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# Social and Behavioral Problems of Children with Agenesis of the Corpus Callosum

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# Social and Behavioral Problems of Children with Agenesis of the Corpus Callosum

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**Abstract** Archival data from a survey of parent observations was used to determine the prevalence of social and behavioral problems in children with agenesis of the corpus callosum (ACC). Parent observations were surveyed using the Child Behavior Checklist (CBCL) for 61 children with ACC who were selected from the archive based on criteria of motor development suggesting a relatively high general level of functioning. Younger children with ACC (ages 2–5) were rated as primarily having problems with sleep. Older children with ACC (ages 6–11) manifested problems in attention, social function, thought, and somatic complaints. The older children with ACC were also compared to CBCL data from 52 children with autism who were selected from a previous study. Children with ACC were generally less impaired than children with autism on nearly all scales, with significantly less severe problems in the areas of attention, anxiety/depression, social function, and unusual thoughts. A further questionnaire related to diagnostic criteria for autism indicated that some children with ACC had traits that are among those that contribute to the diagnosis of autism within the domains of social interaction and social communication, but fewer who manifest repetitive and restricted behaviors.

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## Introduction

Little systematic information is available regarding the social, behavioral, and cognitive outcome of agenesis of the corpus callosum (ACC) among children who seemingly are developing in a typical manner and who are not mentally retarded. As a consequence, there is little information available to parents of children with ACC regarding the most likely trajectory of their child's development or the areas of behavioral difficulties they should anticipate. This report summarizes parent observations of social and behavioral problems in relatively high functioning children (ages 2–11 years) with ACC using the Child Behavior Checklist (CBCL) [1–3] and a questionnaire based on diagnostic criteria for autism.

ACC is a congenital defect of the brain in which the 200 million axons of the corpus callosum are either completely or partially absent [4, 5]. In a large majority of cases of ACC, extra-callosal commissures (e.g., the anterior commissure) are still present [5, 6]. Although these pathways are considerably smaller than the corpus callosum, they serve as alternative pathways allowing for a modicum of information to pass from one cerebral hemisphere to the other. The prevalence of ACC in the general population is not yet well documented. However, the California Birth Defects Monitoring Program suggests that disorders of the corpus callosum are present in approximately 1:4,000 live births (J. Harris, personal communication). Some studies report the prevalence as high as 1:1000 births [7–9]. The prevalence of callosal disorders among children with developmental disabilities is approximately 2–3% [7, 10, 11].

ACC is an anatomical abnormality in which the behavioral outcome and relationship to other disorders is not yet well understood. O'Brien [12] surveyed the behavioral consequences of ACC in a small population of unselected individuals with ACC covering a wide range of levels of disability. "Emotional non-communicativeness" was found in 61.5%, and 16% were characterized by "social indifference." Among those individuals with ACC who had some useful expressive language, echolalia was present in 86%, and "meaningless/out of place" language was apparent in 100%. In general, O'Brien summarizes ACC as having a "behavioral phenotype of emotional non-communicativeness and a linguistic anomaly in association with lethargy, but in the absence of autism" (p. 245).

ACC was, at one time, thought to occur mostly in individuals with mental retardation. However, over the last few decades the increased use of brain scans has resulted in more frequent discovery of ACC among neurologically "asymptomatic" individuals with normal-range IQs [6, 13]. In a previous survey of the same population used in this study, Moes and colleagues (personal communication) report that 77% of 720 respondents were considered to have some form of developmental delay, but only 30% were considered mentally retarded. However, the actual proportion of individuals with ACC who are relatively asymptomatic is unknown, particularly given selection bias of undetected cases.

Recent research is consistent in suggesting that these seemingly "asymptomatic" individuals with ACC nevertheless have areas of specific cognitive deficit or learning disability [13, 14]. As of yet, the pattern of consistent cognitive deficits in ACC has not been fully described. However, our results thus far, and those appearing in the research literature, suggest that high-functioning adults with ACC typically have moderate but

detectable deficits in the following areas: interhemispheric transfer of complex sensory information and learning [15–20]; bimanual motor coordination [18, 21, 22]; complex novel problem-solving [13, 14, 23–26]; processing of subtle phonetic and semantic aspects of language [13, 27–32]; comprehension of second-order meanings of language [33–35]; and psychosocial understanding and behavior [14, 35]. Since the individuals with ACC that we have studied have complete ACC, normal IQs, and few, if any, other structural brain abnormalities, we refer to this form of ACC as Primary ACC. This pattern of cognitive and social deficits provides a preliminary definition of a Primary ACC Syndrome.

