PEPSY Project

Background and rationale

One of the key objectives of modern psychiatry is to identify objective biomarkers that can help improve the diagnosis and prognosis of patients. This objective is more broadly embedded in the promise of 5P medicine: predictive, preventive, personalized, purpose-driven (and participatory). In the context of schizophrenia -one of the most disabling psychiatric disorders- prospective studies have shown that the first few months following a first episode of psychosis (FEP) constitute a crucial time window for optimizing the therapeutic strategy and improving long-term prognosis. Specifically, around 40% of patients will experience treatment failure, i.e. absence of symptomatic remission at 3 months, and these patients will have a considerably increased risk of developing life-long treatment-resistant schizophrenia (at 5 years, at 10 years). Identifying the non-responders early would enable adapting the first-line management of these patients, and consequently deliver precision care in order to preserve long-term prognosis.

In recent years, the combination of functional magnetic resonance imaging (fMRI) and machine-learning methods has made some progress towards the identification of biomarkers capable of predicting individual patient trajectories. Here we aim to use one of the most recent developments in this burgeoning field, that associates naturalistic fMRI (i.e. movie watching in the scanner) and functional connectivity mapping, that has shown great promise in predicting patient evolution, e.g. relapse in substance addiction, but has not yet been applied to schizophrenia.

Aim

In this project, we aim to leverage state-of-the-art analyses techniques applied to naturalistic fMRI, in order to identify functional brain connectivity markers predictive of the absence of remission at 3 months after an FEP. Specifically, we will use connectome-based modeling and dynamic independent component analysis (ICA). In addition, we will follow the evolution of these markers over the first three months and assess their relationship with the clinical and prognostic measures at 6 months and 1 year.

Methodology

FEP patients will be recruited across 4 early intervention centers in France (Lyon, Saint-Etienne, Clermont-Ferrand, Grenoble), before treatment initiation. Patients will be recruited via the extensive network collaborating with these early intervention centers. Initial assessments will include clinical and biological measures (standard workup and toxicology) renewed at 3, 6 and 12 months, in addition to neurocognitive evaluation and naturalistic fMRI, renewed at 3 months.

Experimental design: a training sample will be selected randomly (80% of patients) to build the model predicting the absence of remission, while a validation sample (20% of patients) will be used to assess the model's performance (sensitivity and specificity). After acquisition, fMRI data will be centralized and analyzed at a single site (Lyon). The dynamic ICA analyses will be performed in close collaboration with the group of Prof Fabio Sambataro (University of Padova, Italy), who's a world-leading expert on this approach.

Feasibility

- Long-time collaboration with the 4 early intervention centers for FEP (previous projects PRESTO and PRIMO), ensuring recruitment of patients within the timeframe of a PhD

- Joint supervision by a psychiatrist specializing in schizophrenia (E. Fakra) and a neuroscientist expert in neuroimaging (G. Sescousse), with a history of joint supervision and publications
- Collaborations with expert on machine learning: Institut Pasteur, Paris (V. Guillemot)
- Collaboration with expert on dynamic ICA: University of Padova (F. Sambataro)
- Funding for data acquisition (PHRC) and ethical approval already obtained

Implications

Early assessment of the likelihood of remission would open new avenues for optimal management of FEP, e.g. by prioritizing therapeutic strategies that are currently only offered as second- or third-line treatments. These therapeutic adjustments should have beneficial long-term consequences for schizophrenia, i.e. fewer patients developing a chronic disease, better prognosis and, consequently, a reduction in the considerable direct and indirect costs associated with this illness.

Contact details of supervisors

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Suggestion for secondment

We believe that a secondment in the lab of Prof Fabio Sambataro at the University of Padova would be highly beneficial for the project and the student. Firstly, Prof Sambataro is a recognized authority in the use of advanced methods for analyzing functional brain connectivity —the very methodology crucial to the success of this project. Their extensive expertise in this field is underscored by numerous publications, in particular in the domain of schizophrenia. Secondly, our labs share a history of collaboration, albeit without forging strong ties as of yet. Building upon our past engagements, this collaboration represents an excellent opportunity to strengthen the bonds between our research teams. By combining our respective strengths, we aim to create a synergy that will not only enhance the quality of the proposed project but also foster long-term partnerships between our labs. This collaboration with Prof Sambataro is poised to yield innovative outcomes, capitalizing on our collective knowledge and skills in the field of schizophrenia.
NB: Given the meticulous consideration given to the proposed secondment and the absence of comparable alternatives in terms of relevance, we put forth only one recommendation.