Social and Communication Development in Infants with Isolated Agenesis of the Corpus Callosum

Lynn K. Paul, PhD[1,2,*], Jasmin Turner, MS[1], Sooyeon Sung, PhD[3], and Jed T. Elison, PhD[3,*]

Objective To evaluate the development of social behavior, communication, emotion regulation, and repetitive behaviors in infants with congenital malformation of the corpus callosum, specifically those with isolated agenesis of the corpus callosum (ACC), in comparison with infants who are developing typically.

Study design This case-control longitudinal observation study examined parent report of social behavior, social-communication, emotion regulation, and repetitive behavior development in community-ascertained infants (n = 156) and infants with isolated ACC (n = 57) between 12 and 24 months of age.

Results Infants with isolated ACC produced fewer words at 12 (P = .003) 18 (P < .001), and 24 months of age (P = .003) and fewer gestures at 12 (P < .001), 18 (P < .001), and 24 months of age (P < .001). In addition, the ACC group demonstrated delays in reciprocal social behavior at 18 months (P = .01) and social competence at 12 (P < .001) and 18 months (P = .01). No concerns were noted in emotion regulation or restricted and repetitive behavior, and social behavior appeared to normalize at 24 months.

Conclusions Existing data suggest heterogeneity in developmental outcomes among individuals with isolated ACC. The current findings fill a gap in knowledge about development in the second year of life. Surveillance of social and communication ability in infants with ACC may be warranted. The role of the corpus callosum in facilitating rapid interhemispheric information processing affects skills beyond the motor system. More work is needed to identify intervention targets for infants and toddlers with ACC. *(J Pediatr 2024;14:200118)*.

Agenesis of the corpus callosum (ACC) is a developmental brain malformation that occurs in 1 of ~4000 live births.[1-3] The diagnosis often is made in utero through a combination of ultrasound technology and fetal magnetic resonance imaging (MRI). Variation in neurodevelopmental outcomes partially depends on the presence of additional cerebral malformations or chromosomal syndromes. However, even among those individuals for whom ACC is an isolated finding, there is notable heterogeneity in outcome. Individuals showing normal levels of intellectual functioning also may exhibit subtle deficits in processing speed, problem-solving, and pragmatic communication.[4-6] Despite accumulating data on neurodevelopmental outcomes in children, adolescents, and adults, very little is known about cognitive, social, and motor development in the first 2 years of life. This report attempts to fill this gap by characterizing behavioral development in a sample of 12- to 24-month-old children with ACC for the first time.

As one source of heterogeneity in outcome, children and adults with ACC show an increased likelihood of manifesting autistic traits[7,8] and increased likelihood of receiving a diagnosis of autism spectrum disorder (ASD).[9] In a sample of 26 adolescents and adults with isolated ACC, 30.8% met diagnostic criteria for ASD.[9] In another study that screened 4- to 11-year-old children with isolated ACC for autistic traits using the Autism Spectrum Quotient, or AQ, researchers found that 45% of this sample scored in the autism range.[8] The behaviors that define ASD emerge in first 2 years of life.[10] Atypical corpus callosum development has been implicated in the early ASD phenotype.[11,12] Splenium structure, the most posterior segment of the corpus callosum, has been associated with visual orienting and word production in infants who are developing typically[13,14] and with repetitive behaviors in infant siblings of autistic children who later receive a diagnosis of ASD.[12] Whether these behaviors differentially manifest during infancy and toddlerhood in the absence of the corpus callosum in children with ACC is unknown.

To complement existing work on cognitive and developmental outcomes in young children with ACC,[6,15,16] studies of early development during infancy

ACC	Agenesis of the corpus callosum
ASD	Autism spectrum disorder
ITSEA	Infant-Toddler Social-Emotional Assessment
MB-CDI	MacArthur-Bates Communicative Development Inventories
MRI	Magnetic resonance imaging
P-CBCL	Preschool Child Behavior Checklist
RBS-EC	Repetitive Behavior Scales for Early Childhood
vrRSB	Video-Referenced Rating of Reciprocal Social Behavior

From the [1]Division of Humanities and Social Sciences, California Institute of Technology, Pasadena, CA; [2]International Research Consortium for the Corpus Callosum and Cerebral Connectivity (IRC5), Pasadena, CA; and [3]Department of Pediatrics, Institute of Child Development, Masonic Institute for the Developing Brain, University of Minnesota, Minneapolis, MN

*Contributed equally.