While there are many questions regarding the outcome of callosal agenesis for individuals at all levels of functioning, we have chosen to focus on those with Primary ACC for several reasons: (1) ACC is an anatomical abnormality that can be accompanied by other brain abnormalities which would, in most cases, lead to greater cognitive impairment. Primary ACC, on the other hand, is more likely to reveal the impact of the ACC itself. (2) The Primary ACC subgroup is more likely to be involved in typical school settings and is more likely than those with multiple conditions to face expectations regarding normal school performance and acting in a socially “appropriate” manner. Thus, a better description of the range of behavioral problems that are likely to be associated with Primary ACC would be helpful.

We have included problems with psychosocial behavior and understanding as a part of the Primary ACC Syndrome, although this is a more difficult domain to measure. Family members or friends of adolescents and adults with Primary ACC often describe mild but noteworthy deficiencies in social functioning. Parents report a tendency for their child with ACC to talk in clichés (although not to talk excessively or to be lacking in normal expressive inflection), to have poor social judgment, and to have difficulty understanding facial expressions [12]. In addition, parents have indicated that their child tends to miss the point of jokes and stories [33].

Many of the social and behavioral problems associated with ACC are also associated with Autism Spectrum Disorder. Autism is characterized by problems in social interaction and communication that are manifested within the first 3 years. These problems tend to remain stable throughout the lifespan [36, 37]. According to the DSM-IV-TR [38], to be diagnosed with Autistic Disorder, an individual must show impairment in the areas of social interaction, social communication, and restricted repetitive and stereotyped patterns of behavior, interests, and activities. The autism spectrum includes individuals with Asperger’s syndrome who manifest these autistic characteristics, but who have relatively normal language capacities.

Both anecdotal evidence and accumulating research suggest that high-functioning children with autism and children with Primary ACC have in common certain forms of social disability [14, 39]. In addition, high-functioning individuals with autism and ACC also share diminished ability to infer what other people are thinking, referred to as “theory of mind” [40, 41] and deficits in abstract reasoning [14, 42–45]. However, in both the social and cognitive domains it is uncertain how the deficits associated with ACC and autism compare with respect to specific patterns of disability, severity, or prevalence. In a large survey of persons with ACC from a broad range of levels of functioning ( $N = 733$ ) a diagnosis of autism was found in only 9.5% of those surveyed [46]. When a smaller sample ( $N = 231$ ) of higher-functioning individuals with ACC was selected from this group, 4.3% were reported as having a diagnosis of autism.

Exploring similarities and differences between individuals with ACC and autism is of particular interest given recent findings regarding white matter abnormalities in individuals with autism, including reduced size of subregions of the corpus callosum [47–51]. For

example, Just and colleagues [50] recently report that individuals with autism have a smaller genu and splenium, and that reduced callosal size was correlated with diminished functional cortical connectivity as measured by synchronization of fMRI. Diffusion tensor imaging of individuals with autism showed reduced fractional anisotropy in the corpus callosum [52].

The CBCL [1–3] is used to determine the extent of behavioral anomalies in children and adolescents. We have reported preliminary results of the CBCL ratings of parents of a small group of 18 older children and adolescents (ages 7–18) with Primary ACC that have participated in laboratory testing [53]. Among this group significant CBCL elevations were found on Social Problems and Attention Problems. Brown and Paul [14] reported that two adolescents with ACC who had normal intelligence rated themselves (using the Youth Self Report version of the CBCL) high on the Thought Problems scale, but low on Social Problems, whereas their parents rated them low on Thought Problems and high on Social Problems.

With respect to individuals with autism, parental reports utilizing the CBCL showed attention, social, and thought problems [54]. Even when compared to clinical norms, the group with autism scored strikingly above the clinical populations on these scales. Another study of Brazilian children with autism using the CBCL found that the Thought Problems scale significantly differentiated the children with autism from both a normative population of schoolchildren and from a clinical population of children with other psychiatric disorders [55].

While previous studies have elucidated some of the social and behavioral problems among adults, adolescents, and older children with ACC, little information exists regarding very young children with Primary ACC. In addition, many of the previous studies yielding behavioral descriptions of ACC included in their study-groups lower-functioning individuals [12]. Since ACC can occur in persons with an IQ score in the normal range, lower cognitive functioning suggests the presence of other significant congenital brain abnormalities.

