

Abnormal global cortical dynamics at rest and during failures of working memory binding in Alzheimer's disease

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BACKGROUND

- Associative binding is key to normal memory function and is impaired in Alzheimer's disease (AD)
- Electrophysiological abnormalities are frequently reported in AD, including during tasks requiring associative binding
- We use a precision spatial working memory test to investigate the binding of distinct visual features (object and location) in working memory
- We test the hypothesis that misbinding is related to dynamic electrophysiological abnormalities in AD

METHODS

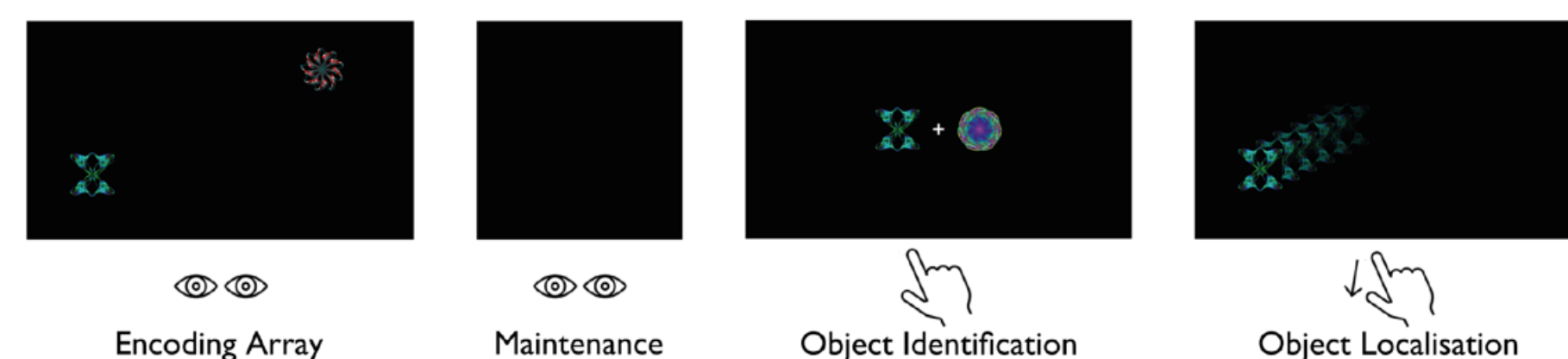
40 Alzheimer's disease patients (AD)

55% Male; Age 75.7 (62-90 years); 13 years education*; ADAS-COG*** = 37.85 (±11.75)

30 Healthy age-matched controls (HC)

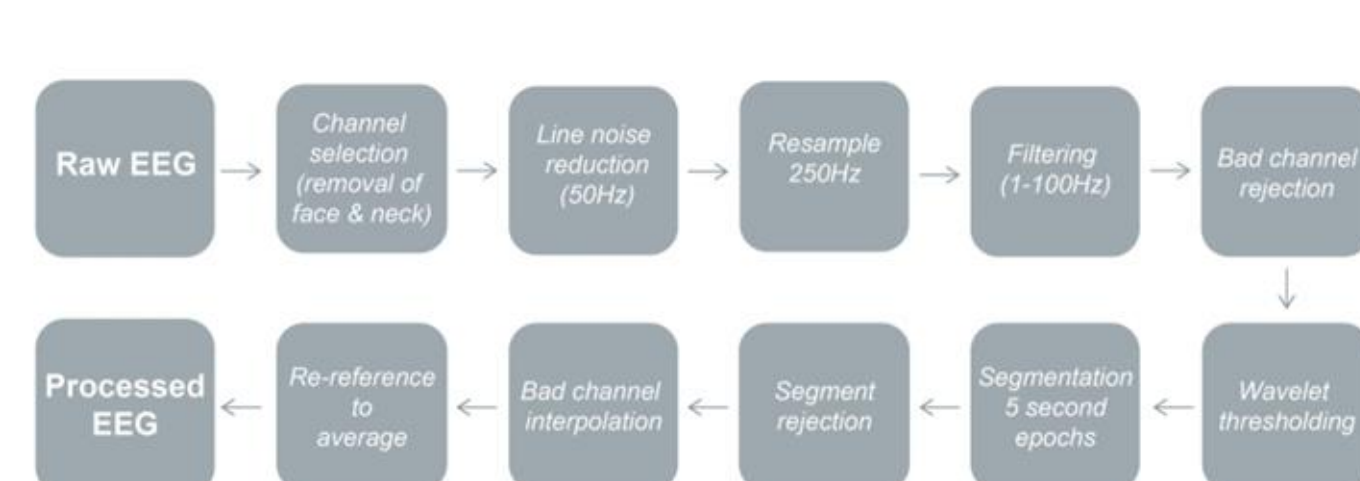
50% Male; Age 77.1 (63-85 years); 15 years education*; ADAS-COG*** = 10.23 (±4.43)

