28.3 MINIMAL SELF IN SCHIZOPHRENIA: THE TIME PERSPECTIVE

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**Background:** The feeling of being one continuous individual in time is a natural evidence, which seems to be lost for patients with schizophrenia who display ‘minimal’ or ‘bodily’ self disorders. The continuity in time is a property of the ‘minimal’ self and its alteration could disrupt the sense of self. It has long been proposed that patients with schizophrenia experience a breakdown of the experience of time continuity. This proposal relies on the patients’ self-reports and the phenomenological analysis of their verbal descriptions. We will discuss to which extent recent experimental evidence supports this proposal and provides insight on the mechanisms underlying the perturbation of the experience of time continuity.

**Methods:** We used two original experimental approaches to test the link between the sense of self and time disorders in stabilized patients with schizophrenia and controls. The first relies on the parallel measure of time expectation and minimal self disorders, as evaluated with the EASE (phenomenological scale). Time expectation is indexed by the ability to benefit from the passage of time to react to a visual target: expectation increases with time, leading to shorter reaction times. The second approach consists in asking subjects to evaluate their feeling of control when tapping with a stylus on a virtual surface. The feeling of control is a component of agency, i.e. related to the bodily self. It can be altered even when subjects know the action to be their own, and may thus show alterations in the absence of delusions. In order to test the link between the feeling of control and timing, the haptic feedback (tactile and kinesthetic) was manipulated, with perceptible or imperceptible delays.

**Results:** Both tasks show that patients can expect sensory signals and react to unusual events to some extent: they increase their reaction times after trials with missing targets, and their feeling of control decreases when sensory feedbacks are delayed. However, the patients who feel as not being immersed in the world (EASE) do not benefit from the passage of time, consistent with previous results suggesting that patients have a difficulty to fluently follow the events flow. In the motor task, contrary to controls the patients’ feeling of control drops as soon as there is an imperceptible delay in the haptic feedback, and patients have difficulty to adjust sensory anticipation in case of delayed haptic feedback.

**Discussion:** The results suggest a link between timing and minimal self disorders. The patients are able to expect well-learned sensory signals. However, the patients with minimal self disorders (altered immersion in the world) display time disorders consistent with a breakdown of time continuity. All patients display disrupted time expectation when events become unusual or uncertain. Expecting events in time helps to link events with one another and thus participates to transform a chain of discontinuous events in a continuous flow. Conversely, fragile time expectations may lead to a sense of discontinuity, which could disrupt perceptions and especially the flow of bodily signals, thus contributing to bodily self disorders.

28.4 FLEXIBLE BODY BOUNDARY AND ALTERED MAPPING OF THE BODILY SELF IN THE SCHIZOPHRENIA SPECTRUM: CAUSES, PROCESSES AND POTENTIAL INTERVENTION

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**Background:** Our sense of embodied self depends on continuous spatiotemporal integration and predictive coding of multisensory signals to yield a stable internal landscape. However, schizophrenia is characterized by inconsistent mapping of the physical and parasomatic body space, autoscopic hallucinations and flexible body self boundary. We aimed to elucidate the specific roles of exteroceptive, proprioceptive and interoceptive systems in generating self disturbances. Lastly, if schizophrenia represents one end of the spectrum of bodily self disorders, it is also important to understand what lies at the other extreme end, represented by those whose prediction coding is honed to perfection from years of training (athletes) to gain insight into potential remediation strategies.

**Methods:** In Study 1, components of bodily self-disturbances were examined in individuals with schizophrenia (SZ), matched controls (CO) and prodromal participants (P) with tasks that assessed tactile perception (2-point discrimination task), susceptibility to proprioceptive-tactile illusions, multisensory integration, visual body mapping of emotions (emBODY), and interoceptive awareness (heartbeat detection task). Phenomenological dissociative experiences were captured with a novel picture-based inventory (BODI). In Study 2, we recruited healthy participants with extraordinary expertise to coordinate interoceptive, proprioceptive and exteroceptive signals to perform physical tasks (athletes), and compared their embodiment of emotions with that of matched controls and individuals with schizophrenia.

