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Causal Associations between Sleep Traits, Sleep Disorders, and Glioblastoma: A Two-Sample Bidirectional Mendelian Randomization Study

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Abstract

Background: Glioblastoma (GBM), a highly aggressive brain tumor predominantly affecting individuals over 40, often co-occurs with sleep disorders. However, the causal relationship remains unclear. This study employed a bidirectional Mendelian randomization (MR) approach to investigate the causal links between sleep traits/disorders and GBM. **Methods:** Sleep trait and disorder data were obtained from the IEU Open GWAS Project, while GBM data came from the Finn cohort. Primary analysis utilized inverse-variance weighted (IVW), complemented by MR-Egger, weighted median, and weighted mode methods. MR pleiotropy residual sum and outlier (MR-PRESSO) was applied to detect potential outliers, and MR-Egger regression explored horizontal pleiotropy, with Cochran's Q test assessing heterogeneity. **Results:** IVW analysis indicated a significant negative association between sleep duration and GBM risk (OR=0.13, 95% CI=0.02-0.80, P=0.027). Conversely, GBM was positively associated with evening chronotype (OR=1.0094, 95% CI=1.0034-1.0154, P=0.002). No significant associations were found for other sleep traits or disorders. Midday napping showed potential pleiotropy, and significant heterogeneity was noted in the reverse analysis. MR-PRESSO identified no outliers. **Conclusion:** Shorter sleep duration may elevate GBM risk, and GBM might influence circadian preference toward eveningness. Further studies are warranted to validate these findings.

Keywords: Glioblastoma; Mendelian randomization; chronotype; sleep; sleep duration.