

State-dependent Spectral Slowing in Lewy Body Dementia Using Resting-state MEG and Hidden Markov Modeling

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Rationale

Significance

- Lewy Body dementia (LBD) is the second most common neurodegenerative dementia
- Previous studies have identified spectral slowing in LBD as a potential biomarker for diagnosis and disease progression
- Cognitive Fluctuations (CF) are a core feature of LBD, and little is known about the mechanisms of CF in relation to spectral slowing

Knowledge Gap

- Resting-state electrophysiological slowing is a promising biomarker in LBD, but objective markers of its temporal instability are limited
- The relationship between spectral slowing and CF severity is poorly understood

Emerging Field

- LBD, while being a common type of dementia, remains underrecognized in clinical practice
- The application of Hidden Markov models to MEG now allows characterization of temporal brain-state dynamics that static spectral measures miss

Study Focus

- Identify whether resting-state MEG with hidden Markov modeling (HMM) can identify state-dynamic and spectral signatures associated with LBD and CF severity.

Methods

Groups

This study was comprised of 60 participants spread across 4 groups:

- LBD (n = 9; 71 ± 6 years; 7 male)
- Alzheimer's Dementia and amnesic Mild Cognitive Impairment (AD/aMCI, n = 8; 72 ± 11 years; 5 male)
- Parkinson's Disease (PD, n = 11; 72 ± 6 years; 7 male)
- Healthy Controls (HC, n = 32; 71 ± 7 years; 11 male)

Experimental Protocol

- Each participant underwent five 2-minute eyes-closed resting-state MEG scans
- Cognitive Fluctuations were assessed with the Clinical Assessment of Fluctuation (CAF)

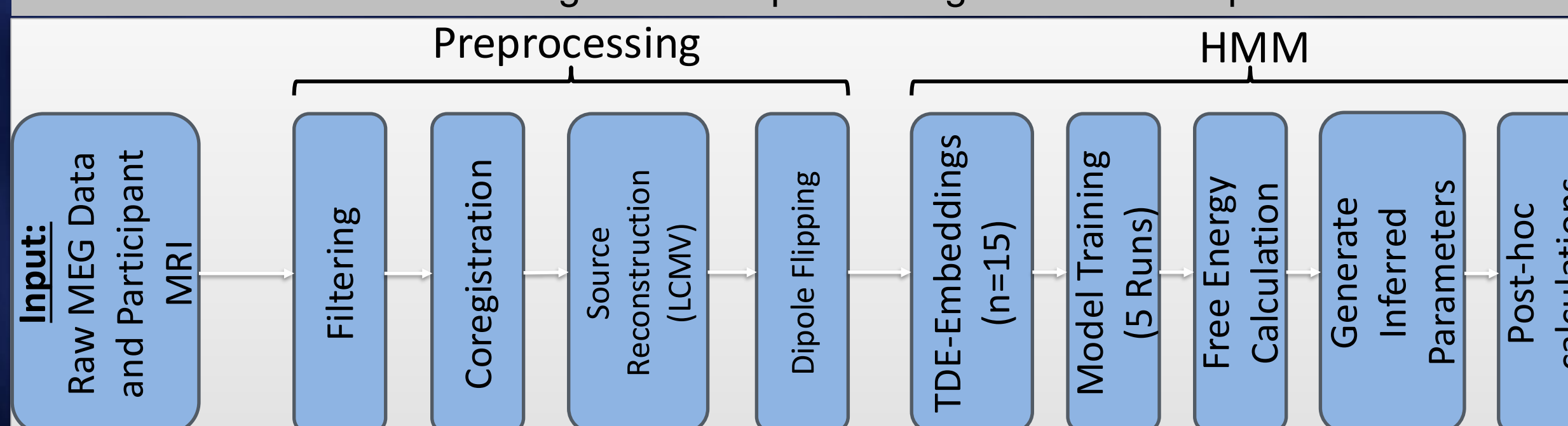
MEG Preprocessing

Resting-state MEG data were preprocessed using a 0.5–125 Hz bandpass filter and a notch filter to remove powerline noise. Automated bad segment and bad channel detection were applied prior to 40-component ICA decomposition, with ECG and EOG components rejected and bad channels interpolated from surrounding channels. Each subject's structural MRI was co-registered with MEG sensor digitization points using RHINO. An LCMV beamformer was then applied to project sensor-level data into source space, parcellated into 52 cortical regions using the Glasser atlas.

