

The corpus callosum is the largest transverse white matter fiber tract connecting the two hemispheres of the brain. It plays an essential role in the interhemispheric transfer and bihemispheric coordination involved in perception and sensory-motor integration, as well as higher level cognition (e.g., memory, executive functioning). The corpus callosum forms prenatally (10-15 weeks gestation) and continues to develop through early adulthood. Damage to the corpus callosum throughout the lifespan, but especially later in life, can result in sensory and motor coordination deficits and produces disconnection syndromes. However, individuals born with a partial or fully absent corpus callosum, known as Agenesis of the Corpus Callosum (ACC), do not exhibit a full disconnection syndrome and may, in fact, demonstrate many intact skills including broadly average intellectual abilities. Agenesis of the corpus callosum (ACC) is a relatively common congenital brain malformation that occurs in 1 out of ~4000 live births (Glass, Shaw, Ma, & Sherr, 2008; Paul et al., 2007). There is significant heterogeneity in outcomes for these individuals, often related to the presence of additional neuropathology, and the presence of co-occurring medical and genetic conditions. In adults for whom ACC is the primary neurological finding, there is a core constellation of cognitive symptoms that include reduced interhemispheric transfer, slowed processing, and difficulty with complex novel problem solving (Brown & Paul, 2019). There is also an elevated likelihood of autism spectrum disorders in this population as well (Paul et al, 2014).

Modern ultrasound technology facilitates diagnosis of ACC in utero, offering a unique opportunity to study these individuals' development from infancy. However, no studies to date have examined early development in this population using validated measures, leaving neuropsychologists, neurologists and primary care providers to make educated guesses about what families should expect and appropriate therapies/treatment.

This symposium presents a series of studies examining the early development of individuals with primary ACC across domains including language, adaptive skills, autism symptomology, and temperament/anxiety. We will provide the first in-depth prospective characterization of

development in ACC relative to typically developing children at 6, 12, 18 and 24 months and discuss what these findings reveal about brain development and plasticity more broadly (e.g. how does early disruption in interhemispheric connection impact cognitive development across key domains?).

Finally, while ACC is defined specifically by corpus callosum anatomy, the corpus callosum has been implicated in other neurodevelopmental conditions (Paul, 2011). Utilizing extant comparison, we also assess how early development in ACC both overlaps and differs from two monogenic conditions (e.g. Fragile X and Down Syndrome) and a developmental behavioral diagnoses (e.g. autism) and discuss how early disruptions in interhemispheric transfer may contribute to shared behavioral phenotypes in these conditions.

Keyword 1: corpus callosum

Keyword 2: pediatric neuropsychology

Keyword 3: brain development

1 Early Development of Adaptive Skills in Young Children with Agenesis of the Corpus Callosum: A Comparison to Monogenic and Neurodevelopmental Conditions

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Objective: Differences in adaptive functioning present early in development for many children with monogenic (Down Syndrome, Fragile X) and neurodevelopmental disorders. At this time,

it is unclear whether children with ACC present with early adaptive delays, or if difficulties emerge later as functional tasks become more complex. While potential delays in motor development are frequently reported, other domains such as communication, social and daily living skills are rarely described. We used a prospective, longitudinal design to examine adaptive behavior from 6-24 months in children with ACC and compared their trajectories to those with monogenic and neurodevelopmental conditions.

Participants and Methods: Our sample included children with primary ACC (n= 27-47 depending on time point) whose caregivers completed the Vineland Adaptive Behavior Scales-Interview 3rd Edition, via phone at 6, 12, 18 and 24 months. Comparison samples (using the Vineland-2) included children with Down Syndrome (DS; n = 15-56), Fragile X (FX; n = 15-20), children at high familial likelihood for autism (HL-; n=192-280), and low likelihood (LL; no family history of autism and no developmental/behavioral diagnosis; n = 111-196). A subset of the HL children received an autism diagnosis (HL+; n = 48-74). The DS group did not have an 18-month Vineland.

Results: A series of linear mixed model analyses (using maximum likelihood) for repeated measures was used to compare groups on three Vineland domains at 6, 12, 18 and 24 month timepoints). All fixed factors (diagnostic group, timepoint, and group X timepoint interaction) accounted for significant variance on all Vineland domains ($p < .001$). Post hoc comparisons with Bonferroni-correction examined ACC Vineland scores compared to the other diagnostic groups at each timepoint. At 6 months, parent-ratings indicated the ACC group had significantly weaker skills than the LL group in Communication and Motor domains. At 12, 18 and 24 months, ratings revealed weaker Communication, Daily Living and Motor skills in the ACC group compared to both the LL and HL- groups. Compared to the other clinical groups, the ACC group had stronger Socialization and Motor skills than Fragile X at 6 months, and at 24 months had stronger Communication and Socialization skills than both the DS and FX groups, as well as stronger Socialization than the HL+ group.

Conclusions: Compared to children with low likelihood of ASD, children with primary ACC reportedly have weaker Communication and Motor skills from 6 to 24 months, with weakness in Daily Living Skills appearing at 12 months and

all differences increase with age. Compared to Fragile X, the ACC exhibited relative strengths in socialization and motor skills starting at 6 months. By 24 months, the ACC group was outperforming the monogenic groups on Socialization and Communication. In general, the ACC scores were consistent with the HL+ sample, except the ACC group had stronger Social skills at 18 and 24 months. The results clearly inform the need for early intervention in the domains of motor and language skills. Additionally, as we know that children with ACC are at increased risk for social difficulties, research is needed both using more fine-grained social-communication tools, and following children from infancy through middle childhood.

Categories: Behavioral Neurology/Cerebral Lateralization/Callosal Studies

Keyword 1: corpus callosum

Keyword 2: pediatric neuropsychology

Keyword 3: adaptive functioning

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2 Early Presentation of Autistic Features in Infants with Agenesis of the Corpus Callosum

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Objective: Agenesis of the Corpus Callosum (ACC), a congenital disorder in which the corpus callosum partially or completely fails to develop properly, occurs in ~1 in 4,000 live births. ACC has been identified as a major risk factor for receiving an Autism Spectrum Disorder (ASD) diagnosis (~10% diagnosis rate, as compared to 2.3% in the general population), but little is currently known about behavioral and social development during infancy and early childhood in this disorder. In this study we aim to 1) characterize the manifestation of autistic features in 24-month-old children (a common age for early diagnosis of ASD) with ACC and a convenience sample of age matched comparison children from the community, and 2) determine if parent reports of autistic features during the first year of life are associated with