Direct Brain Stimulation Modulates Encoding States and Memory Performance in Humans

Highlights

- Intracranial brain stimulation has variable effects on episodic memory performance
- Stimulation increased memory performance when delivered in poor encoding states
- Recall-related brain activity increased after stimulation of poor encoding states
- Neural activity linked to contextual memory predicted encoding state modulation

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In Brief

Direct brain stimulation is a promising tool for modulating cognitive function. Ezzyat et al. show that stimulation differentially affects episodic memory encoding depending on its timing relative to the brain’s encoding state. The data suggest applications for closed-loop treatment of memory dysfunction.

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Direct Brain Stimulation Modulates Encoding States and Memory Performance in Humans

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SUMMARY

People often forget information because they fail to effectively encode it. Here, we test the hypothesis that targeted electrical stimulation can modulate neural encoding states and subsequent memory outcomes. Using recordings from neurosurgical epilepsy patients with intracranially implanted electrodes, we trained multivariate classifiers to discriminate spectral activity during learning that predicted remembering from forgetting, then decoded neural activity in later sessions in which we applied stimulation during learning. Stimulation increased encoding-state estimates and recall if delivered when the classifier indicated low encoding efficiency but had the reverse effect if stimulation was delivered when the classifier indicated high encoding efficiency. Higher encoding-state estimates from stimulation were associated with greater evidence of neural activity linked to contextual memory encoding. In identifying the conditions under which stimulation modulates memory, the data suggest strategies for therapeutically treating memory dysfunction.

INTRODUCTION

Memory depends on encoding processes that lay down neural representations of experiences for long-term storage [1]. Recordings taken during laboratory memory tasks demonstrate that neural activity in the hippocampus, medial temporal lobe (MTL) cortex, frontal lobe, and parietal lobe [2, 3] differentiates learned information that is likely to be remembered from information likely to be forgotten. These effects extend to other brain areas [4] and exist both during and prior to when a to-be-remembered stimulus is present [5–8]. This suggests that coordinated activity in a distributed neural network generates states that are responsible for effective memory encoding.

If variability in distributed neural network activity reflects fluctuation of encoding states that leads to differences in memory performance, then it should be possible to modulate memory by perturbing the brain’s encoding state directly [9]. We test this hypothesis using electrical stimulation delivered through electrodes implanted in the brains of epilepsy patients. Direct electrical stimulation allows for targeting focal brain structures in order to modulate activity in complex neural networks [10–12] and can be precisely timed to target specific encoding events, offering some advantages over non-invasive methods [13].

We predicted that stimulation’s effects on memory would depend on the brain’s encoding state at the time it is delivered. If the memory network is operating efficiently, stimulation should...
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