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413 - SEX-DIFFERENTIAL EFFECTS OF AIR POLLUTION AND TELOMERE LENGTH ON COGNITIVE PERFORMANCE IN INDIVIDUALS AT RISK OF ALZHEIMER'S DISEASE

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Resumen

Background/Objectives: Investigate sex-specific effects of air pollution and telomere length on cognitive performance in cognitively unimpaired individuals at risk of Alzheimer's disease (AD).

Methods: We included 1,472 middle-aged adults at risk of AD (89.7% with family history of AD) from the ALFA study. We estimated residential exposure to air pollutants (nitrogen dioxide [NO2], particulate matter [PM2.5, PM10]) using land use regression models. Leukocyte telomere length (LTL) was determined by qPCR from DNA extracted from peripheral blood leukocytes and residualized against chronological age and sex (rLTL). Participants were categorized into short and long groups according to the percentile 50^{th} of rLTL. Cognitive testing covered verbal memory, psychomotor speed, visual processing, and executive function. We calculated episodic memory (EM), executive function and Preclinical Alzheimer Cognitive Composite (PACC) composites by averaging normalized subtest raw scores. Models accounted for chronological age, education and APOE-ε4 status. Sex- and rLTL-specific effects were explored through interaction and stratified models.

Results: Sex-stratified analyses revealed that elevated NO2 and PM2.5 levels were associated with reduced EM in men. rLTL modified these associations; men with longer

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rLTL experienced negative impacts on EM and PACC with higher NO2 and PM2.5 exposure. Conversely, men with shorter rLTL exhibited a positive association between NO2 and PACC. Global models did not show significant associations.

Conclusions/Recommendations: Air pollution adversely affected EM and the PACC in men at risk of AD, with no such effects observed in women. These associations appeared to be amplified in men with longer rLTL and reversed among those with shorter rLTL. Further analyses will explore sex-and gender-specific factors as potential mediators of these associations.

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