Diffusion spectrum imaging connectomics: a biomarker for staging in psychotic disorders

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Target audience: Researchers and clinicians interested in psychosis investigation, clinical staging, brain network analysis, connectomics.

Purpose: Schizophrenia is a severe psychiatric disorder hypothesized to result from brain connectivity impairment. Precocious brain alterations can already be highlighted in the early stages of the pathology. According to the concept of clinical staging in psychotic disorders, brain connectivity might be more abnormal in more severe stages of the pathology, and altered connectivity measures might show progressive changes from prodromal to chronic phase. In a recent diffusion-based analysis on 16 chronic schizophrenia patients and 15 healthy controls, we identified a spatially distributed set of brain regions, dubbed affected core or a-core, driving the loss of global brain network properties. Investigating a cohort of 59 early psychosis patients, in the present study we question: (i) whether alterations of global brain network properties are already present in the early stage of the disease, and (ii) whether the a-core is precociously affected in the disease. We propose affected core network measures as possible markers of illness progression.

Methods: 59 first episode psychosis patients having met the threshold for psychosis according to the CAARMS criteria1 (FEP, 42M/17F, 26±6yo), and 59 age and gender matched healthy controls (CTRL, 40M/19F, 26±6yo) underwent an MRI session composed by MP-RAGE and diffusion spectrum imaging (DSI) sequences. Moreover, 16 chronic schizophrenia patients (SCHZ, 10M/6F, 26±6yo) and 15 age and gender matched healthy controls (CTRL, 8M/7F, 41±9yo) underwent the same MRI, as reported in7. For FEP patients, the number of hospitalizations before the MRI scan was recorded. Subject-wise structural connectivity matrices were generated combining MP-RAGE segmentation into 82 cortical and subcortical regions, and DSI reconstruction and streamline tractography, according to8. Brain connectivity matrices were weighted by the relative streamline density as in8. Global and local integration and segregation network properties were quantified through classical graph measures, and particularly global efficiency, transitivity, nodal closeness centrality, and nodal local efficiency. The affected core subnetwork was previously identified as driving the loss of global network properties in the cohort of 16 SCHZ patients and 15 CTRL, and includes 26 brain regions (figure (a)). In the present study the a-core of CTRL, FEP and SCHZ subjects was characterized by the following measures: efficiency and transitivity computed within the a-core subnetwork; generalized fractional anisotropy (gFA) and inverse apparent diffusion coefficient (iADC) averaged over the a-core edges; a-core centrality within the overall brain network. As in8, the a-core centrality was characterized by comparing targeted attack toward the a-core itself with repeated random attacks, and computing the efficiency z-score (a-core centrality disruption) after targeted attack relative to its reference distribution9. Non-parametric Mann–Whitney U test (MWU, α=0.05) was used for group comparison. Multiple comparison correction was applied when necessary (FDR=0.05). A generalized linear model (GLM) was used to assess the relationship between a-core measures and illness stages, i.e. early psychosis patients to chronic schizophrenia stages, while controlling by age and gender.

Conclusion: This study investigates psychosis progression with a neuroimaging and graph theory perspective. A distributed set of brain regions (a-core) affected in the chronic stage of the disease is precociously impaired in the early stages. We propose a-core network measures as possible markers of illness progression, while loss of global network efficiency and transitivity might characterize the advanced stages of the disease.