effective at identifying pragmatic difficulties that affect everyday communication. The Children's Communication Checklist-2 (CCC-2) [Bishop, 2003b] was developed for this purpose.

Here we report findings from a study in which the CCC-2 was completed by a subset of parents from families who had participated in the Western Australia Family Study of Autistic Spectrum Disorders (WAFSASD). Mothers reported

on communicative characteristics of siblings of children with autistic spectrum disorder (ASD), or on children who formed part of a non-autistic control group. The hypothesis that we tested was that the rate of reported communicative difficulties, especially pragmatic impairments, would be elevated in siblings of children who had ASD (i.e., autistic disorder or PDDNOS).

MATERIALS AND METHODS

Participants

Characteristics of participants in the original WAFSASD cohort are described in full by Bishop et al. [2004b]. Index families were recruited by advertisements on the basis that they had two or more children, at least one of whom had an ASD in the absence of a known cause (such as identified metabolic or genetic disease). ASD probands included 57 children who met algorithmic diagnostic criteria for autism on the Autism Diagnostic Interview—Revised [ADI-R; Rutter et al., 2003b], and 21 probands who were designated as cases of PDDNOS. These children were referred as having a disorder on the autistic spectrum, but scored above threshold on only one (N = 3) or two (N = 18) of the three symptom domains assessed by the ADI-R.

Control families were recruited by brochures sent to schools, and mailouts in the Perth Metropolitan Region. The goal was to select a typically developing sample that was similar to the index sample in terms of age and sex distribution. Because reliance on volunteers tends to yield a sample biased in favor of children with above average IQ, some lower ability control probands were recruited by screening IQ in children attending a mainstream school and then inviting parents of less able children to take part in the main study. Control probands were screened to exclude cases with autistic symptomatology (see below), and any child with signs of PDDNOS was excluded. The full WAFSASD sample included 59 control probands.

The current study was conducted 4–5 years after the initial sample was recruited. Parents of all probands were approached and asked to complete the CCC-2 for participating siblings (in cases where the proband had autistic disorder or PDDNOS) or for the proband and siblings (for typically developing controls). The CCC-2 has been normed for children aged 4–16 years, and siblings outside this age range were excluded. Data were also excluded for one sibling of an autism proband and one sibling of a control child where the mother reported that the child had a hearing loss, and for one family where the only sibling of the proband also had a diagnosis of autism. The CCC-2 scoring manual has guidelines for identifying inconsistent patterns of responding, but no data had to be excluded on this basis. Valid checklists were available for 30 siblings of 20 children with autistic disorder, 13 siblings of 9 children with PDDNOS, and 46 typically developing control children from 26 families.

Assessments

Assessment of ASD symptoms. When the sample was first recruited, children were screened using the Social Communication Questionnaire [SCQ: Rutter et al., 2003a] to assess autistic symptomatology in siblings of probands and to exclude cases of ASD in the control probands. The full ADI-R was administered to any child scoring above 10 (cutoffs for PDD and autism are 14 and 21, respectively). No child who scored above threshold for autism on any of the three domains assessed by the ADI-R was included in the control sample. Presence of autistic symptomatology in ASD siblings was not used to include or exclude families, but was taken into account in the data analysis (see below).

IQ assessment. Probands and their siblings were given the vocabulary, similarities, picture completion, and object assembly subtests of the age-appropriate Wechsler Scales (WPPSI-R, WISC-III, or WAIS-III), which were prorated to give short form estimates of verbal and performance IQ. This assessment was carried out when the children were first recruited to the WAFSASD sample.

Non-word repetition. The non-word repetition test, devised by Baddeley et al. [in preparation], is described in detail by Bishop et al. [2004b]. The testee listens to tape-recorded, polysyllabic non-words and repeats them. Responses were scored on-line as right or wrong and converted to age-scaled z-scores. Non-word repetition is a good marker of heritable language impairment [Newbury et al., 2005], but is not deficient in relatives of children with ASD [Bishop et al., 2004b].