The current research analyzed available data from a survey of parents of higher-functioning (i.e., nonretarded and apparently typically developing) children with ACC. The survey included the CBCL, as well as items that operationalized abnormal behaviors used in the DSM-IV diagnostic criteria for autism. The CBCL data were compared to data from parents of children with autism. We hypothesized (1) that behavioral problems of children with ACC would be consistently evident to parents, as demonstrated by the CBCL; (2) that the CBCL profiles would overlap but differ for children with ACC and children with autism; and (3) that symptoms contributing to the diagnosis of autism would be present to some degree among children with ACC.

## Methods

### Participants

In order to exclude children who were particularly low functioning, surveys from parents of children with ACC were selected from a larger database of parents who responded. Reports were selected where the child with ACC was reported to be of appropriate age and to have met developmental milestones for specific motor abilities (see below). Due to the survey nature of the dataset, IQs were not systematically available. The resulting group included 33 males and 28 females between 2 and 11 years old (mean =  $6.3 \pm 3.0$  years). All children were reported by their parents to have received a definitive diagnosis of complete

or partial ACC subsequent to a CT scan (33%) or MRI (67%). In addition, 34% of the children had been prenatally identified via ultrasound as likely to have ACC. The children that were selected had sat without support by an average of 7 months (range: 4 months to the cutoff of 10 months), and walked independently by an average of 15 months (range: 9 months to the cutoff of 20 months). Of these 61 cases, 40 (68.2%) had complete ACC and the remainder had partial ACC. Thirty-one parents (51%) reported that their child had some other findings identified on neuroradiological reports (but these could not be systematically surveyed). A majority of these children (72%) were receiving some form of special education services. Fourteen (23%) had received a diagnosis of Asperger's syndrome or autism. These individuals were not eliminated since it is the specific aim of this study to describe behavioral difficulties in higher functioning individuals with ACC, regardless of current behavioral diagnosis, and to compare these individuals to a group with an autism diagnosis.

Since different versions of the CBCL are applicable to younger and older children and since we were interested in differences between younger and older children with ACC, we analyzed the data separately for younger children between 2 and 5 years ( $n = 28$ ; mean age =  $3.5 \pm 1.0$ ) and older children between 6 and 11 years ( $n = 33$ ; mean age =  $7.9 \pm 1.5$ ).

CBCL data from the older group of children with ACC were compared to a group of 52 children with autism recruited at the Department of Child and Adolescent Psychiatry in Frankfurt/M., Germany. This group was comprised of cases reported in Bölte et al. [54] as well as new cases. The sample included 43 males and 9 females aged between 6 and 11 years (mean age =  $8.3 \pm 2.0$ ). IQ ranged between 71 and 134 (mean IQ =  $100.2 \pm 19.8$ ).

## Procedures

The survey was mailed by the ACC Network to 2,015 families that are known to have a family member with ACC. While survey data were collected from all individuals with ACC who were 18 months or older and from all functional levels, the current study focused on children between the ages of 2 and 11 (at the time of the survey) with partial or complete ACC who were not mentally retarded. Responses were received from 398 families (19.8%), which is less than the 35% return from a previous survey of the same population [46]. However, this 19.8% return rate is most likely an under-estimate of the actual return rate. The 2,015 mailed surveys in this study represent two distinct groups of families in the ACC Network: (1) those for whom the age of the individual with ACC was known to be at least 18 months or older and (2) those that had not identified the age of the individual with ACC. Since some individuals with ACC in this latter group very likely were younger than 18 months of age, they would not have been eligible to be included in the study and their parents were asked not to return surveys. Without knowing the proportion of this group that was less than 18 months of age, the actual return rate cannot be calculated.

The individuals with ACC represented in the current sample and previous survey of the same population [46] were similar in age and level of disability. Of the 398 surveys returned, 274 were from families of 2- to 11-year-olds, of which 61 described children who met the inclusionary criteria regarding developmental milestones. These 61 children constituted the sample for this study.