Precision spatial working memory task paradigm



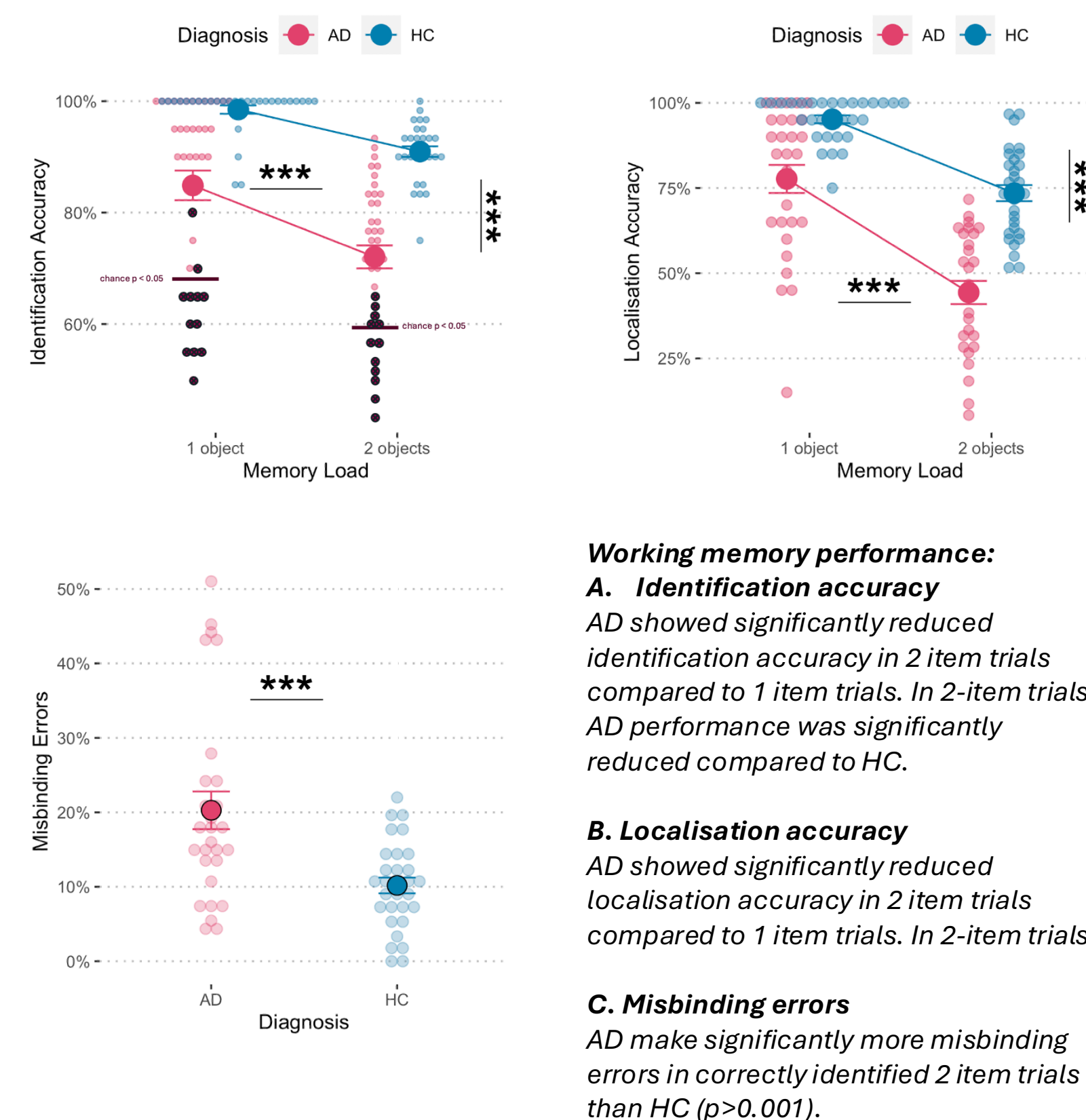
A precision working memory paradigm requiring the association of object and location information was delivered on a 27" touch-screen computer. The task consisted of 20 1-item trials and 60 2-item trials. To assess misbinding only 2 item correctly identified trials were considered.

