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

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1 Sex Differences in Associations Between APOE ε2 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 ε4 on risk for AD. While APOE ε4 increases AD risk in both sexes, women who carry APOE ε4 are disproportionately vulnerable to cognitive impairment and AD compared to their counterpart men. In contrast to APOE ε4, APOE ε2 is associated with slower cognitive decline and a lower risk of AD. Although a less robust literature, APOE ε2 may also have sex-specific effects. Because APOE ε2 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 ε2 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 ε2, ε4, or ε3/ε3 carriers. APOE ε2/ε4 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 (ε2 or ε4 vs. ε3/ε3), 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(%)

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women=1,583(78.8)) met inclusion criteria. Sex modified the association between APOE ε2 and cognitive decline in NHW (β=0.097, 95% CI: 0.023–0.172, pint=.01) but not NHB participants (β=-0.011, 95% CI: -0.153–0.131, pint=.9). In sex-stratified analyses of NHW participants, APOE ε2 (vs. ε3/ε3) carriage was associated with attenuated cognitive decline in men (β=0.096, 95% CI: 0.037–0.155, p=.001), but not women (β=-0.001, 95% CI: -0.044–0.043, p=.97). In analyses comparing men and women APOE ε2 carriers, men exhibited slower cognitive decline than women (β=0.120, 95% CI: 0.051–0.190, p=.001). Analyses performed separately in NACC and ROS/MAP revealed the same pattern of male-specific APOE ε2 protection in NHW participants in both data sources.
Conclusions: In light of the longstanding view that APOE ε2 protects against AD and dementia, our results provide evidence that APOE ε2 is associated with attenuated cognitive decline in men but not women among NHW adults. This male-specific protection may contribute to sex differences in AD-related cognitive decline. Our findings have important implications for understanding the biological drivers of sex differences in AD risk, which is crucial for developing sex-specific strategies to prevent and treat AD dementia.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: apolipoprotein E
Keyword 2: aging disorders
Keyword 3: dementia - Alzheimer's disease
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2 Predictors of Memory Deficits in Patients with Subjective Cognitive Decline, Mild Cognitive Impairment, and Alzheimer's Disease – Do Disease Severity Moderate the Association?

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Objective: Age, sex, education, memory, and the APOE e4 allele are related to Alzheimer's disease (AD) risk. Recently it was suggested that low body mass index (BMI) contributes to the development of AD. The objective of this study was to examine how delayed recall of a word list was influenced by demographic variables, APOE and BMI in people with memory problems, and to investigate whether the impact of these variables was smaller at higher disease severity levels.
Participants and Methods: The participants were 1206 patients in the Norwegian NorCog registry diagnosed with either subjective cognitive decline (SCD) (n=274), mild cognitive impairment (MCI) (n=444), or AD (n=488). ANOVAs and hierarchical regression were applied to examine whether the delayed recall part of the 10-word test of the CERAD-WL was associated with age, sex, education, APOE (e4/non-e4) and BMI. Analyses were run separately for SCD, MCI and AD patients.
Results: There were significant bivariate differences (p<.001) between the three patient groups for all variables; the AD patients were older, less educated, more were women, more had APOE e4 alleles, and they had lower BMI. For the SCD group, 34% of the total variance (R^2) of the dependent variable was explained. All independent variables except BMI (p=.07) had a significant contribution in the prediction. For MCI, 18% of the total were explained. All variables except education and sex showed significant contribution to R^2. For the AD group, R^2 was 13%. Sex and BMI did not contribute significantly.
Conclusions: As expected, the performance on CERAD-WML was influenced by age, education and sex in the SCD group, whereas the associations between memory function and the three demographic variables were less clear among patients with MCI and AD. ApoE genotype influenced on the CERAD-WML

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