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# Drowsiness increases slow oscillations in rs-fMRI signal before sleep onset

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## Introduction:

Sleep can significantly affect the functional MRI (fMRI) signal as reported in previous studies where subjects were allowed to fall asleep during the examination (Fukunaga et al., 2006, Duyn 2019). Fluctuation in the MRI signal has been associated with the increase in functional connectivity observed during light slow wave sleep (Tagliazucchi et al., 2014). Nevertheless, a major concern arises regarding the limited understanding of the evolution of fMRI signals as a function of drowsiness, when subjects are instructed to remain awake, as typically prescribed in standard resting-state exploration (rs-fMRI). This knowledge gap primarily results from the challenge of quantifying such vigilance-related events during fMRI, as they mostly occur within the complex period of wakefulness-to-sleep transition (Ogilvie, 2001). In this study, we used the percentage of eye closure (PERCLOS index (Wierwille et al., 1994)) as a proxy of drowsiness to explore its effect on the evolution of the rs-fMRI signal.

## Methods:

A 45 min T2\* gradient echo sequence (MRI GE 3T SIGNA Premier, TR = 1 s, TE = 30 ms, flip angle = 62°, 2700 volumes) was performed in 50 healthy subjects (26 Females, 24 Males, age = 23.3 ± 4.45) with instructions not to move, not to do constructed mental tasks and to keep their eyes open without sleeping. Subjects were asked to sleep for only 5 hours the night before and all examinations were carried out at 1 p.m.

Drowsiness was assessed using video from the MRI surveillance camera allowing to automatically compute an eye closure degree called Eye Aspect Ratio (EAR). Afterwards, PERCLOS index was calculated based on proportion of the time spent with eyes closed for at least 80% of their size in a 60s window. The drowsiness state was identified according to the following thresholds of the index (awake: [0.0, 0.08]; probably drowsy: [0.08, 0.15]; drowsy: [0.15, 1]; sleep: eyes closed > 5s). Lastly, all signals were resampled to MRI's sampling rate (1s).

MRI signals were preprocessed using fMRIPrep 20.2.6 with each brain region being extracted through python's Nilearn library 0.10.1, using AAL3 v1 1mm atlas. We considered the subject's specific mask and filtered out confounds computed in the preprocessing stage (low frequency drift and motion parameters). Signals were analyzed in a time-frequency manner using a Taper spectrogram (window length: 60s, window step: 1s, time half-bandwidth: 2.5, number of tapers: 4). Each column of spectrogram was classified using our drowsiness scale then grouped by state. Afterwards, mean amplitude by frequency band was calculated and finally projected on an inflated surface of the left hemisphere of the brain.

