APOE ε4 predicts accelerated cognitive and brain aging outcomes in older adults with autism

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BEAR

Autism Brain Aging -Laboratory-

INTRODUCTION

Autism spectrum disorder (ASD) is a developmental and social communication disorder affecting over 75 million individuals worldwide. Recent research evidence suggests that middle-aged adults and older adults with ASD are more likely to be diagnosed with early onset Alzheimer's disease compared to neurotypical (NT) adults. Autistic adults have a 2.6 times higher risk for Alzheimer's disease compared to those without ASD and by 2030, there will be roughly 700,000 older adults diagnosed with ASD in the U.S. Importantly, the Autism and Brain Aging lab is one of the first to examine sex differences in aging for autistic adults. Specifically, facets of aging in adults with autism may include increased likelihood of developing Alzheimer's Disease, Parkinson's Disease, short-term verbal memory vulnerabilities, and learning reduction. Thus, this research aims to test the hypothesis that Alzheimer's related genes (APOE ε4), contribute to accelerated cognitive and brain aging outcomes in older adults with autism. APOE is a gene that may present as different alleles, APOE ε4 is one of the strongest indicators of developing Alzheimer's disease (NIH 2021). Exploring this field bridges a vast knowledge gap surrounding adults with ASD, allowing for increased understanding, resources, and integration of precision medicine.

METHODS

Table 1 Participant Demographics

	NT (N=41) Mean (±SD) Range	ASD (N=35) Mean (±SD) Range
Age (Years)	53.90 (±8.44) 40-70	53.06 (±8.91) 40-71
Sex (M/F)	27/14	27/8
KBIT2[d] Composite	109.07 (±12.09) 85-141	108.97 (±14.52) 70-131

- Intellectually-able adults (IQ>70) over the age of 40 were recruited for the study
- DNA extracted from saliva was used to conduct APOE genotyping, assessed by TapeStation methods.
- Verbal learning and memory was assessed using the Auditory Verbal Learning Test. Short-term memory was measured via the immediate recall of the first trial. Long-term memory was measured via the twenty-minute delayed trial. Total words (A1-A5) measured learning.
- Data was analyzed using SPSS with a general linear model evaluating the main effects of ASD, age, and their interaction, controlling for sex.

AIM

Assess whether the Alzheimer's risk allele (APOE ε4) contributes to accelerated cognitive and brain aging outcomes in older adults with autism. We hypothesized that older adults with ASD and the ε4 allele may have exacerbated declines in short term verbal memory and learning reduction as they age.

RESULTS

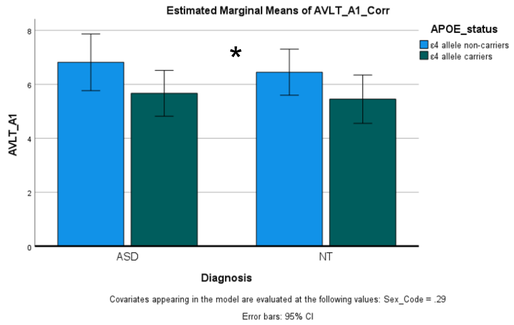

Figure 1. Short-term verbal memory (A1) showed a main effect of the ε4 allele with carriers remember fewer words (*p=0.025).

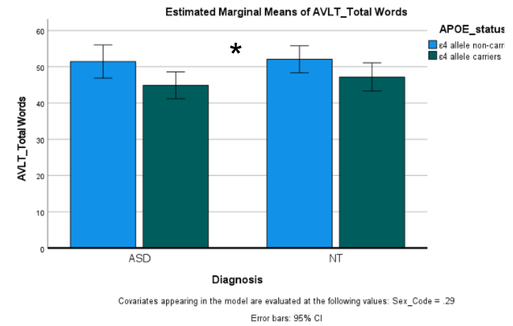

Figure 2. Total learning showed a main effect of the ε4 allele with carriers learning fewer words (*p=0.006).

