

BIOMARKERS (NON-NEUROIMAGING)

ABCA7 high-risk genotype predicts working memory decline among older cognitively healthy African Americans

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Abstract

Background: Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive cognitive decline¹. APOE- ϵ 4 has been identified as the most prevalent genetic risk factor for the early onset of AD, while ABCA7-80 (rs115550680) has been shown to have a stronger effect size than the APOE- ϵ 4 allele and is associated with the development of late-onset of AD among African Americans^{2,3}. Although the efficiency of executive functions declines with age, some basic attentional functions and preserved knowledge may help mitigate the effects of aging on working memory⁴. Nevertheless, the impact of APOE ϵ 4 and ABCA7-80 genotypes on attention and executive function in preclinical AD remains unclear⁵. This study investigated the influence of APOE ϵ 4 and ABCA7-80 genotypes on working memory among cognitively unimpaired older African Americans.

Method: Participants were drawn from the ongoing longitudinal study, Pathways to Healthy Aging in African Americans conducted at Rutgers University–Newark. 838 participants (ages \geq 60) completed saliva collection for genotyping and neuropsychological battery for cognitive assessment with a fraction repeating each assessment multiple times as part of returning visits. Simple linear mixed models were applied for longitudinal statistical analysis.

Result: ABCA7-80 high-risk genotype was found to be a risk factor for decreased cognitive performance, as assessed by Trail Making Test Part A ($\beta = 5.819$, $p = 0.030$) and Part B ($\beta = 39.964$, $p < 0.001$), Digit Span Total ($\beta = -2.092$, $p = 0.045$), Controlled Oral Word Association ($\beta = -4.708$, $p = 0.019$), as well as a significant association with increased depression.

Conclusion: The ABCA7-80 high-risk genotype may indicate early working memory declines in preclinical AD and may serve as a predictive biomarker among cognitively impaired older African Americans.

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