Sleep Decoded: Decoding and Predicting NREM Sleep Stages Based on fMRI

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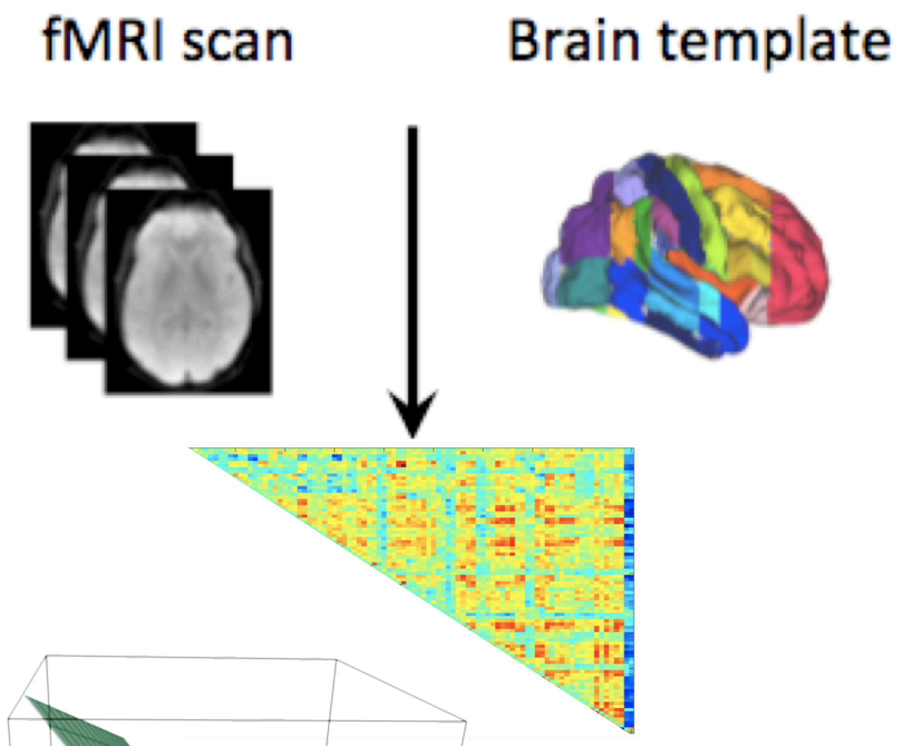
Introduction

Resting state (rs) conditions, especially rs-fMRI, have become a dominant experimental paradigm. An obstacle of rs-fMRI data acquisition is the length of the scan combined with the subjects' instruction to rest with their eyes closed and "think of nothing". Subjects may easily drift from wakefulness into light sleep during a scan. This change in vigilance may cause changes in functional connectivity (FC) patterns, which may in turn confound results. Ideally, simultaneous EEG recordings are used to monitor the subjects' alertness during the scan, but simultaneous fMRI/EEG recordings are rarely feasible. We developed a classifier that detects sleep from fMRI data alone and investigated its predictive components.

