

Multimodal neural modeling links hippocampal excitation/inhibition balance to pattern separation and completion in healthy older adults

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Hippocampal E/I balance is stable in cognitively normal aging; and it sets a bias between pattern separation and completion.

INTRODUCTION

Hippocampal **hyperactivation** in preclinical Alzheimer's is linked to an excitation-inhibition (E/I) imbalance, and maladaptive dysfunction

Two episodic memory processes

PATTERN SEPARATION

Similar inputs → **distinct** representations

PATTERN COMPLETION

Similar inputs → **indistinct** representations

In the mnemonic similarity task (MST)

similar Lure → "SIMILAR" ✓

similar Lure → "OLD" ✗

THE QUESTION

Does E/I balance set a bias between pattern separation and completion in cognitively normal older adults?

METHODS

30 cognitively normal adults Aged 56-85 [70 ± 7] years

Multi-echo resting-state fMRI

Multi-echo MST fMRI

Multimodal analysis pipeline

rs-fMRI AFNI → Multiscale Neural Model Inversion → Hippocampal E/I balance

MST-fMRI AFNI → Lure-Similar (separation) vs Lure-Old (completion) → Task activation β coefficient

Linear regression E/I balance vs task activation

RESULTS

E/I balance is stable near zero

Inhibition → separation
Excitation → completion

Right Hippocampus

No significant finding in the left hippocampus

REFERENCES

1. Maestú Ageing Res Rev 2021; 2. Bakker Science 2008; 3. Yassa PNAS 2011; 4. Stark Trends Cogn Sci 2019; 5. Li Commun Med 2025.

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CONCLUSIONS

BALANCED E/I

Inhibitory control supports selective, efficient activation → robust pattern separation.

NORMATIVE

↓

LOSS OF INHIBITION

Reduced synaptic inhibition lowers representational specificity.

EARLY SHIFT

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TOWARD EARLY DETECTION

An accessible fMRI window into E/I balance, and the completion bias it predicts, as a candidate early marker of Alzheimer's risk.

PRECLINICAL ALZHEIMER'S

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