**Results:** Individuals with schizophrenia and prodromal participants were impaired in interoceptive awareness, exteroceptive tactile discrimination, and audio-visual integration compared with matched control groups. SZ and P also showed increased sensitivity to proprioceptive illusions, which was associated with increased dissociative experiences and positive syndromes. Bodily sensations associated with emotions were reduced in SZ and P compared to CO. Importantly, the spatial locations of embodied emotions were different in SZ compared with CO. Interestingly, athletes showed highly precise localization of embodied emotions compared with matched controls. Self-disturbances were exacerbated by social isolation regardless of diagnosis.

**Discussion:** These results suggest that mapping of internal signals to the experience of external world is inconsistent or incoherent, contributing to fragmented and discontinuous self experience in persons with schizophrenia. More specifically, proprioceptive prediction errors seem to contribute to abnormally flexible self boundary. Diminished access to interoceptive signals may lead to reduced mapping of bodily sensations. Embodied emotions were reduced in SZ and P compared to CO. Athletes seemed to have much more precisely tuned awareness of embodied emotions. These results are consistent with the framework of increased internal neural noise in schizophrenia, which could lead to both weakened and poorly integrated interoceptive, proprioceptive and exteroceptive signaling, and a fragmented sense of self. Athletes data suggest that it may be possible to remediate bodily self disturbances via physical training. These findings underscore the importance of bringing back the body to psychiatry.

**Plenary**

29. THE COMPLEX INTERACTIONS BETWEEN MIND AND BODY: IT TAKES A BRAIN TO CONTROL IMMUNITY

Asya Rolls
Israel Institute of Technology

**Overall Abstract:** Thoughts and emotions can impact physiology. This connection is evident by the emergence of disease following stress or recovery in response to placebo treatment. Nevertheless, this fundamental aspect of physiology remains largely unexplored. We have recently shown that activation of the brain’s reward system, which is active in positive emotional states and positive expectations, boosts immunity. In this talk, I will discuss how brain activity can regulate anti-bacterial and anti-tumor immunity and...
the potential implications for health and cancer therapy. Given the crucial role of the reward system in emotional processes, our findings offer a new mechanistic insight to the association between the patient’s psychological state, physical health and cancer progression.

**Concurrent Symposia**

**30. AN IMMUNE PATHOGENESIS OF PSYCHOSIS? EVIDENCE AND CHALLENGES FROM BENCH TO BEDSIDE**

Rachel Upthegrove  
University of Birmingham

**Overall Abstract:** The immune pathogenesis story of schizophrenia is gathering momentum, with increasing evidence from animal models, genetic, circulating biomarker and neuropathological studies. Potentially ground breaking new treatment approaches are proposed. However, it is vital that basic science and is equally matched by deep understanding of the complexity of clinical samples and management of multiple confounding factors when moving from bench to bedside. This presentation will pull together key speakers from a variety of fields, demonstrating the need for continued dialogue in translational, and reverse translational, approach. We will present findings from preclinical studies, genetic insights, longitudinal modelling of immune markers from population-based samples and detailed analysis from clinical samples. Data will include evidence of a prenatal immune activation and the potential transgenerational transmission of behavioural and neuronal abnormalities, co-variation of gene sets associated with both increased risk of schizophrenia and immune function (eg CSMD1, DPP4) together with CRP and peripheral inflammatory cytokine association with symptom profiles in both larger population and clinical samples. Thus, evidence presented will move from large data to fine grain analysis, animals to man and from bench to bedside. We aim to provide insights into early pathophysiological processes and forward avenues of research to the ultimate aim of elucidating the immune dysfunction impact on psychosis and future avenues for effectiveness of treatment.

