

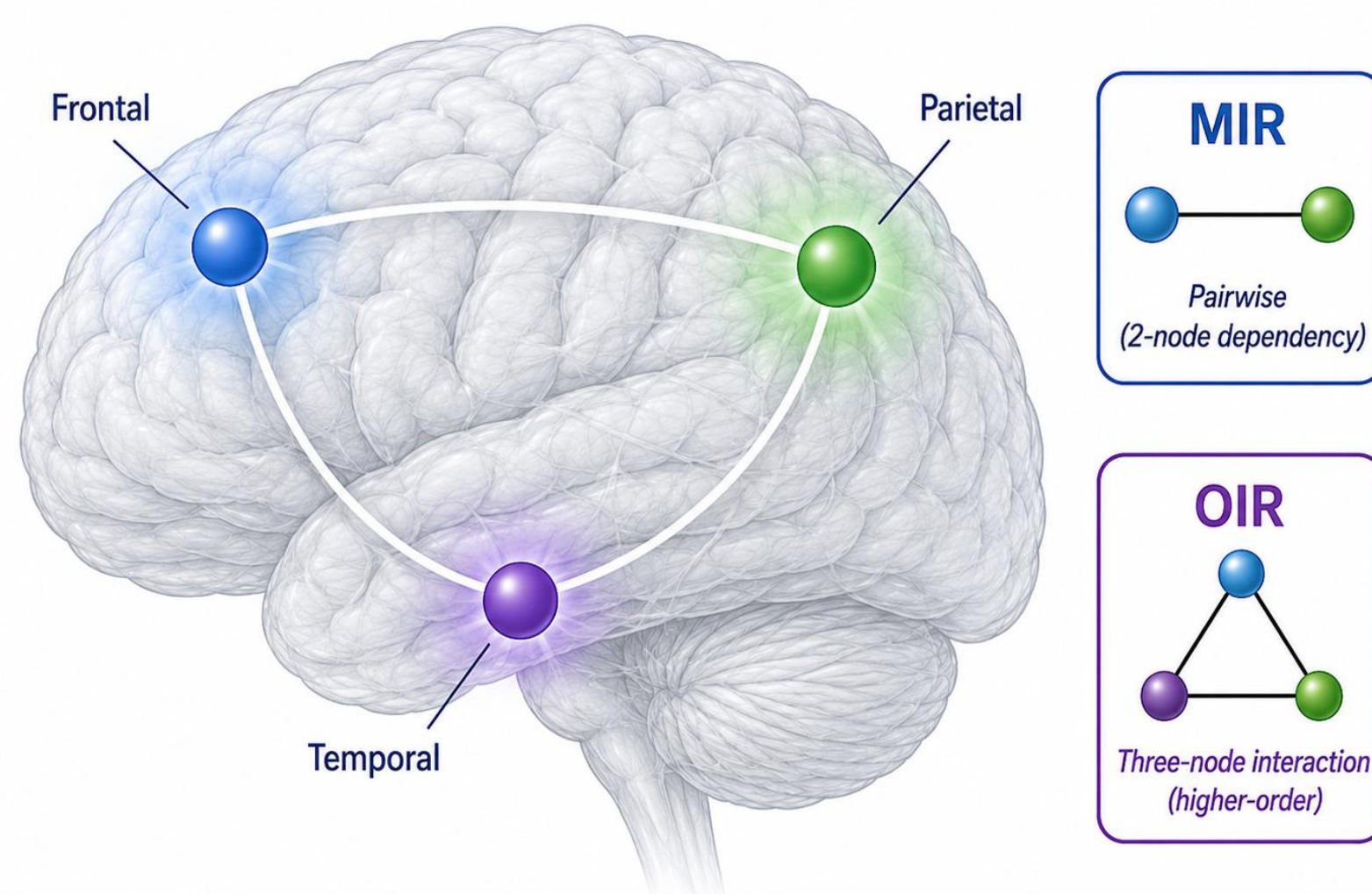
Three-Order Interactions in the Alpha Band of Default Mode Network EEGs Based on O-Information Rate: Insights from Aging and Alzheimer's Dementia

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Background

- ❖ Alpha-band DMN connectivity is disrupted in aging and Alzheimer's dementia (AD).
- ❖ Most EEG connectivity studies rely on pairwise measures, such as Mutual Information Rate (MIR).
- ❖ Pairwise methods cannot capture higher-order interactions among multiple brain regions.
- ❖ O-information rate (OIR) quantifies three-node interactions and distinguishes redundant from synergistic information processing.
- ❖ We tested whether OIR declines with aging and AD, improves classification beyond MIR, and correlates with global cognition (MoCA).



Methods

- Resting-state EEG from two independent cohorts (95 younger & 93 older; 44 healthy controls or HC & 84 amnesic mild cognitive impairment or aMCI & 41 AD) was source-localized using eLORETA.
- 14 DMN ROIs were grouped into frontal, temporal, and parietal blocks and analyzed in the alpha band (8–13 Hz).
- MIR quantified pairwise connectivity, whereas block-OIR quantified three-order interactions and their redundancy/synergy components using multivariate spectral analysis.
- Group differences used t-tests/ANCOVA with multiple-comparison correction; classification used repeated stratified 10-fold cross-validation with logistic regression, linear SVM, and random forest.