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and toddlerhood promise to inform models of ACC pathogenesis. In addition, early identification of behavioral patterns that predict outcomes will augment early clinical intervention, when necessary, for children with ACC. In the current study, we longitudinally characterize social, communication, emotional regulation, and repetitive behavior development across the second year of life in infants with isolated ACC as compared with a sample of community-ascertained infants who are developing typically. These domains were selected, as they represent putative intervention targets for deficits that emerge later in development,[4,5] along with evidence that ACC may differentially affect auditory processing in early infancy,[17] and subsequent communication development. We hypothesized that callosal absence impedes the rapid information integration necessary to meet increased symbolic and conceptual processing inherent to social interactions during the second year of life, manifesting as attenuated social and communicative development accompanied by intact development in emotion regulation and absent evidence of restricted and repetitive behaviors.[9] To our knowledge, the data that follow represent the first characterization of behavioral development in infants/toddlers with ACC in this age range.

Methods

This case-control, longitudinal observation study included convenience samples of 96 children with ACC and 156 typically developing comparison participants (10-26 months), the latter drawn from the Baby Connectome Project.[18] English-speaking parents of infants with ACC were recruited through social media and study announcements that were shared with family support group organizations (eg, the National Organization of Disorders of the Corpus Callosum, Australian Disorders of the Corpus Callosum, and Corpal). Data were collected remotely in 2017-2019. Twenty-three (24%) children with co-occurring neuropathology (eg, heterotopia, abnormal pituitary, cerebellar dysplasia) and/or corpus callosum hypoplasia were excluded from the current study. Development in these children will be characterized in a separate article describing the total sample of children with ACC. An additional 16 (16.7%) children were excluded from the ACC cohort, as specific neuroanatomical diagnoses could not be confirmed from medical records or because parents didn't provide more detailed information than "dysgenesis of the corpus callosum." Of the remaining 57 included herein, diagnostic information was ascertained from detailed parent report (n = 23) or from medical records (n = 34), and included 47 infants with isolated complete ACC and 10 infants with isolated partial ACC. Children with neuroanatomical findings secondary to ACC, including colpocephaly, interhemispheric cyst, untreated "hydrocephalus," absence of septum pellucidum, or interhemispheric lipoma, were included in the current report. See **Table I** for the characterization of participant information. Written informed consent was obtained from the parents of the children who served as research participants in the current study.

Table I. Participant information

Variable	Isolated ACC, n = 57	Controls, n = 156
ACC type		
Complete, No. (%)	47 (82.5)	
Partial, No. (%)	10 (17.5)	
Male, No. (%)	34 (59.6)	81 (51.9)
Ethnicity/race, No. (%)		
Non-Latino	52 (91.2)	1 (0.006)
White	47 (82.5)	130 (83.3)
Multiracial	6 (10.5)	25 (16.0)
Other	2 (3.5)	0
Unknown	2 (3.5)	0
Birth weight, g, mean (SD)	3394.1 (627.4)	3516.2 (440.8)
Gestational age at birth, wk, mean (SD)	38.5 (1.9)	39.9 (1.1)
Age of diagnosis, No. (%)		
Prenatal	45 (78.9)	
Postnatal	9 (15.8)	
Unknown	3 (5.3)	
Parent education, college degree min, No. (%)	43 (75.4)	142 (91.0)

Clinical MRI scans and radiologic reports were collected from medical records to confirm diagnoses. To focus principally on callosal agenesis, we excluded individuals with ACC who also had additional severe neural malformations, including polymicrogyria, microcephaly, trisomy chromosomal diagnoses, holoprosencephaly, tumors, and cerebrovascular incidents, as well as individuals with very low birth weight (<1500 g), very preterm birth (<32 weeks), or intractable epilepsy. Since ACC is associated with greater-than-normal risk of epilepsy and intellectual disability, as well as comorbid medical issues, an updated medical history was obtained at each time point to screen for any participants who must be excluded because of new information.

The participants represented in this report consist of all children with ACC recruited into a pilot study, funded by nonsponsored research funds at Caltech and the University of Minnesota, that motivated R01HD092430. Our target sample size for children with isolated ACC was determined of the basis of effect sizes observed in Lau et al.[8] Missing time points were largely the result of family availability and are treated as missing at random in the linear mixed effects model.