The children that were selected from this sample were assumed to be relatively high functioning (i.e., not mentally retarded), as indicated by attainment of two developmental



milestones: age the individual sat without support ( $\leq 10$  months), and age at which the individual walked independently ( $\leq 20$  months). These milestone cutoffs were derived from a previously studied large group of high-functioning persons with ACC ( $n = 733$ ) [46]. From this previous survey, a subgroup ( $n = 355$ ) was selected who were rated as normal in their achievement of both receptive and expressive language. From this subgroup we determined the mean and standard deviation of ages for sitting and walking, and used this information to create the criteria for an early indication of the likelihood of individuals in the current sample being within the normal range of functioning (i.e., sitting alone  $\leq 10$  months, and walking alone  $\leq 20$  months). The ages for these milestones are slightly older than what is considered the typical rate of development in children with a corpus callosum.

Individuals with ACC were compared to a group of 52 children with autism. The diagnosis of autism was made using the German forms of the Autism Diagnostic Interview Revised (ADI-R) [3, 56, 57]; and Autism Diagnostic Observation Schedule (ADOS) [58], and IQ was assessed with the German versions of the WISC-R (HAWIK-R) [59]. Individuals between 6 and 11 years old with IQs greater than 70 were selected for comparison to the older group of children with ACC.

## Tests Administered

The ACC survey instrument included the CBCL (2000 edition for ages 1½–5, and the 2001 edition for ages 6–18), as well as additional questions specifically related to diagnostic criteria for autism. The CBCL is a broadband clinical questionnaire designed to record behavioral problems and competencies of young individuals aged 4 through 18 as reported by their parents or parent-surrogates. The relevant time period assessed is the past six months. The behavior problem scale contains 118 items (plus two optional questions; all rated on a 0-to-2 scale) of which 85 items constitute eight syndrome-scales: Withdrawn, Somatic Complaints, Anxious/Depressed, Attention Problems, Aggressive Behavior, Social Problems, Thought Problems, and Rule-breaking/Delinquency. The CBCL for younger children (2–5 years old) does not include the last three of these scales, but adds scales of Emotionally Reactive and Sleep Problems. For both versions of the CBCL, there are two higher-order scales, Internalizing and Externalizing.

Confirmatory factor analysis supports the use of the CBCL by providing evidence of its construct validity [60]. Furthermore, the CBCL was found to have long-term stability in a 5-year follow-up study in that children originally categorized by a particular profile type using the CBCL were found to be categorized by that same profile type at follow-up [61]. Similarly, it has been found that ratings of a group of 5- to 6-year-olds based on the CBCL corresponded to interview-defined diagnoses 1½ years later [62].

Although the US version of the CBCL was used in the ACC survey and the German version was used by Bölte et al. [54], these two versions are highly comparable regarding form, content, psychometrics, and data collection [63–65]. Most importantly, Döpfner and colleagues [64] provide evidence for cross-cultural comparability of CBCL parent ratings of behavior problems of children and adolescents (aged 4–18) in Germany ( $n = 1,622$ ), and The Netherlands ( $n = 2,076$ ), compared to the data published by Achenbach [1] for the US sample. Only relatively minor differences could be detected between the three samples and it was concluded that the “American norms can serve as an orientation for German studies using the CBCL.”

In addition, questions were included that asked about behaviors specifically used in the *DSM-IV-TR* diagnostic criteria for autism. Questions directly reflecting autism diagnostic

criteria included such questions as: “Has difficulty using nonverbal communication.” (Category 1); “Has difficulty developing peer relationships.” (Category 1); “Is able to adequately communicate desires.” (Category 2); and “Excessively preoccupied with a specific interest.” (Category 3). Parents answered questions on this survey with “never,” “sometimes,” “frequently,” or “always.” Additional questions were added to this part of the survey that reflected other behaviors sometimes found in autism, such as: “Has difficulty understanding nonverbal communication”; “Shows anti-social behavior”; and “Has difficulty taking another person’s perspective.”

The methods and procedures of this research were approved by the Institutional Review Board of the Fuller Graduate School of Psychology. All parents who returned surveys also returned a signed form consenting for the information they provided to be included in this research.

## Statistics

The CBCL scores of individuals with ACC were evaluated with respect to the probability that the observed proportion of individuals with ACC would exceed the Borderline threshold or above ( $T \geq 65$ ), or exceed the Clinical threshold ( $T \geq 70$ ), by chance. Fisher’s Exact test was used to compare the actual proportion exceeding the particular threshold with that expected based on the normative sample ( $p < .01$ , 2-tailed, not adjusted for multiple comparisons). Fisher’s Exact test is an alternative to a Chi-square in the case of a  $2 \times 2$  comparison where probabilities are exact calculations from a hypergeometric distribution. Individuals with ACC and autism were compared based on the frequency of exceeding these thresholds, again using a Fisher’s exact test. Since a normative sample was not available for the additional questions regarding diagnostic criteria for autism, these results are reported as descriptive clinical information with respect to the sample of older children with ACC, exclusively.

