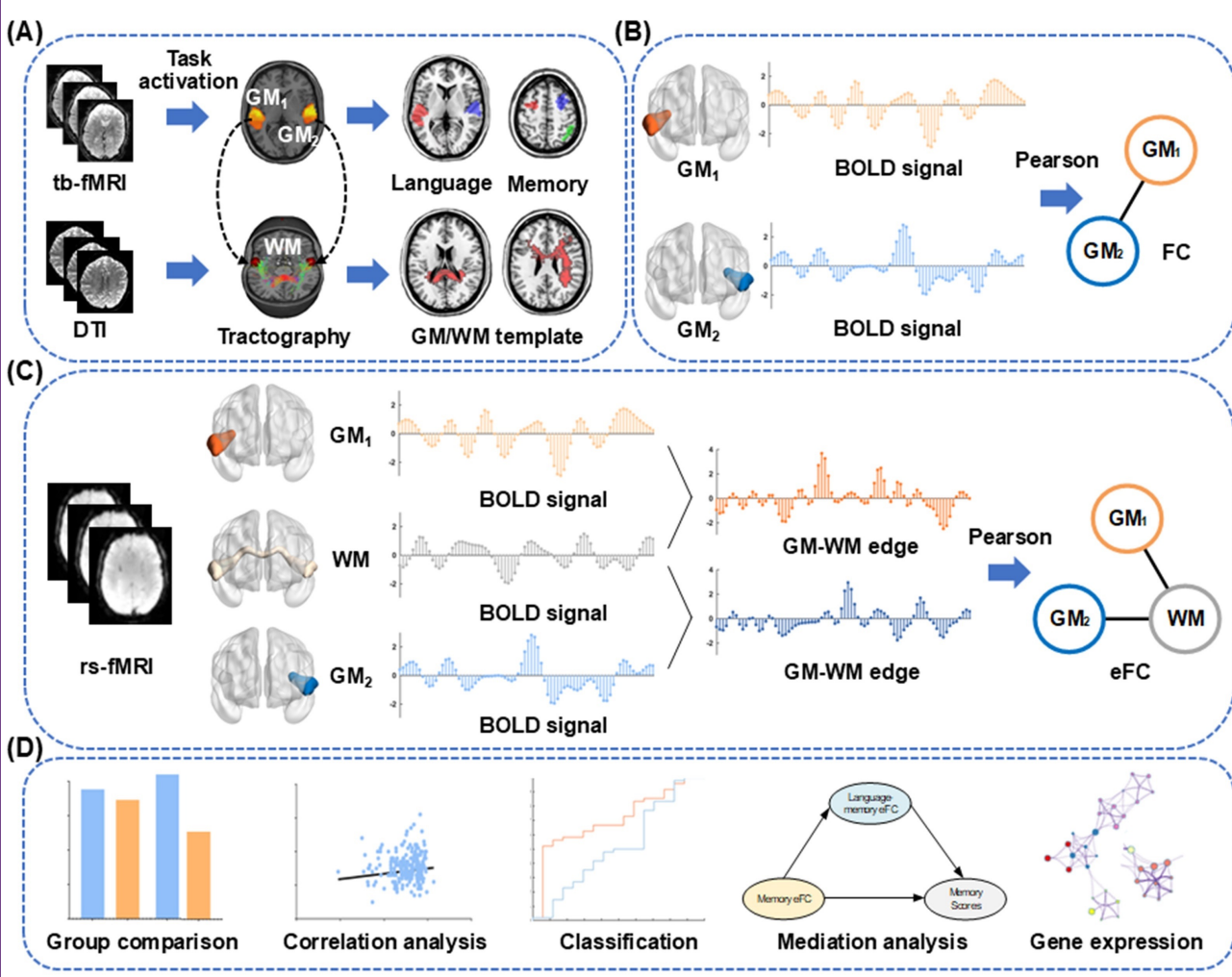
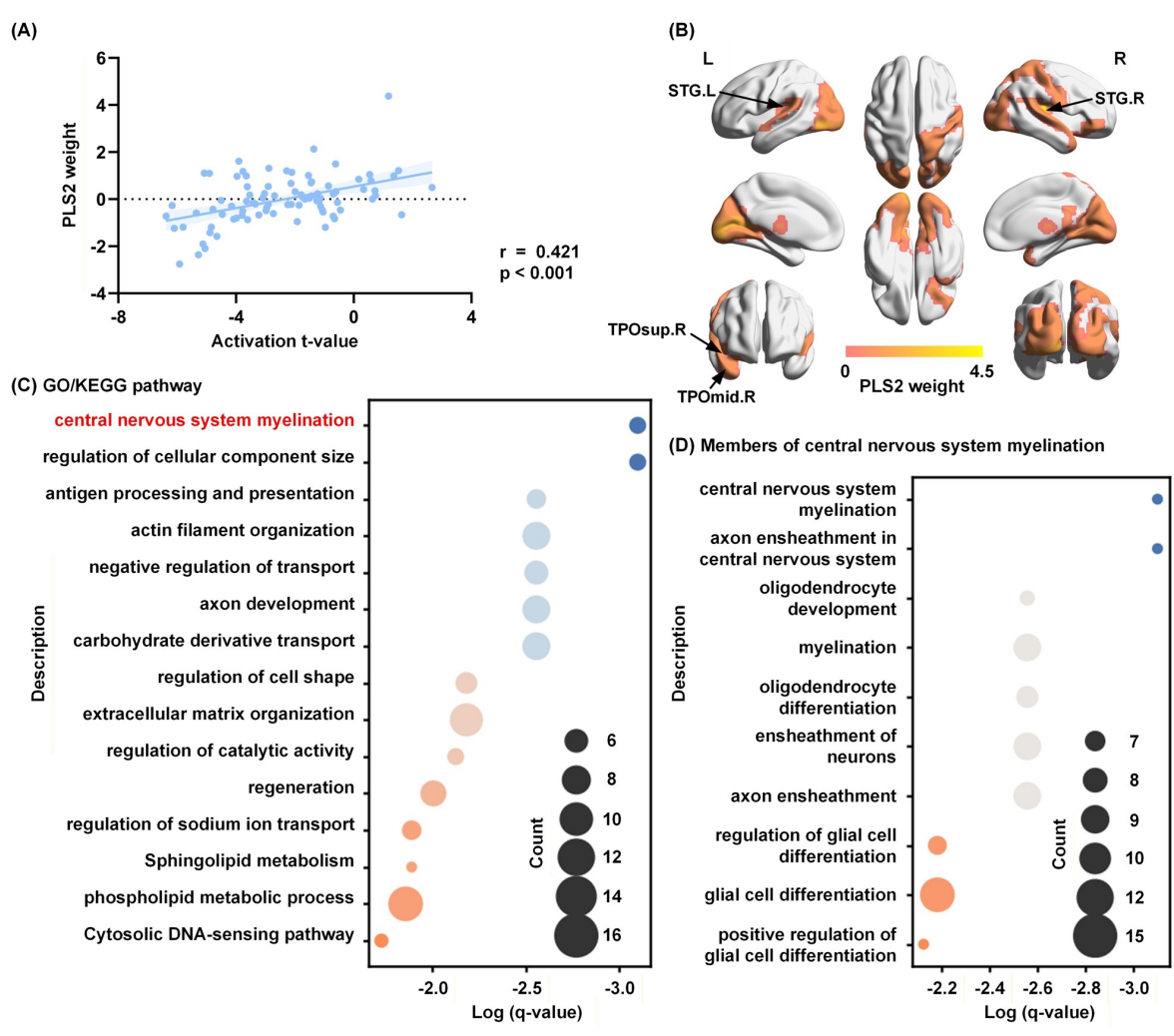


Brain Edge-centric Network Reveals Superior Temporal Gyrus Pathway As A Biomarker For Language-impaired Mild Cognitive Impairment

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Language-impaired mild cognitive impairment (iLMCI) is a heterogeneous pre-dementia stage, driven by distinct pathological mechanisms. We identified bilateral superior temporal gyrus edge-centric functional connectivity as a cross-culturally robust imaging biomarker for iLMCI. Integrating this imaging feature with plasma GFAP achieved an AUC of 0.835 for early pathological subtyping of iLMCI.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	CONTACT
To identify cross-culturally robust biomarkers for precise subtyping of language-impaired mild cognitive impairment (iLMCI). 	We developed a multi-modal framework integrating gray-white matter edge-centric functional connectivity (eFC) and plasma biomarkers in 609 cross-cultural participants. First, we constructed language- and memory-specific gray-white matter network templates from 244 healthy adults via task-based fMRI. We then validated this panel in 365 individuals from two independent Chinese/Western cohorts (controls, iLMCI, amnesic MCI). We analyzed correlations between imaging metrics and plasma biomarkers (Aβ, p-tau217, GFAP, NfL), and stratified iLMCI into Alzheimer's disease (AD)-origin and non-AD-origin subgroups using plasma p-tau217 as the pathological gold standard.	iLMCI exhibited consistently reduced bilateral superior temporal gyrus (STG) language network eFC across both cohorts ($p < 0.001$). This shared imaging abnormality was driven by distinct pathological mechanisms: AD-related tau pathology (elevated p-tau217, $r = -0.351$, $p < 0.012$), and astrocytic activation (elevated GFAP, $r = -0.445$, $p = 0.001$). The integrated eFC + GFAP model achieved an AUC of 0.835 for pathological subtyping, significantly surpassing single-modal models.	This study provides a novel, cross-cultural subtyping tool of iLMCI that facilitates early differential diagnosis and personalized intervention with strong clinical translational potential. 	Name: Qihao Guo Department of Gerontology, Shanghai Sixth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, 200233, China 