Autism Quotient (AQ) [Baron-Cohen et al., 2001]. Parents were asked to complete the AQ at the start of the WAFSASD data collection. This is a self-report instrument that is sensitive to autistic features. Bishop et al. [2004a] showed that a summed score on the social skills and communication scales of the AQ acts as an index of the broad phenotype, insofar as high scores (11 or above) are more common in parents of probands with ASD than in control parents.

Children's Communication Checklist-2 [CCC-2; Bishop, 2003b]. The CCC-2 was designed to be completed by parents, who report on aspects of their children's communicative strength and weakness that are not amenable to more conventional forms of assessment. The CCC-2 contains 70 items divided into 10 scales. The first four scales assess structural aspects of language: A: speech, B: syntax, C: semantics, and D: coherence. The next four scales assess aspects of communication that are impaired in children with pragmatic difficulties: E: inappropriate initiation, F: stereotyped language, G: use of context, and H: non-verbal communication. The final two scales assess behavioral domains relevant to autism: I: social relations and J: interests. For each scale, five items describe weaknesses and two describe strengths. For instance, a "weakness" item on the "coherence" scale is: "It is hard to make sense of what she is saying (even though the words are clearly spoken)," and a "strength" item on the "use of context" scale is: "Appreciates the humor expressed by irony. Would be amused rather than confused if someone said 'isn't it a lovely day!' when it is pouring with rain." The respondent is asked to rate the frequency with which a specific behavior is observed, with options of (0) less than once a week (or never), (1) at least once a week, but not every day (2) once or twice a day, or (3) several times (more than twice) a day (or always). The CCC-2 has been standardized on 542 children in the UK aged from 4–16 years old. Scores on individual subscales are converted to age-scaled scores with mean of 10 and SD of 3. Two composite scores can also be obtained: a General Communication Composite (GCC) formed by summing the first eight scales (A–H), and a Social Interaction Deviance Composite (SIDC) formed by summing scales E, H, I, and J, and then subtracting scales A, B, C, and D, to give an index of mismatch between structural language skills and pragmatic/social skills. In a validation study [Norbury et al., 2004], the GCC was effective in distinguishing between children with communication impairments (including both SLI and autism) and typically developing children. The SIDC was usually negative in children with ASDs, with particularly large negative values being seen in children with a diagnosis of Asperger syndrome.

RESULTS

Characteristics of the subset of WAFSASD children for whom CCC-2 data were obtained are shown in Table I. On ANOVA, the groups did not differ significantly in terms of age,

TABLE I. Characteristics of the Subset of Western Australia Family Study of Autistic Spectrum Disorders (WAFSASD) Cases for Whom CCC-2 Data Were Available

	Sibling of proband with autistic disorder	Sibling of proband with PDDNOS	Typically developing control
N families	20	9	26
N children	30	13	46
N children with above threshold score on 1+ scales of ADI-R	4	0	0
Age in months	155.8 (32.64)	148.7 (31.87)	146.3 (36.51)
Mean (SD) VIQ	103.9 (16.44)	106.3 (15.56)	107.7 (16.63)
Mean (SD) PIQ	110.5 (18.41)	110.9 (16.55)	104.4 (18.08)

verbal IQ (VIQ) or performance IQ (PIQ) (all P-values in excess of 0.29). Four of the siblings of autistic probands scored above our cutoff of 10 on the SCQ and on at least one scale of the ADI-R, raising the question of whether they should be excluded as potential cases of the broad phenotype and regarded instead as having ASD. One child had a pre-existing diagnosis of autism and scored above threshold on all three ADI-R scales; his data are omitted from CCC-2 analyses. The other three cases were more problematic to classify: two of them had prior diagnoses of language disorder, and one had no pre-existing diagnosis. It is likely that such cases would have been categorized as instances of the broad phenotype in some prior studies, although if we use our study criteria, they would count as affected cases of PDDNOS. Because there is no hard and fast boundary between PDDNOS and broad phenotype, we analyzed the data with these three cases both included and excluded, so we could see whether low CCC-2 scores in siblings were confined to those who also showed significant autistic symptoms on the ADI-R.

