Whole-brain network states predict behavioral responses to transcranial magnetic stimulation

Thomas A. Dorfer[1,7], Conor N. Robinson[1,6], Luca Cocchi[1,6], Jason B. Mattingley[4,5], Martin V. Sale[3], Andrew Zalesky[2], Leonardo L. Gollo[1,6]

1 QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia. 2 Department of Psychiatry, The University of Melbourne, Melbourne, Australia. 3 School of Physiotherapy, The University of Queensland, Brisbane, Australia. 4 Queensland Brain Institute, The University of Queensland, Brisbane, Queensland, Australia. 5 School of Psychology, The University of Queensland, Brisbane, Australia. 6 School of Biomedical Sciences, The University of Queensland, Brisbane, Australia. 7 Faculty of Medicine, The University of Queensland, Brisbane, Australia.

QIMR Berghofer Medical Research Institute

The University of Queensland AUSTRALIA

Motivation

Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique used for treating various psychiatric disorders. However promising, TMS is very expensive and time-consuming and reported response rates are only between 45% and 60%. Having a predictive tool for TMS responsiveness would therefore significantly improve patients' prognoses by referring responders to TMS therapy and non-responders to alternative treatments (i.e. electroconvulsive therapy or pharmacotherapy). We hypothesize that simple resting-state connectivity features prior to stimulation are predictive of post-TMS behavioral outcomes. Our findings suggest that these features – derived from whole-brain and sensorimotor systems – bare indeed the potential to significantly predict the responsiveness to two forms of TMS – intermittent theta burst stimulation (iTBS) and continuous theta burst stimulation (cTBS).

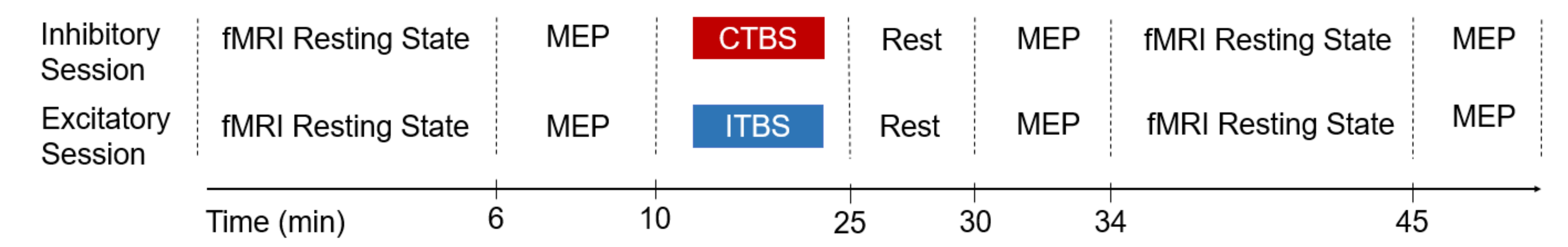


Fig. 1: Experimental design for the theta-burst stimulation (TBS) and resting-state functional neuroimaging (rsfMRI) protocols. All 24 participants performed 2 experimental sessions comprised of rsfMRI and TBS. The 2 sessions were scheduled at least 24 hours apart. MEPs, motor-evoked potentials; cTBS, continuous TBS (inhibitory); iTBS, intermittent TBS (excitatory). Adapted from Cocchi et al. (2015).

