Altered plasticity of microcircuit dynamics explains working memory and sleep alterations in anti-NMDAR encephalitis and schizophrenia

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. 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 previously characterized one alteration that points to altered cortical dynamics: 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. Here we present an analysis of EEG collected in these patients while they sleep. We find that slow waves do not show the dynamics of potentiation during individual deep sleep periods that are characteristic of healthy participants. In addition, we assessed longitudinally the within-subject changes, suggesting a possible biomarker. A computational model of the cortical microcircuit can accommodate both working memory and sleep alterations 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 variety of dynamics and functions of cortical networks.