Parent-Report Assessments

Parents of all children completed questionnaires about their child's behavior remotely, through an online survey platform using best practices.[19,20] These assessments included the MacArthur-Bates Communicative Development Inventories (MB-CDI),[21] the Preschool Child Behavior Checklist (P-CBCL),[22] the Infant-Toddler Social-Emotional Assessment (ITSEA),[23] the Video-Referenced Rating of Reciprocal Social Behavior 2.3 (vrRSB),[24-26] and the Repetitive Behavior Scales for Early Childhood (RBS-EC).[27,28] Each instrument is described in detail to follow. Parents provided consent, and

permission to collect data about their child according to the Declaration of Helsinki and study activities were approved by the institutional review boards at the California Institute of Technology and University of Minnesota, respectively. The study followed Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines. Analyses were conducted between January and December 2022.

The MB-CDI[21] is a widely used parent-report questionnaire designed to index expressive language, receptive language, and communicative gesture use. An advantage of this parent report measure is the avoidance of situational and temperamental factors that may interfere with test performance. Parents of children with ACC completed the MB-CDI Words and Gestures at 12-, 18-, and 24-month time points.

The P-CBCL[22] is a 99-item widely used, norm-referenced, parent-report instrument that evaluates a wide range of internalizing and externalizing disorders based on 6 subscales (emotionally reactive, attention problems, anxious/depressed, somatic complaints, withdrawn, and aggressive behavior) and a Diagnostic and Statistical Manual of Mental Disorders-Pervasive Developmental Problems scale, which corresponds to *Diagnostic and Statistical Manual of Mental Disorders*, *Fourth Edition*, criteria. Parents of children with ACC completed this questionnaire at the 18- and 24-month time points.

The ITSEA[23] is a 166-item parent report questionnaire that assesses 4 primary domains of dimensional functioning that include externalizing behaviors, internalizing behaviors, dysregulation, and social competencies. The assessment also captures low base-rate, clinically relevant, social behaviors that include maladaptive behaviors, atypical behaviors, and social relatedness. This measure was included to augment the vrRSB and P-CBCL at 18 and 24 months while also providing preliminary data on these competencies at 12 months.

The vrRSB[24,25] represents a downward extension of the Social Responsiveness Scale,[26] among the most widely used instruments to assess autistic traits. The first 13 items (of a total of 48 items) are scored in reference to a 3-minute video of a 19-month-old typically developing child demonstrating a variety of reciprocal social behaviors (eg, expressing feelings through changes in facial expression, cooperating with an adult's request, performing showing and requesting behaviors, etc). Thirty-five additional questions reflect quantitative aspects of social behavior, and 2 final questions ask the parent to report specifically about the number of words produced by the child and to provide an example of a complex/sophisticated sentence produced by their child. Parents of children with ACC completed the vrRSB at 18- and 24-month time points.

The RBS-EC[27,28] is a measure of repetitive behaviors for children ages 8 months to 8 years of age. Repetitive behaviors range from simple motor movements to complex patterns of interests and routines and represent diagnostic criteria for ASD. Many of these behaviors occur as part of healthy early development, and variation in the manifestation of these behaviors extends across the typical to atypical continuum. Parents of children with ACC completed this questionnaire at the 12-, 18-, and 24-month time points.

A background and demographics questionnaire was designed for this study to collect basic demographic and medical history information on families entering the project. The history form includes questions regarding pregnancy, labor and delivery, callosal disorder diagnosis, developmental history, medical history, and family background. This form was completed upon enrollment. At subsequent time points, an abbreviated version of the history form was completed to acquire updated or additional information regarding callosal disorder diagnosis, developmental history, medical history, and family background. This information complemented medical records acquired from participants. Background Questionnaires are available on GitHub.

Statistical Analysis

Scores from isolated complete ACC and isolated partial ACC were largely overlapping and thus combined for subsequent analyses (**Supplement Figure S1**, online; available at www.jpeds.com). Of the 57 infants with isolated ACC, 17 contributed data at 3 time points, 27 contributed data at 2 time points, and 13 contributed data at 1 time point. Normality and equal variance assumptions were tested, and the Box-Cox transformation was conducted when the assumptions were violated. Linear mixed effects modeling with a random intercept was implemented for longitudinal models of communication (MB-CDI words produced and total gestures), social/internalizing/externalizing behaviors (vrRSB total score, P-CBCL, and ITSEA), and repetitive behaviors (RBS-EC). When relevant, Poisson regressions were implemented (eg, RBS-EC self-injurious, restricted, and ritual subscales). A modified-Bonferroni correction was implemented for analyses within each measure to adjust for multiple comparisons. This analytic approach allows for unbalanced sample size between cases and controls.