## Results

### CBCL Scores

Table 1 shows the percentage of younger and older children with ACC who scored above the Borderline threshold, and those who also scored above the Clinical threshold, for each CBCL scale. It can be seen that few problems are recognized by parents of younger children with ACC. For both the Borderline and Clinical cut-off levels, the only frequency that significantly exceeded the percentage expected based on the normative population was the Borderline level for Sleep Problems (36%; Fisher’s exact test,  $p < .01$ ). Other problems that were frequently noticed were behavioral withdrawal and attention, although these were not significant at either level. In addition, 25% of this younger group with ACC had Externalizing scores above the Clinical threshold, but again this did not statistically exceed the proportion that would be expected based on norms.

The number of individuals that were rated above both test score thresholds increased dramatically in the case of older children with ACC (Table 1). At the Borderline threshold, all of the scales (including the Broad-band scales) exceeded expectations based on norms ( $p < .01$ ), with the exception of the Withdrawn and Rule-Breaking/Delinquency scales. At the Clinical threshold, all of the scales (including the Broad-band scales) exceeded the threshold

**Table 1** Percentage of younger and older children with ACC whose CBCL *T*-scores are above the borderline threshold or above the clinical threshold

	ACC ( <i>n</i> = 28) 2- to 5-year-olds		ACC ( <i>n</i> = 33) 6- to 11-year-olds	
	Borderline	Clinical	Borderline	Clinical
<i>Symptom Scale<sup>a</sup></i>				
Emotionally Reactive	14	1	–	–
Anxious/Depressed	11	4	42*	15
Somatic Complaints	11	7	45*	30*
Withdrawn	18	18	33	12
Sleep Problems	36*	14	–	–
Attention Problems	21	18	79*	48*
Aggressive Behavior	14	7	42*	30*
Social Problems	–	–	64*	39*
Thought Problems	–	–	64*	30*
Rule-Breaking /Delinquency	–	–	27	9
<i>Broad-band Scale<sup>b</sup></i>				
Internalizing Score	29	11	58*	45*
Externalizing Score	36	25	45*	45*

<sup>a</sup> Symptom Scales: *Borderline* range =  $T \geq 65$  ( $\geq 93$ rd percentile); *Clinical* range =  $T \geq 70$  ( $\geq 97$ th percentile)

<sup>b</sup> Broad-band Scales: *Borderline* range =  $T \geq 60$  ( $\geq 84$ th percentile); *Clinical* range =  $T \geq 64$  ( $\geq 90$ th percentile)

\*Greater than expected % exceeded this cutoff,  $p < .01$ , two-tailed, Fisher's exact test

level at a statistically significant rate with the exception of the Anxious/Depressed, Withdrawn, and Rule-Breaking. The most remarkable areas of behavioral difficulties were attention and problems in social interactions, where 48% and 39% (respectively) of older children with ACC were rated as having a clinically significant level of problem.

The older children with ACC were also compared to children with autism of similar age and level of functioning from the data of Bölte et al. [54] Since different versions of the CBCL were used in these two samples (the English version in the group with ACC and the German version in the group with autism), the groups were compared only with respect to differences in the percentages that exceeded the Borderline and Clinical thresholds and not in terms of mean scores.

In general, the group with autism was more likely than the group with ACC to manifest behavioral problems on most CBCL scales at both Borderline and Clinical thresholds (Table 2). At the Borderline and Clinical levels, individuals with autism were significantly more likely to be anxious/depressed and withdrawn. At the Clinical level, the group with autism was also more likely to have attention difficulties, problems in social interactions, and unusual thoughts. On the Attention scale (the highest rated area in older children with ACC), the likelihood of being rated as Borderline was not significantly greater for individuals with autism, but the group with autism was above the Clinical threshold significantly more often than the group with ACC. This suggests that the attention problems, while remarkable in ACC, are less likely to be as severe as in autism. Individuals with ACC were seen to have *more* clinical-level somatic complaints and aggression than children with autism, but these differences were not statistically significant.