Because the sample included more than one child from some families, to ensure independence of observations, the mean scores on the CCC-2 scales were computed for each set of sibs in a family before comparing the three groups. As shown in Table II, there was only one scale, syntax, where there was a significant mean difference between groups. However, the Levene test for homogeneity of variance revealed significant differences in variance between the three groups for six of the scales, suggesting that there might be over-representation of ASD siblings in the tails of the distributions. This was confirmed with a further analysis in which individual siblings were classified on each scale according to whether or not they obtained a scaled score below 6 (roughly corresponding to the 10th centile in the normative sample). The relevant data are

shown in Table III. Fisher exact test indicated significant over-representation of ASD siblings in the tail of the distribution for four of the subtests, with several other subtests showing trends in the same direction. The subtests showing this effect were not confined to those assessing pragmatic aspects of language, but included those evaluating structural language skills as well.

As noted above, the conventional method for scoring of the CCC-2 involves computation of the GCC (sum of scales A–H). However, because the ASD siblings showed a trend for low scores on scales I and J, as well as on the eight communication scales, we also computed an overall CCC-2 total based on all 10 scales. Compared to the GCC, this gave similar but stronger group differences between ASD and control siblings, and so we report here just results for the CCC-2 total composite, based on all 10 scales, as well as the SIDC (scales $[E + H + I + J] - [A + B + C + D]$).

The scatterplot of scores on the two composites is shown for all participating siblings in Figure 1. The mean score on the CCC-2 total for controls was 105.9, SD = 15.34. Ten of the ASD siblings (23.8%) compared with only one of 46 controls (2.2%) obtained a total score below 75 (2 SD below control mean). On Fisher exact test, using 75 as the cutoff for low CCC-2 total, with autistic and PDDNOS cases combined, there was a significant association between CCC-2 total and group status, P (1-tailed) = 0.002. Of the ten children with low CCC-2 totals, two had scored above threshold on at least one ADI-R scale, and the remaining eight had scored below the cutoff of 10 on the SCQ and so had not been given the ADI-R. If analysis is restricted to the latter eight siblings, the association between proband diagnosis status and sibling low CCC-2 total remains significant (1-tailed $P = 0.007$ on Fisher exact test), indicating that there are elevated rates of impairment in siblings of

TABLE II. Mean Scores on CCC-2 Subscales for Siblings in Each Family

	Proband status								
	Autistic[a] N = 20		PPDNOS N = 9		Control N = 26				
Scale	Mean	(SD)	Mean	(SD)	Mean	(SD)	F	Significance	Levene P
A: speech	8.41	(3.09)	9.35	(2.69)	10.10	(1.46)	2.88	0.065	0.003
B: syntax	9.68	(2.91)	11.00	(1.20)	11.23	(0.75)	3.97	0.025	<0.001
C: semantics	10.27	(3.60)	11.80	(2.78)	11.42	(1.81)	1.39	0.258	0.024
D: coherence	9.29	(2.92)	9.31	(3.52)	10.96	(1.96)	2.74	0.074	0.020
E: inapprop. initiation	10.13	(2.59)	9.76	(3.45)	10.50	(2.61)	0.27	0.765	0.547
F: stereotyped language	10.15	(2.31)	10.54	(2.72)	11.21	(1.52)	1.54	0.224	0.002
G: use of context	9.33	(3.44)	9.94	(3.19)	10.53	(1.90)	1.07	0.351	0.149
H: non-verbal communication	10.21	(2.66)	11.50	(1.54)	10.96	(1.78)	1.35	0.269	0.002
I: social relations	9.52	(2.85)	9.28	(2.84)	9.94	(2.56)	0.26	0.775	0.738
J: interests	9.92	(3.07)	10.11	(3.47)	10.25	(2.71)	0.07	0.931	0.326

[a]Excluding one sibling with a diagnosis of autism.

