IS THE LENGTH OF THE WHITE MATTER FIBER BUNDLES UNDERLYING THE THALAMO-CORTICAL LOOP ASSOCIATED WITH SLEEP SPINDLES? – A PRELIMINARY STUDY

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Limit: 658/750 words

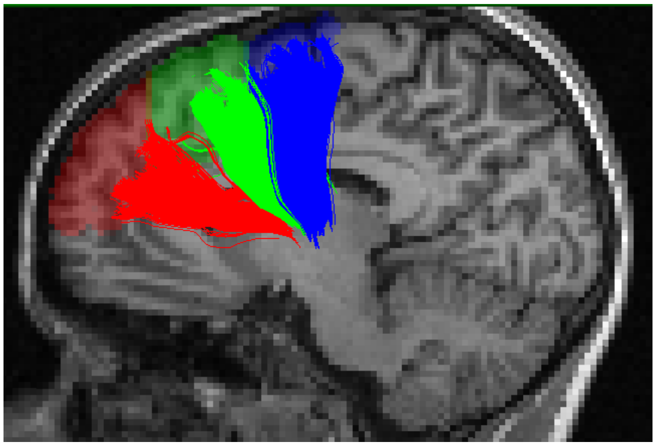
Introduction: Sleep spindles are electroencephalographic manifestations occurring during non-rapid eye movement sleep which are characterized by bursts of oscillatory brain activity with a frequency varying between 12 and 16 Hz. Studies showed that sleep spindles play a significant role in sleep-related cognitive processes such as declarative and procedural memory consolidation as well as in more global cognitive abilities such as the intelligence.[1-4] The generation of sleep spindles imply a complex activation of the thalamo-cortico-thalamic loop.[5] The literature suggests that sleep spindles reflect dynamic connectivity in-between neuronal networks in the brain but also more stable white matter networks as demonstrated by a recent study that showed in young subjects an association between sleep spindles power and white matter microstructure using tract-based spatial statistics, a voxel-based approach.[6] Thus, this study aimed at investigating whether sleep spindles variables were associated to characteristics of the thalamo-cortical loop using a streamline-based and bundle specific approach measuring streamline length between the thalamus and the frontal cortex.

Methods: Twenty-five subjects (20-30 years, 11 females) underwent a whole-night of polysomnographic recording and a 3T MRI acquisition including a diffusion sequence (EPI, 64 gradient directions, b-value 700 s/mm^2) and a structural T1 weighted image. Sleep spindles were automatically detected on artefact-free non-rapid eye movement sleep using a previously published detection algorithm on F3, F4, C3, and C4 electrodes referred to linked-earlobes[7]. Sleep spindles detected in N2 sleep stage were analysed. Sleep spindles amplitude (µV) and frequency (Hz) were averaged across night for each electrode. Diffusion images where denoised for rician noise and motion corrected using FSL eddy[8]. The fiber orientation distribution functions were computed using constrained spherical deconvolution[9] and streamlines were obtained using anatomically constrained particle filter tractography.[10] The T1 image was registered to the motion corrected b0 image and segmented using FreeSurfer.[11] Streamlines were clustered based on their starting and ending regions and outliers were removed using QuickBundles.[12] In addition to the thalamus, three cortical regions of interest were considered because of their proximity to the electrodes: the superior frontal gyrus, the middle frontal gyrus and the anterior cingulate cortex. To reduce the size of the regions of interest, the superior frontal gyrus was further segmented into 3 sub regions as illustrated in Figure 1. Linear regression analyses were performed between the median length of the streamlines connecting the thalamus to each cortical region and the sleep spindle amplitudes and frequencies.

Results: The length of the streamlines connecting the thalamus and the middle part of the left superior frontal gyrus significantly predicted sleep spindle amplitudes on F3, F4, C3, and C4 (β ranging from -0.465 to -0.503, $p < 0.05$) whereas the streamlines connecting to the anterior part of the left superior frontal gyrus predicted the amplitudes only on frontal derivations (F3: $\beta = -0.525$, $p < 0.01$; F4: $\beta = -0.479$, $p < 0.05$). Similarly, bilateral streamlines connecting the thalamus to the anterior part of the superior frontal gyrus significantly predicted sleep spindles frequency on F3, F4, C3, and C4 (left part: β ranging from -0.389 to -0.540, $p < 0.05$; right part: β ranging from -0.412 to -0.559, $p < 0.05$). No significant associations were detected between the sleep spindles amplitude or frequency and the length of the streamlines connecting the thalamus to the middle frontal gyrus and the anterior cingulate cortex.

Discussion and conclusion: In this preliminary work, we investigated the association between the anatomical structure of the thalamo-cortical loop and features of sleep oscillations. Our results are in agreement with previous results which link sleep-related EEG events and white matter characteristics. However, our metric being streamline bundle specific, we highlight white matter fiber bundles connecting the thalamus to the frontal cortex which may be associated with sleep spindles. More specifically, we found that the length of the of the streamlines connecting the thalamus to the anterior portion of the superior frontal gyrus significantly predicted both sleep spindle amplitudes and frequencies. This promising approach may allow to further increase our understanding of sleep regulation mechanisms.

Figures:



1 - Caption: Example of recovered bundles reaching the left superiror frontal gyrus and color coded sub regions The superior frontal gyrus was segmented into 3 sub regions (anterior in red, middle in green, and posterior in blue). Streamlines connecting the thalamus to each subregions where bundles.

2 - Graphs showing significant correlations with trendline.

References:

1- Schabus et al. 2004
2- Schabus et al. 2006
3- Ulrich et al. 2016
4- Fogel and Smith, 2011
5- Clawson et al. 2016
6- Piantoni et al. 2013
7- Martin et al. 2013
8- Jesper L. R. Andersson and Stamatios N. Sotiropoulos. An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging. *NeuroImage*, 125:1063-1078, 2016.
9- Tournier et al. 2007
10- Girard et al. 2014
11- Dale et al. 1999
12- Garyfallidis et al. 2012