age-related cognitive change was moderated by CR, such that only patients with low CR showed evidence of exaggerated fluid reasoning decline that paralleled the exaggerated age-related deterioration of underpinning brain structures seen in all patients.

Conclusions: In schizophrenia–spectrum illness, CR may negate ageing effects on fluid cognition by conferring resilience against pathologically exaggerated structural brain deterioration through some form of compensation. CR may represent an important modifier that could explain inconsistencies in brain structure - cognition outcomes evident in the extant literature.

4.2 NETWORK CONNECTIVITY IN DISTINCT COGNITIVE SUBTYPES ACROSS THE PSYCHOSES

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Background: Substantial cognitive heterogeneity exists both within and between diagnostic categories in patients with psychosis. Given that cognitive deficits are highly predictive of outcomes in patients and are believed to be underpinned by neurobiological abnormalities in relevant circuits, characterization of cognitive heterogeneity is a critical step toward understanding neurobiological and functional correlates of this key symptom dimension. Thus, we identified patients with psychosis with intact or impaired cognitive profiles, and examined clinical, functional, and resting state connectivity both between patient groups and compared to controls. We also compared findings in patients in the early course of illness versus chronicity to explore these associations across illness stages.

Methods: Patients with affective or non-affective psychosis (n=120) and healthy controls (n=31) were assessed using measures of cognition, clinical symptoms, and community functioning, and administered an FMRI scan to measure resting state functional connectivity (RSFC). Cognitive scores were used to group patients with and without cognitive dysfunction. Clinical, functional, and resting state data were compared across all three groups; RSFC data were examined controlling for demographic and clinical variables.

Results: Compared to controls, both cognitively intact and cognitively impaired patients showed decreased network connectivity in frontoparietal control and motor networks. Patients with cognitive impairment showed additional frontoparietal connectivity reductions compared to patients with intact cognition, particularly in subnetwork A, even after controlling for measures of illness severity (e.g. clinical symptoms, medication). Similar findings were detected in both early and chronic illness phases.

Conclusions: Heterogeneity in cognitive ability among patients with psychosis can be leveraged to disentangle the relative effects of cognitive dysfunction and presence of an underlying psychotic illness using RSFC. Additionally, early and chronic patients showed similar patterns of association between cognition, network connectivity, and functioning. These findings suggest at least partially separable effects of presence of a psychotic disorder and neurocognitive impairment contributing to network connectivity in psychosis that is detectable across illness stages.

4.3 HIPPOCAMPAL SUBFIELDS AND VISUOSPATIAL ASSOCIATIVE MEMORY ACROSS STAGES OF SCHIZOPHRENIA-SPECTRUM DISORDER

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Background: Previous studies indicate that visuospatial associative memory ability deteriorates over the course of psychotic illness, with substantial impairments observed in individuals with chronic schizophrenia. However, the neural underpinnings of poor performance on this task in schizophrenia have not previously been investigated. While previous studies have identified relationships between hippocampal volumes and memory performance in schizophrenia, few studies have examined the role of hippocampal subfields in illness-related memory deficits, and no study has examined potential differences across varying illness stages. The current study aimed to investigate whether individuals with early and established psychosis exhibited differential relationships between visuospatial associative memory and hippocampal subfield volumes.

Methods: Measurements of visuospatial associative memory performance and MRI scans were obtained from 52 individuals with a chronic schizophrenia-spectrum disorder, 28 individuals with first-episode psychosis (FEP), 52 older healthy controls, and 28 younger healthy controls.

Results: Both chronic and FEP patients had impaired visuospatial associative memory performance relative to healthy controls. However, only chronic patients showed hippocampal subfield volume loss relative to healthy controls. Both chronic and FEP patients demonstrated relationships between visuospatial associative memory performance and hippocampal subfield volumes in the CA4/dentate gyrus and the stratum that were not observed in healthy controls. There were no group by volume interactions when chronic and FEP patients were compared.

Conclusions: The current study extends the findings of previous studies by identifying particular hippocampal subfields, including the hippocampal stratum layers and the dentate gyrus, that appear to be related to visuospatial associative memory ability in individuals with both chronic and first-episode psychosis. These regions are particularly vulnerable to the effects of chronic stress and inflammation, suggesting that these factors may contribute to memory impairment in psychotic disorders.

4.4 THE INFLAMMATORY CASCADE AND COGNITIVE OUTCOME IN A TRANSDIAGNOSTIC COHORT

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Background: There is evidence of an inflammatory response during acute episodes in patients with schizophrenia (SZ) and bipolar disorder (BD), which is believed to contribute to cognitive and functional deficits. Less is known about inflammation during remitted phases of these disorders and to date, sample sizes and included markers have been limited.