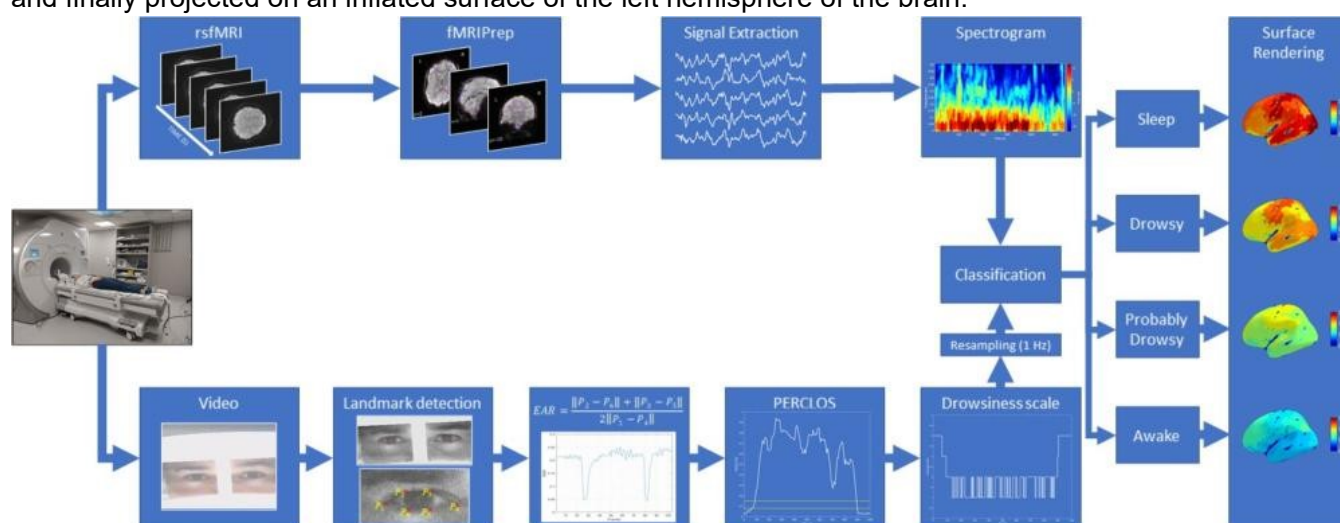
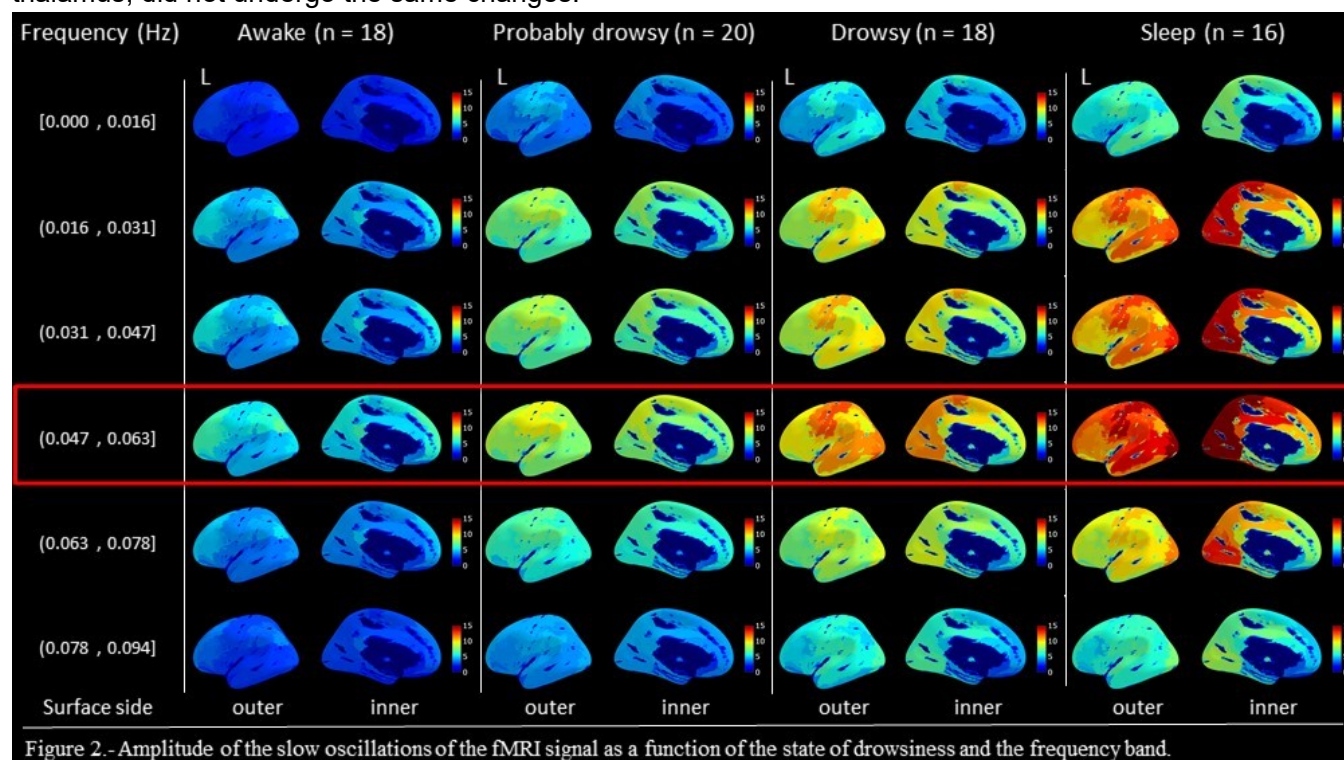


Figure 1.- Processing pipeline

## Results:

Figure 2 shows the evolution of the power spectral density of the rs-fMRI signal as a function of the drowsiness states. We can observe that the amplitude of slow oscillations, particularly in the [0.047-0.063] Hz band, increases overall at the first sign of drowsiness. This increase clearly predominates within primary

cortices (motor, somesthetic, visual and auditory), as demonstrated by a drowsiness effect in the generalized linear models computed in each 165 brain regions and corrected for Bonferroni multiple comparisons test (Wald's  $\chi^2$  ranging from 21,96 to 334,1). Conversely, the deep gray structures, notably the thalamus, did not undergo the same changes.



## Conclusions:

This study is the first attempt in exploring rs-fMRI signals while subjects struggle against sleep by considering 4 drowsiness states. The increase in slow oscillations observed, which may underlie an increase in functional connectivity and which predominate in the primary cortices, is paradoxical given the progressive isolation of the cortex induced by the thalamus during the descent into sleep and requires further investigation.

## Modeling and Analysis Methods:

Methods Development

Task-Independent and Resting-State Analysis <sup>1</sup>

## Novel Imaging Acquisition Methods:

BOLD fMRI <sup>2</sup>

## Physiology, Metabolism and Neurotransmission :

Neurophysiology of Imaging Signals

## Keywords:

Sleep

Somatosensory

Other - drowsiness

<sup>1|2</sup>Indicates the priority used for review

## Abstract Information

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation" study.

Resting state

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Other, Please specify - Resting State Functional MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

Other, Please list - fMRIPrep, nilearn

Provide references using author date format

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