Network feature selection

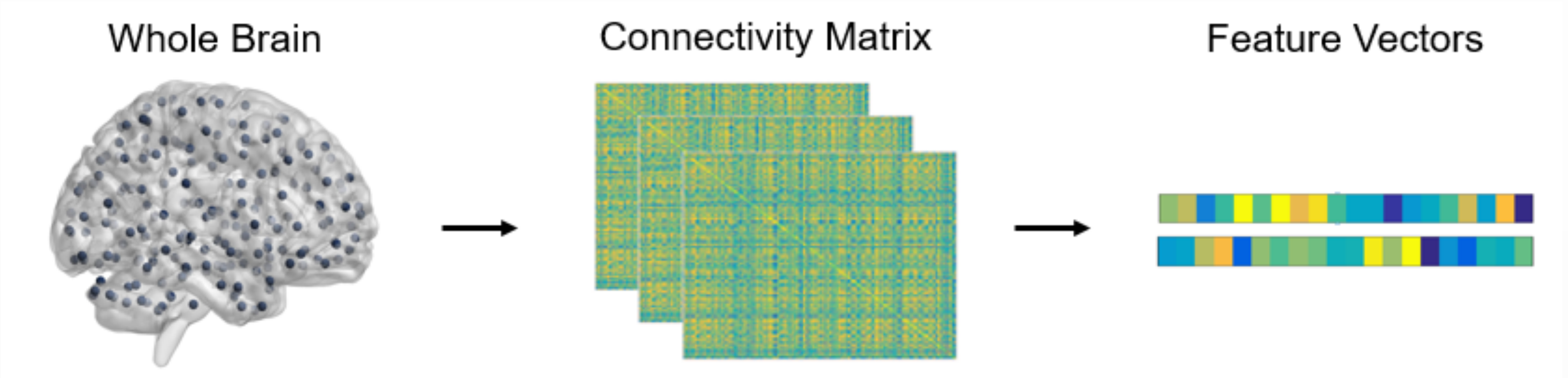


Fig. 2: Whole-brain features were extracted from participants' pre-TMS rsfMRI functional connectivity matrices (generated with MNI coordinates, Craddock et al.,2012).

The following 11 brain network features were extracted and fed into a max-relevance feature selection algorithm (Peng et al., 2005):

1 Age
2 Betweenness Centrality
3 Clustering Coefficient
4 Global Efficiency
5 Standard Deviation
6 Mean
7 ALFF (Power)
8 Median
9 Modularity
10 Path Length
11 Small Worldedness