Results

Figure 1. Alpha-band OIR and redundancy were significantly lower **(A)** in older versus younger healthy adults and **(B)** in AD versus HC and aMCI; synergy showed no significant group differences. No significant HC–aMCI differences were observed.

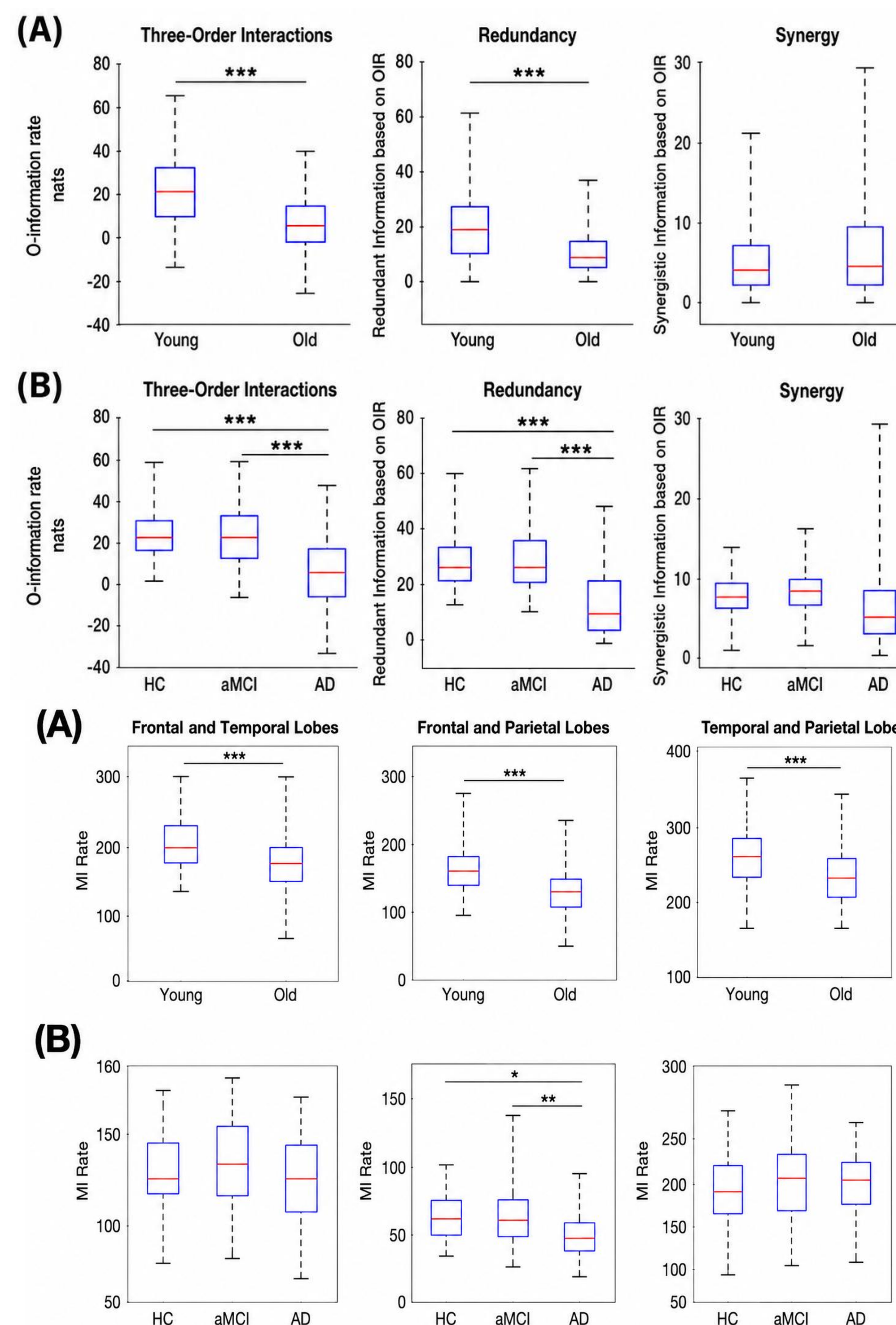
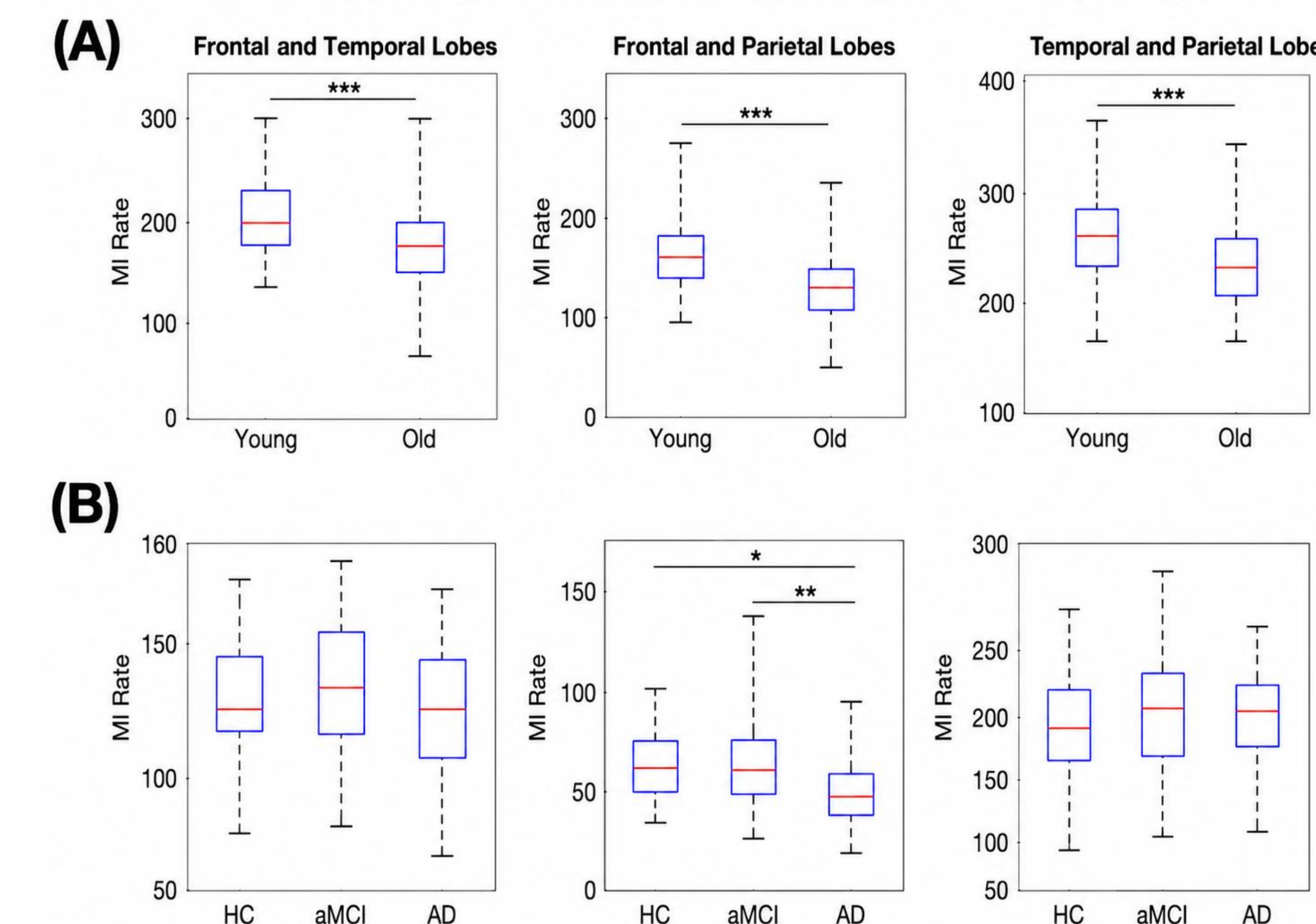


