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Prevention (nonpharmacological) / Lifestyle factors (e.g., smoking, etc.)

Mendelian randomization of smoking behavior on cognitive status among older Americans

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Abstract

Background: Smoking is associated with dementia status, and smoking behavior has a genetic component. In this study, we jointly test the associations between cumulative genetic risk for smoking, smoking behavior, and cognitive status.

Method: We conducted a cross-sectional study using the 2010 wave of the Health and Retirement Study. First, we used logistic regression to test the relationship between cumulative genetic risk for smoking and current smoking behavior. Second, we tested the association between smoking behavior and cognitive status. Third, we checked the assumption that cumulative genetic risk for smoking was not associated with cognitive status. All analyses were adjusted for age, sex, years of education, rural/urban residence and five ancestry-specific genetic principal components. Analyses were stratified by ancestry. Finally, a Mendelian randomization framework was used to test inferred causal relationships between smoking behavior and cognitive status via genetic instruments.

Result: Among European ancestry participants (n = 8,735), one standard deviation increase in smoking polygenic score was associated with 1.28 times odds of current smoking behavior (95% confidence interval: 1.18, 1.38) relative to never smoking. Current smoking was associated with 1.62 times odds of cognitive impairment (95% confidence interval: 1.29, 2.01) relative to never smokers and those with normal cognition. No association was observed between smoking polygenic score and cognitive status, an important assumption of the Mendelian randomization framework. Using the smoking genetic instrument, a significant inferred causal relationship was observed between current smoking and cognitive impairment (P=0.02, 1.53 odds ratio, 95% confidence interval: 1.07, 2.18).

Conclusion: These findings demonstrate current smoking is likely causally related to cognitive impairment. Promotion of smoking cessation is important for public health and brain health specifically. Studies on dose and duration of smoking on cognition are critically needed, as well as in research non-European ancestries.