Results

Communication

Overall, the isolated ACC group produced fewer words and gestures than the control group, $F(1,193.42) = 26.95$, $P < .0001$, $\eta^2 = 0.12$ and $F(1,188.70) = 39.63$, $P < 0.0001$, $\eta^2 = 0.17$ respectively. **Figure 1** depicts data at 12, 18, and 24 months. This omnibus difference was also reflected at each time point (post-hoc pairwise comparisons are summarized in **Table II** and full results for all measures in **Supplemental Table S1**, online; available at www.jpeds.com).

Social Behaviors

Total vrRSB scores revealed less-developed reciprocal social behavior in the ACC group than the comparison group overall, $F(1,160.85) = 7.17$, $P = .008$, $\eta^2 = 0.04$. Specifically, reciprocal social behavior was less developed in the ACC group at 18 months, but groups did not differ at 24 months (**Figure 2** and **Table II**). These findings were replicated with a separate control group as reported in **Supplemental Table S2**, online;

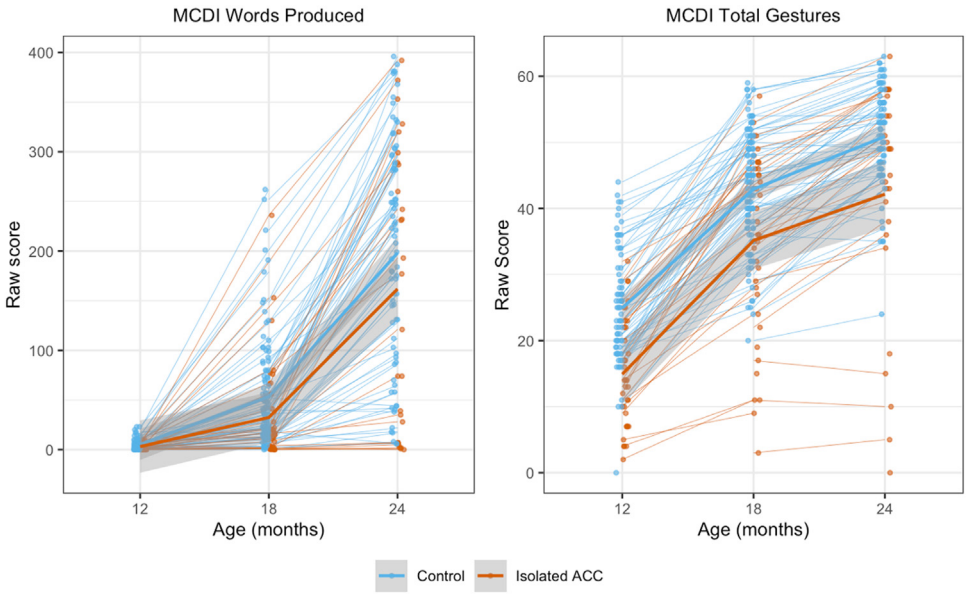

Figure 1. Trajectories of words produced and total gestures. Individual data points are represented by *closed circles*, with lines connecting longitudinal time points. *Blue* represents the control group and the *rust color* represents infants with isolated ACC. The *shaded area* around the mean trajectory for each group (*bolder thick lines*) represents 95% CI.

available at www.jpeds.com). Likewise, ratings on the ITSEA indicated reduced social competence in the ACC group overall, $F(1,172.81) = 22.43$, $P < .0001$, $\eta^2 = 0.11$, with significantly lower competence in ACC at 12 and 18 months, but no difference from controls at 24 months (**Figure 3** and **Table II**). The ACC group exhibited greater T scores on the P-CBCL Diagnostic and Statistical Manual of Mental Disorders-Pervasive Developmental Problems scale, indicating more pervasive developmental problems overall $F(1,146.46) = 8.77$, $P = .004$, $\eta^2 = 0.06$ (**Figure 2** and **Table II**) at 18 months, but no difference from the control group at 24 months.

