Optimizing prediction models of sleep as confound for large scale resting state fMRI studies

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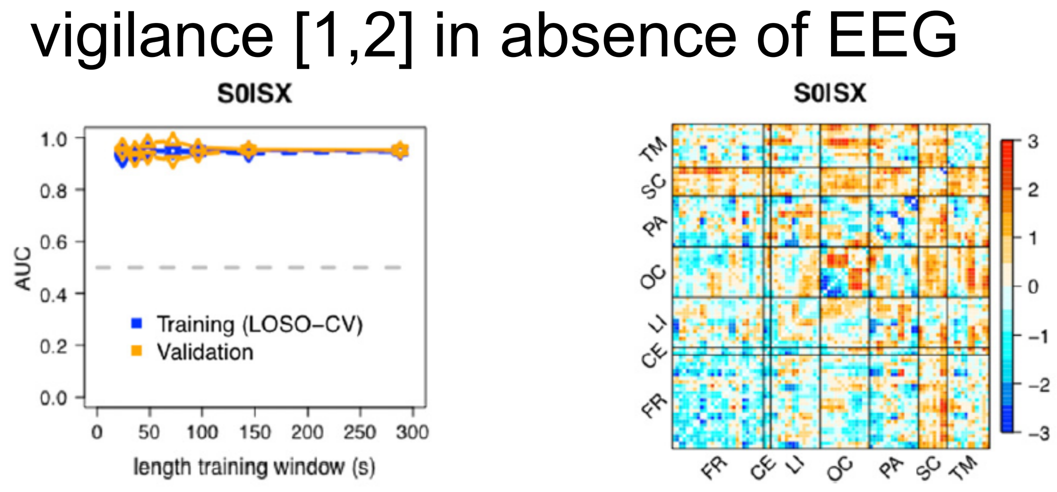
Participants get sleepier during the course of rs-fMRI sessions. Using pre-trained sleep classifiers requires site-specific adjustment factors.

INTRODUCTION

- Vigilance drifts – up to the point of subjects falling asleep during the experiment – may severely confound rs-fMRI based measures and biomarkers
- fMRI data-driven methods can monitor vigilance [1,2] in absence of EEG



Performance (left) and connection weights (right) for the wakefulness (S0) vs sleep (SX) SVM [1].

- We challenged the generalizability of our sleep decoding algorithm [1] on a large heterogenous dataset
- We study possibilities to fine-tune the prediction model for an optimal performance in multi-site studies

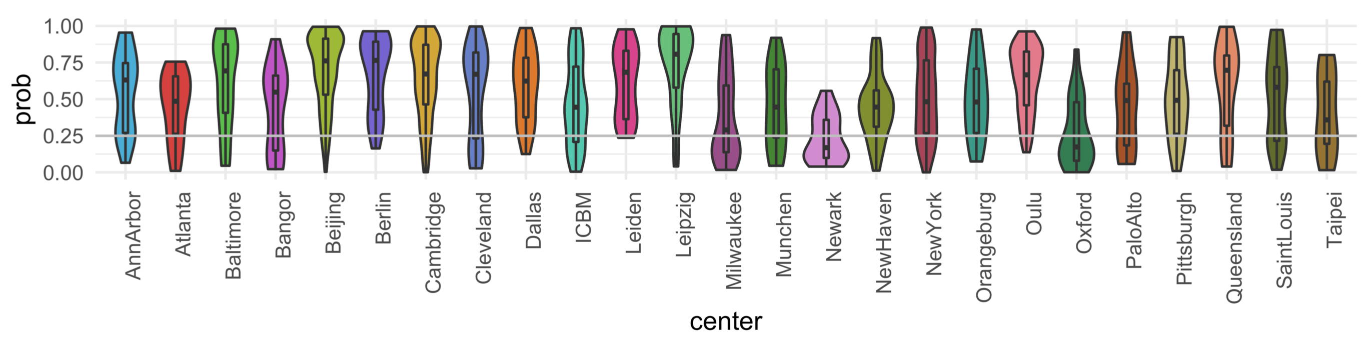
METHODS

1. N=1480 rs-fMRI sessions of the 1000 Functional Connectomes Project [3] from 25 centers
2. Windows of 60s were sleep-rated with our SVM-based classifier [1]; windows shifted by 1 frame to cover the entire session