TABLE III. Numbers (%) of Siblings With Scaled Score Less Than 6

| | Proband status | | | | | | |
| | Autistic[a] | | PDDNOS | | Control | | Fisher exact |
Scale	N	(%)	N	(%)	N	(%)	P (1-tailed)[b]
A: speech	$4+1^c$	(17%)	1	(8%)	1	(2%)	0.042
B: syntax	3	(11%)	—	—	—		0.105
C: semantics	$2+1^c$	(10%)	1	(8%)	1	(2%)	0.153
D: coherence	$5+2^c$	(24%)	1	(8%)	2	(4%)	0.032
E: inappropriate initiation	2	(7%)	—	—	2	(4%)	0.657
F: stereotyped language	$1+1^c$	(7%)	—	—	—		0.225
G: use of context	$5+2^c$	(24%)	1	(8%)	1	(2%)	0.010
H: non-verbal communication	$4+2^c$	(21%)	—	—	1	(2%)	0.042
I: social relations	$3+2^c$	(17%)	1	(8%)	3	(7%)	0.199
J: interests	$4+2^c$	(21%)	1	(8%)	3	(7%)	0.123
Total N	29		13		46		

[a]Excluding one sibling with a diagnosis of autism.
[b]Siblings of autistic and PDDNOS probands combined for this analysis.
[c]Denotes sibling with at least one ADI-R scale above threshold.

children with ASD even when those with evidence of autistic symptomatology are excluded. It had been anticipated that siblings of children with autism might have a low SIDC, indicating disproportionate pragmatic problems, but though most of those with a low CCC-2 total scored below zero on SIDC, two did not, and had a profile that was more similar to that seen in SLI, with a positive SIDC indicating problems largely affecting the structural language scales [Norbury et al., 2004]. We also anticipated that siblings who met our ADI-R criteria for PDDNOS would all obtain abnormal scores on CCC-2, but there was one child in this group who scored in the normal range. He had no clinical diagnosis, but on the ADI-R he scored above threshold on social interaction (score 13 vs. cutoff 10) and communication (score 12 vs. cutoff of 8).

Further details of the 10 ASD siblings with low CCC-2 totals are shown in Table IV, together with summary statistics for the 32 other siblings of ASD probands. There were two pairs of siblings among the 10 children with low CCC-2 totals. Furthermore, the sibling who was excluded from analysis

because he had a diagnosis of autism came from family #2 (see Table IV).

Children with low CCC-2 totals did not differ from other ASD siblings in terms of sex, age, or non-verbal ability, but they had significantly lower VIQ. However, there was no evidence of any deficit on non-word repetition.

Further analysis was conducted at the family level, with ASD families classified as CCC− if they included a sibling with a low CCC-2 total, and as CCC+ if they did not. We first considered whether there were any verbal difficulties in the *probands* with ASD for CCC− vs. CCC+ families. The mean VIQ of the probands with ASD did not differ significantly for the two types of family: for the eight CCC− families, the mean proband VIQ was 88.6 (SD = 24.9) and for the 21 CCC+ families it was 74.8 (SD = 27.6), F(1, 27) = 1.53, P = 0.226. Turning to consider evidence of the broad phenotype in parents, following Bishop et al. [2004b], we regarded a total score on communication and social scales of the AQ of 11 or more as indicative of the broad phenotype. All mothers had
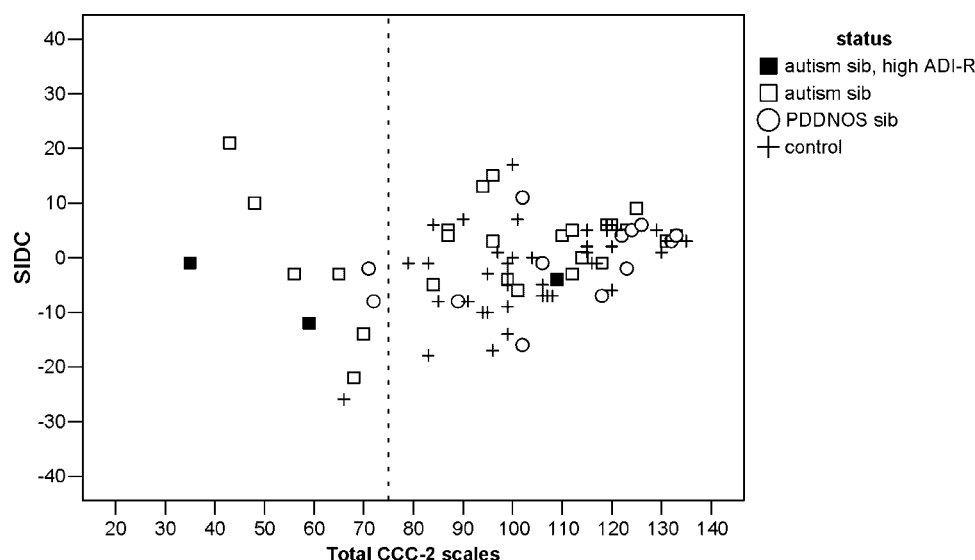

