F142. THE USE OF NEUROIMAGING MARKERS IN STRATIFIED DIAGNOSIS AND THERAPY OF SCHIZOPHRENIC AND AFFECTIVE DISORDERS

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Background: Neuroimaging techniques have been developed as important tools to investigate brain dysfunctions that underlie mental disorders. In particular, modern functional magnetic resonance imaging (fMRI) holds the promise to provide neurofunctional biomarkers for improved diagnosis, prognosis, and optimized treatment of schizophrenic and affective disorders.

Methods: Neurofunctional connectivity MRI using advanced experimental paradigms permits targeted investigation of the functional integrity of brain systems involved in the pathomechanisms of schizophrenic and affective disorders. From these investigations, pathophysiologically relevant neuroimaging biomarkers can be derived for differential diagnosis and tailored treatment selection.

Results: Possible neuroimaging biomarkers will be presented for the prediction of development and clinical course of schizophrenic and affective disorders as well as for the prediction of individual treatment responses. Further, recent neuroimaging findings on possible pathophysiological subtypes of schizophrenic and affective disorders will be discussed.

Discussion: These findings from functional neuroimaging studies may help to foster the development of precision medicine in psychiatry.

F143. PREDICTORS OF RELAPSE: PATIENT, DISEASE, COGNITIVE, AND FUNCTIONAL CHARACTERISTICS WITH COMT GENE VAL158MET POLYMORPHISM IN A 2-YEAR FOLLOW-UP

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Background: Schizophrenia is a severe and chronic mental illness characterized by continual relapses that may require hospitalization, changes in medications, arrests, emergency room hospitalizations, self-harm or suicidal behavior. Research has shown that costs associated with treatment received following relapse may constitute the largest share of treatment costs psychiatric illnesses. Although, demographic and clinical characteristics associated with relapse have been examined in previous research, information about potential predictors of relapse are limited. The aim of this study was to evaluate the effect of patient and disease characteristics, cognitive, functioning, and COMT gene polymorphism (rs4680) on relapse during 2-year following completion of an inpatient rehabilitation and cognitive treatment.

Methods: Data were taken from a COMT genotype and response to cognitive remediation study of schizophrenia in the United States conducted between 07/2005 and 10/2015 for inpatients with schizophrenia who were also participating in psychiatric rehabilitation. Patients with and without relapse 2 years following completion of the study were compared on clinical, demographic, cognitive, functional and COMT genotype characteristics. The COMT gene rs4680 polymorphism was genotyped using a DNA sequence detection system. Relapse or events identified as treatment failures include: arrest, psychiatric re-hospitalization, suicide, discontinuation of antipsychotic treatment due to inadequate efficacy, treatment supplementation with another antipsychotic due to inadequate efficacy, discontinuation of antipsychotic treatment due to safety or tolerability, or increase in the level of psychiatric services. Baseline (end of study, start of 2-year follow-up) predictors of subsequent relapse were also assessed. Univariate analysis and Cox’s regression was used to examine the effect of potential predictors on outcome.

Results: Of 140 subjects with eligible data, 91 (65.00%) relapsed during the 2-year follow-up period. Patients who relapsed were younger (< 45 years), higher number of previous hospitalizations, shorter chronicity of illness (< 10 years), PANSS baseline score of > 4 on the core PANSS items (conceptual disorganization, hallucinatory behavior, suspiciousness, unusual thought content), higher negative symptom factor, substance use, PSP score of < 60 and lower MCCB composite T score (> 2 SD below the mean). Univariate analysis shows that COMT rs4680 gene variants were different between relapse and stable groups. The COMT rs4680 gene had an interaction with PANSS baseline core item scores and MCCB composite score. Number of previous antipsychotic trials did not predict relapse.

Discussion: There is a high relapse rate within 2 years in chronic schizophrenia. Behavioral symptoms, aided by genetic and environmental factors common to this population (homelessness, unemployment, and social isolation) frequently lead to treatment failure. Knowing potential triggers of relapse can help in developing resources for this population to reduce treatment failures and associated costs.

F144. MUSCARINIC M1 RECEPTOR SIGNALLING UNDERLYING COGNITION IN PSYCHOTIC DISORDERS

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Background: Antipsychotic treatment has failed to improve cognitive deficits associated with psychotic disorders. This has led to an increased interest to revisit earlier implications from post-mortem studies that lowered muscarinic M1 receptor signaling may underlie these symptoms. This receptor is highly expressed in important regions for cognition such as the dorsolateral prefrontal cortex (DLPFC) and hippocampus, and administration of anti-muscarinic agents gives induce cognitive deficits in healthy volunteers. Administration of xanomeline, a M1/4 agonist in patients with schizophrenia resulted in improved learning and memory scores and decreased psychotic symptom severity. Therefore, the current study sought to examine alterations in muscarinic M1 receptor signaling in relation to cognitive functioning in medication free subjects with psychotic disorders and matched controls.

Methods: Muscarinic M1 binding potential (BPND) was measured using single photon emission computed tomography (SPECT) with the M1 selective radiopharmaceutical 123I-iiododextemide in the DLPFC and hippocampus in the psychotic group. Pharmacological functional magnetic resonance imaging (phMRI) with the M1 antagonist biperiden was used to assess differences in functional response on
the paired associate learning task (PAL) and emotion recognition task (ERT) adapted for fMRI from The Cambridge Neuropsychological Test Automated Battery in all subjects. The PAL task assessed encoding phase (learning) and retrieval (memory) of figure-place associations and the ERT task social cognition, both highly predictive of functional outcome. Cluster significance was set at Z>2.3, with cluster threshold correction at p<0.05.