Hidden Markov Model Analysis

An 8-state HMM was used to identify transient brain states. Fractional occupancy (FO), switching rate (SR), and transition-probability metrics were derived. Spectral slowing was quantified using power spectral density and theta/beta ratio (TBR).

Chart 1. Diagram of Preprocessing and HMM Steps



Results

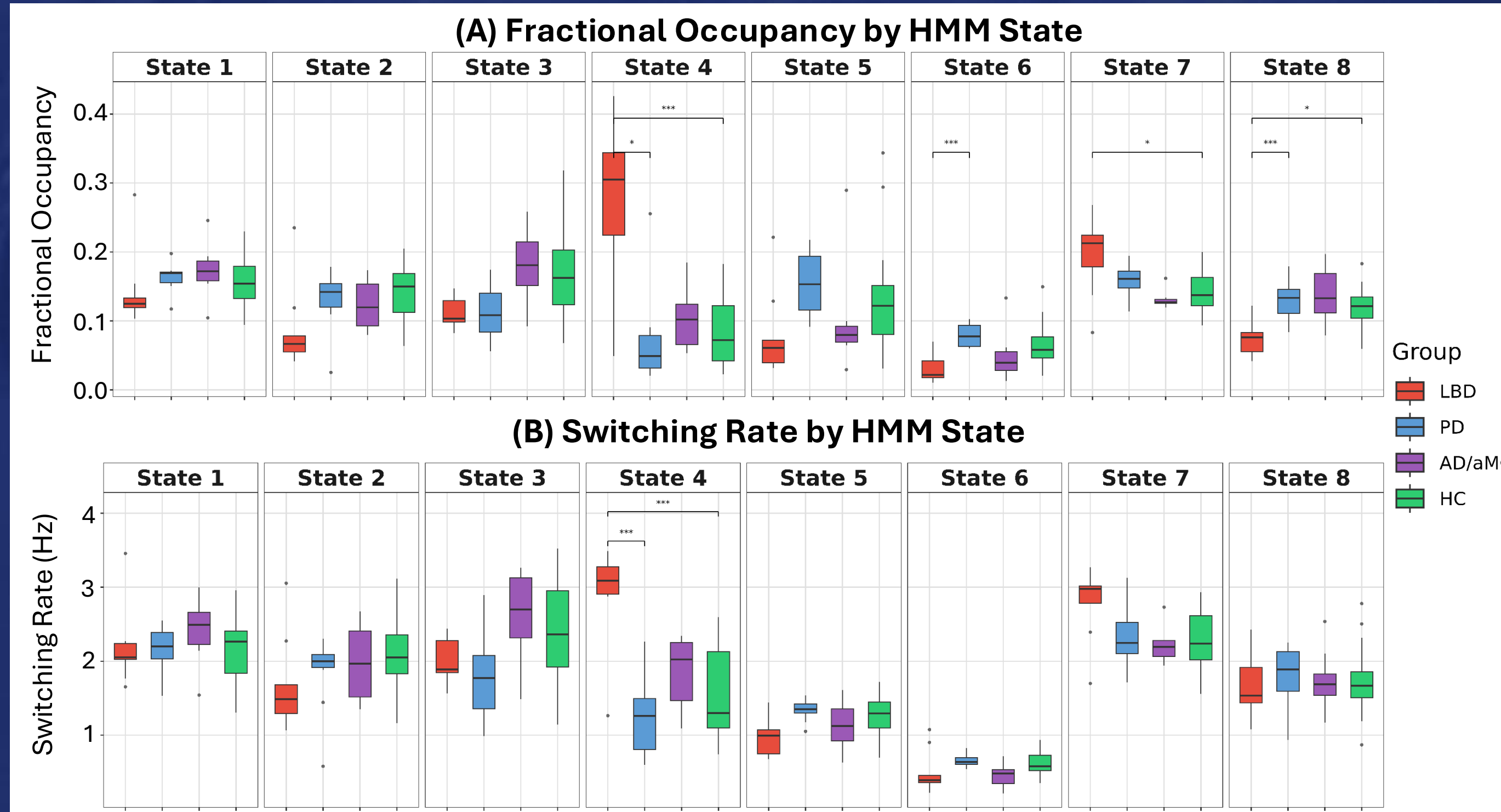


Figure 1. Group differences in HMM-derived state dynamics from resting-state MEG. Data are shown for participants with Lewy body dementia (LBD, n = 9), Parkinson's disease (PD, n = 11), Alzheimer's disease/amnesic mild cognitive impairment (AD/aMCI, n = 8), and healthy controls (HC, n = 32). (A) Fractional occupancy, defined as the proportion of total time spent in each state, is shown across groups and states. In the LBD group, State 4 showed the highest fractional occupancy. (B) Switching rate, defined as the mean number of visits to each state, is shown across groups and states. The LBD group tended to enter State 4 more frequently than other states.

