Discussion: In both HC and FESz, greater hippocampal gray matter volume was associated with better performance on a battery of cognitive tasks. In FESz, greater hippocampal volumes were associated with worse positive symptoms and a longer DUP. As these relationships appear paradoxical, it can be speculated that the individuals with greater hippocampal volumes have greater cognitive ability that potentially contributes to more elaborate and severe positive symptoms and greater resilience before needing first clinical contact. There were no group differences in volumes, but future studies following these individuals longitudinally will examine these relationships and whether hippocampal gray matter volume declines.

T93. DISRUPTED WHITE MATTER INTEGRITY OF THE SUPERIOR CEREBELLAR PEDUNCLE IS ASSOCIATED WITH NEUROCOGNITIVE IMPAIRMENTS IN PATIENTS WITH RECENT-ONSET SCHIZOPHRENIA

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Background: Increasing evidence has shown that the cerebellum is involved in cognitive controls in cooperation with higher-order association areas of the cerebrum. The superior cerebellar peduncle (SCP), a major output route from the cerebellum, conveys modulatory signals to the cerebral cortex to fine-tune cognitive mental activities. In line with the concept of "cognitive dysmetria," we investigated white matter integrity of the SCP and its associations with neurocognitive functioning in patients with recent-onset schizophrenia (ROS).

Methods: Fifty-seven ROS patients (male 20, female 37; mean age = 33.5 ± 9.7 years) and 38 healthy controls (HCs; male 20, female 18; mean age = 33.6 ± 6.1 years) participated in this study. Diffusion tensor imaging (DTI) data were acquired from all participants using a 3-Tesla magnetic resonance imaging (MRI) scanner. We used the Tract-Based Spatial Statistics software to estimate fractional anisotropy (FA) of the bilateral SCPs. Neurocognitive function was measured using the Korean version of the Wechsler Adult Intelligence Scale (K-WAIS) and Rey-Kim memory test in ROS participants.

Results: The FA values of the left SCP were significantly lower in ROS participants compared to HCs (HCs: 0.82 ± 0.02, ROS: 0.81 ± 0.02; F = 6.36, p = 0.013). We found that FA of the right and left SCPs have positive correlations with general intellectual functioning measured using the full-scale intelligence quotient (right: r = 0.415, p = 0.012; left: r = 0.380, p = 0.022) in ROS participants. FA of the right SCP also showed positive correlations with memory encoding (r = 0.330, p = 0.033) and retention (r = 0.325, p = 0.036) of the Rey-Kim memory test in the verbal domain.

Discussion: The present findings suggest that white matter connectivity between the cerebellum and cerebrum is disrupted in patients with schizophrenia. Furthermore, impaired cortico-cerebellar communication through the SCP may contribute to neurocognitive dysfunction, particularly in the verbal domain. Given that neurocognitive impairments is one of the core characteristics of schizophrenia, disrupted cortico-cerebellar connectivity would provide some clues to understand the pathogenesis of schizophrenia.

T94. CORTICAL THICKNESS TRAJECTORIES IN RELATION TO CHANGES IN EXECUTIVE FUNCTION AMONG FIRST EPISODE PSYCHOSIS PATIENTS

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Background: Disorganized thinking and executive function impairments are often present in patients with psychosis. Several studies have found associations between cognitive abilities and cortical thickness in schizophrenia; however, only a few studies have investigated cortical thickness relative to executive function (EF) in patients with a first episode of psychosis (FEP) compared with healthy controls (HC), using cross-sectional study designs. Moreover, the direction of findings from these studies have been inconsistent, although results converge on the idea that EF are differentially related to brain structure in patients. The present study aims to examine longitudinal relationships between changes in cortical thickness and EF in individuals with a FEP relative to HC using structural brain imaging.

Methods: Structural T1-weighted images were acquired on a 3T scanner for patients (n=21) and controls (n=28). Two to four timepoints were completed per subject, over a period of approximately 3–21 months. The Groton Maze Learning test and Set Shifting test from the CogState computerized battery were collected as measures of EF. Images were processed using the CIVET pipeline, and all cortical thickness-related analyses were performed across 81,924 vertices of the cortical surface, using the SurfStat toolbox in Matlab. A slope of CT at every vertex across the brain and a slope of EF across available timepoints per subject were independently calculated and subsequently used in the analysis. A linear model was applied to test for the main effect of change in EF to change in CT per group, and to assess the interaction between group and change in EF on cortical thickness rates of change. Models controlled for age and sex. For both sets of analyses, resultant t-statistic maps were thresholded and corrected for multiple comparisons with Random Field Theory (RFT), with a stringent cluster-threshold of p=0.005. Exploration of results was also done with a more relaxed threshold of p=0.01.