Support vector machine classifier

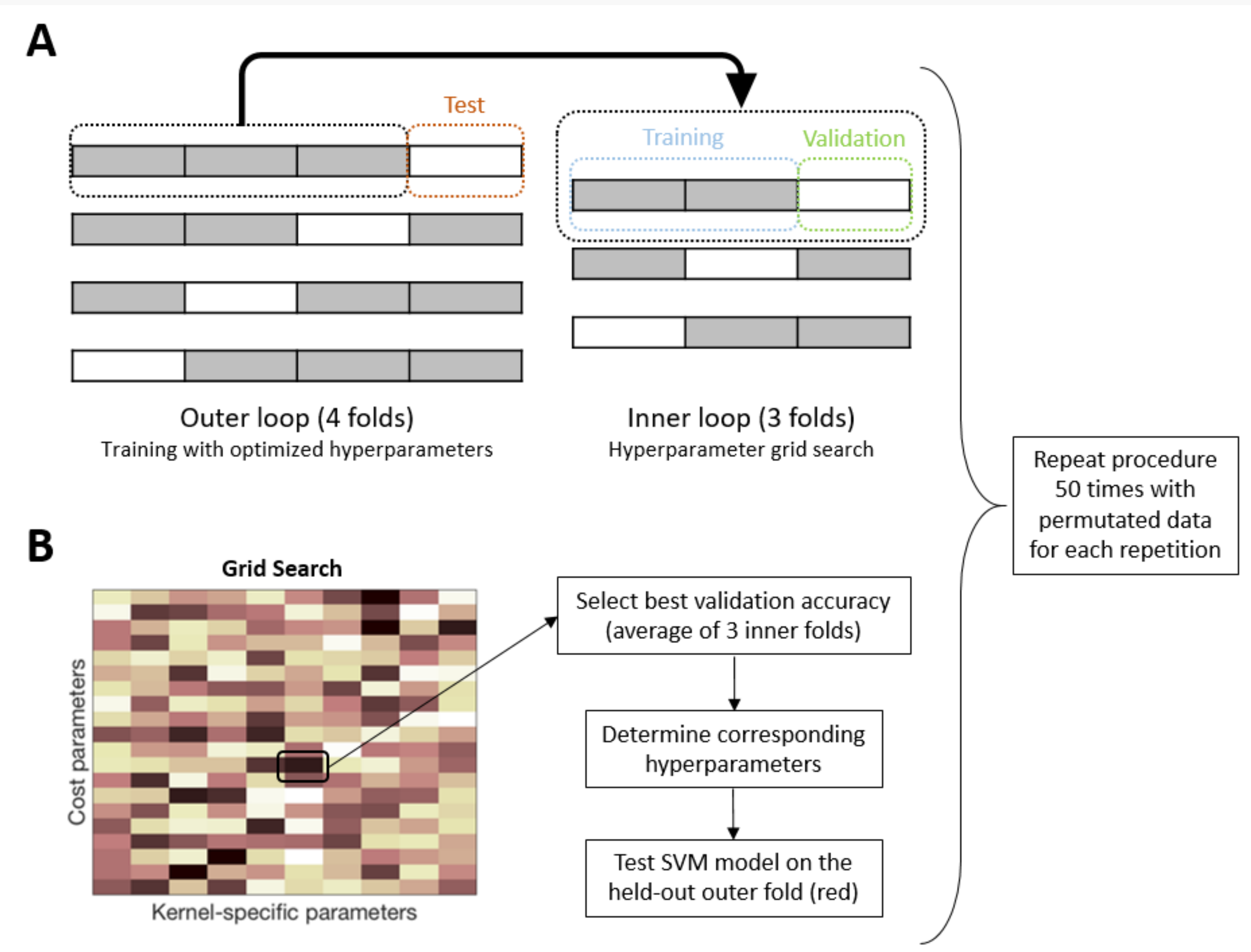
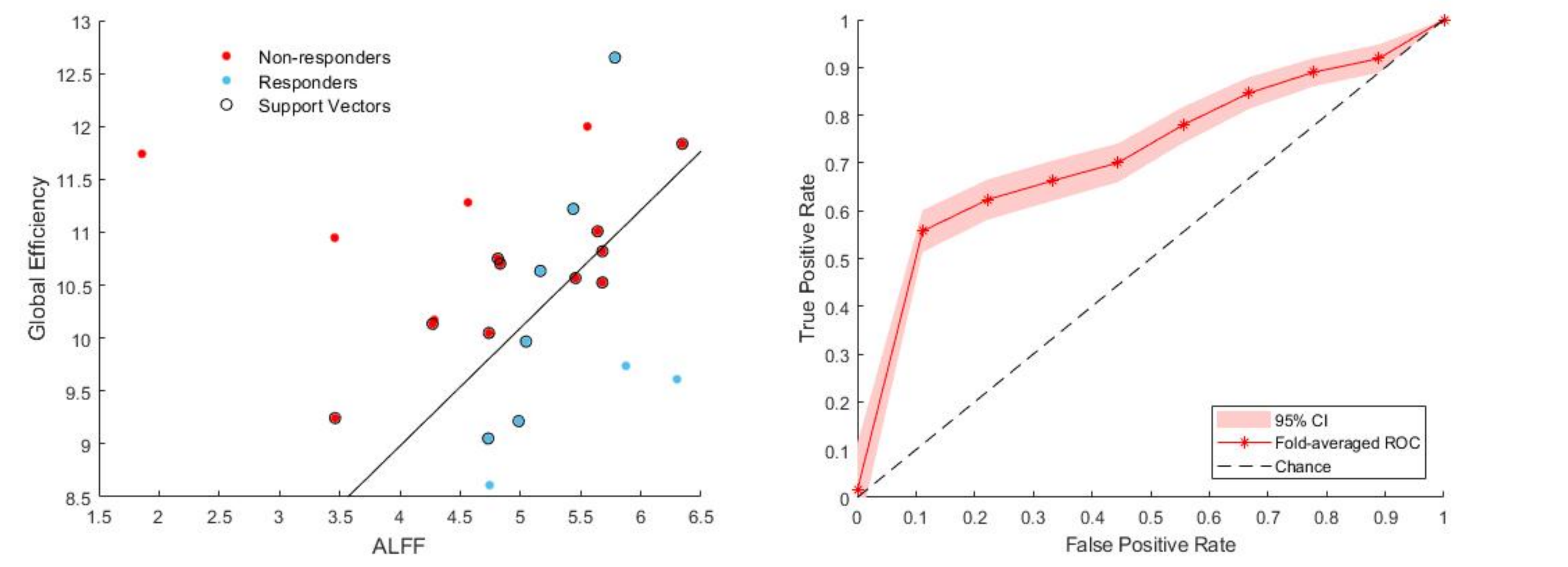


Fig. 3: SVM classifiers were trained using 70% of the available data in which the efficacy of the model was assessed against the remaining subjects (leave-one out cross-validation). In the inner loop, grid search was performed, whereby the optimal hyperparameters were identified and averaged across the outer folds. The final model was then trained on these hyperparameters.

Results

cTBS

For cTBS, the features identified as most relevant and least redundant were global efficiency and ALFF, with an mean (across folds) accuracy rate of **77.68 ± 2.41%**.



iTBS

For iTBS, the same feature selection pipeline identified ALFF and betweenness centrality as the most relevant feature, performing at an average accuracy of **67.22 ± 4.14%**.

