

The Relationship Between Sleep Duration and Severity of Cognitive/Functional Impairments Differ by *APOE*-ε4 Carrier Status in Middle-aged and Elderly Indigenous Africans

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In middle-aged and elderly indigenous Africans, the link between sleep duration and severity of cognitive/functional impairment(s) differed by *APOE*-ε4 carrier status, underscoring the importance of gene × behavior interactions for cognitive function and Alzheimer’s disease risk.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
- Older adults in sub-Saharan Africa experience a high and rising burden of both sleep disturbance and Alzheimer's disease (AD) yet remain among the most understudied populations for the sleep–dementia relationship. <i>APOE</i>-ε4 is the strongest genetic risk factor for late-onset AD, with <i>APOE</i>-ε4/ε4 carriers having the highest genetic risk. - Short (≤6 h) and long (≥10 h) sleep are both correlated with worse cognitive/functional impairment; however, whether sleep and <i>APOE</i>-ε4 interact remains unclear. Objective: To test if the link between sleep duration and severity of cognitive/functional impairments differs by <i>APOE</i>-ε4 carrier status in middle-aged and elderly indigenous Africans.	Design: Subsample from cross-sectional, population-based DAWN-ADSP study. Sample: <i>N</i>=2,121 from Africa; 56.3% female; aged 73.9±9.4y. Sleep: Self-reported hours/24 h, then classified as short (≤6 h), average (7–9 h), or long (≥10 h). <i>APOE</i>-ε4: non-carriers (50.8%), heterozygotes (38.4%), homozygotes (10.8%). Outcomes: Clinical Dementia Rating (CDR) Scale Sum of Boxes and Global Scale; higher scores = worse impairment. Analysis: Ordinal logistic models tested if an <i>APOE</i>-ε4 × environmental interaction between self-reported sleep durations and <i>APOE</i>-ε4 status associated with severity of cognitive/functional impairments, including extraneous factors that may influence this link as covariates (age, sex, body mass index, years of education, African subregion (West/East), financial strain, and CVD/hypertension/stroke history); and stratified by <i>APOE</i>-ε4 group.	A B Figure 1. Predicted CDR-SB (A) and CDR-GS (B) by sleep duration × <i>APOE</i>-ε4. Error bars = 95% CI; ***<i>p</i><0.001. Post hoc <i>APOE</i>-ε4 stratification analysis: Non-carriers: long (but not short) sleep = worse impairment. Heterozygotes: both short and long sleep = worse impairment. Homozygotes: similar levels of cognitive impairment regardless of sleep durations	- Sleeping 7–9 hours nightly may be protective in <i>APOE</i>-ε4 heterozygotes, which may reflect that having one <i>APOE</i>-ε4 allele may not significantly disrupt glymphatic clearance of AD-linked neuropathological proteins (amyloid-β, tau), and obtaining sufficient sleep can still drive effective glymphatic waste removal in these individuals. <i>APOE</i>-ε4 homozygotes had the greatest severities of cognitive/functional impairments, regardless of sleep duration, which may reflect significant impairment in glymphatic clearance during sleep and may render sleep as less effective in protecting against cognitive/functional impairments in these individuals. Future work: future studies should replicate this work in other ancestral groups and include objective sleep measures.	1. World Health Organization. Global status report on the public health response to dementia. 2021. 2. Alzheimer's Association. 2024 Alzheimer's disease facts and figures. <i>Alzheimers Dement</i>. 2024;20(5):3708-3821. 3. Mayeda ER, et al. Inequalities in dementia incidence between six racial and ethnic groups. <i>Alzheimers Dement</i>. 2016;12(3):216-224. 4. Corder EH, et al. Gene dose of apolipoprotein E type 4 allele and risk of Alzheimer's disease. <i>Science</i>. 1993;261(5123):921-923. 5. Ray NR, et al. Extended GWAS identifies novel AD susceptibility loci in individuals of African ancestry. <i>Alzheimers Dement</i>. 2024;20(8):5247-5261. CONTACT Brittany A. Larsen, Ph.D., R.D.N. Department of Psychiatry & Behavioral Sciences University of Miami Miller School of Medicine Email: bal184@miami.edu  ALZHEIMER'S ASSOCIATION AAIC 26