Figure 2. MIR decreased broadly with aging but showed limited AD-spectrum differences, mainly in frontal–parietal connectivity: **(A)** younger vs older healthy adults; **(B)** HC, aMCI, and AD groups.



Results

- ✓ OIR and redundancy were significantly reduced in older adults and in AD, whereas synergy showed no significant group differences.
- ✓ OIR-based metrics outperformed MIR for AD vs HC (AUC 0.93 vs 0.73) and AD vs aMCI (0.93 vs 0.71).
- ✓ OIR and redundancy correlated positively with MoCA after adjustment for age and education; MIR and synergy did not.

Discussion and Conclusions

- Higher-order DMN interactions decline with aging and AD, driven primarily by reduced redundancy, not synergy.
- OIR captured AD-related network disruption more sensitively than pairwise MIR, suggesting complementary information beyond conventional connectivity.
- OIR-based features showed strong discrimination for AD vs HC and AD vs aMCI (AUC = 0.93 for both contrasts).
- OIR and redundancy correlated positively with MoCA, supporting their relevance to cognitive status.
- OIR may serve as a promising network-level EEG biomarker, warranting validation alongside established AD biomarkers in larger independent cohorts.

Reference

- H. Azami, Y. Antonacci, D. M. Blumberger, H. J. Brooks, L. Faes, C. E. Fischer, A. Flint, N. Herrmann, S. Kumar, D. Gallagher, L. Mah, B. H. Mulsant, N. Schoer, B. G. Pollock, and T. K. Rajji, "Three-Order Interactions in the Alpha Band of Default Mode Network EEGs Based on O-Information Rate: Insights from Aging and Alzheimer's Disease," Alzheimer's Research & Therapy, in press, 2026.