Results: A significant negative main effect of change in EF on change in CT was observed for HC in the right insula (i.e. improvement in EF was related to cortical thinning); additionally, the right cingulate gyrus was significant with a relaxed threshold of p=0.01. The main effect of change in EF on changes in CT was not significant for FEP patients. The interaction between change in EF and group was found to be significant, where negative associations between change in EF and change in CT were driven by HC. Specifically, a negative association of change in EF was found in right insula, right supramarginal gyrus and the left ventrolateral prefrontal cortex, whereas no such relationship was observed in patients.

Discussion: To our knowledge, longitudinal changes in cortical thickness relative to changes in EF have not been investigated before in FEP. Findings from this study suggest there are no significant associations between change in CT and change in EF among individuals early in the course of psychosis. Significant associations found in controls suggest that steeper improvements in EF is associated with cortical thinning in frontal-parietal regions. These results are consistent with a cross-sectional study in healthy adolescents suggesting that rapid structural maturation in higher-order brain regions characterized by protracted development is associated with improvement in cognitive abilities. It is possible that in patients, these maturational patterns are altered and/or more diffuse and, thus, not as readily localized with a univariate analysis. We suggest that future studies should examine such brain-behaviour relationships in FEP with brain network approaches.

T95. FREE WATER IMAGING REVEALS DIFFERENTIAL PATTERNS OF WHITE MATTER ALTERATIONS IN INDIVIDUALS WITH ADOLESCENT-ONSET SCHIZOPHRENIA AND BIPOLAR DISORDER

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¹SIRS 2019 Abstracts
Background: Recent studies using an advanced diffusion model, Free Water Imaging (FWI), have demonstrated that fractional anisotropy (FA) reductions in schizophrenia (SZ) patients were mostly associated with increases in extracellular free-water (FW) in the early stages of the illness, while patients with chronic SZ predominantly showed decreases in FA of the tissue (FAt). Conversely, a study comparing patients with chronic bipolar disorder (BP) and healthy individuals (HC) reported that FW was increased in BP subjects suggesting a different trajectory compared to the one found in SZ patients. The present study is the first to investigate WM properties in adolescent-onset SZ and BP together. Utilizing conventional diffusion tensor imaging and FWI, we aim to identify imaging biomarkers that could help differentiate the biological nature of these two disorders.

Methods: Forty-eight (20F/28M) SZ patients (mean age: 16.28), 15 (7F/8M) BP patients (mean age: 15.52) and 35 (18F/17M) HCs (mean age: 15.65) were included in the study. The mean duration of psychosis (DOP) was 0.97 years in BP subjects and 1.84 years in SZ subjects. All participants underwent diffusion MRI scanning (1.5 T Siemens Magnetom Sonata, 60 gradient directions with b = 1000 m/s^2 and 5 images with b = 0 m/s^2). Each scan was repeated three times to increase the signal-to-noise ratio and was subsequently corrected for motion and eddy currents before getting averaged. FA, FAt, and FW maps were calculated and then skeletonized using Tract-Base Spatial Statistics (TBSS). Voxel-wise, non-parametric statistics were conducted with 5000 permutations and threshold-free cluster enhancement controlling for age, sex and motion.

Results: Significant ANOVA effects were explained by pairwise post-hoc t-tests revealing the expected global FA decrease in SZ and BP subjects compared to HCs. Further, lower FA restricted to the corpus callosum was found in BP compared to SZ individuals. Applying FWI, BP subjects had both spatially limited decreased FAt and widespread increased FW compared with HCs, while SZ subjects had extensively decreased FAt but not increased FW. Comparing between the BP and SZ groups, there was no difference in FAt, but significantly higher FW in BP in most regions of the WM skeleton.

Discussion: Our results are in line with previous studies suggesting a perturbation of WM health in individuals suffering from BP and SZ. The use of FWI in the present study allows for the further clarification of the biological nature of FA reductions: while SZ patients showed only reductions in FAt compared to HCs, the BP group also had marked increases in FW both compared to HCs and the SZ group. These increases in FW spatially overlapped with FA decreases, suggesting that an extra-cellular pathology is driving the observed FA reductions. The present alterations of WM properties in adolescent-onset BP are similar to those previously described in chronic BP and indicate that FW increases might be a biomarker of BP disorder. Interestingly, the adolescent SZ group, unlike recent-onset or first episode adult SZ cohorts, show no FW alterations, but instead FAt reductions similar to those previously reported in chronic SZ subjects. This could be explained by the longer illness duration, or different disease trajectories between adult and adolescent-onset psychosis. Taken together, we show differential patterns of WM aberrations in adolescent-onset SZ and BP, which lend support to the presence of distinct pathologies underlying the neurobiological development and manifestation of these disorders.