Results: The current study included 26 (mean age: 27.68; 19 male/7 female) subjects with a psychotic disorder and 29 (mean age 25.63; 20 male/9 female) matched controls. Subjects with psychotic disorders recalled less figure place associations than controls (t=2.9, p=0.005) and were worse in recognizing different intensities of disgust emotions (t=2.26, p=0.03). Psychotic subjects showed a blunted response in functional reactivity to biperiden in the bilateral superior and medial frontal gyri with decreasing intensity of disgust facial expressions compared to controls, this blunted response was greatest in those with lower M1 BPND in the DLPFC. During encoding processes, psychotic subjects also showed differential reactivity to biperiden in the left middle frontal gyrus, insula, and caudate nucleus showing hypoactivation compared to controls. Greater hypoactivation was significantly associated with lower hippocampal M1 BPND. For retrieval both groups showed lowered activation under biperiden in the inferior frontal gyrus, but psychotic subjects failed to show increased activation with increasing cognitive load in the placebo condition, like the controls. Lower hippocampal M1 BPND in psychotic subjects was associated with lower activation of this region.

Discussion: Results show preliminary evidence for altered M1 signaling of prefrontal areas in psychotic disorders underlying social cognition and learning and memory processes. Additionally, results show an important role for the M1 receptor in the DLPFC and hippocampus in altered fronto-striatal activation underlying encoding processes. Lower hippocampal M1 BPND is related to more severe alterations in underlying functional activation in encoding and retrieval processes. Results further support the need for development of therapeutic strategies that focus on the M1 receptor to improve cognitive functioning and functional outcome in psychosis.

F145. WHAT ARE THE MAIN BRAIN CHANGES IN FMRI AFTER TREATMENT IN FIRST EPISODE PSYCHOSIS? A SYSTEMATIC REVIEW
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Background: There are many studies using structural MRI to explore the longitudinal course of F Episode Psychosis (FEP). On the other hand, there is a lack of functional MRI studies examining the longitudinal course of FEP. The aim of this work is to make a literature systematic review of these studies, to summarize the knowledge about longitudinal course of functional brain activity in FEP.

Methods: We followed the PRISMA guidelines for conducting systematic reviews and combined the use of electronic and manual systematic search methods, in the principal databases (MedLine, PubMed and Web of Science) using the query “longitudinal” AND “fMRI” AND “first episode psychosis” OR “first episode schizophrenia”. This search included (PERIODIC). The inclusion criteria were: a) FEP diagnose; b) at least 2 functional MRI scans (pre-post); c) both task and resting-state scans were included. The exclusion criteria were: a) chronic patients in the studied sample; b) structural imaging results; c) just 1 fMRI scan; d) reviews and metaanalysis.

Results: 202 records were identified through database searching. A total of 10 articles were selected. From them, a total of 276 FES sample were examined by fMRI. In all of these studies patients were diagnosed by structured interviews according to DSM-IV-TR or ICD-10 criteria. The average age of the FES sample was 26.64 years old. Nine of the 10 studies involved 2 scans with a mean interval between them of 7 months. Six of the 10 studies did the first scan without any antipsychotic treatment, but all of them had medication at follow-up scan. Most of the studies used a region of interest (ROI) approach, and examined the role mainly of these areas: limbic system, hippocampus, striatum and prefrontal cortex.

Five of the studies used a resting-state paradigm. The other 5 works implemented some cognitive or emotional task using some visual stimuli. Attending to the imaging results at baseline, most of studies found an hypoactivation of several brain areas, specially the limbic areas, like thalamus, amygdala and hippocampus. There are some other areas less activated compared to controls, including striatum, anterior cingulated cortex, orbito-frontal cortex, temporal gyrus and cerebellum posterior lobe.

At follow-up, almost all studies reported normalization of the hypoaivation levels found at baseline in the same regions. When the results at baseline were an increased activation, it also normalized at follow-up. There is only one study reporting an increased activity at baseline comparing to healthy volunteers which is still increased at follow-up scans.

Discussion: There are very few studies exploring fMRI longitudinal course of FEP patients. Our results in FEP are similar with other recent reviews in chronic schizophrenia samples, finding normalization (increase) of brain activity after antipsychotic treatment.

There are only visual or resting-state paradigms during scanning, which could explain some of the results. More investigations, involving other paradigms and related with psychopathological changes are needed, to test how the brain of the FEP patients change over time.

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F146. S-KETAMINE-INDUCED NMDA RECEPTOR BLOCKADE DURING NATURAL SPEECH PRODUCTION AND ITS IMPLICATIONS FOR FORMAL THOUGHT DISORDER IN SCHIZOPHRENIA: A PHARMACO-FMRI STUDY
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Background: FTD is a dimensional, phenomenologically defined construct, which can clinically be subdivided into positive (pFTD) versus negative (nFTD) as well as objective versus subjective symptom clusters. Structural and functional changes in the lateral temporal language areas have been related to formal thought disorder (FTD) in schizophrenia. Continuous, natural speech production activates the right lateral temporal lobe in schizophrenia, as opposed to the left in healthy subjects. Positive and negative FTD can be elicited in healthy subjects by glutamatergic NMDA blockade with ketamine. It is unclear, whether the glutamate system is related to the reversed hemispheric lateralization during speaking in patients.

Methods: In a double-blind, cross over, placebo-controlled study, 15 healthy, male, right-handed volunteers overtly described 7 pictures for 3 minutes each, while BOLD signal changes were acquired with fMRI. As