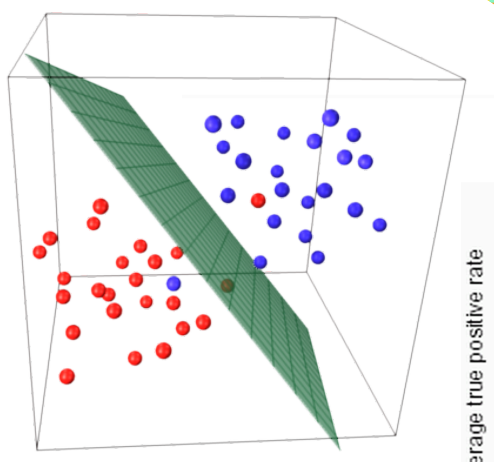
Methods

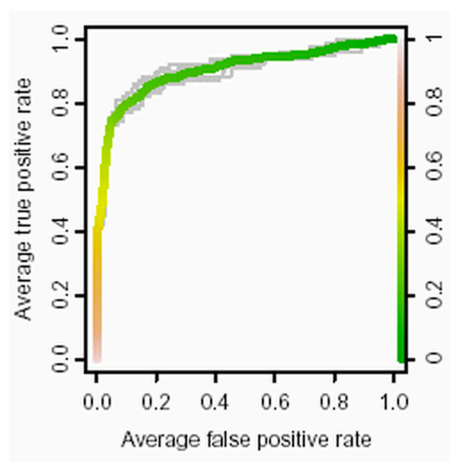
Simultaneous fMRI/EEG. Recordings were obtained in 25 participants (mean age 24.7±2.8 years) during wakefulness **(S0)**, sleep stage 1 **(S1)**, sleep stage 2 **(S2)**, and slow wave sleep **(SW)**. Sleep stages were scored using the criteria by Rechtschaffen and Kales [1]. Intervals comprising 300 sec of one consecutive (i.e., min 85%) sleep stage were extracted from the scan to serve as training data, yielding 92 epochs (5 min). A second **independent sample** comprising 42 epochs for sleep stages S0, S1 and S2 of 19 participants (mean age 27.0±2.7) was obtained to validate the accuracy of the model.

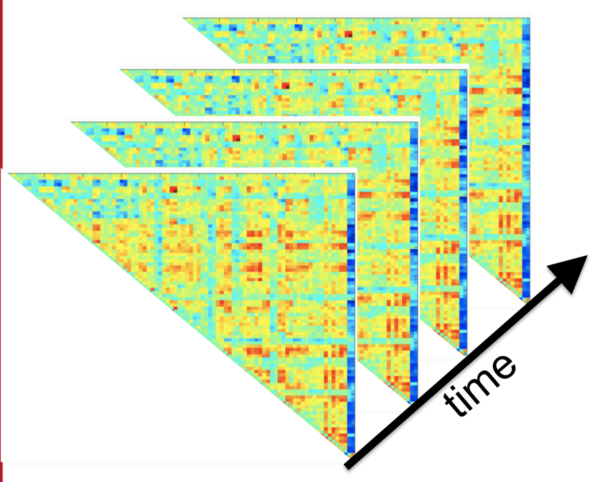
Feature Extraction. Brains were parcellated using 90 cortical regions of the AAL Atlas [2]. Regional time courses were extracted and correlation matrices computed. Correlation coefficients were converted to z-scores using Fisher's transform.



Statistical Learning. We used binary linear **SVM** classifiers for separating pairs of vigilance stages. Performance was evaluated using **Leave-One-Subject-Out Cross-Validation (LOSO-CV)** and the area under the ROC curve (AUC).