**Table 2** Comparison of the percentage of children with ACC and with autism whose CBCL *T*-scores are above the borderline threshold or above the clinical thresholds

	ACC ( <i>n</i> = 33) 6- to 11-year-olds		Autism ( <i>n</i> = 52) 6- to 11-year-olds	
	Borderline	Clinical	Borderline	Clinical
<i>Symptom Scale</i>				
Anxious/Depressed	42	15	83*	77*
Somatic Complaints	45	30	20	13
Withdrawn	33	12	75*	49*
Attention Problems	79	48	92	83*
Aggressive Behavior	42	30	43	21
Social Problems	64	39	83	75*
Thought Problems	64	30	75	75*
Rule-Breaking /Delinquency	27	9	47	30
<i>Broad-band Scale</i>				
Internalizing Score	58	45	75	62
Externalizing Score	45	45	64	47

\*Different from the older individuals with ACC,  $p < .01$ , two-tailed, Fisher's exact test

### Post hoc Analyses of CBCL Scores

Anecdotal reports from parents have indicated equivalent or worse behavioral outcomes in individuals with partial ACC (pACC) compared to those with complete ACC (cACC). To test this possibility, *t*-tests of differences in mean CBCL scale scores were used to compare pACC ( $n = 20$ ) with cACC ( $n = 41$ ). This comparison revealed no significant differences between pACC and cACC on any of the scales.

In some individuals with ACC and relatively normal IQ, other forms of MRI findings were reported by parents in addition to callosal absence. Fifty-three percent ( $n = 31$ ) of the children with ACC were reported by their parents to have "other brain abnormalities" as they understood this from neuroradiology or neurology reports they had received. Post hoc analyses of CBCL scale scores revealed no significant differences on any of the scales in either age group when comparing children with and without reports of other MRI findings.

While absence of a significant difference on these post hoc comparisons cannot rule out the possibility of an impact of either partial versus complete ACC, or the presence or absence of other brain neuropathology (particularly in light of the indirectness of these reports), these additional analyses at least suggest that these variables are not likely to have made a major difference in outcomes on the CBCL. More direct analysis of data from neuroimaging and/or more sensitive behavioral tests may well bring to light effects of both variables.

### Questions Regarding Diagnostic Criteria for Autism

Table 3 shows the results from the additional questions regarding autism diagnostic criteria in terms of the percentage of the entire ACC group of children who were reported by their parents to display the autistic characteristic either "frequently" or "always." Of the three *DSM-IV-TR* categories for autism, the highest percentages of children with ACC were found to have behaviors in the autistic direction for Category 1 (impairment in social interaction).

**Table 3** Presence of autism-like symptoms in ACC (ages 2–11;  $n = 61$ )

DSM-IV Diagnostic Criteria for Autism	(% endorsed)
<i>Category A (deficits in social interaction)</i>	
Using nonverbal communication	38
Developing peer relationships	46
Seeking to share enjoyment or interests with others	34
Showing social and emotional give-and-take	43
<i>Category B (deficits in social communication)</i>	
Adequately communicating desires	25
Initiating and sustaining conversation	51
Using repetitive language	30
Using make-believe or imitative play	33
<i>Category C (restricted/repetitive behavior)</i>	
Preoccupation with a specific interest	28
Engaging in nonfunctional routines or rituals	2
Engaging in repetitive motor movements	16
Preoccupation with parts of objects	10
<i>Other Autistic Tendencies</i>	
Showing antisocial behavior	10
Following rules of society	8
Having empathy for others	11
Acting on own needs first	26
Understanding nonverbal communication	36
Taking another person's perspective	30
Avoiding eye contact	20

On Category 2 (impairment in social communication), only the area of “initiating and sustaining conversation” was frequently noted as problematic. Behaviors in Category 3 (restricted and repetitive behavior) were less likely to be seen by parents of children with ACC. In general, parents reported that the most predominant autistic-like problems were related to deficiencies in social functioning: initiating and sustaining conversation, developing peer relationships, and showing social and emotional give-and-take.

The bottom portion of Table 3 shows the percentage of parents who endorsed for their children with ACC other behavioral tendencies sometimes observed in autism, but not found in the *DSM-IV-TR* diagnostic criteria. Most notably, 36% of the children with ACC were reported to have difficulty in “understanding nonverbal communication” (i.e., slightly different from the *DSM-IV-TR* criteria of “using nonverbal communication”).