High-density EEG

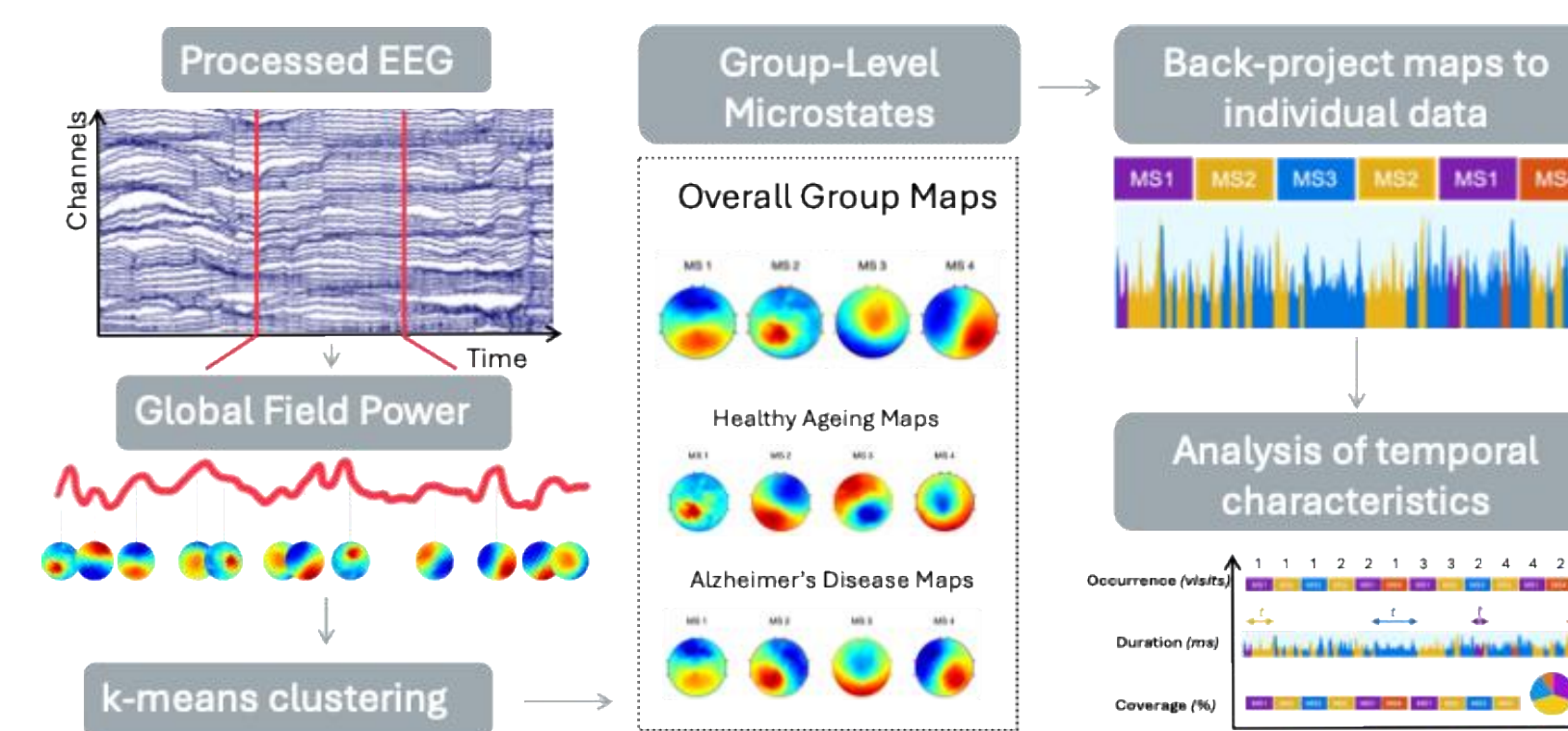


Five-minutes of high-density (256 channel) eyes-closed resting-state EEG was collected to assess electrophysiological abnormalities and their relationship to misbinding. EEG data were pre-processed as above.

