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The relationship between individual circadian phase, subjective amplitude, and brain anatomy

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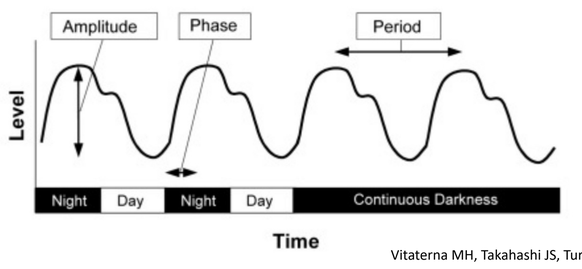
INTRODUCTION

A full description of the daily rhythms requires a characterization of three distinct elements: phase (chronotype or morningness-eveningness, ME), period, and amplitude (distinctness, AM). The ME score represents an individual's preferred time of activity, while the amplitude score - the strength of this preference.

The "larks", or early chronotypes (EC), prefer to get up early in the morning and feel best in the early hours of the day, while "owls", or late chronotypes (LC) have a peak of cognitive performance in the evening. ME aspect of circadian rhythm is well studied, while subjective amplitude (AM), i.e. the distinctness, is overlooked. Unlike the traditional classification of chronotypes, which determines the type of "extreme" or "moderate" phenotypes based on the exact hours of waking up and falling asleep, the AM refers to the perceived intensity of differences in functioning between the morning and evening hours.

The study aimed to elucidate whether the subjective AM and its interaction with ME was a significant predictor of individual brain structure.



Vitaterna MH, Takahashi JS, Turek FW, 2001

MATERIALS AND METHODS

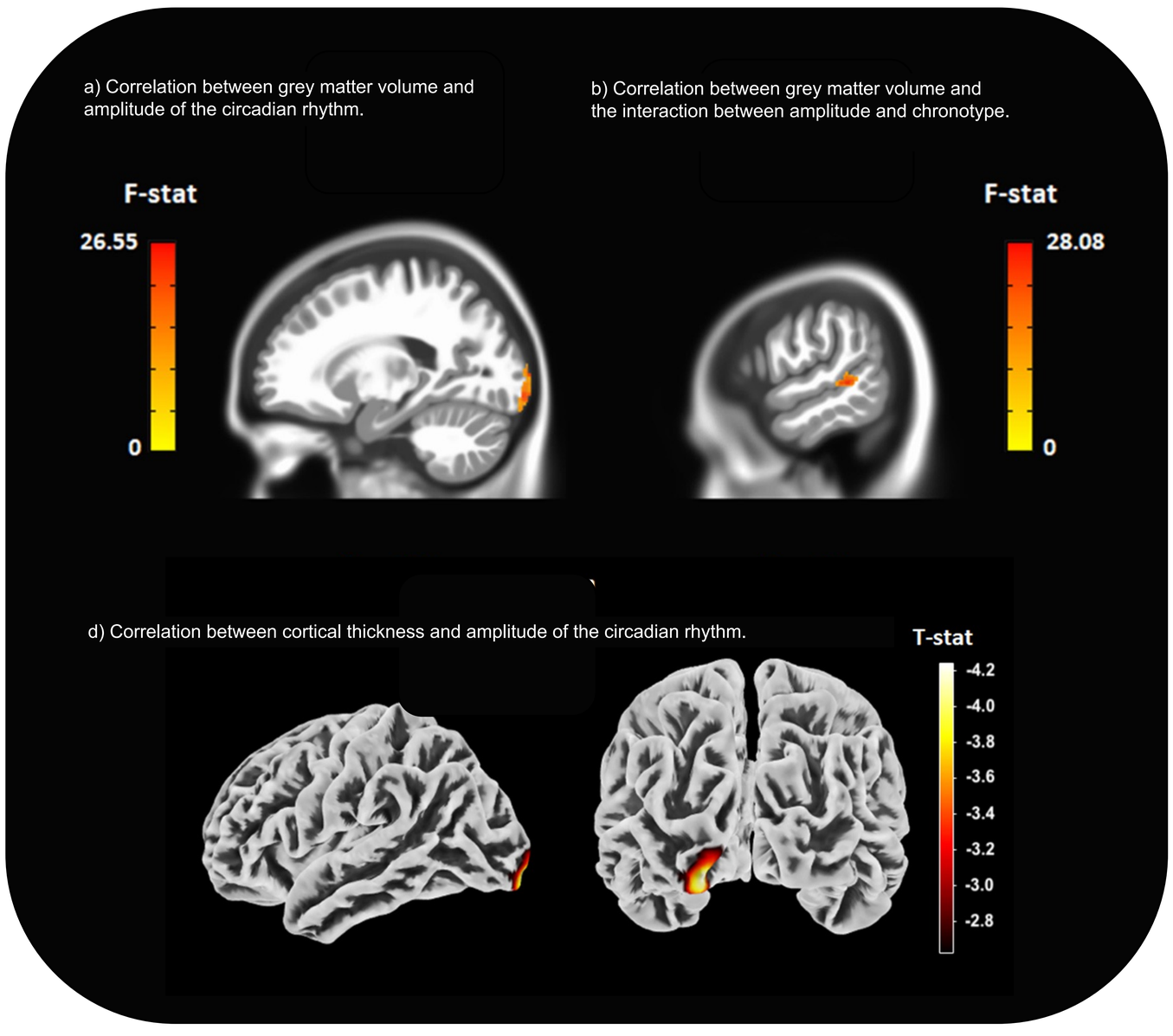
The analyses were performed using a fully anonymized high-resolution structural dataset obtained during fMRI projects (N = 153). All subjects were aged from 19 to 35, right-handed, had normal or corrected-to-normal vision. Trait-like chronotype was assessed using of the Chronotype Questionnaire (ChQ). The tool is particularly useful for distinguishing between the two dimensions of circadian rhythms, i.e. the subjective circadian phase (ME) and the subjective amplitude of diurnal variations in mood and cognition (AM). In the dataset, the sample was divided into two groups: early chronotypes (EC; ME scores from 11 to 22) and late chronotypes (LC; ME scores from 23 to 32). The scores in AM varied from 11 to 29 and followed the normal distribution according to the Kolmogorov-Smirnov test ($p > 0.05$). Magnetic resonance imaging (MRI) was performed on a 3T scanner (Magnetom Skyra, Siemens). All scanning sessions were performed between 4:30 PM and 8:55 PM to minimize the effects of time-of-day on the morphometric measures. Voxel-based morphometry (VBM) analysis and estimation of cortical thickness were performed in the CAT12 toolbox and AFNI. The normalized and modulated GM segments were smoothed with a 4 mm Gaussian filter. Sex, age, and total intracranial volume of the participants were controlled as covariates. The multiple comparisons correction was achieved with the cluster-level family-wise error correction (FWE < 0.05) following the initial voxel-level thresholding ($p < 0.001$).

