42. METABOLISM AND CO-MORBIDITIES IN PSYCHOTIC DISORDERS

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Overall Abstract: Schizophrenia is associated with a reduced life expectancy of 15–20 years due to a high prevalence of cardiovascular disease and metabolic syndrome. Unhealthy lifestyles and pharmacological side effects have been suggested to be a major cause of excess mortality rates in patients with psychotic disorders. However, abnormal glucose homeostasis, hyperinsulinemia and accumulation of visceral fat are already detected in drug-naïve first episode psychosis (FEP) patients, independently of obesity.

The aim of this symposium is to present the latest research on the theme of metabolic co-morbidities in psychotic disorders. Preliminary and published data from the symposium speakers suggests that FEP is associated with altered composition of gut microbiota, inflammation and lipid dysregulation including changes in the endocannabinoid system in the central nervous system. The studies presented in this symposium may offer new insights into the gut-brain axis in psychotic disorders as well as provide new evidence on the role of lipids as a potential underlying link between the aetiology of psychosis and the associated metabolic disturbances.

All four speakers are principal investigators in the European FP7 project METSY, which aims to identify and evaluate multi-modal peripheral and neuroimaging markers that can predict and monitor psychotic and metabolic symptoms, with specific focus on metabolic co-morbidities in psychotic disorders.

Oliver Howes will first introduce the topic, based on his recent meta-analysis (JAMA Psychiatry 2017; 74; 261–269) as well as present his recent research on neuroimaging of the endocannabinoid system in FEP.

Jaana Suvisaari will present her recent research on gut microbiome and inflammation in FEP. The findings so far suggest that FEP patients have specifically altered gut microbiome composition and increased levels of inflammation.

Tuulia Hyötyläinen will introduce the field of metabolomics in psychosis research and discuss the latest findings from at-risk mental state individuals and FEP patients. Recently published findings suggest that FEP patients who later rapidly gain weight are characterised by increased markers of liver fat at the baseline.

Jarmo Hietala will present neuroimaging studies of the endocannabinoid system using PET and the [18F]FMPEP-d2 tracer, a CB1R radioligand. These studies suggest a major sex difference in the brain CB1 receptor system as well as clear evidence for a dysregulated endocannabinoid system in first-episode psychosis.

Given the endocannabinoid system in the periphery promotes the development of fatty liver, the presented work together suggests that the endocannabinoid system may be the underlying link between the psychosis and the associated metabolic disturbances. This intriguing possibility with potential diagnostic and therapeutic implications will be discussed by the presenters. The discussant Matej Oresic is the coordinator of the METSY project.

42.1 BODY AND MIND: CARDIO-METABOLIC AND IMMUNE FUNCTION IN FIRST EPISODE PSYCHOSIS AND COMPARISON WITH CENTRAL NEUROFUNCTIONAL MEASURES

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Background: People with schizophrenia die on average 15–20 years earlier than the general population, and the mortality gap has grown in recent years. Non-CNS, particularly cardio-metabolic, causes account for the majority of this premature mortality. Abnormalities in the cardio-metabolic and immune system are well established in patients with schizophrenia, but it is unknown if abnormalities are present in people at risk of psychosis and at illness onset prior to antipsychotic treatment, and how they compare to neurofunctional measures. To address this, we conducted a series of meta-analyses and meta-regressions to determine the magnitude and consistency of findings and influence of antipsychotic treatment, exercise and other factors across cardio-metabolic parameters at onset of psychosis.

Methods: We conducted a meta-analysis of peripheral gluco-regulatory, immune and lipid measures and comparison with brain neurofunctional outcomes (including N-acetyl aspartate, gray matter volume and auditory P300 measures) in studies of clinical high risk samples and first episode psychosis, focusing on drug naïve patients. The entire PubMed, EMBase and PsychInfo databases were searched to identify relevant studies. Then we conducted a meta-review statistical comparison of cardio-metabolic and immune function with neurofunctional measures.

Results: 35 studies (>1500 patients and controls) were included in the meta-analyses. Interleukin-6 ($g=2.2$, $p=0.013$), and TNF-alpha ($g=0.94$, $p<0.01$) levels and fasting insulin and post-challenge glucose levels were elevated with moderate-large effect sizes ($g=0.4$, $p=0.01$; $g=0.6$, $p=0.007$ respectively) and cholesterol and low density lipoprotein levels were reduced ($g=-0.2$, $p=0.005$, and $g=-0.22$, $p=0.001$ respectively), whilst triglyceride levels were increased ($g=0.14$, $p<0.05$). These findings remained significant in drug naïve patients and after adjusting for the influence of a number of potential confounders (including body mass, exercise levels, smoking). N-acetyl aspartate levels in frontal cortex and auditory P300 amplitude ($g=0.83$, $p<0.0001$) were significantly altered in first episode patients relative to controls. The median effect sizes for cardiometabolic dysfunction ($g=0.41$) was comparable to that of the neurofunctional measures ($g=0.42$, $p>0.3$). Moreover, the median effect size for immune alterations ($g=1.3$) was significantly greater than that for neurofunctional measures ($p=0.002$).

Discussion: We demonstrate that effect sizes for markers of cardio-metabolic and immune disturbance are comparable in magnitude to those for markers of neurofunctional CNS disturbances from the onset of psychosis, suggesting schizophrenia involves multiple organ systems from illness onset. The three main pathoetiological models by which CNS and non-CNS abnormalities may co-occur in schizophrenia will be discussed. The shared genetic and environmental risk architecture between schizophrenia and cardiometabolic disorders suggests common aspects of pathoetiology.

42.2 INFLAMMATION AND GUT MICROBIOME IN FIRST-EPISODE PSYCHOSIS

Jaana Suvisaari*[,1], Outi Mantere[2], Jaakko Keinänen[1], Tuula Kieseppä[3], Maria Saarela[4], Robert Yolken[5], Jarno Honkanen[6]
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Background: Patients with first-onset psychosis have evidence of impaired glucose tolerance, but otherwise are metabolically healthy when traditional cardiovascular risk markers are used. After antipsychotic treatment is started, there is rapid weight gain and emergence of dyslipidemias. Weight gain and development of abdominal obesity is accompanied by worsening chronic low-grade inflammation. Activation of innate immunity is often present at the onset of disease. One unexplored mechanism possibly contributing to these problems is altered gut microbiota.

Methods: The Helsinki Early Psychosis Study recruited 97 patients with first-episode psychosis and 62 controls into a longitudinal study. Here, data on longitudinal changes in inflammation, weight gain and abdominal obesity during the first year of treatment in patients with first-episode