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

Lana Kambeitz-Ilankovic
Ludwig-Maximilian University, Munich

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 assaying 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 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 Paranoic 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 Paranoic 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 other. 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.

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.

5.1 THE NEURAL MECHANISMS OF SOCIAL REWARD IN EARLY PSYCHOSIS

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Background: In chronic psychosis, the loss of trust towards others is associated with a neural insensitivity to social reward and reduced theory of mind (ToM). The aim of this study was to investigate whether these mechanisms are already present in early psychosis.

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 Paranoic Thought Scale. Region of interest analyses included right caudate, medial pre-frontal cortex (mPFC) and reward processing.

Results: Both groups showed similar levels of trust towards other. 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 (CBTs) could benefit patients recently diagnosed with a psychotic disorder.
Methods: A single-blind randomized controlled trial enrolled 99 participants recently diagnosed with schizophrenia or a related disorder that received treatment as usual (TAU; n 50), or TAU plus CBTsa (n 49). Negative symptoms (Brief Negative Symptom Scale) and social withdrawal (Positive and Negative Syndrome Scale) were primary outcomes. Secondary outcome measures included dysfunctional beliefs (Dysfunctional Attitudes Scale-Defeatist Performance Attitude), stigma (ISMIS), and symptom severity and functioning as measured with the Global Assessment of Functioning (GAF). Outcomes were compared directly posttreatment and at follow-up (6 months posttreatment).

Results: Intention-to-treat analyses showed significant improvement in GAF symptoms (p < .02, d = 0.36) and a decrease in negative symptoms on trend level (p = .08, d = 0.29) in CBTsa compared to TAU at posttreatment. These group differences were no longer apparent at 6 months follow-up. Social withdrawal and negative symptoms improved over time in both conditions.

Conclusions: The current trial showed small positive effects on symptom severity posttreatment but did not demonstrate maintenance of long-term effects in favor of the CBTsa group. Findings suggest that the treatment duration may have been too short to change dysfunctional beliefs, a potentially important maintaining factor of negative symptom severity. Longer intervention periods in later, more stable stages of the illness when intensive standard treatment has tapered off may yield more beneficial effects.

5.3 SOCIAL COGNITIVE TRAINING IMPROVES MOTIVATION TO EARN REWARDING OUTCOMES IN PSYCHOSIS

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Background: Amotivation in schizophrenia is a central predictor of poor functioning and is thought to occur due to deficits in anticipating future rewards, suggesting that impairments in anticipating pleasure can contribute to functional disability in schizophrenia. In healthy comparison (HC) participants, reward motivation is associated with anticipatory activity in frontal-striatal networks. By contrast, schizophrenia (SZ) participants show hypoactivation within these frontal-striatal networks during this motivated anticipatory brain state. Here, we investigated whether intensive computerized social cognitive training in schizophrenia could increase activity within frontal-striatal circuits to improve motivation during the anticipatory phase of stimuli that predicted upcoming reward.

Methods: In our double-blind randomized clinical controlled trial, SZ were randomly assigned to either social cognitive training or cognitive training (without the social training component). We used a standard Monetary Incentive Delay task (MID), to assay the neural patterns as associated with immediate anticipation and outcome of monetary reward (gain) in each group, at baseline and after training intervention. In the MID paradigm, at the beginning of each trial, a cue (i.e., marking the onset of an anticipatory period) indicates the amount of money at stake in each group, at baseline and after training intervention. In the MID paradigm, at the beginning of each trial, a cue (i.e., marking the onset of an anticipatory period) indicates the amount of money at stake that the patient won or not won money. We assessed whole-brain activity specifically relating to immediate reward anticipation by contrasting neural activity during the anticipation to win money with no outcome trials (i.e., Win cue vs. Null cue). Group analyses focused on mixed effects repeated measures ANOVA to delineate neural activation that mediated reward motivation, which was specific to the social cognitive group.

Results: After 16 weeks of social cognitive training, we found that patients showed significant increases in the medial prefrontal cortex, which had been initially hypoeactive at baseline (i.e., not activated during reward anticipation). Further, increased medial prefrontal activity induced improvements in patients’ ability to earn rewarding outcomes after social cognitive training compared to baseline. These neural improvements were not observed in our control patients who completed cognitive training (without the social training portion), suggesting that these brain-behavioral improvements were specific to the social cognitive training patient group.

Conclusions: Together, our promising results indicate that cognitive and neural impairments in schizophrenia are not fixed. Promisingly, we can target the points of neural system dysfunction with behavioral interventions to induce significant improvements in social cognition that have critical relevance for real-world functioning.

5.4 INDIVIDUALIZED PREDICTION OF FUNCTIONAL OUTCOMES IN SCHIZOPHRENIA PATIENTS IN RESPONSE TO NEURO-COGNITIVE INTERVENTION: A MACHINE LEARNING ANALYSIS

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Background: Computer-based neurocognitive interventions (cNCI) represent an innovative way to improve cognitive functioning and functional outcome in schizophrenia patients. However, evidence suggests that cNCI can be highly effective in some, though not all patients. This variability is most likely due to intermediate neurocognitive and brain phenotypes that moderate the neuroplastic response induced by the respective training paradigms. Previous studies also suggested that prospective short- and long-term functional outcomes can be individually approximated in early psychosis using not only clinical, but also structural neuroimaging data (sMRI) (Kambeitz-Ilankovic et al., 2015, Koutsouleris et al., 2018). We employed multivariate pattern analysis (MVPA) to identify patterns in sMRI data predictive of functional outcome after 40 hours of cNCI.

Methods: The support vector machine (SVM) pipeline wrapped grey matter (GM) volume matrices into repeated nested, cross-validation that was used to train a multi-modal prediction of good (18) vs. poor functional outcome (17) that underwent 40 hours of neuro-cognitive training including social cognition exercises. The generalization capability of the model was evaluated by applying this model to 18 unseen schizophrenia patients that underwent 50 hours cognitive intervention. Finally, we used General Assessment of Functioning Scale (GAF) to determine good or poor outcome status at baseline and follow up. We aimed to set a clinically meaningful cut-off by applying median split to GAF scores to differentiate poor and good “outcomers” of both samples.

Results: Volume-based pattern classification predicted good vs. poor outcome status at follow-up with a balanced accuracy of 74.5% (sensitivity 64.7%, specificity 84.2%) as determined by nested cross-validation. Neuroanatomical prediction of functional outcome was nearly as accurate when predicting the difference in global level of functioning at two different time points (baseline and follow-up) with balanced accuracy of 65% (sensitivity 66.7%, specificity 64.7%). Both models were significant (p<0.05) and generalizable onto independent intervention sample with balanced accuracy of 68.8% and 58%, respectively. The neuroanatomical markers that showed diagnostic specificity for prediction of poor functional outcome

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