Prediction of TMS-evoked Potentials from Prestimulus Spectral Features: A Machine Learning Approach

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Background

Brain Criticality
A state near phase transition, where neural networks achieve optimal adaptability and computational efficiency.

TMS-EEG
Transcranial Magnetic Stimulation (TMS) combined with EEG provides a non-invasive method to study neural dynamics through TMS-evoked potentials (TEPs).

TEPs
Reflect cortical excitability and connectivity.

Frequency Bands in Brain Function:
- **Delta (1–3 Hz):** Linked to deep sleep and unconscious processes.
- **Theta (4–7 Hz):** Involved in memory encoding and cognitive control.
- **Alpha (8–13 Hz):** Associated with inhibition, sensory gating, and readiness states.
- **Beta (14–30 Hz):** Reflects motor preparation and top-down control.
- **Gamma (31–90 Hz):** Related to local processing, excitability, and cortical responsiveness.

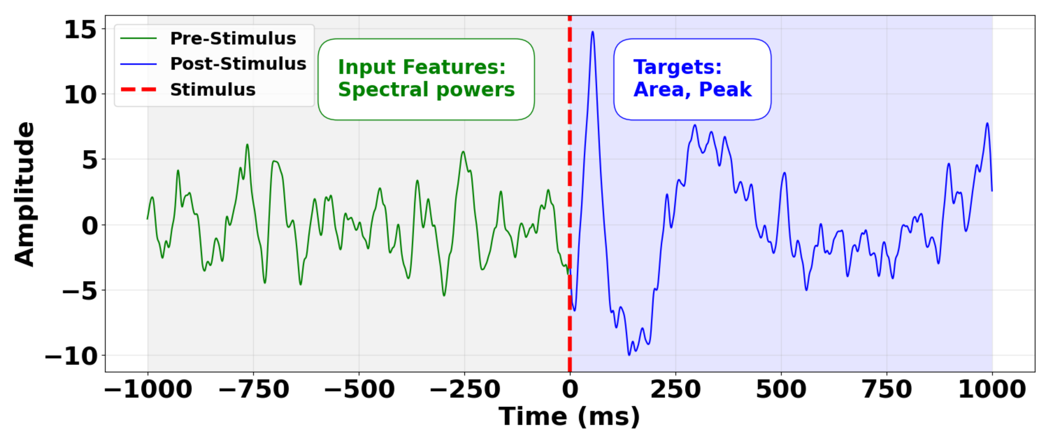
Goal
To examine the predictive relationship between pre-stimulus TEP features and post-stimulus TEP variability.

Methods

Dataset:
- Publicly available TMS-EEG dataset of 20 right-handed healthy volunteers (age: 24.50 ± 4.86 years; 14 females).
- Recorded with a 62-channel EEG system at 1 kHz.
- EEG preprocessed using **EEGLAB** and **TESA** toolbox.

Features Extraction:
- Each trial segmented into 2000 samples (1000 pre-stimulus, 1000 post-stimulus).
- Focused on channel C3, where TMS was applied.
- Morlet wavelet transform (constant=7) applied to pre-stimulus window (−800 to −200 ms).
- Power Spectral Density (PSD) computed in five frequency bands: delta, theta, alpha, beta, gamma

Targets Variables:
- **Area**: Total area under the absolute post-stimulus signal (global response magnitude).
- **Peak**: Maximum amplitude of the post-stimulus signal (most prominent response).



