

Alterations of the Hemodynamic Response in Mild Cognitive Impairment: Evidence for Early Neurovascular Uncoupling.

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INTRODUCTION

Neurovascular dysfunction is increasingly recognized as an early contributor to Alzheimer’s disease (AD), yet task-based fMRI typically emphasizes activation magnitude while assuming a fixed canonical hemodynamic response function (HRF). This approach overlooks potentially informative alterations in HRF shape that may reflect impaired cerebrovascular responsiveness and altered neurovascular coupling.

Objective: To characterize alterations in hemodynamic response during a motor task in older cognitively impaired and unimpaired adults.

METHODS

- Using data from the Alzheimer’s Disease Connectome Project, we examined hemodynamic response dynamics during a bilateral motor fMRI task.
- The analyses reported here were restricted to a motion-curated subset of participants (N = 143; mean framewise displacement < 0.2 mm), comprising 90 cognitively unimpaired (CU), 29 mild cognitive impairment (MCI), and 24 Alzheimer’s disease (AD) participants, with increasing mean age across groups and matching sex distributions and motion.
- We employed a deconvolution-based Finite Impulse Response (FIR) model (TENT function in AFNI).
- This enabled independent estimation of multiple HRF shape features: peak amplitude, time-to-peak (TTP), full-width at half-maximum (FWHM), and area under the curve (AUC), within predefined motor-related regions of interest.

RESULTS

- Across linear mixed-effects models adjusting for age, sex, scanner site, and head motion, effect-size estimates revealed biologically coherent trends despite not exceeding a strict $p < 0.05$ threshold.
- The most consistent finding was a reduction in hemodynamic response dispersion (FWHM) across primary and secondary motor regions in the MCI group relative to CU controls (Cohen’s $d \sim -0.4$).
- A concurrent trend toward reduced HRF peak amplitude ($d \sim -0.3$) was observed, whereas HRF latency (TTP) and integrated response (AUC) showed no consistent group differences. Robust effects were not observed in the AD group.

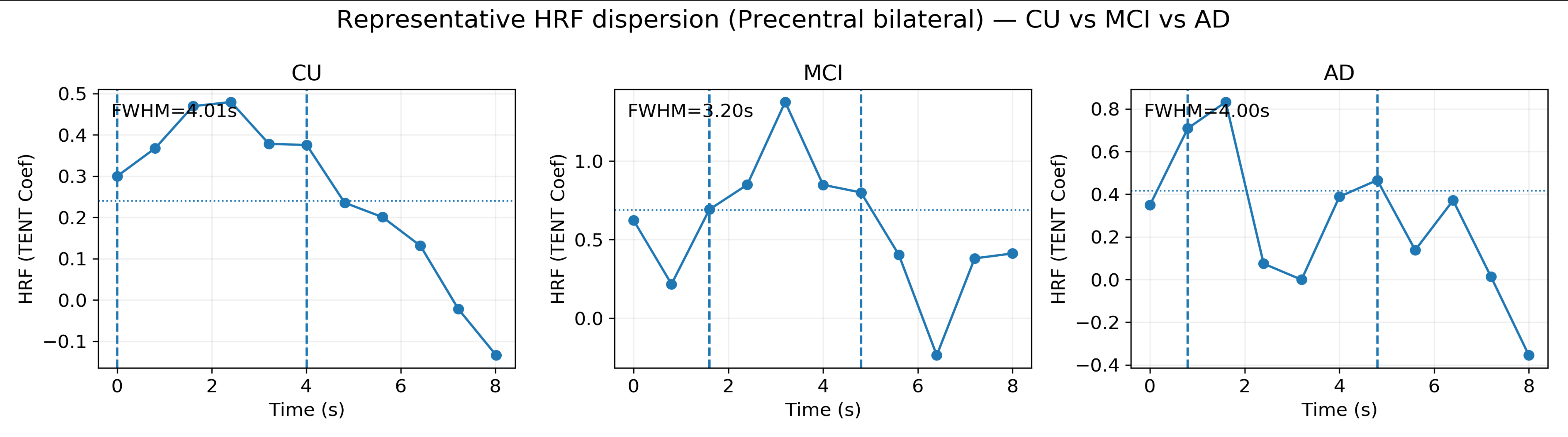
CONCLUSION

- HRF temporal dispersion appears to be a sensitive marker of early neurovascular dysfunction, detectable at the MCI stage.
- Increased inter-subject heterogeneity in AD may obscure group-level effects later in the disease course.
- These findings suggest that HRF shape metrics provide complementary and potentially more sensitive information than amplitude-based BOLD measures alone for characterizing neurovascular alterations in the Alzheimer’s continuum.

Consensus Dx	N	Age mean	Age sd	Education mean	Sex M/F	Handedness	Motion mean	Motion sd	Motion max
AD	24	74.91	7.4	14.7	10/14	Right=20, Left=2, Neither=1	0.114	0.042	0.448
CU	90	66.72	7.27	16.75	34/56	Right=76, Left=12, Neither=2	0.105	0.038	0.363
MCI	29	70.62	8.56	16.17	17/12	Right=25, Left=4	0.126	0.044	0.529

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Representative single-subject HRFs from bilateral motor cortex selected near the group median FWHM values for CU, MCI, and AD groups. Vertical dashed lines indicate FWHM. The MCI participant demonstrates a more temporally compact HRF.