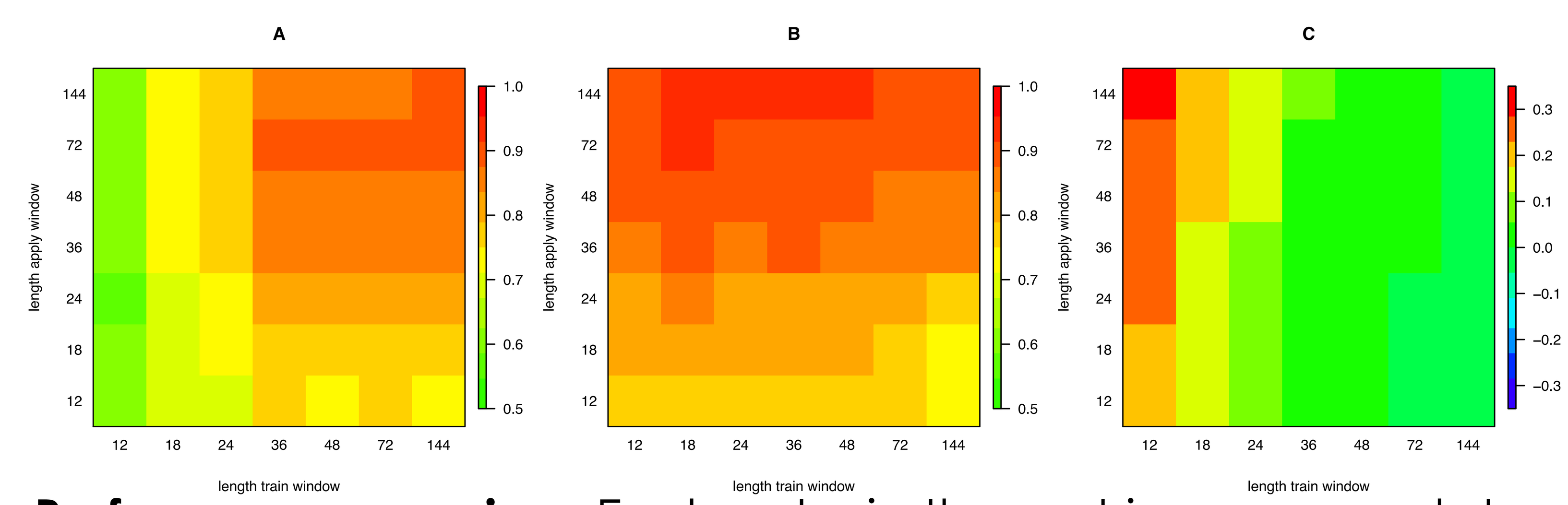




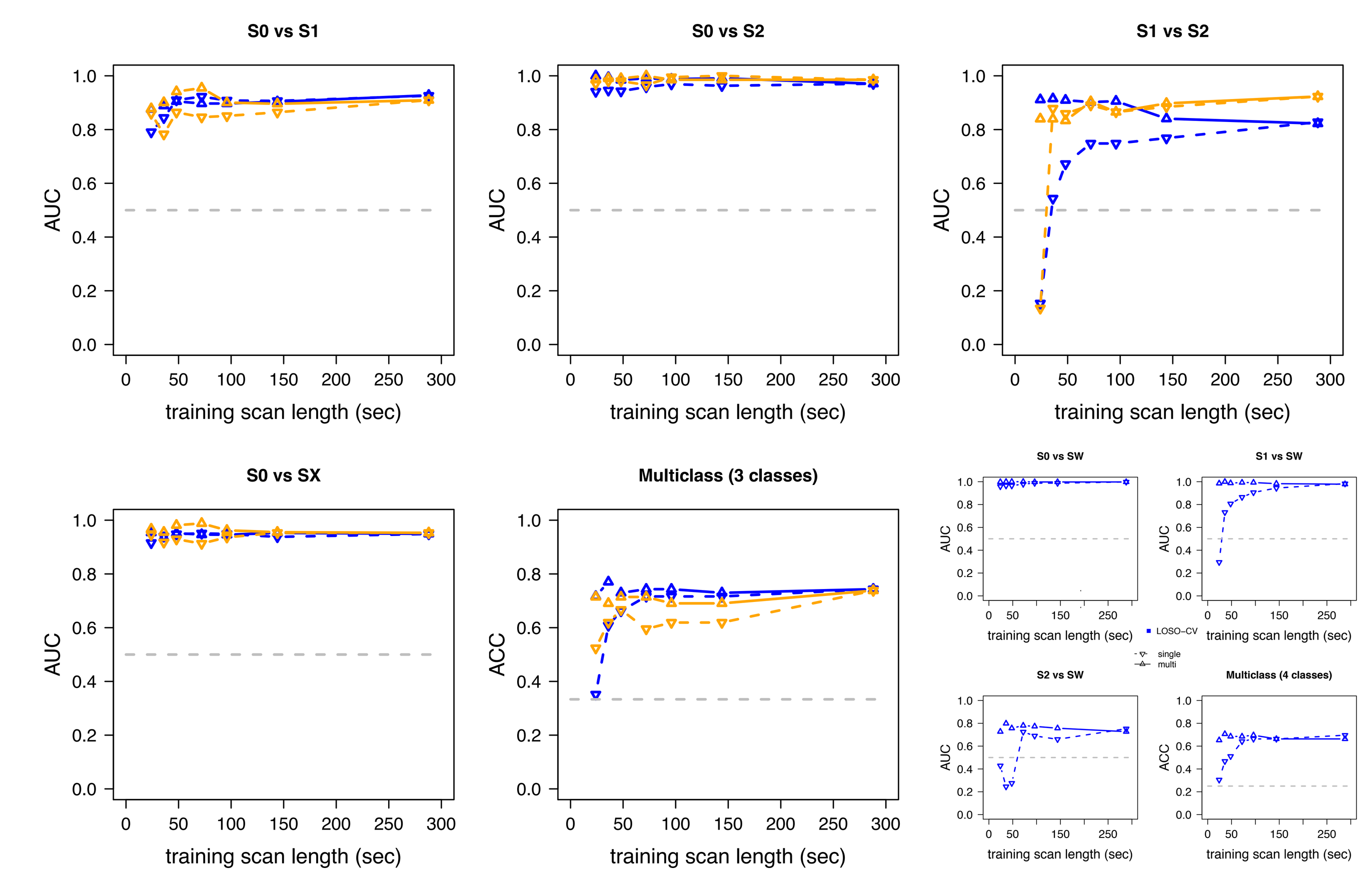


FC Eigennetwork (EN) Analysis. For analyzing the temporal changes in brain connectivity we conducted eigen-network analysis [3] using overlapping (4 sec) windows of 48 sec. for all 92 training epochs.