Methods: In this study we assessed 350 adult participants (230 with BD; 70 with SZ; 50 healthy controls) across a comprehensive battery of tasks including general cognition, social/affectionally-based cognition, and reward processing. We collected peripheral blood at the time of assessment to assay multiple levels of the immune response including primary proinflammatory cytokines (IL-1β), IL-6, TNF-α), soluble antagonists/receptors regulating the primary cytokines (IL-1RA, sIL6-R, sTNF-R1, sTNF-R2), secondary mediators of inflammatory damage (CRP and IP-10), and angio-neurotrophic factors (VEGF, BDNF). We first evaluated each marker for its association with cognition individually and then incorporated the known interactions among these measures in an effort to recapitulate this complex biological process.
Results: Results suggest that inflammation overall contributes significantly to cognitive outcome in both BD and SZ, even in remitted patients. Individual markers may contribute specifically to certain aspects of cognitive impairment (e.g. TNF-α/TNFRI/TNFRII influence cognitive flexibility; VEGF influences reward processing; IL-6/IL-6r influence measures of spatial processing; and IL-1RA/IL-1p influence social cognition). The relationship between course of illness (e.g. age at onset, number prior episodes, psychosis) and inflammation will also be discussed.

Conclusions: The inclusion of both primary and secondary mediators of inflammation is important as the effects of the primary proinflammatory cytokines can be blocked by a number of decoy receptors and soluble antagonists; evidence of increased levels of the secondary mediators provides additional - and novel- information on the overall function of the immune system in major psychiatric disorders.

5. SOCIAL COGNITION AND FUNCTIONING IN PSYCHOSIS: MECHANISMS, INTERVENTION AND PREDICTION OF TREATMENT SUCCESS

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This symposium will combine state-of-art findings from different complementary neuroimaging studies of social interactions and therapeutic interventions that aim to improve social functioning in psychosis. For the first time, we focus on the multi-dimensional concept of social functioning in which we combine pioneering findings on therapeutic interventions to refine prediction and optimization of therapeutic response using machine learning.

Four different speakers with distinct expertise in complementary research will delineate precise methods of assessing neuroimaging-based assessments of social cognition, investigating how social cognition can be modulated by cognitive behavioral therapy and neuro-cognitive training in psychosis, to improve functional outcome. We will conclude the symposium by demonstrating how we can use machine learning to predict response to treatment at the individual level.

Specifically, we will address four key-questions:
1) How is the (in)sensitivity to social reward during social interactions expressed on the neural level?
2) Can social cognitive training increase activity within frontal-striatal circuits and improve reward processing?
3) Does cognitive behavioral therapy that is particularly focused on social activation ameliorate negative symptoms and improve global functioning?
4) Are the effects durable?

First, Dr. Fett will present her recent research on the neural insensitivity to social reward in early psychosis. This group of patients has shown altered caudate and temporo-parietal junction activation as compared to healthy controls in two interactive fMRI trust games which they played against a pre-programmed cooperative and unfair partner during fMRI scanning. Symptoms were assessed with the Positive and Negative Syndrome – and the Green Paranoid Thought Scale. Region of interest analyses included right caudate, medial pre-frontal cortex (mPFC) and right temporo-parietal junction (rTPJ), involved in reward and ToM processing.

Methods: Twenty-two participants with early psychosis and 25 controls (male, 13–19 years) participated in two interactive trust games which were played against a pre-programmed cooperative and unfair partner during fMRI scanning. Symptoms were assessed with the Positive and Negative Syndrome – and the Green Paranoid Thought Scale. Region of interest analyses included right caudate, medial pre-frontal cortex (mPFC) and right temporo-parietal junction (rTPJ), involved in reward and ToM processing.

Results: Both groups showed similar levels of trust towards others. However, individuals with psychosis failed to activate the caudate differentially between the cooperative and unfair conditions while making decisions to trust. During cooperative returns patients showed reduced and controls increased caudate activation, suggesting reduced social reward sensitivity in psychosis. Patients demonstrated greater rTPJ activation relative to controls, possibly pointing towards compensatory cognitive mechanisms, which underlie similar behavior. No group differences emerged in mPFC activation.

Conclusions: Early psychosis is associated with an aberrant neural sensitivity to social reward. This could lead to a feedback loop whereby lacking social reward fosters reduced social motivation and social isolation. Intact trust during cooperation in early, relative to later illness stages could be related to an increased compensatory demand on ToM processing.

5.2 COGNITIVE BEHAVIORAL THERAPY FOR SOCIAL ACTIVATION IN RECENT-ONSET PSYCHOSIS: RANDOMIZED CONTROLLED TRIAL

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Background: Negative symptoms largely account for poor outcome in psychotic disorders but remain difficult to treat. A cognitive–behavioral approach to these symptoms showed promise in chronic schizophrenia patients. We explored whether a combination of group and individual treatment focused on social activation (CBTsa) could benefit patients recently diagnosed with a psychotic disorder.

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