Fig. 1. Scatterplot showing scores on Children's Communication Checklist-2 (CCC-2) total and Social Interaction Deviance Composite (SIDC) scales for siblings categorized according to proband status. Siblings who scored above threshold on one or more Autism Diagnostic Interview—Revised (ADI-R) scales are shown as filled black squares.

TABLE IV. Characteristics of Individual Children With Low CCC-2 Totals, Compared With all Other Siblings of ASD Probands

Family #	Sex	Age (months)	ADI-R scales > threshold[a]	Other diagnosis	CCC-2 total	SIDC	VIQ	PIQ	VP discrep	Non-word repetition z
1	F	161	—	—	48	10	80	97	17	1.17
2	F	147	—	—	43	21	94	113	19	1.71
3	M	108	C	Language dis.	35	−1	93	89	−4	−2.20
4	M	125	B+D	Language dis.	59	−12	74	93	19	−0.92
5	M	208	—	—	56	−3	102	127	25	−1.04
5	F	178	—	—	65	−3	102	127	25	−0.02
6	M	195	—	—	68	−22	118	94	−24	−0.20
6	F	140	—	—	70	−14	87	94	7	0.12
7	F	213	—	—	71	−2	106	116	10	0.10
8	M	154	—	None	72	−8	66	90	24	1.26
All other sibs of ASD probands	17 m 15 f	M: 151.6 SD: 31.5	1: B+C	None	M: 111.4 SD: 14.64	M: 1.78 SD: 6.44	M: 102.3 SD: 13.51	M: 112.9 SD: 18.28	M: 3.66 SD: 19.27	M: 0.08 SD: 0.941
Significance[b]	$\chi^2 = 0.04$ $P = 0.863$	$F = 0.94$ $P = 0.339$	Fisher exact $P = 0.136$		n/a[c]	$F = 3.11$ $P = 0.085$	$F = 11.26$ $P = 0.002$	$F = 1.96$ $P = 0.169$	$F = 1.48$ $P = 0.232$	$F = 0.49$ $P = 0.826$

[a]Scale B is social interaction, C is communication and D is repetitive behavior.
[b]χ^2 tests have 1 d.f. and exclude those with missing data, F-tests have 1 and 40 d.f.
[c]Groups defined on this variable.

completed the AQ. Three families included mothers who had the broad phenotype and one (33.3%) had a child with a low CCC-2 total. This was similar to the percentage seen in non-broad phenotype mothers (7/26; Fisher exact 1-tailed $P = 0.636$). Data were available from fathers in 22 ASD families. Four of five fathers from CCC− families (80%) had evidence of the broad phenotype, compared with 1 of 17 fathers from CCC+ families (6%), an association that is significant on Fisher exact test ($P = 0.003$). In comparison, 2 of 16 fathers from control families and none of 24 mothers had an AQ composite score greater than 11. Although numbers are small, these data suggest that for fathers there may be a familial association between features of the broad phenotype across generations when measured on scales that assess abnormalities of communicative and social behavior.

Rates of impairment in siblings of ASD probands varied according to how impairment was defined. Overall, in this sample, among the 43 siblings of 29 ASD probands, 1 (2.3%) merited a diagnosis of ASD (and was excluded from CCC-2 analyses), a further 1 (2.3%) scored above threshold on two ADI-R scales but did not have a low CCC-2 total, 2 (4.6%) scored above threshold on one or two ADI-R scales and also had a low CCC-2 total, and a further 8 (18.6%) had a low CCC-2 total but no other evidence of autistic symptomatology.

