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Time of the day and coupling between global grey matter BOLD and CSF flow signal in healthy humans: *preliminary results*

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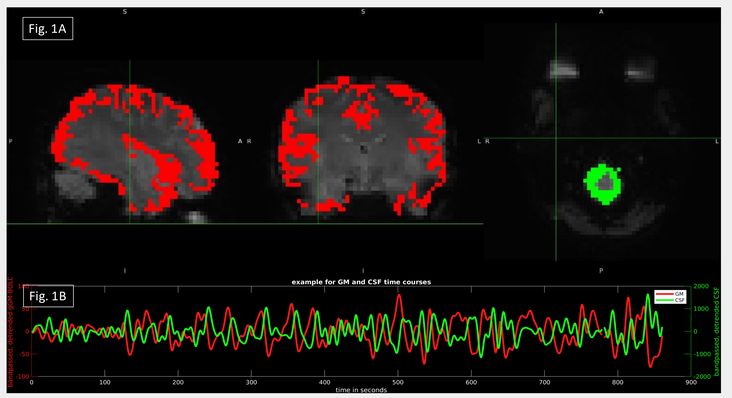
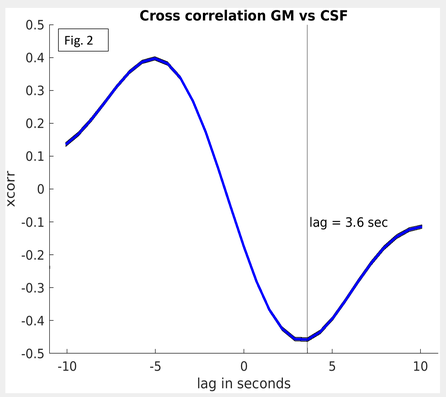
BACKGROUND: The Glymphatic system model describes how cerebral spinal fluid (CSF) bulk movement in and around the brain is mediated by changes in cerebral hemodynamics, thereby removing waste products. Factors such as sleep-wake cycle or synchronous neuronal activity could influence its function (i.e., enhanced during sleep). Novel fMRI tools, e.g., the correlation between global grey matter (gGM) BOLD and CSF flow signal, have enabled neuroimaging researchers to study the system's function. Yet, no studies are looking at whether the time of fMRI acquisition might influence results, especially considering the known circadian variation in arousal across the day. A recent study showed that time of the day is associated with reductions in global signal fluctuations. The aim of our study is to explore whether the macroscopic glymphatic measure changes across the day and, if it changes, whether this is dependent on the reported changes of global signal fluctuations.

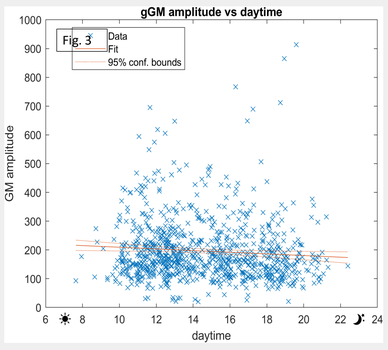
METHODS: We used 14-min resting-state fMRI recordings from 877 healthy young adults from the Human Connectome Project S1200 dataset. Data were minimally pre-processed following current publications. We extracted the mean signal of all grey matter voxels from the cortex (i.e., gGM, Fig. 1) and intensity signals from the bottom slice of the fMRI image (i.e., CSF flow, Fig. 1). Absolute amplitudes of gGM were extracted. A cross-correlation between gGM and CSF flow signal was calculated (coupling value = xcorr at lag 3.6 seconds). We examined the association between coupling values and time of fMRI acquisition (from 7.38 am to 10.23 pm) using a correlation approach. Finally, using a partial correlation we tested whether this change was influenced by gGM amplitude changes.

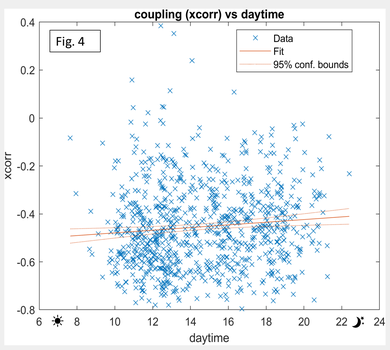
RESULTS: Our results showed that, in line with the previous publication, gGM amplitude decreased with the time of the day ($r = -0.08$, $p < 0.05$, Fig. 3). CSF amplitudes did not reduce ($p = 0.97$, Fig. 5). Absolute values of the coupling also reduced across the span of 14.75 hours ($r = -0.09$, $p < 0.01$, Fig. 4). This relationship stayed when controlling for gGM amplitudes ($r = -0.08$, $p < 0.01$). Important to highlight: strength of correlations are low.

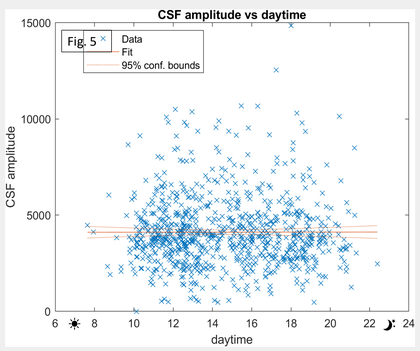
CONCLUSION (preliminary): This analysis show a progressive reduction in glymphatic function across the day which is not dependent on the progressive reduction in gGM fluctuations. If during sleep glymphatic function is the most enhaced, it suggests the longer we stay awake, the worse its function is. We will look into functional connectivity changes in the future.











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