

BACKGROUND

Transcranial magnetic stimulation (TMS) could treat a variety of brain disorders, but its effects are variable.

In some cases, less than half of tested participants show the expected plastic response to TMS interventions.

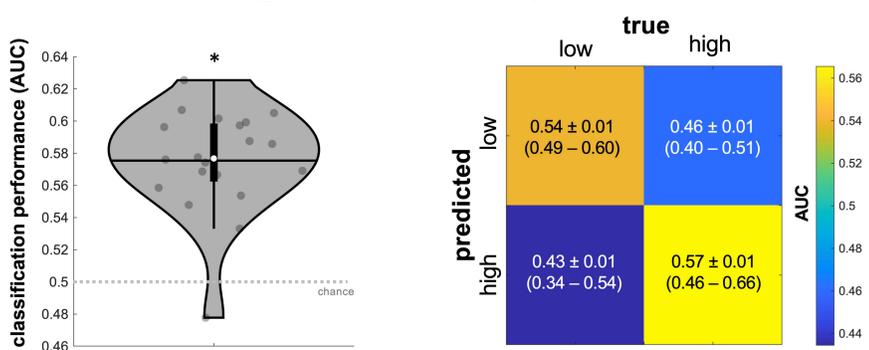
Brain state-dependent TMS may improve reliability of TMS effects by coupling stimulation to periods of low or high excitability.

Current brain state-dependent TMS approaches deliver stimulation during states shown at the group level to correlate with excitability.

Here, we aimed to determine if individual subjects exhibit unique brain activity patterns that discriminate between low and high excitability states.

RESULTS

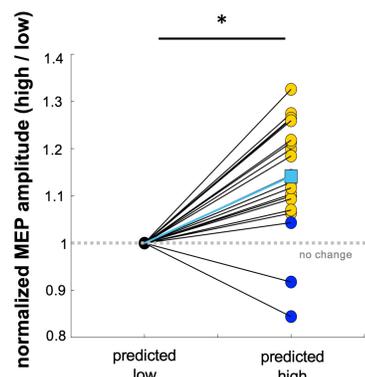
Subject-specific classifiers successfully discriminated between low and high M1 excitability states.



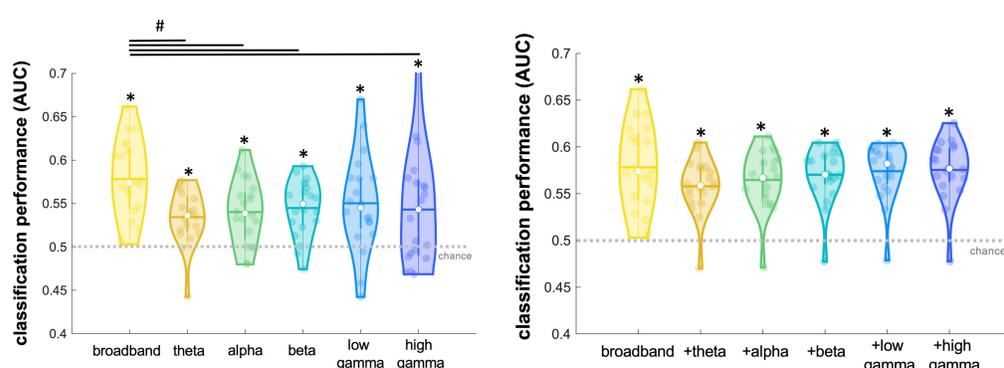
- 17 of 20 subjects showed above-chance classification performance (permutation tests, $p < 0.04$).
- Group-level classification performance ($AUC = 0.59 \pm 0.01$) exceeded chance (one-tailed sign-rank test, $p < 0.001$).
- Accurate classification occurred more often than inaccurate classification.

Classifier-predicted high excitability states were associated with larger MEPs than classifier-predicted low excitability states.

- MEP amplitudes were larger during classifier-predicted high vs. low excitability states in 16 of 20 subjects (one-tailed sign-rank tests, $p < 0.04$).
- Group-level MEP amplitudes were larger during classifier-predicted high vs. low excitability states (one-tailed sign-rank test, $p < 0.001$).
- MEP amplitudes were $14.13 \pm 2.7\%$ larger during classifier-predicted high vs. low excitability states.



