

Astrocytic Biomarkers Show Stronger Links to Memory Brainwaves Than Classic AD Biomarkers



#3371

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Key Takeaway: Astrocyte-mediated processes emerge as primary drivers of working memory dysfunction. Combining astrocyte and amyloid/tau biomarkers is crucial for predicting MCI in asymptomatic older adults.

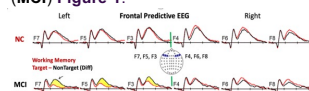
Electronic Poster Presentation: 7/13 Mon 3:30-4:15 pm

Emerging Role of Neurophysiological Signatures and Alzheimer's Biomarkers in Risk and Progression Assessment (Neurophysiology PIA)

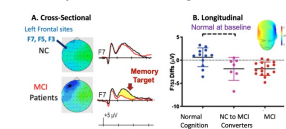
INTRODUCTION

Working memory, the ability to hold and manipulate information, is a core cognitive function and among the earliest to decline in MCI and dementia.

WM relies on precisely coordinated neural oscillations for communication with cortical networks. We have previously reported distinct frontal signature of Working Memory related Potentials (WMP) in older adults with Normal Cognition (NC) versus age-matched older adults with Mild Cognitive Impairment (MCI) Figure 1.



Left frontal WMP is predictive of MCI risk ~5 years before diagnosis.



immunobiomarker GFAP (astrocyte reactivity) and astrocyte-related MMP9 (a zinc-dependent enzyme remodeling extracellular matrix) have been reported in MCI and AD patients.

Res Q: How do astrocyte related biomarkers track WM brainwaves related network hyperexcitability, synaptic stress, and inflammation?

Hypothesis: Astrocytes and extracellular matrix, active partners in synaptic transmission and plasticity, would show a strong association to WMPs.

METHODS

Thirty-four older adults (19 women; mean age = 79 ± 8.5 years) with/without MCI from a longitudinal cohort participated or Lexington KY. 17 people also had biomarkers from UK-ADRC, US.

EEG was recorded during a modified delayed Match-to-Sample Working Memory task. **Principal component analysis (PCA)** on 64-channel EEG data generated PC1 and PC2 scores representing WMPs at frontal and temporal sites.

Multiple linear regressions examined associations between EEG PC scores and plasma biomarkers, including Aβ_{42/40}, pTau₁₈₁, total Tau, GFAP, MMP9, IL-6, and IL-8, and TNFα, adjusting for age, sex, education, and collection gap years.

RESULTS

GFAP and pTau₁₈₁ trends similarly

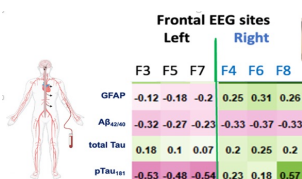
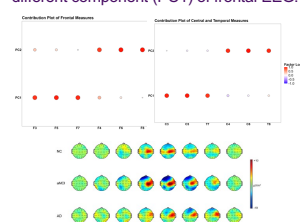


Figure 2. Aβ_{42/40}, pTau₁₈₁, total Tau, GFAP and six left (F3, 5, 7) and right (F2,4,6) frontal sites using difference waves of memory related potentials (Target – Nontarget).

RESULTS

Figure 3. Asymmetry of correlations. The decreased brainwaves (MCI-like) seen in left frontal sites significantly correlate with increased pTau₁₈₁, GFAP, and PC2. GFAP & pTau₁₈₁ trend in similar asymmetry ways, and Aβ_{42/40} & total Tau correlate to different component (PC1) of frontal EEG.



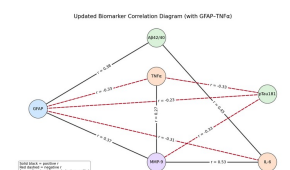
Reduced WMP are more strongly linked to elevated MMP9 and GFAP than Aβ and tau biomarkers.

Working Memory Potentials (WMP)	Table 1. Biomarkers	Correlation (r)
WMP PC1 (Frontal Laterality)	MMP9	-0.58
WMP (Prefront-Temp Target-Distractor)	MMP9	-0.57
WMP (Frontal Laterality)	GFAP	-0.41
WMP (Prefront-Temp Target-Distractor)	GFAP	-0.35
WMP (Frontal Laterality)	IL6	0.34
WMP (Prefront-Temp Target-Distractor)	IL6	-0.34
WMP (Frontal Laterality)	TNFα	-0.39
WMP (Prefront-Temp Target-Distractor)	TNFα	-0.37

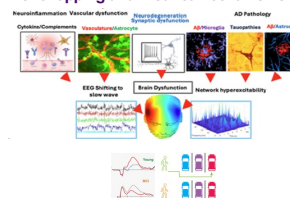
Aβ_{42/40}, pTau₁₈₁, total Tau, showed no or only weak associations (~0.2) with WMP PC1 PC2

CONCLUSIONS

DISCUSSIONS



Overlapping and Distinct Mechanisms



CONCLUSIONS

• **Memory network disruptions may link more to astrocyte reactivity and glial inflammation than amyloid buildup, at the preclinical and MCI stage.**

• **Amyloid and tau impact synapses and interact with glial cells in later disease stages.**

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