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THE RELATIONSHIP BETWEEN SLEEP AND PARKINSON'S DISEASE PROGRESSION: A MENDELIAN RANDOMIZATION STUDY

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Introduction: Sleep disturbances and disorders are common in Parkinson's disease and significantly impact quality of life. Often, such sleep disturbances are considered sequelae of neurodegeneration affecting sleep-wake circuitry. However, there is emerging evidence that sleep disturbance may itself play a causal role in neurodegenerative processes via altered clearance of pathological proteins. Whether sleep disturbance affects the pathological progression of Parkinson's disease is unknown. Recently, a several genetic variants have been discovered for sleep-related parameters through genome-wide association studies (GWAS) providing a unique opportunity to examine the evidence for causal relationships through the use of the Mendelian randomization.

Methods: To elucidate the causality between sleep disorders and progression of Parkinson's disease, we performed two sample Mendelian randomization analysis using genetic variants identified from publicly available GWAS data for sleep variables including insomnia, sleep duration, chronotype, napping and daytime sleepiness as exposure variables. Outcome measures were derived from a large collective GWAS of PD progression (N=4093 cases) including the Unified Parkinson's disease rating scale (UPDRS total and UPDRS- III), motor fluctuations, Age of onset of PD (PD-AOO), Mini-mental state examination (MMSE) and Montreal Cognitive Assessment (MOCA). The robustness of results was examined using conventional Mendelian randomization sensitivity analyses.

Results: Genetic liability to increased sleep duration was associated with a lower rate of progression of motor symptoms in PD using UPDRS-III score. Meanwhile insomnia was associated with increased rate of motor progression of PD. Predisposition to daytime sleep was associated with lower rates of progression of cognitive decline in PD measured using MMSE. No robust relationships were determined between markers of progression and chronotype or daytime napping. Statistical measures showed significant pleiotropy for the relationships identified.

Conclusion: Sleep-related variables may have a deterministic role in the clinical progression in Parkinson's disease and may represent a modifiable target for altering the trajectory of neurodegeneration.

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SYMPTOMS OF INSOMNIA AND DEPRESSION AMONG INDIVIDUALS WITH MULTIPLE SCLEROSIS BEFORE AND DURING THE COVID-19 – RESULTS FROM A PROSPECTIVE LONGITUDINAL STUDY

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Introduction: There is some -- but inconsistent -- evidence that sleep and psychological health have deteriorated in the general population as a result of the COVID-19-pandemic and its related social restrictions. In the present study, we investigated whether and to what extent symptoms of insomnia, depression, fatigue, and paresthesia changed from before to during the COVID-19-pandemic among women diagnosed with multiple sclerosis (MS).

Methods: A total of 90 women with MS (mean age; 37.62 (SD = 8.61) years; EDSS score: median: 2.5 (range: 0-6.50)) completed a series of self-rating scales at two time-points: Nine months before the COVID-19-outbreak in May 2019 (baseline) and during the COVID-19-pandemic (study end; 12 months after baseline: May 2020). Self-rating questionnaires covered sociodemographic and disease-related information, symptoms of insomnia, depression, fatigue, and paresthesia.

Results: Symptoms of depression increased over time (medium effect size: Cohen's d = 0.53), while symptoms of insomnia (small effect size: Cohen's d = 0.43), fatigue (trivial effect size: Cohen's d = 0.19), and paresthesia (trivial effect size: Cohen's d = 0.08) did not. The only predictor for insomnia during the COVID-19-pandemic was insomnia before the COVID-19-pandemic ($\beta = 0.36$; $p = 0.001$); the only predictor for depression during the COVID-19-pandemic was insomnia before the COVID-19-pandemic ($\beta = 0.66$; $p = 0.001$).

Conclusion: Overall, among a sample of female individuals with MS the COVID-19-pandemic and its related social restrictions may have had a modest influence on participants' core concerns of insomnia, depression, fatigue, and paresthesia.

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