Sensitivity Analyses

Emotion regulation scores did not differ between groups overall or at any time point on either internalizing or externalizing scales of the CBCL or ITSEA, the ITSEA dysregulation scale, or the composite RBS-EC frequency scores (**Supplemental Table S1**). However, in exploratory analyses of the RBS-EC subscales, the ACC group showed fewer ritualistic behaviors overall than the control group, $B = -0.93$, $z = -2.74$, $P = .006$. Post-hoc comparisons found significantly fewer ritualistic behaviors in the ACC group at 12 and 18 months but not at 24 months. See **Supplemental Table S1** for full statistical results for the P-CBCL and the RBS-EC.

Discussion

In this case-control longitudinal study, we describe developmental patterns of social and communication development in the second year of life in infants with isolated ACC. In comparison with typically developing controls, infants with isolated ACC produced fewer words and gestures at 12, 18, and 24 months. They also showed delays in reciprocal social behavior and social competence at 12 and 18 months, but not at 24 months. See **Table III** for characterization of the effect sizes, using the Cohen *d*, for each time point and each measure showing a significant omnibus effect. However, the infants with isolated ACC did not differ from the control group on measures of emotion regulation or restricted and repetitive behaviors.

The lack of cross-sectional differences in social behavior at 24 months may reflect diminished power to detect differences at that age, or true developmental change in toddlers with ACC in this domain, such that reciprocal social behavior begins to normalize at this age. More data, beyond 24 months, will determine whether we are observing a time-constrained window of behavior of a broader dynamic process in which reciprocal social behavior oscillates in response to various age-dependent developmental challenges. More data could also illustrate a trajectory of social development defined by persistent normalization over time, consistent with the current observation at 24 months. Nevertheless, delays in reciprocal social behavior at 18 months of age, especially when combined with the communication delays observed, may have cascading effects on more complex social cognitive ability later in development. Indeed, there is evidence to suggest social behavior as a key domain of concern in older children with isolated ACC.[7,8,29]

There are several notable strengths of the current approach. Namely, these behavioral data fill a gap in knowledge about development from 12 to 24 months in infants/toddlers with ACC.

Table II. Estimated marginal means by group for the MB-MCDI, the vrRSB, the ITSEA, and the P-CBCL

	12 mo			18 mo			24 mo		
	Isolated ACC	Control		Isolated ACC	Control		Isolated ACC	Control	
Age of assessment	EMM (95% CI)	EMM (95% CI)	*P* value	EMM (95% CI)	EMM (95% CI)	*P* value	EMM (95% CI)	EMM (95% CI)	*P* value
MB-MCDI									
No. (% male)	35 (61)	78 (50.0)		38 (67)	106 (67.9)		27 (47)	75 (48.1)	
Words produced	1.2 (0.2-2.3)	3.9 (2.4-5.5)	.003	11.5 (5.7-17.4)	32.1 (22.7-41.5)	<.001	68.1 (31.5-104.8)	156.9 (106.2-207.6)	.003
Total gestures	12.7 (8.6-16.8)	24.5 (21.8-27.2)	<.001	34.1 (30.1-38.1)	42.8 (40.3-45.3)	<.001	43.1 (38.7-47.6)	51.5 (48.8-54.2)	<.001
vrRSB									
No. (% male)				41 (70)	104 (66.7)		25 (42)	78 (50.0)	
Total score				27.0 (23.8-30.1)	21.2 (19.2-23.2)	.01	22.2 (18.4-25.9)	19.0 (16.8-21.2)	.54
ITSEA (T scores)									
No. (% male)	34 (60)	59 (37.8)		42 (74)	43 (27.6)		26 (46)	82 (52.6)	
Competence	35.6 (32.4-38.7)	44.1 (41.8-46.4)	<.001	39.7 (37.2-42.3)	45.8 (44.0-47.5)	.01	43.9 (40.5-47.3)	47.4 (45.3-49.5)	.21
Internalizing	45.8 (42.6-48.9)	44.6 (42.3-47.0)	.99	45.8 (43.3-48.3)	45.0 (43.3-46.7)	.99	45.9 (42.5-49.3)	45.3 (43.2-47.4)	>.99
Externalizing	43.7 (40.9-46.4)	46.3 (44.3-48.3)	.12	45.2 (43.1-47.3)	46.5 (45.1-48.0)	.99	46.7 (43.8-49.6)	46.7 (44.9-48.5)	.97
Dysregulation	46.1 (41.9-50.3)	43.8 (40.8-46.9)	.99	44.0 (40.4-47.5)	41.6 (39.2-44.1)	.99	41.8 (37.3-46.2)	39.4 (36.6-42.2)	.98
P-CBCL (T scores)									
No. (% male)				41 (70)	30 (19.8)		27 (47)	78 (50.0)	
DSM Mental				53.0 (51.5-54.5)	50.4 (49.0-51.7)	.006	52.2 (50.7-53.8)	50.7 (49.6-51.8)	.18