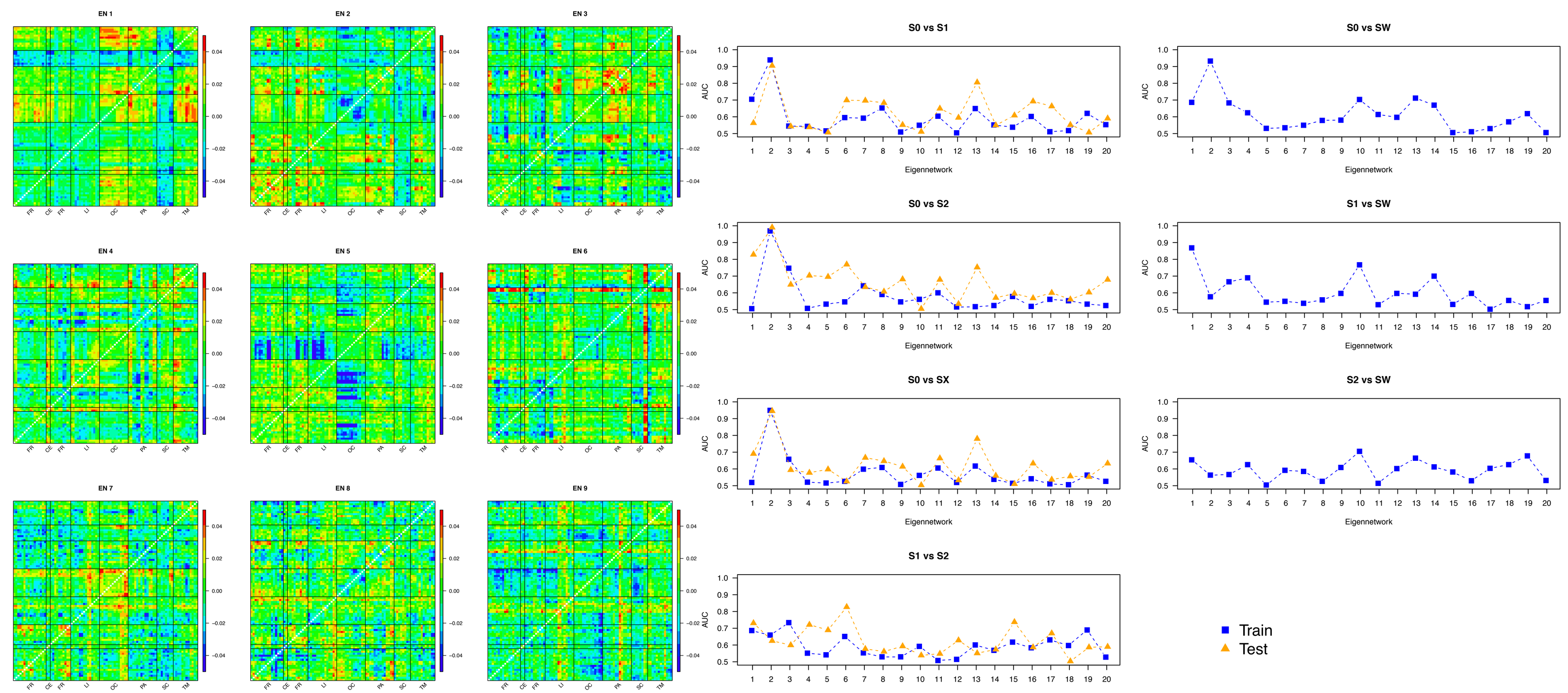
Results



Performance overview. Each entry in the matrix corresponds to the average AUC across the six binary classification tasks (S0|S1, S0|S2, S0|SW, S1|S2, S1|SW, and S2|SW) for one pair of window length used for training the classifier (x-axis) and for applying it in a LOSO-CV manner (y-axis). Inlet **(A)** shows the performance when only one window per epoch is used, while **(B)** all non-overlapping windows are used, and **(C)** is their difference.



