Glutamatergic modulation of working memory precision and serial biases

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Continuity of mnemonic contents in time contributes to integrating information into coherent memory representations. Recently, attractive response biases towards previously memorized locations in visuospatial delayed response tasks have been reported as evidence for continuous integration of memory contents between trials. These serial attractive biases emerge specifically during working memory (WM) delay. Assuming a beneficial role of attractive biases for the coherence of memory representations, psychiatric and neurological disorders could be characterized by atypical serial memory biases, along with impairments in memory maintenance and precision. We tested a unique population of patients recovering from anti-NMDAR encephalitis to study possible synaptic mechanisms of memory maintenance and continuous memory integration. These patients still have a decreased NMDAR mediated neurotransmission and reportedly suffer from long-term and WM deficits. We collected behavioral and electroencephalography (EEG) data from anti-NMDAR encephalitis patients and healthy control subjects performing a visuospatial delayed response task. While healthy controls' responses were significantly biased towards previous memoranda, serial attractive biases were absent in patients with reduced glutamatergic synaptic transmission. Moreover, encephalitis patients reported memorized spatial positions with lower precision than healthy controls. Both serial biases and WM precision normalized with recovery from the synaptopathy. In EEG data, we analyzed task-related changes in alpha-band power during WM delay and prior to stimulus onset. Both during WM encoding and delay, encephalitis patients showed reduced decodability of the stimulus, compared to healthy controls. Similarly, past stimulus locations could be decoded just before the onset of the new stimulus in healthy controls, but not in encephalitis patients. Persisting target-specific neural activity during delay and in the inter-trial interval might play a role in explaining behavioral differences between anti-NMDAR encephalitis patients and controls. Taken together, our findings suggest a fundamental role of the NMDAR in the within- and between-trial maintenance of short-term memory traces, potentially leading to deficits in the continuous integration of memory contents in NMDAR synaptopathies.

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