SIRS 2019 Abstracts

(b) 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.

(c) 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.

(d) 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

Adrienne Lahti*,1, Gregory Overbeck1, Timothy Gawne1, Nina Kraguljac1, Meredith Reid3
1The University of Alabama at Birmingham; 2Auburn University

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 in SZ. 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 7T 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 absent 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

Hilleke Hulshoff Pol*,1, Rene Mandl2
1University Medical Center Utrecht Brain Center; 2University Medical Center Utrecht

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 excitation 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 damage or death through excitotoxicity.

Methods: We measured GABA/creatinine ratios, and glutamate, NAA, 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

Sophia Frangou*,1, Gaelle Doucett1, Won Hee Lee1, Emma Sprooten2
1Icahn School of Medicine At Mount Sinai; 2Donders Institute for Brain, Cognition, and Behaviour, Radboud University

Background: Abnormal myelination has been proposed as a pathogenetic mechanism for schizophrenia. Ultra-high-field magnetic resonance imaging
30.4 IDENTIFYING THE REDOX SUBTYPE OF SCHIZOPHRENIA USING ULTRA-HIGH FIELD 7T IMAGING

Lena Palaniyappan*,1, Kara Dempster2, Michael Mackinley3, Jean Theberge4, Peter Jeon1
1University of Western Ontario; 2London Health Sciences Center; 3St. Joseph’s Health Care London

Background: Ultra-high field 7T imaging greatly enhances the estimation of altered structure-function correspondence in disease states and provides unprecedented access to estimate neurometabolites with high specificity. Glutathione and glutamate have emerged as promising therapeutic targets for patients showing inadequate response. Nevertheless, the role of these non-dopaminergic treatment targets in the neurobiology of treatment response is poorly understood.

Methods: Using a longitudinal design and ultra-high field 7-Tesla magnetic resonance spectroscopy (MRS), we investigated the association of glutamate and glutathione with time to response in the dorsal anterior cingulate cortex (dACC) in patients with drug-naïve or minimally medicated first-episode psychosis (n=26) and healthy controls (n=27). Time to response was defined as the number of weeks it took to reach a 50% improvement on the PANSS-8 from baseline. We also studied the time-course of glutamate and glutathione changes using 7T functional spectroscopy and related metabolite dynamics at the onset to the early clinical course of psychosis.

Results: Higher dACC glutathione at baseline was associated with decreased time to response, while higher dACC glutamate was associated with functional impairment at baseline. There were no significant differences between patients and controls on measures of glutamate, or glutathione. Glutamate and glutathione levels are highly correlated in healthy controls, but this association is weakened among patients.

Conclusions: In a sample of acutely psychotic drug-naïve first-episode subjects, the highly resolved dynamic spectroscopic measures emerge as promising markers of early prognostic course. We believe these results add credibility to the claim that an aberrant redox subtype of schizophrenia can be identified early on at the time of first episode psychosis.

31.1 COMBINING EXERCISE PHYSIOLOGY, RECREATIONAL THERAPY, VIRTUAL REALITY GAMING TECHNOLOGY, AND PSYCHOSOCIAL REHABILITATION TO PROMOTE PHYSICAL EXERCISE IN SERIOUS MENTAL ILLNESS

Jimmy Choi*,1, Beth Taylor2, Joanna Fiszdon3, Robert Astur4, Lawrence Haber5, Dana Shagan6, Cenk Tek6, Matthew Kurtz7, Godfrey Pearlson1
1Olin Neuropsychiatry Research Center; 2UCONN Institute for Collaboration on Health, Intervention, and Policy; 3VACH/Yale University; 4UCONN; 5The Institute of Living; 6Yale University School of Medicine; 7Wesleyan University

Background: Physical exercise (PE) is a safe, non-stigmatizing, and side-effect free intervention that has the potential to mitigate neurocognitive dysfunction in psychosis, as well as reduce anxiety and paranoia. Developing and promoting PE programs for people with SMI in the community where participants cannot be paid to participate requires an interdisciplinary approach to activate motivation for exercise. We report the initial development and pilot results of a PE community program developed to enhance motivation and engagement in adults with schizophrenia, merging expertise from the fields of exercise physiology, recreational therapy, virtual reality (VR) gaming technology, and neuropsychiatric rehabilitation.

Methods: Adult outpatients diagnosed with schizophrenia (N=29) were enrolled in 18 hours (40 min session, 3x/week for 3 months) of exergaming. Exergaming uses interactive exercise equipment connected to a computer and monitor so the patient is engaged in a virtual game while exercising. For example, while pedaling on an exergaming stationary bike, the can have the experience of racing or biking through the countryside, either using a virtual reality headset or simply looking at the monitor. The PE regimen was tailored for each participant based on input from a (1) exercise physiologist about optimal methods to achieve volitional exhaustion and reduce the risk for injury, (b) recreational therapist who set up the overall exercise milieu to promote enjoyment, (c) expert in VR technology who calibrated and