

## The Role of Educational Attainment and APOE $\epsilon$ 4 in Alzheimer Disease among Puerto Ricans: Disparity in Resilience

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**Background:** Cognitive reserve research in African Americans shows that higher educational attainment (EA) can mitigate Alzheimer disease pathology (ADP), though this effect is less pronounced in APOE $\epsilon$ 4 carriers, suggesting resilience disparities influenced by the interplay of educational and genetic factors. Our study examines whether similar patterns exist in Puerto Ricans (PR), a population with distinct social and ancestral backgrounds. We aim to explore education as a modifiable risk factor in AD among PRs and to determine whether the APOE $\epsilon$ 4 allele affects resilience between carriers and non-carriers.

**Methods:** We analyzed 732 PRs, focusing on their education years, plasma pTau181 levels, and APOE genotypes. We derived a composite functional score, CDR-FUNC (0–12), by summing the non-memory components of the Cognitive Dementia Rating scale. EA was classified as low ( $\leq 9$  years) and high ( $> 9$  years). Plasma pTau181, used as a proxy for ADP, identified advanced pathology if  $\log_{10}(\text{pTau181})$  was  $> \text{mean} + 1\text{SD}$ . We used the Mann-Whitney U test to assess associations between EA and CDR-FUNC in those with advanced pTau181 levels and the APOE $\epsilon$ 4 allele.

**Results:** We found a significant association between EA and functional difficulties in participants with high pTau181 levels. Individuals with high EA showed better functional ability than those with low EA ( $p = 3.2 \times 10^{-4}$ ). Additionally,  $\epsilon$ 4 carriers with low EA had worse functional outcomes compared to non-carriers ( $p = 0.045$ ). No difference was observed in functional outcomes among individuals with high EA.

**Conclusion:** Our study demonstrates that education functions as a modifiable risk factor for AD in PRs, contributing to resilience against ADP. Notably, APOEε4 carriers with low EA had worse functional outcomes than non-carriers. Understanding the combined influence of education, genetics, and functional resilience in PRs is essential for creating targeted interventions to improve health outcomes in this distinct population.