

Network properties underlying remission mechanisms at early stages of psychosis (EP): bridging hierarchical levels with a whole-brain computational approach.

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Psychotic disorders are characterised by great heterogeneity of disease progression, and the neural mechanisms underlying remission and relapse after a first psychotic episode remain unclear.

Here, we included resting-state fMRI and DTI data from 128 healthy controls and 88 patients with early psychosis, stratified based on their ability to recover after the first episode. We focused on differences between stage-III remitting-relapsing (EP3-R) and stage-III non-remitting (EP3-NR) patients. We first of all searched for stage-specific resting-state functional connectivity (FC) alterations. We then combined functional and structural empirical information of each condition into diverse generative whole-brain models to explore the interplay between the global and local dynamics underlying pathological mechanisms.

Opposite alterations in FC could be found in different subgroups of patients as compared to controls. In EP3-NR we observed a reduction of FC, aligned with the reduced structural connectivity found in previous studies, while EP3-R shows increased FC, potentially indicating a relevant compensatory mechanism. Using a theoretical model to fit the empirical data, we showed that, in the healthy condition, a subset of areas is characterized by increased stability to filter out irrelevant stimuli and prevent over synchronisation of the network. Additionally, we proved that node stability strongly correlates with combined functional-structural properties across nodes. We then showed how such crucial property is lost in EP3 patients. Notably, this alteration is more relevant in the remitting than in non-remitting patients, and correlates with changes in empirical functional strength. Therefore, it probably indicates a compensatory response to the reduced structural conductivity (global coupling) highlighted by the model in both EP3 conditions as compared to controls. Finally, we used a mean-field model approach to prove the role of excitation/inhibition modulation underlying this compensatory mechanism.

These results allow us to progress in understanding some of the key mechanisms in emergence and progression of psychosis.