

Epidemiology: Lifestyle risk factors

Lifestyle and genetic risk: Revisiting the association with incident dementia

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Abstract

Background: Previous work using data from the UK Biobank has shown that both unfavorable lifestyle and genetic risk are associated with higher dementia risk; however, it is not known whether these results transfer to more representative samples and across country.

Methods: Data come from the Health and Retirement Study (HRS), a cohort study of Americans 65 years of age and older without dementia at baseline. Adults of European descent are included in the analyses. Dementia was determined using Medicare claims from 2000-2016. 6,870 individuals were followed for an average of 11 years (Median 12; IQR 8.6 – 15.6 years) with mean age of 68.8 (5.4). Polygenic scores (PGS) for dementia from 2 large, replicated genome-wide association studies (Lambert et al. and Kunkle et al.) were used along with a weighted lifestyle score (including measures of smoking, drinking, and physical activity) to predict incident dementia. The association between the PGS and lifestyle was assessed using ordered logistic regression. Cox proportional hazard regression models were used to examine the association of genetic risk, lifestyle, and the interaction with time to incident dementia.

Result: Overall, 22.9% (n=1,580) were diagnosed with dementia during the observation period. 23.8% of participants had a favorable lifestyle, 50.7% had a moderately favorable lifestyle, and 25.5% had an unfavorable lifestyle. There was no significant association between the lifestyle score and either PGS. The effect of PGS on time to dementia was significant with and without adjustment for covariates (age, sex, education, wealth, comorbidities) with higher genetic risk conferring an increased risk for dementia (hazard ratio highest PGS group compared to lowest 1.37 [95% CI [1.17, 1.61]). Individuals with a favorable lifestyle at baseline were significantly less likely to develop dementia adjusting for PGS and covariates (adjusted hazard ratio 0.85 [95% CI, 0.74-0.99]). Results were similar regardless of which PGS was used. There was no significant interaction between genetic risk and lifestyle.

Conclusion: These findings demonstrate that an unhealthy lifestyle and genetic risk are associated with higher dementia risk. Results from a nationally-representative sample of older adults in the United States are comparable with those from UK Biobank.