DSM, Diagnostic and Statistical Manual of Mental Disorders; *EMM*, estimated marginal means.

A relatively recent meta-analysis reveals the standard approach to the vast majority of studies that have examined neurodevelopmental outcomes in children with ACC.[5] Namely, the presumed goal is to derive data to inform clinical counseling regarding cognitive, intellectual, and/or developmental *outcome* of children diagnosed with ACC. However, there is a striking paucity of data informing what parents should know about the *development* of their children in the first years of life. Here, we provide data indicating that social and communication development may represent domains for parents and clinicians to monitor during this age period.

The use of a community-ascertained control group of typically developing children is also a strength. Most previous studies base results on comparisons with published norms from a given standardized instrument. However, there are documented limitations to reliance on published norms for elucidating differences between clinical cases and controls (eg, Raznahan et al[30]). The utility of comparison groups, be

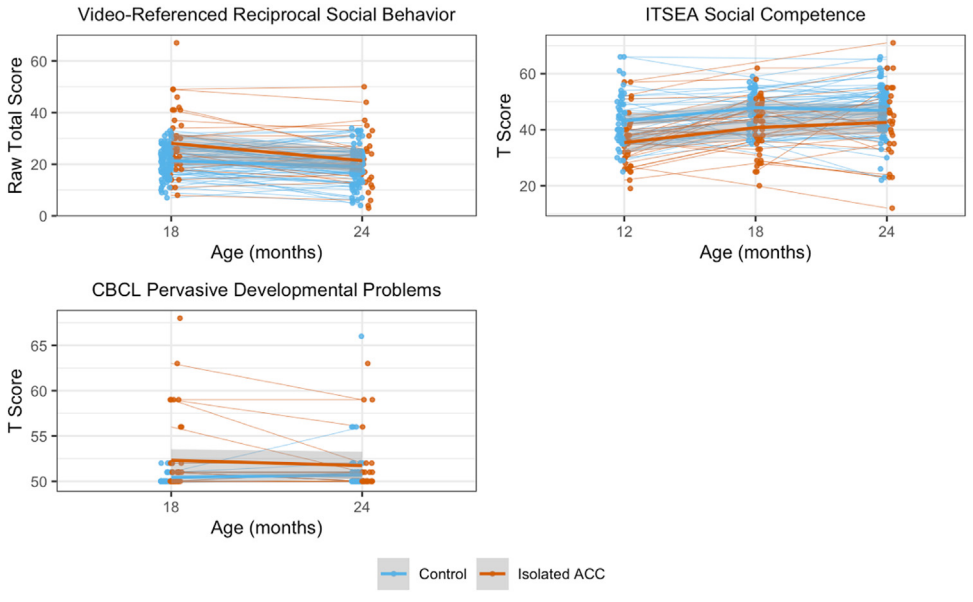

Figure 2. Social behavior from 3 separate instruments. Individual data points are represented by *closed circles*, with lines connecting longitudinal time points. *Blue* represents the control group and the *rust color* represents infants with isolated ACC. The *shaded area* around the mean trajectory for each group (*bolder thick lines*) represents 95% CI. Differences in social behavior are present at 18 months in the vrRSB, ITSEA, and P-CBCL and at 12 months in the ITSEA.