## Discussion

The intent of this study was to summarize parent observations of children with ACC who are relatively high functioning and typically developing. To give some additional perspective on these results, we compared these parent reports with those from parents of a

group of high-functioning children with autism for whom the behavioral outcome is already relatively well known by clinicians.

## CBCL Results

The behavioral impairments observed by parents of older children with ACC involved multiple areas of functioning (see Table 1). These older children significantly exceeded the Clinical cut-off on the scales involving Attention Problems, Social Problems, Thought Problems, Somatic Complaints, Aggressive Behavior, and Anxious/Depressed. In a comparable small-group study of individuals with ACC brought to our laboratory for testing (and in whom Full Scale IQ was known to be  $>80$ ), we also found significantly high ratings on the Attention and Social Problems scales [53].

The most remarkable behavioral disorder among children with ACC noted in the parent responses was difficulties in attention. From CBCL parent ratings, it is difficult to distinguish between problems in focal attention and problems created by difficulty assimilating complex new information. The Attention Problem scale of the CBCL includes questions about daydreaming, staring, being confused, inability to sit still, failing to finish tasks, and wandering away. Thus, parents might endorse these items on the CBCL as a result of their child's inability (or unwillingness) to maintain attention to a constant task over a longer period of time (i.e., task persistence). Alternatively, apparent attention problems could be the result of a difficulty in thoroughly understanding all of the complex ramifications of the situation. Without adequate comprehension, children with ACC may appear to be daydreaming or inattentive. With respect to focused attention, evidence suggests that this form of attention is not markedly deficient in individuals with ACC. In a previous study, we found no difficulties among individuals with ACC in establishing spatially focused visual attention, but some difficulty in shifting attention between the right and left visual fields [66].

The ratings of parents with respect to problems in social interactions are consistent with anecdotal reports from parents, as well as our own observations of individuals with ACC who have been tested in our laboratory. We have previously hypothesized that reduced ability to adequately comprehend complex information will translate into difficulty tracking complicated, rapidly evolving social situations [14]. A number of studies have demonstrated that individuals with ACC have difficulty on tasks involving complex novel problem solving [13, 14, 23–26, 67–69]. In addition, individuals with ACC have deficits in comprehension of the second-order meanings of language [33–35].

Younger children with ACC were rated by parents as having much less pervasive behavioral problems. Thus, there appears to be a trajectory toward greater manifestation of observable behavioral impairment as children with ACC get older. This trajectory may be due to one or a combination of several factors: First, age-related changes in the test norms reflect (in part) the continuing development and myelination of the corpus callosum in children without ACC, such that the corpus callosum (when present) is an increasingly important contributor to behavioral regulation as children mature [70]. Thus, younger children with ACC will look more similar to their peers who have a corpus callosum (and, thus, similar to test norms), while older children with ACC will appear increasingly dissimilar. Second, greater behavioral problems in older children with ACC may reflect changes in the complexity of a child's context (i.e., the social and academic demands as he/she enters school). Children with autism are also reported to have more obvious behavioral problems during the school years [39, 71]. A third possibility is that parents' perceptions

may change as children get older, resulting in acknowledgement of behavior problems that were previously dismissed.

A somewhat surprising result of this survey is the high rate of endorsement of sleep problems among younger children with ACC. This problem may reflect some other as yet unknown disorder not visible in an MRI that is typically associated with ACC (unrelated to absence of the corpus callosum). Doherty and colleagues [72] report that children with ACC have significantly more problems getting to sleep, waking up in the night, and enuresis than their siblings who have a corpus callosum.

## Comparison of ACC and Autism

To further clarify the nature of the behavioral deficits of the older children with ACC, this study compared these children to high-functioning children with autism (see Table 2). The value of this comparison is that the nature, range, and severity of disorders in high-functioning autism are relatively well known to clinicians, whereas the impact of Primary ACC is not well known. However, since ACC is an anatomical abnormality and autism is based on behavioral observations, one should keep in mind that these could be concomitant issues in some cases.

It is clear in these results that, at both the Borderline and Clinical thresholds, a higher percentage of individuals with autism are rated as having behavioral difficulties than are individuals with ACC. This difference was most clear at the threshold representing a clinically significant disorder. The largest differences between groups are in areas that are generally considered characteristic of autistic psychopathology (anxiety, withdrawal, attention, social function, and thought problems).