DISCUSSION

The total composite score from the CCC-2 detected evidence of abnormalities in 10 children from 8 families with an ASD proband, in a total sample of 42 children from 29 families. The CCC-2 is considerably quicker and more convenient to administer than a diagnostic interview, and this study suggests that it may play a useful role in the screening of relatives in family studies of autism. However, the pattern of results was not entirely as predicted. We had anticipated that siblings of children with ASD would show specific deficits on the SIDC, an index that is sensitive to disproportionate pragmatic impairments and has been shown in previous research to be unusually low in children with an autism-related diagnosis, especially in those with Asperger syndrome [Norbury et al., 2004]. This was not, however, seen in the current sample. Impairments were found on a wide range of CCC-2 subscales, including those assessing structural language skills as well as communicative use. This might suggest that an alternative scenario is a better description of the data, namely that some children with the broader phenotype have characteristics of SLI [cf. Tager-Flusberg and Joseph, 2003]. This seems supported by the finding that children who did poorly on the CCC-2 total tended to have lower verbal IQs than other siblings, and two of them had diagnoses of language disorder. However, overall, those scoring low on the CCC-2 showed no deficit on a test of non-word repetition, which is a sensitive index of heritable SLI.

One issue that needs to be considered is the validity of ratings of children's communication when made by a parent of a child with ASD, who may be unusually sensitive to abnormal communicative features, or who may themselves have problems in understanding. It seems unlikely that response bias can explain the findings obtained here, because if that were the case, we would not expect to see any relationship between CCC-2 results and psychometric test data. The finding of a specific association with VIQ provides some external validation.

The data reported here also offer some tantalizing evidence that there may be a link between the broad phenotype in fathers and the similar characteristics in their non-autistic offspring. Social and communicative difficulties in parents were assessed by self-report on the AQ, whereas such difficulties in children were assessed by maternal report on the CCC-2. There were five families in which a father scored in

the broad phenotype range, and in four of these cases there were siblings in the family with low CCC-2 total, in addition to the proband with ASD. This result needs replicating in a larger sample, but it suggests that subclinical problems with social and communicative behavior may "breed true" in families.

One point to note is that probands participating in our study had to be able to attempt a battery of cognitive tests that were included in the study to characterize the phenotype, and so very low-functioning children were excluded. Verbal IQs in probands ranged from 46 to 145, with mean of 79.6. Starr et al. [2001] found rates of "broad phenotype" in relatives of children with autism who had IQs below 50 that were similar to those reported in higher functioning samples, but rates of scholastic impairment were slightly higher when autism was accompanied by profound mental handicap. Thus it is possible that inclusion of non-verbal and severely mentally impaired probands might have revealed a higher proportion of cases of mild communicative impairment in siblings.

Our results are consistent with findings by Constantino et al. [in press], who used a different parental questionnaire, the Social Responsiveness Scale [SRS; Constantino, 2005], as a quantitative measure of autistic traits. Constantino et al. [in press] compared parental report from 149 brothers of children with ASD (including autistic disorder, Asperger syndrome, and PDDNOS) versus 45 brothers of children with non-autistic psychiatric diagnoses. They excluded siblings who themselves met criteria for an ASD. Their data suggest that the broad phenotype may be particularly prevalent among non-autistic siblings from multiplex families, where the genetic loading is likely to be particularly strong. Among non-autistic brothers from multiplex families with an autism proband, 43% had SRS scores of 70 or above. For a consecutive clinical series of cases or autism or PDDNOS, 25% of brothers had scores this high, compared with only 5% of brothers of non-autistic psychiatric cases. This 25% rate is comparable to the rate of low scorers on the CCC-2 (23.8%) in our sample (which included only one multiplex family), though our rate reduced to 20.5% if we excluded siblings with a high score on at least one ADI-R scale. It is likely that these slight differences reflect sampling error, though the SRS may be more sensitive to the broad phenotype because its focus is broader than CCC-2, including items assessing social, emotional, and sensory behaviors. There would be considerable interest in future in conducting a study that directly compared the SRS and CCC-2 in the evaluation of the same siblings of children with ASD to establish whether they identify the same children as cases of "broad phenotype."

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