RESULTS

VBM analysis revealed two significant clusters: one for the main effect of AM and one for the interaction between AM and ME (voxel-level $p < 0.001$, cluster-level FWE < 0.05). The GM volume in the **left primary visual cortex** (Brodmann Area (BA) 17) was negatively correlated with the individual AM scores **(r = -0.396)**, independently of the ME grouping. In turn, the GM volume of the **right middle temporal gyrus** (BA21, BA37) had a differential association with AM scores depending on whether the individuals were classified as EC or LC. In the former group, the structural measure was positively linked to AM **(r = 0.251)** whereas in the latter group, a negative relationship was found **(r = -0.402)**. The cortical thickness analysis performed at the threshold of vertex-level $p < 0.001$ and cluster-level FWE < 0.05 revealed no significant findings for both the direct effect of AM and its interaction with ME. However, an exploratory analysis with slightly less stringent thresholding (vertex-level $p < 0.005$ and cluster-level FWE < 0.05) revealed that across the entire sample AM scores were negatively correlated **(r = -0.309)** with the cortical thickness of the **left primary visual cortex** (BA17).

a) Correlation between grey matter volume and amplitude of the circadian rhythm.

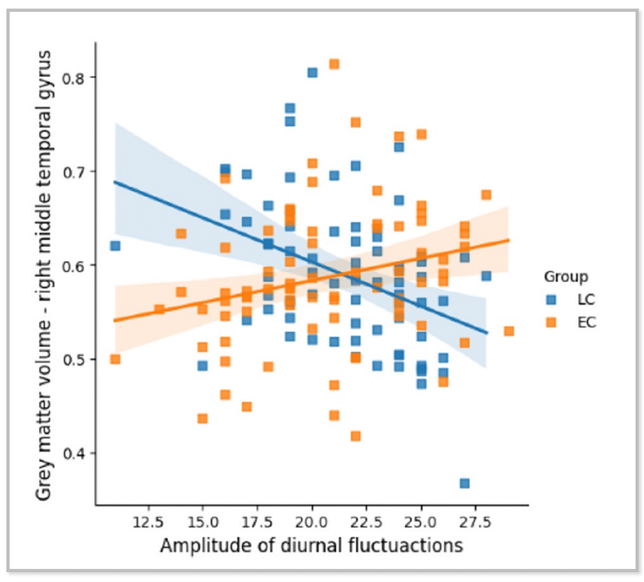
b) Correlation between grey matter volume and the interaction between amplitude and chronotype.



CONCLUSIONS

The current study underlines the importance of the visual system in circadian rhythmicity. Furthermore, the fact that the volume of the right middle temporal gyrus has a differential association with AM in the two groups suggests that behavioral and neuronal differences might become more pronounced in individuals with both extremely low and high values of perceived diurnal differences in mood and cognition. This, in turn, raises an important question in relation to the previous studies. If the AM dimension is not accounted for as one of the factors, it may lead to an unwanted bias in the reported results. An extreme owl with a very distinct rhythm may be characterized by different features than an owl with a less pronounced biological rhythm. For this reason, we underline the importance of considering AM as a factor potentially modulating the results of all studies on chronotypes.

c) Correlation between grey matter volume in the right temporal gyrus and the amplitude (divided into the groups of late and early chronotypes)



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