The hypothesis that social problems in individuals with ACC originates from problems in complex problem-solving [14] is similar to the idea that a primary deficit in individuals with autism is in the area of executive function [73–75]. This theory would suggest a similar origin of social disability in ACC and autism. However, the hypothesis of problems in empathy and theory of mind in individuals with autism [76] might suggest a different origin of social problems in the two disorders. However, there is as yet little information regarding empathy and theory of mind in individuals with ACC [41].

## Autistic-like Behaviors in Children with ACC

Children with ACC were generally reported to share diagnostic characteristics in the *DSM-IV* autism category of social interaction, with somewhat less overlap for social communication, and clearly less impairment within the *DSM-IV* autism category of repetitive and restricted behavior (see Table 3). Overall, the most frequently endorsed autistic-like behavior was a deficiency in initiating and sustaining conversation (51%). From parental anecdotes, this deficit seems to be one of social impropriety when engaging in conversation (e.g., not informing the listener of a change in the topic of conversation), rather than a lack of interest in social interaction (which might be expected in individuals with autism) [39]. O'Brien's survey [12] of the behavioral consequences of ACC found “meaningless/out of place” speech to be characteristic of nearly the entire group. Problems in social communication in persons with ACC could be related to deficits in comprehension of nonliteral language expressions or in use of linguistic pragmatics [34, 35, 44].

Autistic-like behaviors in the area of *repetitive and restricted behavior* were markedly less frequent in children with ACC. While 28% of children with ACC were reported as having a preoccupation with a specific interest, very few were rated as engaging in nonfunctional routines or rituals, engaging in repetitive motor movements, or having a preoccupation with parts of objects. Thus, it is in this third domain of autistic symptoms that ACC and autism show the least similarity. Unlike ACC, children with autism have been reported in previous research [77] as showing higher rates of obsessive behaviors, such as “can’t get mind off thoughts” (66%), “obsessive ideas” (60%), and “needs to be perfect” (52%).

## Survey Participants

The children with ACC selected for this study were chosen based on the child’s meeting specific developmental milestones. These criteria were meant to focus the research on the children with ACC who are relatively high-functioning and could reasonably be assumed to have at least low-normal intelligence. Thus, while these data do not reflect the entire functional spectrum that is represented in ACC, the research findings are more likely to represent the outcomes related specifically to absence of the corpus callosum, rather than to the various other neurological anomalies that sometimes accompany ACC. That the data reflect primarily the impact of ACC and not that of other brain abnormalities is supported by the absence of any statistically significant differences between the subgroup whose parents reported other MRI findings or thought their child had some other brain abnormality and those who thought their child had ACC only. There was also a high degree of similarity in the CBCL results of this survey group and that of the smaller group of individuals with ACC tested in our laboratory, all of whom had a FSIQ greater than 80 [53].

There are also caveats to our comparison of children with ACC and children with autism. First, the data regarding autism comes from a study done in Germany [54], whereas the data on ACC come from data collected in the United States. While autism is a disorder that is similar in all cultures, there is the possibility of cultural differences in the observations of parents and their willingness to report. However, Döpfner and colleagues [63–65] provide evidence for comparability of CBCL results in German and US populations. These studies concluded that the American norms can serve as a basis for German studies using the CBCL.

In addition, both samples were taken from existing data sets which used different criteria to select higher-functioning subgroups. The selection criteria for the ACC group included omitting children who had significant language delay or significant delay in motor milestones (i.e., for sitting and walking). These criteria were meant to identify a group of children with ACC who are likely to be within the normal range of intelligence. The selection criteria for the autism group was based on psychometrically assessed IQ, and it is at least possible that some children in the autism sample would not have met one or the other milestone cut-offs used for children with ACC. While these two selection criteria allowed us to compare children with autism who had normal-range intelligence to children with ACC with presumably normal intelligence, these different approaches in selection may have influenced the outcome.

## Summary

Together, these findings suggest that children with ACC exhibit problems in multiple behavioral domains, most particularly in the realms of attention problems, social problems,



somatic complaints, and thought problems. While behavioral problems are generally less severe, children with ACC share symptoms with children with autism in the areas of social interaction and social communication. Although there are limitations to conclusions from surveys and parent reports, these data provide the first published behavioral description of children with Primary ACC, and can serve as the basis for further work involving laboratory tests.

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