ABSTRACT
A BEHAVIORAL AND NEURAL INVESTIGATION OF THE IMPACT OF AGE AND GENETIC RISK FOR ALZHEIMER’S DISEASE ON INHIBITORY CONTROL

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Significant advances have been made in understanding Alzheimer’s disease (AD), but our ability to accurately predict who will develop AD remains limited. Executive functioning has been neglected as a preclinical marker of AD, despite the vital role of these abilities (e.g., planning, set shifting, inhibition) in everyday functioning. Inhibitory deficits in particular have been found to predict impairment in activities of daily living, an important criterion in the diagnosis of AD.

This study examined differences in behavioral task performance and underlying neural processing based on event related potentials (ERPs) during an inhibition task as a function of age and genetic risk for AD based on apolipoprotein-E (APOE) ε4 status. Participants included 49 healthy, cognitively intact older adults and 42 young adult college students. Genetic testing was conducted for older adults, 24 of whom were APOE ε4 carriers. Participants completed the Parametric Go/NoGo/Stop (PGNGS) task while EEG data was collected for later extraction of ERPs.

Significant ERP differences by genetic risk emerged such that APOE ε4+ participants exhibited significantly more negative amplitudes than APOE ε4- participants at midline electrodes in response to Stop trials (Fz: \( p < .001 \), FCz: \( p = .002 \), Cz: \( p = .012 \)). These neural differences were seen in the absence of genetic risk differences in behavioral task performance, suggesting that psychophysiological measures may be more sensitive to early disease stage differences than neuropsychological testing alone. Expected age differences also emerged, with older adults exhibiting slower response times and longer ERP latencies in most task conditions and at most electrode sites.

In conclusion, this study revealed significant ERP differences across genetic risk groups in cognitive intact older adults, revealing a new early marker of AD risk. Moreover, these findings underscore the importance of considering executive abilities, such as inhibition, as preclinical markers of risk for AD.