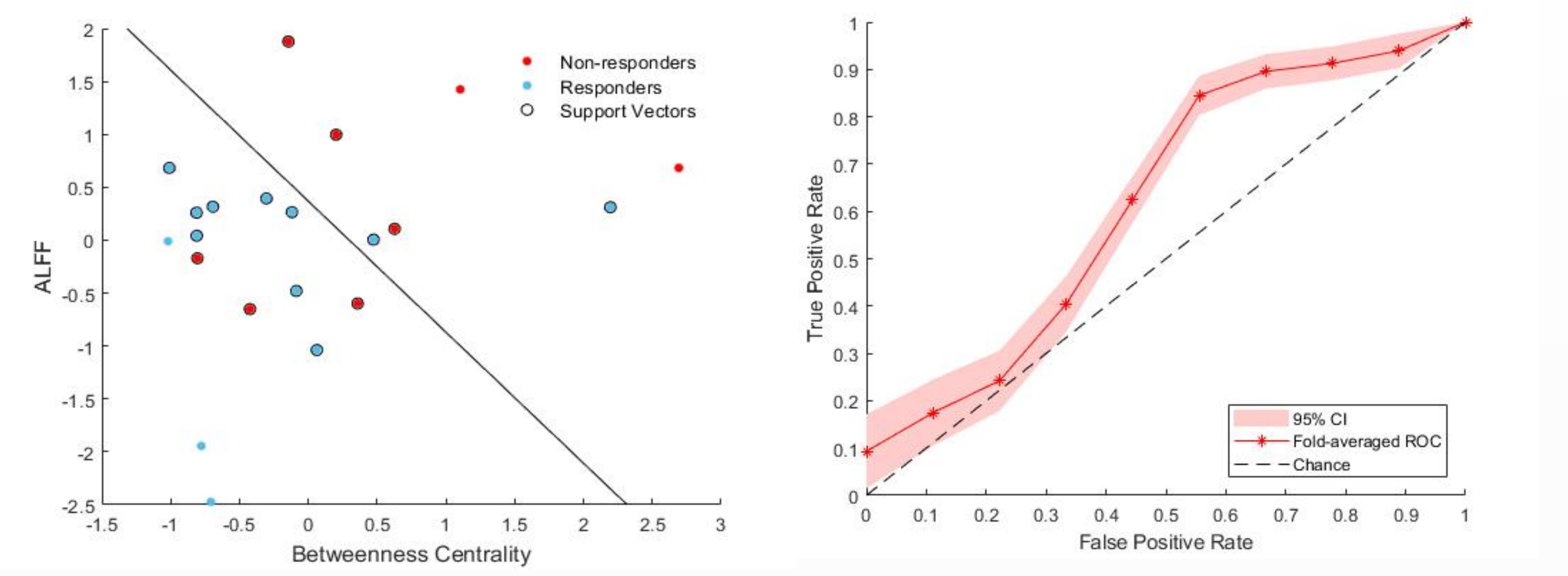


Fig. 4: Top left: Scatter plot of best-performing cTBS features (global efficiency and ALFF) separated by a linear hyperplane. Top right: Receiver operating characteristic (ROC) curve, showing specificity and sensitivity of the classifier. Bottom left and right are equivalent graphs for iTBS. It is apparent that iTBS features demonstrate a lower sensitivity compared to their cTBS counterparts.

Discussion & Future Work

Our results demonstrate that network connectivity features at baseline –easily extractable from the Brain Connectivity Toolbox (Rubinov & Sporns, 2010) – can significantly predict the behavioral response to inhibitory and excitatory repetitive TMS with an accuracy of approximately 77% and 67%, respectively. It is worth highlighting that resting-state whole-brain activity is particularly predictive of TMS responsiveness for the cTBS paradigm, which is in alignment with previous findings that suggest that cTBS induces more robust changes in connectivity compared to its iTBS counterpart.

Furthermore, it should be noted that these features only contribute partially to the behavioral outcome of TMS and cannot fully account for it. Future work could entail the identification of other factors that can further predict these behavioral outcomes to make these predictions even more accurate and thus start moving toward clinical applications.

Similar studies could also be performed using electroencephalography (EEG) instead of rsfMRI data to validate (and perhaps improve) our findings.

References

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