***: P (Bonferroni-adjusted) < 0.001; *: P (Bonferroni-adjusted) < 0.05

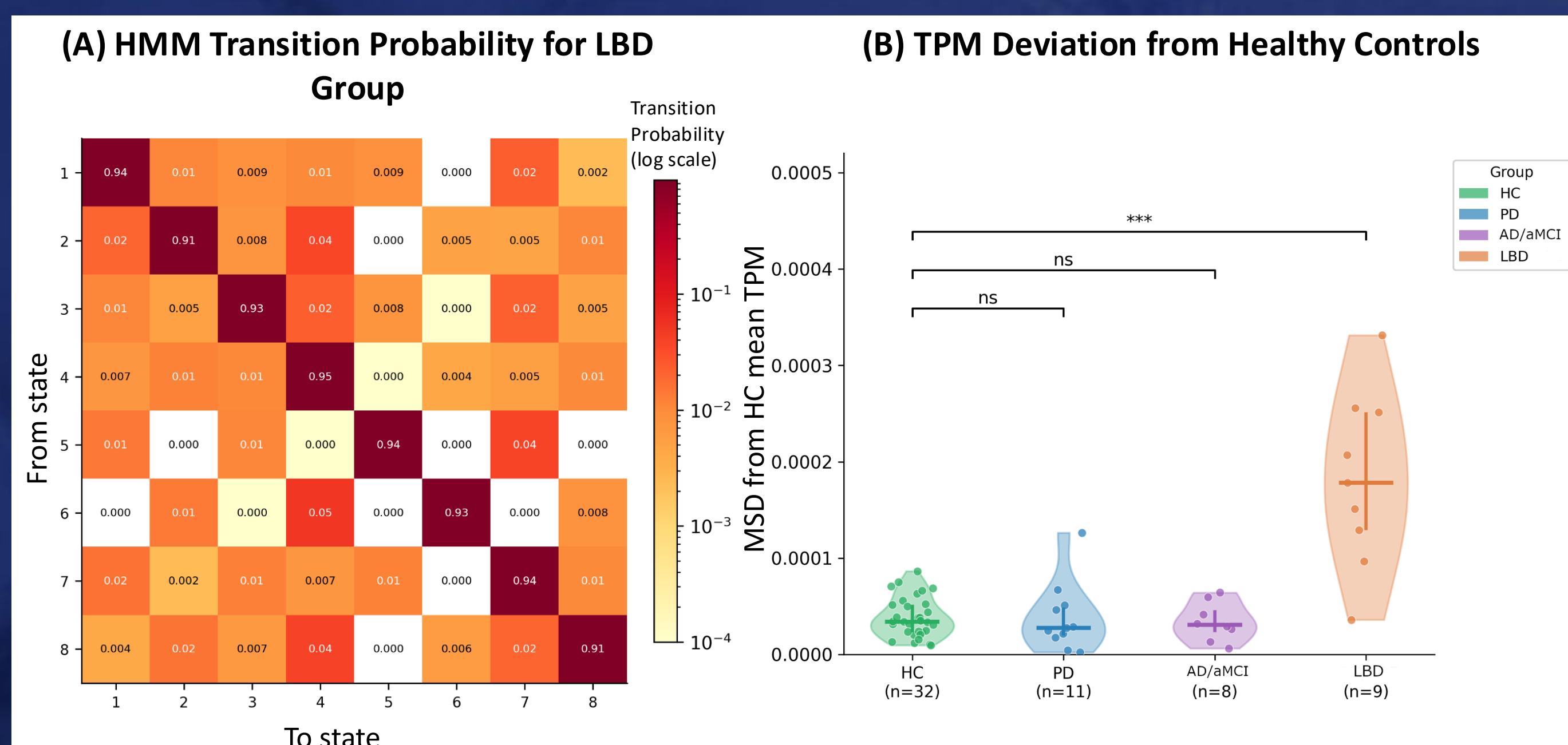


Figure 2. LBD is associated with increased instability of state-transition probabilities relative to healthy controls. (A) State transition matrix. Each element represents the probability of transition from one state to another. (B) Violin plots show the mean squared deviation (MSD) of each subject's run-averaged transition probability matrix (TPM). Each point represents one subject, and horizontal lines indicate the median and interquartile range. The LBD group showed greater TPM deviation than HC, indicating increased state-switching instability. PD and AD/aMCI did not differ significantly from HC.

***: P (Bonferroni-adjusted) < 0.001

Key Findings

- Compared with PD, AD/aMCI, and HC, the LBD group showed a shift toward lower oscillatory frequencies, with significantly higher TBR ($P < 0.05$).
- State 4 emerged as the dominant LBD state, with significantly higher FO and SR than PD and HC (Bonferroni-adjusted $P < 0.05$); similar increases relative to AD/aMCI did not reach significance (**Figure 1**).
- LBD showed greater deviation of the run-averaged transition-probability matrix than HC, indicating less stable state transitions (**Figure 2**).
- State 4 showed the greatest TBR elevation in LBD relative to the other groups (**Figure 3A**).
- Within LBD, higher CAF scores correlated with higher TBR in multiple areas, including visual, inferior parietal, left inferior frontal, and right insular cortices (**Figure 3B**).