AD show significant precision spatial working memory deficits

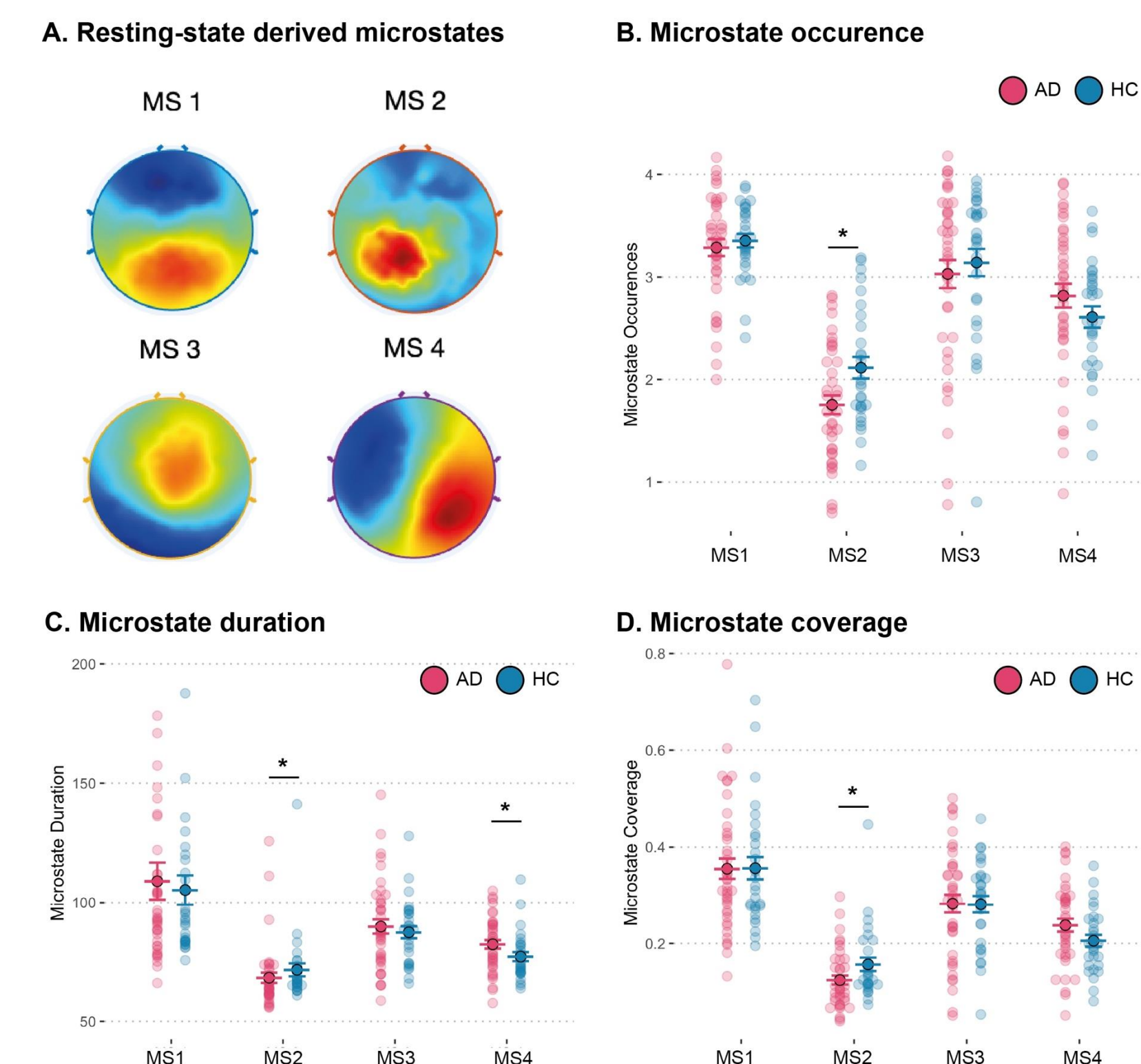


EEG microstate analysis



Microstate analysis was conducted separately for rest and task data. Global field power (GFP) was computed across all channels and peaks in GFP were extracted. Topographical maps at GFP peaks from all participants were submitted to k-means clustering. A common set of microstate templates were then back-projected to the continuous data. Subject-level temporal characteristics were computed for each microstate.