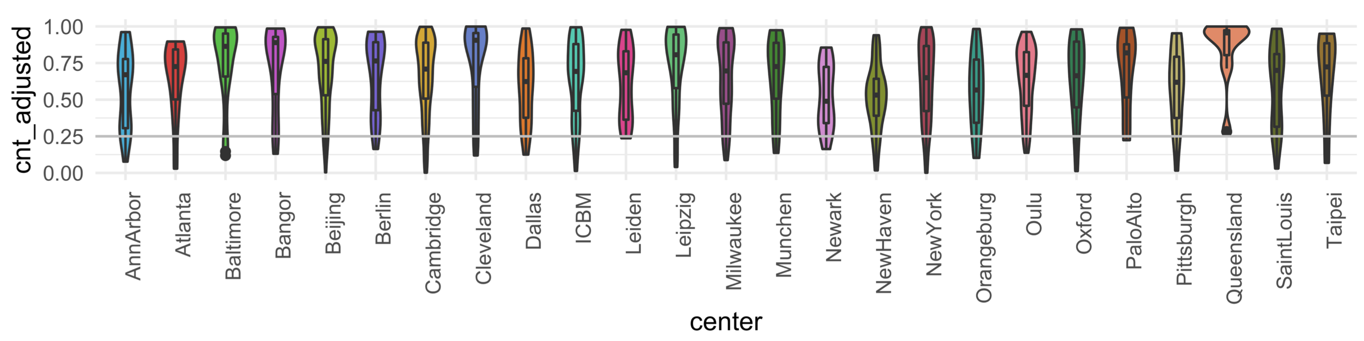
RESULTS

Vigilance declines during scan: Using linear mixed effect models we found that the raw SVM value for the first 60s was significantly higher (P=8.9e-12, T=6.896) corresponding in to 6% (SE 1%) higher wakefulness probability.

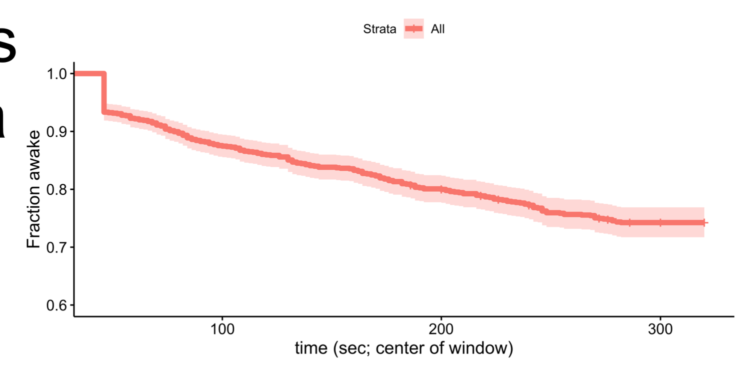
Variation across centers: Substantial differences in the first 60s across centers. Extremes are Newark and Oxford with majority of subjects classified as *asleep*.



We computed a center-specific adjustment factor to ensure 90% of subjects to be awake at session start (this also removed detected biases):



After adjustment 74% of participants exhibited at least a stretch of 30s of reduced wakeful-ness until minute 4-5 in the session.



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ADDITIONAL INFORMATION

Sample numbers:

- 1480 fMRI sessions
- 1241 subjects (i.e., without repeat measures)
- 1195 surviving QC

fMRI processing details:

- slice timing correction, realignment, spatial normalization to MNI space based on an anatomical MRI, spatial interpolation to 2x2x2 mm^3 and denoising using multiple regression
- After quality control, 1195 datasets from 25 centers of distinct participants with sufficient brain coverage and fMRI/T1 co-registration quality were available
- The Automated Anatomical Labeling (AAL) atlas was used to extract whole brain (cerebellum excluded) connectivity matrices for 90 regions of interest

Stratified analysis:

On stratified subsets we screened for score shifts introduced by technical, demographic or instructional biases.

Variable	N	P	Note
Sex	508	>0.14	eyes stratified
Age	227	0.004	eyes closed
TR	233	0.017	
Field Strength	533	0.12	
Eyes open vs closed	323	5.84E-05	
Slice Order	185	0.006	Small dataset

Outlook:

We are currently working on assessing the effect of the pre-processing pipeline on the sleep rating. Especially, how our original pre-processing compares to the ENIGMA pipeline.

References:

1. Altmann A, Schröter MS, Spoormaker VI, Kiem SA, Jordan D, Ilg R, Bullmore ET, Greicius MD, Czisch M, Sämann PG. Validation of non-REM sleep stage decoding from resting state fMRI using linear support vector machines. *Neuroimage*, **125,** 544-555 (2016).
2. Tagliazucchi E, Laufs H. Decoding wakefulness levels from typical fMRI resting-state data reveals reliable drifts between wakefulness and sleep. *Neuron*, **82**, 695-708 (2014).
3. http://fcon_1000.projects.nitrc.org

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