Classifier performance for individual tasks. Each panel depicts the performance of one classifier trained on the training data using either LOSO-CV **(blue)** or the test data **(orange)**. X-axis denotes the window length on which the classifier was trained using either a singe n-second window **(down facing triangles)** or all non-overlapping n-second windows **(up facing triangles)**.



First nine eigennetworks. The connection strengths in each component are color coded with warm (increase) and cold (decrease) colors. FR (frontal), CE (central), LI (limbic), OC (occipital), PA (parietal), SC (subcortical), and TM (temporal).

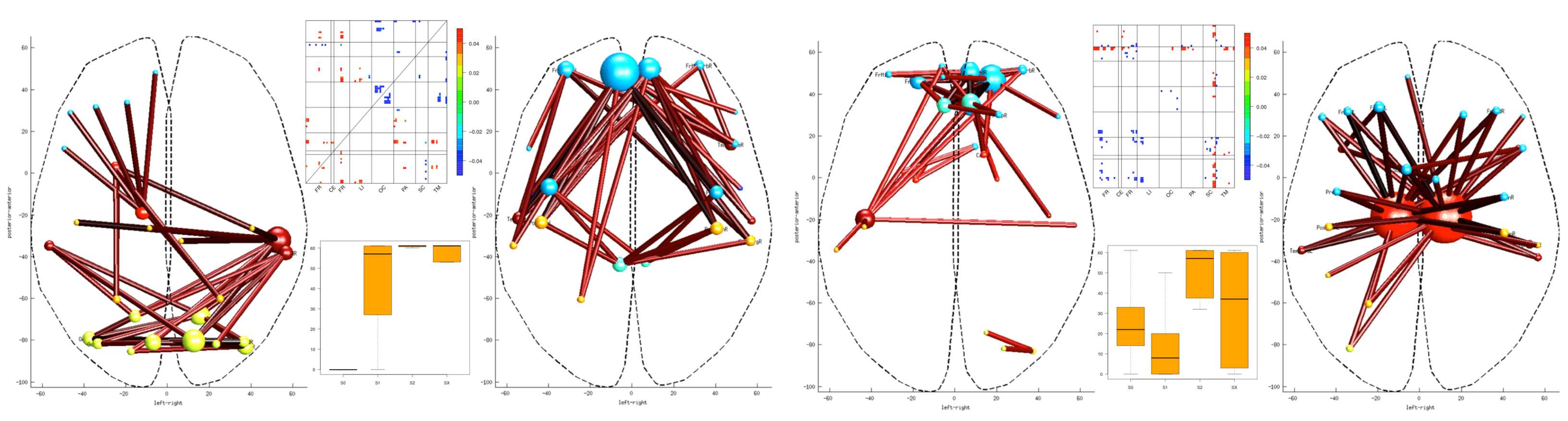
Discriminative power of the first 20 eigennetworks. Discriminative performance of a single EN for a pair of vigilance states measured in AUC. (blue) LOSO-CV (orange) test data.

Conclusions

Other than a previously suggested SVM approach to classify sleep stages based on FC [4], we approached the question free of any anatomical hypothesis. We validated our model in a clean cross-validation setting and on independently acquired data.

Detection of sleep close to perfect. Classifiers separating wakefulness from any sleep stage achieve close to perfect performance in LOSO-CV and on independent test data.

Connectivity within OC and FR lobes and thalamus highly predictive for wakefulness. During wakefulness stronger connectivity within OC lobe and reduced connectivity within FR lobe (left, EN2). Thalamocortical connectivity is increased in S0 and S2 and reduced in S1 (right, EN6).



References

1. Rechtschaffen & Kales (1968) A manual of standardized terminology, techniques and scoring system of sleep stages in human subjects.
2. Tzourio-Mazoyer et al. (2002) Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage vol. 15 (1) pp. 273-89.
3. Leonardi et al. (2012) Functional Connectivity Eigennetworks reveal different brain dynamics in multiple sclerosis patients.
4. Tagliazucchi et al. (2012) Automatic sleep staging using fMRI functional connectivity data. Neuroimage vol. 63 (1) pp. 63-72.

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