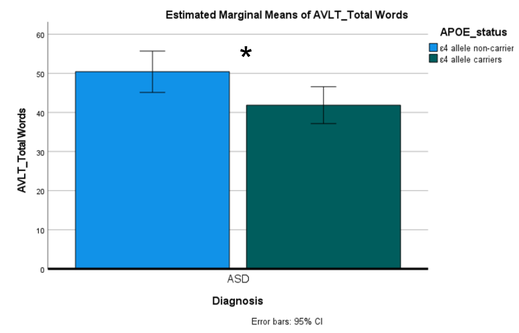

Figure 3. Total learning exploratory analyses in autistic males showed the ε4 allele was associated with learning fewer words (*p=0.020)

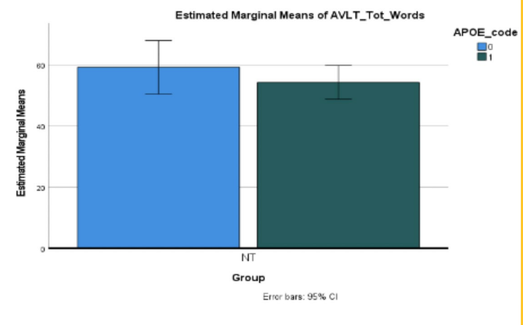

Figure 4. Total learning exploratory analyses in neurotypical females showed the ε4 allele was not associated with learning (n.s. p=0.318)

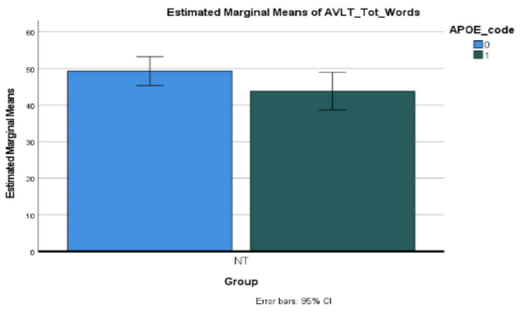

Figure 5. Total learning exploratory analyses in neurotypical males showed the ε4 allele was not associated with learning (n.s. p=0.094)

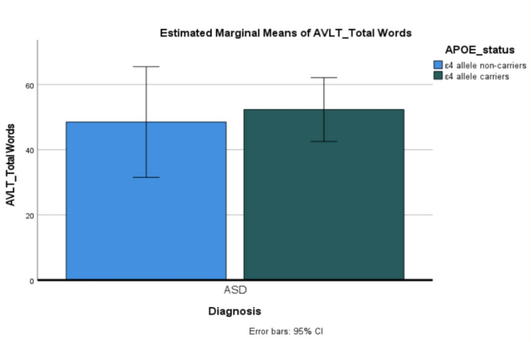

Figure 6. Total learning exploratory analyses in autistic females showed the ε4 allele was not associated with learning (n.s. p=0.649)

CONCLUSIONS

- We replicated previous findings that carrying the APOE ε4 allele is associated with reduced verbal learning and short-term memory in older adults.
- Exploratory analyses of verbal learning in individual sex and diagnosis groups were conducted because sex accounted for a significant amount of variance in this model. Findings suggests the APOE ε4 allele may have the greatest negative impact on autistic males.
- Higher prevalence of the APOE ε4 allele may be an important factor in the increased risk of Alzheimer's disease for those diagnosed with ASD.
- Thus, aging and autism may lead to verbal learning discrepancies that are evident when compared to neurotypical controls.
- In order to fully elucidate cognitive related changes, it is paramount to replicate this study using a larger sample size with longitudinal data.
- In the future, DNA genotyping will be performed on Illumina Global Diversity Array (>1.8 million markers), a high-density single nucleotide polymorphism global microarray with 180k neurodegenerative disease markers assigned to a whole-genome coverage.

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