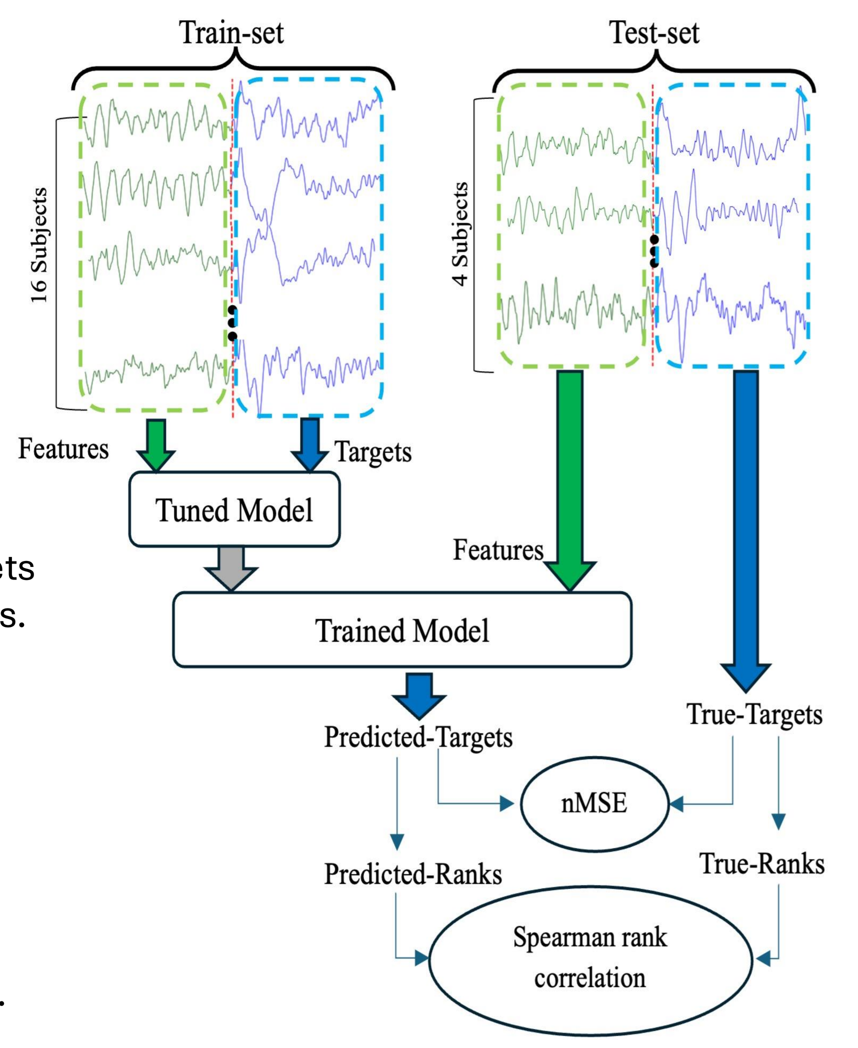
Pre- and post-stimulus from a single trial TEP, with pre-stimulus features predicting post-stimulus targets, separated by the stimulus onset.

Machine Learning Pipeline

Train-Test split: 5-fold stratified cross-validation was applied at the **subject level**, ensuring that training and test sets contained data from **non-overlapping subjects**.
In each fold:
- 16 subjects → training
- 4 subjects → testing
- 3-fold cross-validation was used for

Machine learning model: A **Random Forest Regressor** was used to predict post-stimulus targets (Area and Peak) from pre-stimulus spectral features.

hyperparameter tuning: Input features were standardized before training.



Model Evaluation Metrics:
- **Normalized Mean Squared Error (nMSE):**
  Quantifies prediction error relative to variance.
  Values < 1 indicate better-than-mean prediction.
- **Spearman's ρ:**
  Measures how well predicted rankings match actual trial order.
  ρ > 0.7 = strong
  0.5–0.7 = moderate
  < 0.3 = weak

Interpretability & Visualization:
SHAP analysis: identified the most influential frequency bands.
Quartile-based visualization: compared predicted vs. true trial groupings across response magnitude.

Results

Performance Metric Table

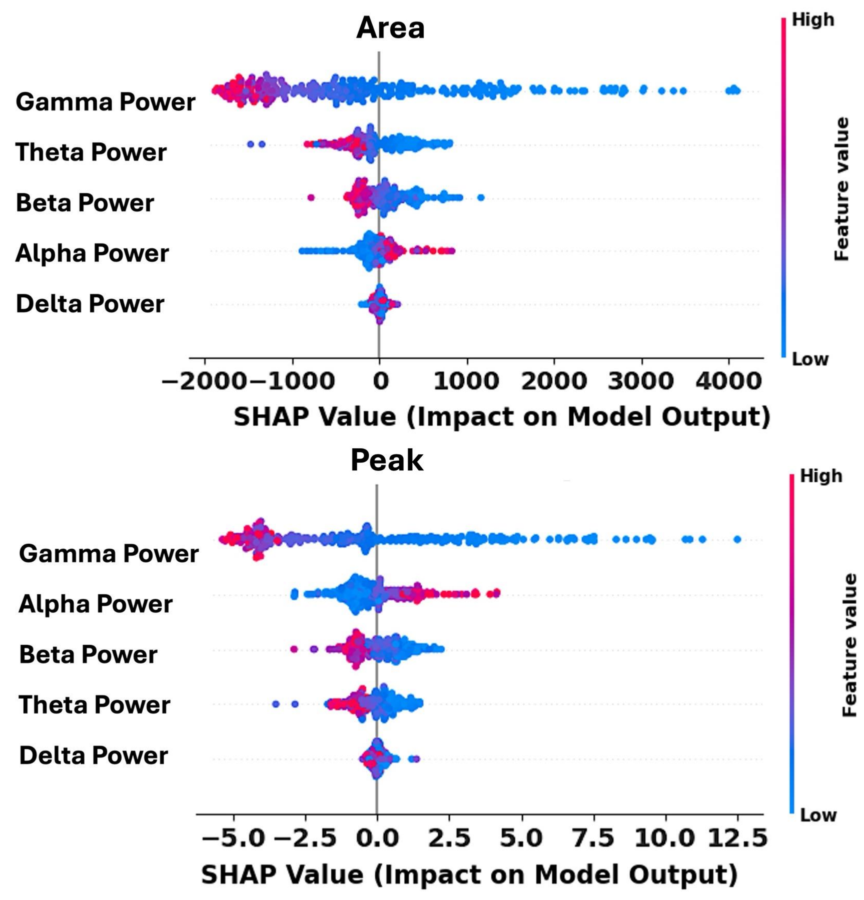
Target Method	nMSE [95%Confidence Interval]	Spearman's ρ [95%Confidence Interval]
Area (all freq bands)	0.49 [0.44-0.54]	0.76 [0.73 – 0.78]
Peak (all freq bands)	0.8 [0.74 – 0.88]	0.6 [0.57 – 0.63]
Area (alpha band)	1.78 [1.67 – 1.9]	0.11 [0.06 – 0.16]
Peak (alpha band)	1.76 [1.65 – 1.88]	0.11 [0.07 – 0.17]