**30.1 IMMUNE PATHOGENESIS OF PSYCHOSIS: THE CHALLENGE OF CO-MORBIDITY**

Rachel Upthegrove*, 1, Carl Krynicki1, Annalisa Gordianno1, Carmine Pariante2, Toby Rowland1, Nicholas Barnes1, 2, Steven Marwaha3, Benjamin Perry1, Paola Dazzan2, John Deakin4  
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**Background:** The immune pathogenesis story of schizophrenia is gathering momentum, with increasing evidence from genetic, circulating biomarker and neuropathological studies. New treatment approaches are being trialled. However immune dysfunction is not unique to schizophrenia, and circulating proinflammatory biomarkers identified in schizophrenia have also been identified in bipolar disorder and major depressive disorders. Similarly, in recent times there has been an increasing recognition of commonality across categorical diagnoses at a symptom level; as RDoC criteria acknowledge. For example, depressive symptoms are common in schizophrenia, hallucinations and delusional beliefs common in mood disorders and anhedonia a cross diagnostic challenge.

**Methods:** This presentation will include data of altered circulating proinflammatory markers from recently completed meta-analysis in first episode psychosis, established schizophrenia and bipolar disorder, highlighting the potential pluripotent inflammation pathway to mental disorders and outline a circulating cytokine profile at the onset and development of mental disorder as related to symptom specific profiles.

**Results:** Data on circulating inflammatory markers as related to symptom profiles cross-sectional and longitudinally will also be presented from the recently concluded NIHR funded BeneMin (The Benefits of Minocycline on negative symptoms in early phase psychosis) study.

**Discussion:** Future research should recognise co-morbidity, adopt a dimensional approach, or investigate symptom specific biomarkers at early stages of illness with numbers large enough to explore an immune specific clinical profile. This knowledge is essential in the developing story of inflammation and psychosis with the most potential in decades to translate into tailored effective treatment options.

**30.2 GENETIC VARIATION RELATED TO IMMUNE FUNCTION AND SCHIZOPHRENIA RISK: EVIDENCE FOR EFFECTS ON COGNITION**

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**Background:** Altered immune response is associated with many psychiatric disorders, but whether and how these changes confer increased risk remains unclear. In schizophrenia, robust association between illness risk and the MHC region general, and complement component 4 (C4) specifically, has been demonstrated, along with evidence from both gene enrichment and other genetic analysis highlighting the broader role of genetic variation in additional immune related networks to schizophrenia risk.

**Methods:** In a series of recent studies from our group, we examined the effects of immune-related genetic variation, based on gene ontology, implicated in neural function both behaviourally in samples of ~1200 cases and controls, and cortically in samples of ~150 cases and controls.

**Results:** We found that (1) increased predicted C4A RNA expression predicted poorer performance on measures of memory recall (p=0.016, corrected) and a pattern of reduced cortical activity in middle temporal cortex during a measure of visual processing (p<0.05, corrected); (2) variation in a curated gene set associated with both increased Schizophrenia risk and immune function (CSMD1, DPP4, SRPK2, TRIM8, STAT6, FES, EP300, TNFRSF13c) were associated with both variation in both episodic memory and general cognitive ability.

**Discussion:** Based on these findings we conclude that schizophrenia risk associated with variation within immune related genes is likely to be conferred at least partly via effects on cognition, and the molecular mechanisms involved may include effects on inflammatory response.

**30.3 ASSOCIATION BETWEEN SERUM C-REACTIVE PROTEIN, POSITIVE AND NEGATIVE SYMPTOMS OF PSYCHOSIS IN A GENERAL POPULATION-BASED BIRTH COHORT**

Golam Khandaker*, 1, Jan Stochl1, Stanley Zammit1, Robert Dantzler3, Glyn Lewis3, Peter B. Jones1  
1University of Cambridge; 2Cardiff University; 3University of Houston in Texas MD Anderson Cancer Centre; 4University College London

**Background:** An association between low-grade inflammation and symptoms commonly shared between psychiatric disorders may explain the trans-diagnostic effects of inflammation, and lead to novel mechanistic hypotheses. Schizophrenia includes diverse symptoms, but the relationship