Title: Association of circadian sleep-wake regulation and brain structure in older adults: a multi-modal approach

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Abstract

Introduction: The temporal organization of sleep and wakefulness evolves throughout the lifespan, leading to an increased sleep-wake fragmentation with ageing. However, how circadian aspects of sleep-wake regulation relate to brain structure during ageing is not known. We aimed at exploring whether grey matter volume and surface measures are associated to an electrophysiology-derived index of circadian sleep-wake regulation.

Methods: Eleven older participants (55-75 years; 7 men) underwent a 40-h multiple nap protocol encompassing 10 nap periods. Nap sleep efficiency over the circadian cycle was obtained with polysomnography and used as an index of circadian sleep-wake promotion. The difference between the sleep ability during the night and day sleep, here called circadian sleep amplitude (CSA) was taken as an indicator of circadian integrity. T1-weighted brain scans were analysed with two complementary approaches: Voxel-Based Morphometry (VBM) to extract total grey matter volume, and Surface-Based Morphometry to extract total cortical thickness.

Results: Contrary to our hypothesis, a correlation analysis revealed that grey matter volume was negatively associated with CSA (r^2= 0.385, p= 0.042), while cortical thickness was not significantly correlated. Remarkably, grey matter volume was also negatively associated with cortical thickness (r^2= 0.454, p= 0.023). Since VBM fails to properly detect folding structures inside the brain, we calculated the local gyrification index for each participant using a surface-based morphometry approach. We observed that the mean of local gyrification indices across the brain showed a trend for a positive correlation with CSA (r^2= 0.324, p= 0.067).

Conclusions: Despite the small sample size, our data suggest that a less folded brain has more “visible” grey matter detectable with the VBM approach, explaining the negative link between grey matter volume and cortical thickness but also with CSA. The results highlight the necessity of analysing surface indices in addition to volumetry. Within this context, our data suggest that a more “folded” brain, an index of brain fitness at older age, is associated with circadian integrity and should be considered in models linking sleep-wake regulation to brain ageing. Future region-based analyses of brain surface indices will be performed.
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