SIRS 2019 Abstracts

Dr. Palaniyappan shows that the highly resolved, dynamic course of glutamate and glutathione changes using 7T functional spectroscopy is a promising marker of early prognostic course that advances our approach to identifying an oxidative stress-prone subgroup of patients with schizophrenia.

Dr. Lahti used magnetoencephalography (MEG), 7T Spectroscopy, and 7T fMRI during task performance to show that illness-related changes in MRI and MEG signals were correlated, while changes in the highly resolved glutamate and NAA represented an independent underlying pathological mechanism.

Dr. Hulshoff Pol will leverage the power of cortical layer-specific investigations using 7T as well as spectroscopy to demonstrate illness-related abnormalities in the GABAergic system. She will present data showing that patients with SCZ have significantly lower prefrontal GABA/Cr ratios that were inversely correlated with cognitive functioning.

Dr. Laura Rowland will lead the discussion, proffering further means to probe mechanistic aspects of psychosis as well as highlighting the future of a discovery-led approach in 7T neuroimaging in psychotic disorders.

### 30.1 RELATIONSHIP BETWEEN CORTICAL EXCITATION AND INHIBITION, TASK-INDUCED BOLD RESPONSE AND FUNCTIONAL CONNECTIVITY: A COMBINED MR SPECTROSCOPY AND FUNCTIONAL MRI STUDY AT 7T IN FIRST EPISODE PSYCHOSIS

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**Background:** Schizophrenia (SZ) is a disorder of brain connectivity characterized by faulty interactions between spatially distinct brain regions. An imbalance between cortical excitation/inhibition has also been implicated, but the link between these abnormalities remains unclear. The present study used proton magnetic resonance spectroscopy (H-MRS) and fMRI to investigate how measurements of glutamate and GABA relate to the blood-oxygen-level-dependent (BOLD) response during a cognitive task and to functional connectivity (FC) between brain regions during a resting state, and how these relationships are altered inSZ. The use of a high field 7T scanner allowed for the separate measurements of glutamate, GABA, and glutamine.

**Methods:** Twenty-one first episode psychosis patients (FEP) and matched healthy controls (HC) completed a Stroop task and a resting state fMRI scan. Neurochemical levels were measured in the dorsal anterior cingulate cortex (ACC). Within and between group comparisons of the BOLD Stroop response (incongruent>congruent trials) and of the ACC functional connectivity were performed. Multiple-regressions investigated how glutamate, glutamine, and GABA related to the BOLD response and to the ACC functional connectivity in HC and FEP separately. Another multiple-regression investigated between group-differences in the relationships between the BOLD response, the ACC functional connectivity and each of these neurochemicals.

**Results:** Compared to HC, FEP showed increased BOLD response within regions of the executive and default mode networks. There were significant between groups' differences in ACC functional connectivity to the precuneus, right inferior parietal cortex, bilateral insula and, bilateral dorsolateral prefrontal cortex. Glutamate levels, but not glutamine or GABA, were significantly lower in FEP compared to HC. In FEP, the relationship between ACC glutamate levels and the BOLD response in regions of the posterior default mode network (DMN) was opposite to that of HC. Likewise, the relationship between ACC glutamate and ACC functional connectivity to the precuneus, a key region of the posterior DMN, was opposite between the groups. In FEP, but not HC, ACC GABA correlated with the local BOLD response and with the Stroop reaction time. FEP showed a significant relationship between ACC GABA and the ACC functional connectivity to the caudate; this relationship was absence in HC. In both groups, glutamine negatively correlated with the BOLD response in diverse regions, but these relationships were stronger and broader in HC. Between groups analysis revealed that in FEP, the relationship between ACC glutamine and the ACC functional connectivity to the right dorsolateral prefrontal cortex was significantly more positive in FEP compared to HC.

**Conclusions:** These results suggest a mechanism whereby, in FEP, alterations in the relationship between cortical glutamate/GABA, and both the BOLD response during the Stroop and the ACC functional connectivity during a resting state is disrupting the dynamic of major neural networks, including DM, executive and fronto-striatal networks.

### 30.2 GABA SPECTROSCOPY AND COGNITIVE FUNCTIONING IN SCHIZOPHRENIA AT ULTRA-HIGH MAGNETIC FIELD STRENGTH OF 7 TESLA

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**Background:** Schizophrenia is characterized by loss of brain volume, which may represent an ongoing pathophysiological process. This loss of brain volume may be explained by reduced neuropil rather than neuronal loss, suggesting abnormal synaptic plasticity and cortical micro-circuitry. Schizophrenia is also characterized by cognitive impairments. A possible mechanism in schizophrenia is hypofunction of the NMDA-type of the glutamate receptor in the medial prefrontal cortex, which reduces the excitatory drive of inhibitory GABAergic interneurons, resulting in a disinhibition of glutamatergic pyramidal neurons. Disinhibition of pyramidal cells may result in excessive stimulation by glutamate, which in turn could cause neuronal death or damage through excitotoxicity.

**Methods:** We measured GABA/creatine ratios, and glutamate, NAA, creatine and choline concentrations in the prefrontal and parieto-occipital cortices and general cognitive functioning in 17 patients with schizophrenia and 23 healthy controls using proton magnetic resonance spectroscopy at an ultra-high magnetic field strength of 7 Tesla.

**Results:** Significantly lower GABA/Cr ratios were found in patients with schizophrenia in the prefrontal cortex as compared to healthy controls. Moreover, GABA/Cr ratios in the prefrontal cortex were inversely correlated with cognitive functioning in the patients. No significant differences in metabolite concentrations in the parieto-occipital cortex were found between the groups.

**Conclusions:** Our findings support a mechanism involving altered GABA levels distinguished from glutamate levels in the medial prefrontal cortex in schizophrenia, particularly in high functioning patients. Intracortical signal variation, representing myeloarchitecture-based laminar information at 7 Tesla can provide additional insights into cognitive functioning in schizophrenia.

### 30.3 DEPTH-DEPENDENT EXAMINATION OF INTRACORTICAL MYELIN IN SCHIZOPHRENIA USING ULTRA-HIGH FIELD IMAGING

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**Background:** Abnormal myelination has been proposed as a pathogenetic mechanism for schizophrenia. Ultra-high-field magnetic resonance imaging...