

Causality of Abdominal Obesity on Cognition: a Trans-ethnic Mendelian Randomization study

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Background

Obesity has been associated with cognition in observational studies; however, whether its effect is confounding or a reverse causality remains inconclusive.

Aims & Objectives

This study aimed to investigate the causal relationships of overall obesity, measured by body mass index (BMI), and abdominal adiposity, measured by waist-hip ratio adjusted for BMI (WHRadjBMI), and cognition across European and Asian populations using Mendelian randomization (MR) analysis.

Methods

We used publicly available genome-wide association study (GWAS) summary data of European ancestry, including BMI (n=322,154) and WHRadjBMI (n=210,088) from the GIANT consortium, and cognition performance (n=257,828) from the UK Biobank and COGENT consortium. Data for individuals of Asian ancestry were retrieved from Taiwan Biobank to perform GWAS for BMI (n=65,689), WHRadjBMI (n=65,683), and Mini-Mental State Examination (MMSE, n=21,273). MR analysis was carried out using the inverse variance weighted method for the main results. Further, we examined the overall pleiotropy by MR-Egger intercept, and detected and adjusted for possible outliers using MR PRESSO.

Results

No causal effect of BMI on cognition performance (beta [95% CI] = -0.00 [-0.08, 0.08], p-value = 0.90) was found for Europeans; however, a 1-SD increase in WHRadjBMI was associated with a 0.07 standardized score decrease in cognition performance (beta [95% CI] = -0.07 [-0.12, -0.02], p-value = 0.006). Further, no causal effect of BMI on MMSE (beta [95% CI] = 0.01 [-0.09, 0.11], p = 0.91) was found for Asians; however, a 1-SD increase in WHRadjBMI was associated with a 0.17 standardized score decrease in MMSE (beta [95% CI] = -0.17 [-0.30, -0.03], p = 0.02). In both populations, overall pleiotropy was not detected, and outliers did not affect the robustness of the main findings.

Discussion & Conclusion

This trans-ethnic MR study reveals that abdominal adiposity, as measured by WHR adjusted for BMI, impairs cognition, whereas weak evidence suggests that BMI impairs cognition.