AD show abnormal cortical dynamics across EEG microstates



A. Four group-level microstates were derived from eyes-closed resting-state EEG.

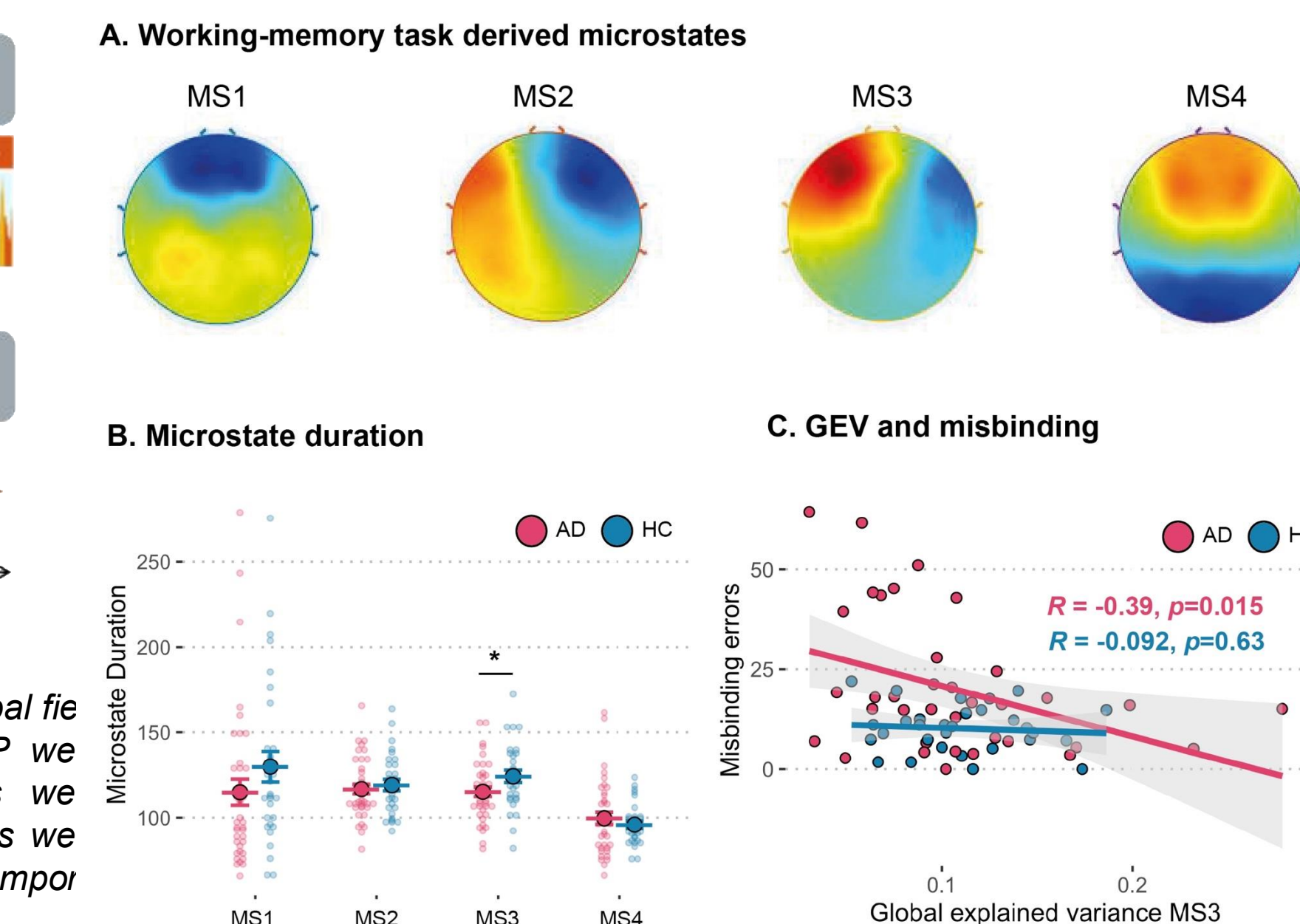
B. Microstate occurrence. AD showed significantly reduced transitions into MS2 compared to HC ($p > 0.05$).

C. Microstate duration. For each transition, AD dwelled for a shorter duration in MS2 and a longer duration in MS4 ($p > 0.05$).

D. Microstate coverage. The proportion of total time spent in MS2 was significantly reduced in AD compared to HC ($p > 0.05$).

AD is associated with abnormal cortical dynamics. At rest, patients show abnormalities in the time spent in microstates. These microstates are less consistently sustained, indicating a fragmentation of cortical activity.

Abnormal task induced microstates are associated with misbinding in AD



A. Four task-specific group-level microstates derived from the working-memory task.

B. Microstate duration. AD showed significantly reduced dwell time in MS3 compared to HC ($p > 0.05$).

C. Global explained variance. of MS3 was significantly associated with misbinding errors in AD.

During working memory binding, AD patients spend less time in a task-related microstate, which is less prominent when misbinding is greater.

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