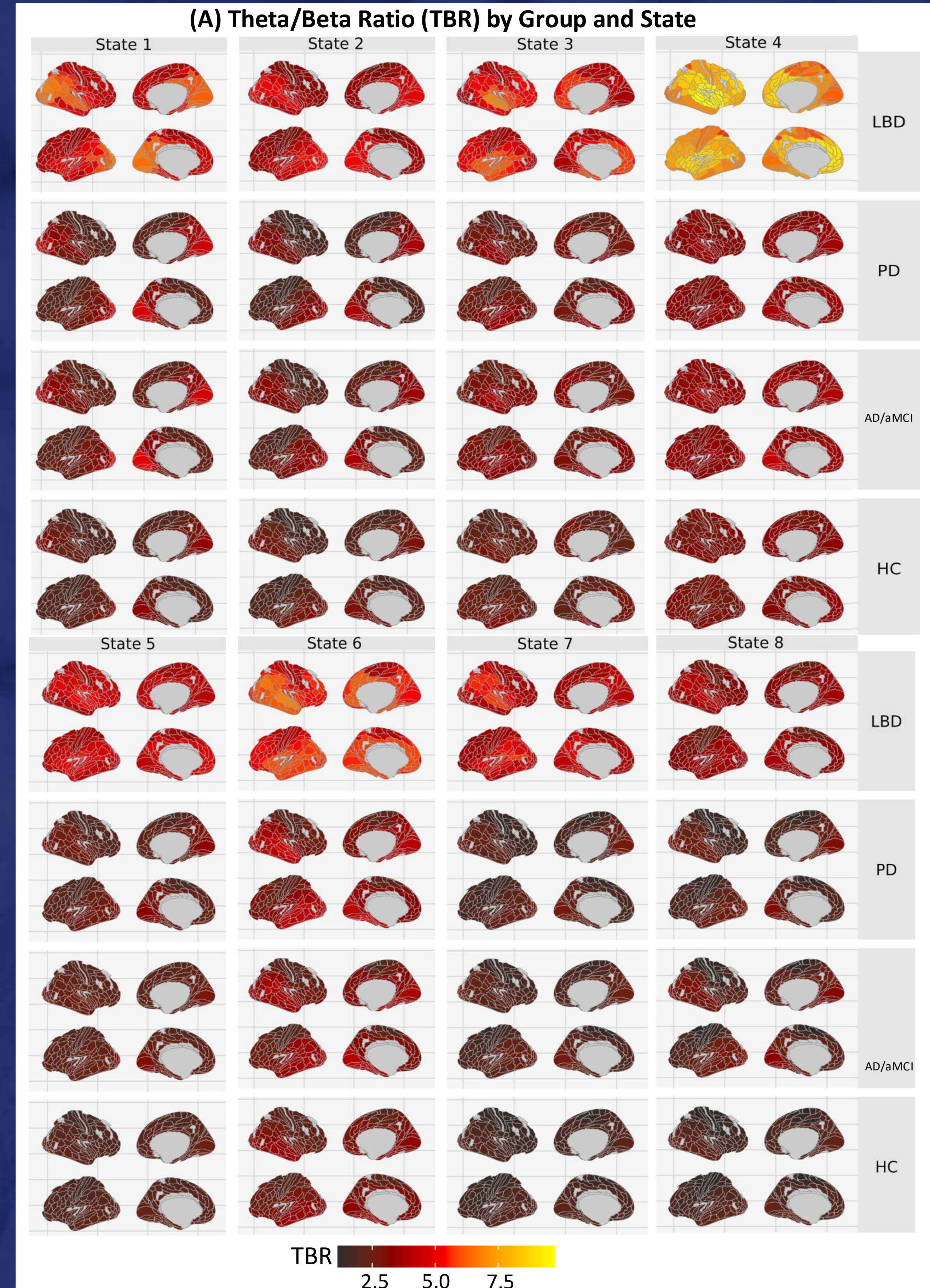


Figure 3. State-dependent cortical spectral slowing and its association with cognitive fluctuations in LBD. (A) Cortical surface maps of theta-to-beta ratio (TBR) across the eight HMM states in each diagnostic group. Higher TBR, indicating greater spectral slowing, is shown in yellow, whereas lower TBR is shown in dark red. In the LBD group, State 4 exhibited the highest TBR across multiple areas, relative to the same state in PD, AD/aMCI, and HC, as well as relative to the other states within LBD. (B) Cortical surface maps show Spearman correlations between CAF scores and regional TBR in the LBD group, highlighting cortical regions in which greater spectral slowing is associated with more severe cognitive fluctuations.

Conclusions

- LBD was characterized by a dominant brain state, increased transition instability and spectral slowing.
- Greater CF severity was associated with stronger regional slowing.
- These findings support resting-state MEG state dynamics and spectral slowing as candidate measures of LBD and CF, with utility for differential diagnosis and treatment monitoring.

Acknowledgments

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