Title: Analysis and modelling of slow-wave changes in anti-NMDAR encephalitis and schizophrenia during sleep

Authors: Adrià Moran[1], Kanthida van Welzen[1], Amaia Muñoz-Lopetegi[1], Heike Stein[1], Mireia Rosa-Justicia[1], Helena Ariño[2], Eugenia Martinez-Hernandez[2], Laia Prades[1], Josep Dalmau[1], Joan Santamaria[1], Albert Compte[1]

Institution: [1] FRCB-IDIBAPS, Barcelona, [2] Hospital Clínic, Barcelona

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis (NMDARE) is an autoimmune disease with a variety of acute neuropsychiatric symptoms, including psychosis and sleep disturbances. Despite favorable response to treatment, complete recovery of cognitive function lasts months, suggesting residual NMDAR hypofunction. We hypothesized that NMDAR hypofunction could impair synaptic plasticity mechanisms engaged normally during slow-wave sleep. Here, we aimed at studying and modelling the mechanisms by which patients with NMDARE and schizophrenia (where NMDARs are likely involved in pathophysiology) had alterations in deep-sleep EEG (parameters/structure...) **I**n a longitudinal, single-center study, 43-channel EEG recordings were obtained from NMDARE patients (N=26, ages 10-57), shortly after successful treatment and in 3 successive sessions at 3, 6 and 12 months. Schizophrenia patients (N=22, ages 16-49) and healthy controls (N=34, ages 15-60) were tested in two sessions (1-year interval). Deep sleep slow waves were detected using the YASA algorithm and we characterized the slope changes along the night in the frontal cortex using mixed linear models. To control for strong age effects, we used the healthy control data to analyze departures in our patients from the predictions for their specific age. Relative to controls, encephalitis and schizophrenia patients showed a reduction in the slow-wave sleep potentiation phase that occurs at the start of each deep-sleep cycle. The rate of slow-wave changes later in the sleeping period was instead unchanged relative to healthy controls for both patient groups. We successfully replicated this phenomenon in a spiking network with short-term synaptic potentiation, previously used to explain working memory alterations in these patients (Stein et al. Nat Commun 2020), which transitioned to deep-sleep dynamics through cholinergic neuromodulation.