ABSTRACT
CORTICO-CEREBELLAR CONNECTIVITY DURING INHIBITION AS AN INDEX OF AGE- AND SEX-LINKED RISK FACTORS FOR ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) may best be described as a "disconnection syndrome" in which symptoms are explained by impaired neural communication between brain regions. While intra-network connectivity typically decreases with age, these trends are impacted by inheritance of the apolipoprotein-E ε4 allele. Carriers of the ε4 allele demonstrate increased activation and connectivity (i.e., compensatory recruitment of neural resources) at younger ages, and depletion of these resources precedes symptoms of cognitive decline. Additionally, women develop AD at a greater rate than men and are more negatively impacted by ε4, presenting a need to assess the contributions of sex in aging trajectories. The cerebellum may be particularly sensitive to these differences, as it is one of the earliest brain structures to undergo age-related changes. Indeed, connectivity between the cerebral cortex and posterolateral regions of the cerebellum is crucial in maintaining aspects of executive functioning (EF) such as inhibitory control. Recent advances in source localization allow cerebellar activity and connectivity to be examined using electroencephalography (EEG), which possesses great temporal precision and can reveal subtle changes in network connectivity during inhibitory subprocesses that may indicate future risk for cognitive decline. Thus, the current dissertation evaluated the influence of age, sex, and ε4 on cortico-cerebellar connectivity during a go/no-go inhibitory control task in healthy, cognitively intact adults ($N = 86$). Multiple hierarchical regressions revealed that lower cortico-cerebellar connectivity in the P300 window was predicted by age, with response time (i.e., processing speed) mediating the effect. Additionally, multiple moderation models identified that biological sex moderated the effects of age on N200 frontal-cerebellar connectivity such that men had greater connectivity in older age, signifying compensatory recruitment. No effect of age was observed in women, potentially signaling depleted neural resources, and no influence of ε4 on cortico-cerebellar connectivity was observed, possibly due to the lower task demand in go/no-go compared to stop signal inhibitory control tasks. Thus, cortico-cerebellar connectivity during EF is influenced by both age and biological sex, highlighting the importance of evaluating sex differences in aging and AD studies.