

who do and do not have a confirmed ASD diagnosis (HL+ n=81, HL- n=282), and low-likelihood controls (LL- n=152).

Results: Overall, the ACC group demonstrated blunted affect, with significantly lower positive and negative emotionality than LL controls at both timepoints. Specifically, the ACC group exhibited lower activity and approach dimensions of positive emotionality at both timepoints, with lower high-intensity pleasure at 6 months and lower vocal reactivity at 12 months. On negative emotionality subscales, the ACC group exhibited lower distress to limitations and sadness at both timepoints, as well as lower falling reactivity at 6 months.

The ACC and HL groups did not differ significantly on positive emotionality at either timepoint. However, negative emotionality was lower in the ACC group than the HL- group at both timepoints and lower than the HL+ group at 12 months, with lower distress to limitations and sadness ratings than both HL groups at both timepoints.

Conclusions: These findings highlight the importance of interhemispheric connections in facilitating active engagement and pursuit of pleasurable activities during the first year of life, as well as expression of sadness and distress to limitations. Notably, similarities between infants with ACC and infants at elevated familial risk of ASD suggest that disrupted callosal connectivity may specifically contribute to reductions in positive emotionality.

Categories: Behavioral Neurology/Cerebral Lateralization/Callosal Studies

Keyword 1: corpus callosum

Keyword 2: language

Keyword 3: pediatric neuropsychology

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4 Language Development in Infants and Toddlers (12 to 24 months) with Agenesis of the Corpus Callosum

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Objective: It is unclear how agenesis of the corpus callosum (ACC), a congenital brain malformation defined by complete or partial absence of the corpus callosum, impacts language development. fMRI studies of middle childhood suggest that the corpus callosum plays a role in the interhemispheric language network (Bartha-Doering et al., 2020), and that reduced interhemispheric functional connectivity is correlated with worse language abilities in children with ACC (Bartha-Doering et al., 2021). Additionally, accumulating evidence suggests structural abnormalities of the corpus callosum play a role in neurodevelopmental disorders. While children who go on to receive an autism spectrum disorder (ASD) diagnosis may show early signs of altered word and gesture acquisition (Iverson et al., 2018), the same is not known about ACC. This study examined language development during the second year of life in children with ACC in comparison to neurotypical control participants, as well as other children at elevated risk of ASD.

Participants and Methods: The MacArthur-Bates Communicative Development Inventories (MCDI): Words and Gestures scales were administered to parents of 74 children with isolated ACC at 12, 18 and 24 months of age. Children whose first language was not English and children who were bilingual were excluded. Comparison groups consisted of individuals with a low familial likelihood of ASD (LL- n=140) and individuals with high familial likelihood of ASD who do and do not have a confirmed ASD diagnosis (HL+ n=68, HL- n=256).

Results: Compared to LL controls, the ACC group produced fewer words at 18 and 24 months of age, and demonstrated fewer words understood at all three timepoints. Similarly, compared to the HL- group, the ACC group demonstrated fewer words produced and understood at 18 months of age, and fewer words produced at 24 months of age. The ACC and HL+ groups did not differ in words produced or words understood at any timepoint.

Conclusions: Overall, infants with ACC demonstrated delayed vocabulary expansion from 12 to 24 months of age. These findings illustrate the role of callosal connectivity in the

development of language across the first 2 years of life, and highlight the need for support and interventions that target vocabulary production and comprehension.

Categories: Behavioral Neurology/Cerebral Lateralization/Callosal Studies

Keyword 1: language

Keyword 2: corpus callosum

Keyword 3: autism spectrum disorder

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Paper Session 08: Alzheimer's disease related topics

4:00 - 5:25pm

Thursday, 2nd February, 2023

Town & Country Ballroom C

Moderated by: Robin Hilsabeck

1 Sex Differences in Associations Between APOE $\epsilon 2$ and Longitudinal Cognitive Decline

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Objective: Women have a greater lifetime risk of developing Alzheimer's disease (AD) dementia than men, a sex/gender disparity that cannot be explained by female longevity alone. There is substantial evidence for sex differences in the effects of APOE $\epsilon 4$ on risk for AD. While APOE $\epsilon 4$ increases AD risk in both sexes, women who carry APOE $\epsilon 4$ are disproportionately vulnerable to cognitive impairment and AD compared to their counterpart men. In contrast to APOE $\epsilon 4$, APOE $\epsilon 2$ is associated with slower cognitive decline and a lower risk of AD. Although a less robust literature, APOE $\epsilon 2$ may also have sex-specific effects. Because APOE $\epsilon 2$ is the rarest major APOE allele, well-powered studies are needed to examine sex-specific effects. The objective of the present study was to examine sex-specific associations of APOE $\epsilon 2$ carriage with longitudinal cognitive decline in a large cohort of clinically unimpaired adults.

Participants and Methods: We used observational data from two sources: the National Alzheimer's Coordinating Center (NACC) and the Rush Alzheimer's Disease Center (ROS/MAP/MARS) studies. We included data from clinically unimpaired adults who were ≥ 50 years old at baseline who self-identified as non-Hispanic White (NHW) or non-Hispanic Black (NHB). Participants were categorized as APOE $\epsilon 2$, $\epsilon 4$, or $\epsilon 3/\epsilon 3$ carriers. APOE $\epsilon 2/\epsilon 4$ carriers were excluded. The same battery of neuropsychological tests was used to assess global cognition in participants from both data sources. Linear mixed models examined interactive associations of genotype ($\epsilon 2$ or $\epsilon 4$ vs. $\epsilon 3/\epsilon 3$), sex, and time on longitudinal cognition in NHW and NHB participants separately. Analyses were first performed in a pooled sample of NACC and ROS/MAP/MARS participants and if significant they were repeated separately in each data source.

Results: Across both data sources, 9,766 NHW (mean (SD) age=73.0(9.00) years, mean (SD) education=16.3(2.83) years, n(%) women=6,344(65.0)) and 2,010 NHB participants (mean(SD) age=71.3(7.59) years, mean(SD) education=14.9(3.10) years, n(%)