Predicting **Area** yields better results than **Peak** amplitude:
- Lower nMSE
- Higher Spearman's ρ

Using **all frequency bands** significantly improves performance.

SHAP Summary Plot

SHAP values quantify how each frequency band influences model predictions.
The plots show feature importance for predicting **Area** and **Peak** targets.

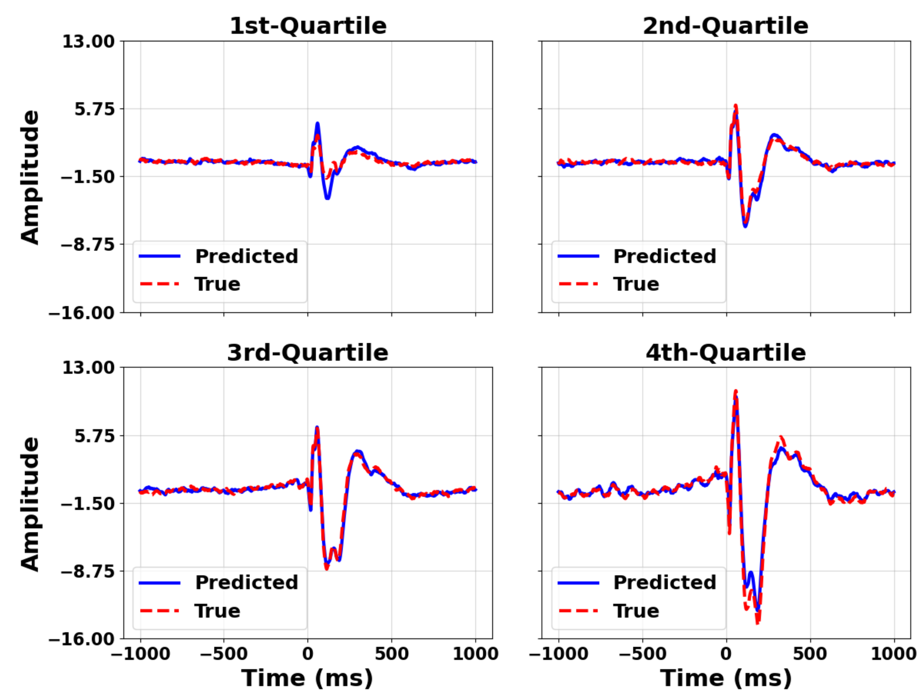


Findings:
- **Gamma power** is the strongest predictor for both targets.
- For **Area**: Gamma > Theta > Beta
- For **Peak**: Gamma > Alpha > Beta
- **Alpha** is more relevant to transient peak fluctuations, while **gamma** is linked to sustained excitability.

Color gradient (blue → red): indicates low-to-high feature values and their corresponding SHAP

Quartile Plot

Trials were ranked based on both **true** and **predicted** values of the **Area** target.
Trials were divided into four quartiles to analyze prediction accuracy across response magnitudes.



What It Shows:
Each subplot displays the **average post-stimulus EEG** signal (C3) for each quartile.
Solid **blue line** = predicted signal
Dashed **red line** = true signal

Strong overlap across quartiles confirms:
The model generalizes well across subjects
Pre-stimulus features retain meaningful information about trial-level variability

Conclusion

- **Machine learning** successfully predicted TMS-evoked responses using **pre-stimulus spectral features.**
- **Gamma power** was the most influential feature for both signal **Area** and **Peak**.
- **Alpha power** was more relevant to transient **Peak** responses, while **theta** and **beta** contributed to **Area.**
- **Delta power** showed minimal impact.

These results confirm that:
- The **full spectrum of frequency bands** is essential for accurate prediction.
- **Gamma activity** may reflect a more excitable or desynchronized cortical state that facilitates stronger TMS responses.
- **Alpha rhythms** may exert inhibitory control, especially over sensorimotor areas.

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Github Repository

Brain Lab Unit