Background: The response to antipsychotic treatment in patients with psychosis is difficult to predict on the basis of the patient’s clinical features. As a result, patients are generally treated in a similar way, even though their response can vary dramatically.

Recent neuroimaging studies suggest that the pattern of brain abnormalities in patients with psychosis may vary in relation to treatment response. However, in many of these studies, patients had already been treated, and it was unclear if this had contributed to the findings.

Methods: In Optimise we obtained a structural Magnetic Resonance Imaging data from n=203 minimally treated patients at their first presentation for a psychotic episode. All patients then started treatment with standard doses of amisulpride. After 4 weeks, 56% were in symptomatic remission.

Results: We identified brain neoplasms in 3 patients, but the most common radiological findings were non-specific white matter T2-weighted hyperintensities (n=48); cavum septi pelludici (n=34); and arachnoid cysts (n=9). Cortical thickness, surface area, and gyriication were measured using Freesurfer (). Preliminary analyses applying machine learning to these measures at baseline indicated that symptomatic remission at 4 weeks could be predicted with an accuracy of 64%.

Discussion: These findings suggest that radiological assessment can identify abnormalities that require an alternative to conventional treatment in a minority of patients. In most patients with psychosis, neuroimaging abnormalities may be better detected using statistical approaches, and these have greater potential for the stratification of patients according to future antipsychotic response.

Concurrent Symposia

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31.4 GENETIC, IMMUNOLOGICAL AND BIOCHEMICAL MARKERS OF TREATMENT RESPONSE IN SCHIZOPHRENIA

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Background: One of the major shortcomings in the current treatment of schizophrenia is that we have no valid criteria in clinical practice to decide which antipsychotic treatment should be chosen first. This is why we need to define a blood-based biological signature of treatment response that can be easily tested at patient bedside and would also help to identify molecular mechanisms of treatment response by determining biological changes associated with symptom improvements.

Methods: Through a European consortium on Optimization of Treatment and Management of Schizophrenia in Europe (FP7, OPTiMiSE), we conducted a clinical trial on treatment response with Amisulpride in 500 subjects with first episode psychosis. For each patient, biological samples (DNA, RNA, plasma and serum) have been collected before treatment and during follow-up visits at weeks 4, 10 and 22, to measure biological changes associated with treatment initiation and with symptoms improvements. We combined multiple high-throughput technologies for transcriptome, genome, metabolome, proteome analyses before and after treatment.

Results: The transcriptome analysis conducted on 10,683 genes expressed in peripheral mononuclear cells identified significantly more genes differentially expressed after treatment in 112 patients who will be in remission after 4-weeks treatment than in 51 non-remitters. Using interaction network analysis, we identified biological pathways affected by Amisulpride. For some genes, the expression level was significantly correlated with symptom improvement. Moreover, some genes were already differentially expressed before treatment between remitters and non-remitters, suggesting they might be used to predict treatment outcome. In addition, we identified genetic variations associated with gene expression level and thus may explain individual difference in treatment response.

In parallel, as recent biological data have suggested a preponderant role of innate and adaptive immune system in the vulnerability to schizophrenia or in antipsychotic treatment response (Fond et al, 2015), we paid a particular attention to the analysis of inflammatory markers and the presence of auto-antibodies in patients’ sera. Circulating autoantibodies against glutamatergic N-methyl-D-aspartate receptor (NMDAR-Ab) have been reported in up to 10% of patients with psychotic disorders. In our study, we demonstrated the advantage of using cutting-edge methods to ascertain the presence of NMDAR-Ab in seropositive patients that cannot be clinically identified ([Jezekul et al, 2017]). Indeed, the only clinical characteristics found in NMDAR-Ab seropositive patients, was the high frequency of female patients, the presence of mild neurologic symptoms and signs of antipsychotic intolerance. In addition, using an advanced statistical classification algorithm, we defined clinically-based subgroups of patients who had specific cytokine signature associated to remission after 4-weeks of treatment, suggesting that these markers may be used to predict treatment response.

Discussion: Altogether, our multilevel biological approach resulted in the identification of promising biomarkers, which may be used both to predict drug response and remission in first psychosis episode.

32. DIGGING DEEPER IN THE PROTEOME OF SCHIZOPHRENIA

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Overall Abstract: Advances in genomics and transcriptomics have yielded novel insights for the pathophysiology of schizophrenia, moving the field forward by providing new substrates for the development of treatment strategies. Interestingly, this has led to a large gap in knowledge in the field, as the impact of genomic variability or alterations in transcript expression is dependent on the next level of gene expression. While proteomics has lagged behind other disciplines in schizophrenia research, several groups are utilizing proteomics approaches to ask and answer the largest possible questions in translational schizophrenia research. Proteomics has evolved as a field very quickly, going beyond the characterization of expression levels of one or a few proteins. With precise quantification of protein expression and degradation, characterization of post-translational modifications as well as the detection of low abundant proteins as putative biomarkers, we will show several different state-of-the-art proteomics approaches applied to the schizophrenia substrate. James Meador-Woodruff (University of Alabama at Birmingham) will provide a brief overview of the field, and present new data showing abnormalities of lipid and carbohydrate modifications on receptor proteins in schizophrenia, as well as abnormal levels of key enzymes associated with these abnormal protein modifications. Robert McCullumsmith (University of Cincinnati, USA) will add pivotal work analysis, we identified biological pathways affected by Amisulpride. For some genes, the expression level was significantly correlated with symptom improvement. Moreover, some genes were already differentially expressed before treatment between remitters and non-remitters, suggesting they might be used to predict treatment outcome. In addition, we identified genetic variations associated with gene expression level and thus may explain individual difference in treatment response.

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