Classification performance varied depending on the power spectral features used



- Regardless of the features used, classification performance exceeded chance (one-tailed sign-rank tests, $p < 0.01$).
- Classifiers trained using broadband power features only outperformed classifiers trained using theta, alpha, beta, or low gamma power features only (two-tailed sign-rank tests, $p < 0.02$).

METHODS

Dataset

- 600 single TMS pulses delivered during 28-channel EEG
- Site: L. FDI hotspot
- Intensity: 120% RMT
- ISI: 5 s with 15% jitter
- Type: Monophasic posterior-to-anterior across central sulcus
- Available at: <https://openneuro.org/datasets/ds002094>

Classification of motor cortex (M1) excitability states

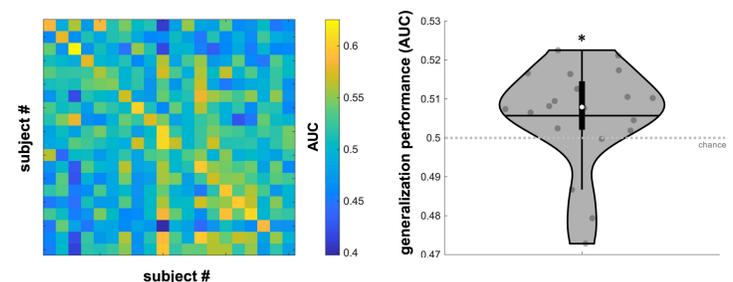
- Linear Discriminant Analysis with 10-fold cross-validation
- Grid search to optimize each subject's lambda value
- Features: Theta (4-7 Hz), alpha (8-12 Hz), beta (13-35 Hz), low gamma (36-60 Hz), high gamma (61-100 Hz), and broadband (4-100 Hz) power per channel
- Classes: low versus high excitability (median split)

Statistics

- Comparison to standard chance level (one-tailed sign-rank test)
- Subject-specific permutation tests
- Pairwise comparisons (two-tailed sign-rank test)
- All p-values are FDR-corrected where appropriate

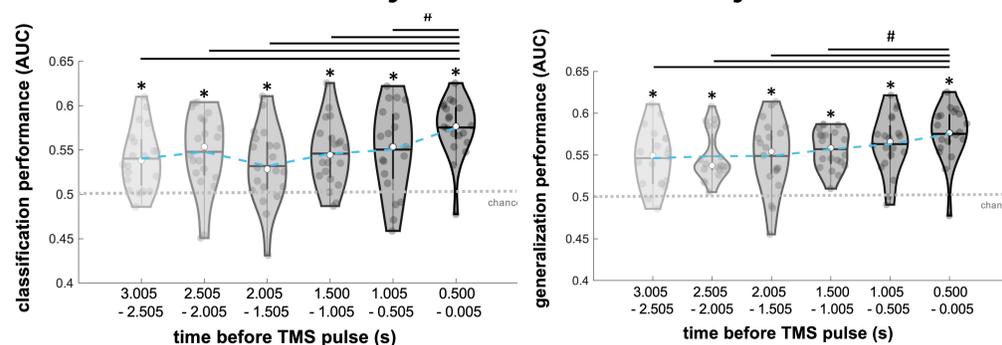
RESULTS CONTINUED

Subject-specific classifiers generalized weakly across subjects.



- Classifiers showed above chance generalization performance in 4 of 20 subjects (one-tailed sign-rank tests, $p < 0.04$).
- Group-level generalization performance ($AUC = 0.51 \pm 0.003$) exceeded chance (one-tailed sign-rank test, $p = 0.02$) but was significantly worse than group-level classification performance (two-tailed sign-rank test, $p < 0.001$).

Classifiers performed best when trained using features obtained immediately before TMS delivery.



- Classification and generalization performance exceeded chance at all time points within 3 seconds of TMS (one-tailed sign-rank tests, $p < 0.002$).
- Overall, classifier performance was highest immediately before TMS (two-tailed sign-rank tests, $p < 0.03$).

CONCLUSIONS

Individual subjects exhibit unique brain activity patterns that discriminate between periods of low and high M1 excitability.

Results provide a framework for fully individualized, decoding-based state-dependent TMS in the future.

Decoding-based state-dependent TMS using the approach described here has multiple advantages:

- 1) It does not require *a priori* knowledge of the relationship between brain activity and excitability.
- 2) In principle, it does not require any specific cortical morphometry.
- 3) It is compatible with threshold-based real-time implementation due to long-lasting excitability states.