Table III. Effect sizes (Cohen *d*) at each time point for the MB-MCDI, the vrRSB, the ITSEA, and the P-CBCL

	Cohen *d*		
Instrument/Subscale	**12 mo**	**18 mo**	**24 mo**
MB-MCDI			
Words produced	0.41	0.56	0.40
Total gestures	0.72	0.58	0.46
vrRSB			
Total score		0.42	0.17
ITSEA (T scores)			
Competence	0.55	0.39	0.27
Internalizing	0.05	0.06	0.02
Externalizing	0.30	0.06	0.10
Dysregulation	0.05	0.04	0.08
CBCL (T scores)			
DSM Mental		0.52	0.31
Internalizing		0.10	0.14
Externalizing		0.04	0.11

they typically developing or other high-risk comparison groups, promises to advance our understanding of heterogenous phenotypic manifestation in ACC. Future work should include comparisons with neurogenetic syndromes (eg, fragile X syndrome and Down syndrome), other neurologic disorders (eg, tuberous sclerosis complex), and infants at high likelihood for developing ASD.

Further, although the use of standardized developmental/intellectual assessments is necessary, global scores of IQ or development quotients often lack precision with regard to specific domains of development.[31] The use of standardized instruments and normed reference scores also often yields truncated summaries of outcomes such as normal, moderate concerns, and severe concerns.[15,16] The use of instruments that target specific behavioral domains, for example repetitive motor behavior as compared with meeting typical motor milestones, is another strength of the current approach. More precise phenotypic characterization promises to inform more precise etiologic characterization, which in turn will improve prognosis and inform early intervention strategies in this population.

As the primary conduit for interhemispheric structural connectivity, the corpus callosum is positioned to support many cognitive and perceptual functions that rely on rapid information integration. Revealing statistically equivalent emotion regulation among the ACC group and the typically developing group suggests (1) either the corpus callosum is not instrumental for these skills or (2) plastic reorganization is occurring very early in development. Further, identifying differences in social and communication development early in life suggests that the corpus callosum may be necessary but not sufficient for enabling functional specialization for these skills. More work is needed to determine whether a subgroup of children who later meet diagnostic criteria for ASD in the ACC group is driving observed group differences in social behavior and communication development.

Several limitations of the current study warrant consideration. Convenience samples may introduce bias in ascertainment. The sample described herein was rather homogenous in race/ethnicity and socioeconomic background, limiting the generalizability of the findings. Inferences also would be strengthened by increased sample size. In addition, although there are strengths of parent-report measures (ie, avoidance of situational/contextual effects that may affect direct assessment performance), weaknesses include the potential of reporter bias and the potential for the halo effect in which parents' positive impressions of their children may exaggerate true ability. Although there are advantages and disadvantages to both parent-report and direct assessments,[32] direct assessments of global and targeted domains of development in conjunction with parent report measurement promises to strengthen future investigations of longitudinal development in infants and toddlers with ACC. Further, although we limited our analyses to the second year of life, more work is needed to expand the age range, the breadth of domains assessed, and as mentioned previously the modality of assessment (ie, direct assessment, clinical interviews, and parent report). Indeed, a comprehensive prospective longitudinal study beginning early in infancy that follows children with ACC and families through school age and adolescence would be invaluable for families, their clinicians, and the basic scientists hoping to elucidate pathogenesis. Lastly, curating more complete medical records, including prenatal ultrasound and perinatal MRI data, will augment the characterization of the sample moving forward. Relying on parent report of the diagnosis in a proportion of children is a limitation of the study.

In conclusion, clinical counseling of families with a child diagnosed with isolated ACC during the perinatal period requires information about development across the first years of life. This case-control longitudinal study suggests that surveillance of social and communication behaviors in infants and toddlers with isolated ACC may be clinically warranted. ■

CRediT authorship contribution statement

Lynn K. Paul: Writing – review & editing, Visualization, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Jasmin Turner:** Writing – review & editing, Visualization, Resources, Investigation, Formal analysis. **Sooyeon Sung:** Writing – review & editing, Visualization, Resources, Investigation, Formal analysis. **Jed T. Elison:** Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of Competing Interest

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of Mental Health (NIMH). The funders had no role in the design, data collection, analysis, data interpretation, or the writing of this report. The authors report no conflicts of interest.

Drs Paul and Elison had full access to the data in this study and take full responsibility for the integrity of the data and the accuracy of the results. We are indebted to the families who graciously provided their time for this research.

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Reprint requests: Jed T. Elison, PhD, Institute of Child Development, 51 East River Parkway, Minneapolis, MN 5455. E-mail: jtelison@umn.edu

Data Statement

Data sharing statement available at www.jpeds.com.

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