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Altered Plasticity of Microcircuit Dynamics in Anti-NMDAR Encephalitis and Schizophrenia

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Anti-NMDA receptor encephalitis is an autoimmune disease in which antibodies mistakenly attack NMDA receptors. Interestingly, anti-NMDAR encephalitis patients often present with initial psychosis similar to schizophrenia, another disease that has been associated with hypofunctional NMDARs. After treatment and hospital discharge, patients with anti-NMDAR encephalitis still have a pattern of cognitive impairment that parallels that of stabilized schizophrenia, and it normalizes after one or two years [1]. We have been investigating altered brain mechanisms in these two groups of stabilized patients longitudinally, seeking to generate hypotheses about what network dynamics deficits underlie their functional impairment. We have collected three pieces of evidence that point to altered cortical dynamics: (1) when performing a visuospatial working memory task, patients demonstrate in their reports a repulsive influence of previously memorized locations, contrary to the common attractive serial bias observed in neurotypical individuals [2]; (2) in the course of this task, memory decoding from EEG signals is diminished in patients and previous-trial code reactivations, which associate with attractive serial bias [3], are abolished [4]; and (3) in sleeping patients, slow waves do not show the dynamics of potentiation during individual deep sleep periods that are characteristic of healthy participants. Here, I will present a computational model of the cortical microcircuit that can accommodate all this evidence through the interaction of synaptic plasticity with different network dynamics of the model. Our simulations suggest that patients treated for anti-NMDAR encephalitis and persons with stabilized schizophrenia share a common substrate of impaired plasticity mechanisms that affects the dynamics and functions of cortical networks.

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