Discussion: We obtained multimodal neuroimaging in a group of healthy volunteers (n = 15) during a saline and during a ketamine infusion (0.27mg/kg bolus over 10 minutes, followed by a continuous infusion of 0.25mg/kg/hour for 50 minutes). We acquired 2D pCASL scans (TR/TE = 5200/33ms, excitation flip angle = 90°, in-plane resolution = 3.75x3.75mm2, matrix=64x64, slice thickness=6mm, label time 1s, delay time 1s, labeling offset 5cm) with 30 pairs of labeled and unlabeled images to measure regional cerebral blood flow (rCBF) and MR spectroscopy scans in the left hippocampus (TR/TE=1500/80ms; 1200 Hz spectral bandwidth; 1024 points; 640 averages, and 8 averages without water suppression, voxel size: 2.7x1.5x1cm) to measure Glx (glutamate+glutamine). We examined changes in rCBF and metabolic connectivity, as well as their associations with clinical symptom severity (measured with the Brief Psychiatric Rating Scale [BPRS]) and Glx levels.

Results: Voxelwise analysis comparing rCBF during a saline infusion and ketamine challenge demonstrated regionally selective increases in the prefrontal, orbitofrontal and cingulate cortices as well as the insula, angular gyrus, caudate, putamen, thalamus and hippocampus. No areas showed a decrease in rCBF. Metabolic connectivity analyses revealed a complex pattern of ketamine related rCBF changes. Positive correlations between the anterior cingulate/ frontal pole and insula decreased. Negative correlations between the hippocampus and the dorsolateral prefrontal cortex as well as the putamen decreased. We also found that the increase in rCBF in the bilateral putamen and left hippocampus was positively correlated with psychosis severity during the ketamine challenge while change in anterior cingulate cortex rCBF was negatively correlated with change in hippocampal Glx.

Discussion: Here we find regionally selective patterns of rCBF changes and metabolic connectivity changes at the level of large-scale brain networks that are thought to be central to the schizophrenia psychopathology. Our study adds to the efforts to confirm putative links between an imbalance in glutamate metabolism and dysconnectivity of large-scale brain networks. Development of glutamatergic compounds that alleviate disease burden, possibly through normalizing glutamate excess related increased rCBF, are direly needed.

T96. KETAMINE INDUCED CHANGES IN REGIONAL CEREBRAL BLOOD FLOW, METABOLIC CONNECTIVITY, AND GLUTAMATE METABOLISM

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Background: Several neuroimaging studies have attempted to characterize the contribution of glutamatergic dysfunction to functional dysconnectivity of large-scale brain networks using ketamine models. However, findings from blood oxygen level dependent signal (BOLD) imaging studies have been conflicting, in part because the signal stems from a complex interaction between blood flow, blood volume, and oxygen consumption.

Methods: We obtained multimodal neuroimaging in a group of healthy volunteers (n = 15) during a saline and during a ketamine infusion (0.27mg/kg bolus over 10 minutes, followed by a continuous infusion of 0.25mg/kg/hour for 50 minutes). We acquired 2D pCASL scans (TR/TE = 5200/33ms, excitation flip angle = 90°, in-plane resolution = 3.75x3.75mm2, matrix=64x64, slice thickness=6mm, label time 1s, delay time 1s, labeling offset 5cm) with 30 pairs of labeled and unlabeled images to measure regional cerebral blood flow (rCBF) and MR spectroscopy scans in the left hippocampus (TR/TE=1500/80ms; 1200 Hz spectral bandwidth; 1024 points; 640 averages, and 8 averages without water suppression, voxel size: 2.7x1.5x1cm) to measure Glx (glutamate+glutamine). We examined changes in rCBF and metabolic connectivity, as well as their associations with clinical symptom severity (measured with the Brief Psychiatric Rating Scale [BPRS]) and Glx levels.

Results: Voxelwise analysis comparing rCBF during a saline infusion and ketamine challenge demonstrated regionally selective increases in the prefrontal, orbitofrontal and cingulate cortices as well as the insula, angular gyrus, caudate, putamen, thalamus and hippocampus. No areas showed a decrease in rCBF. Metabolic connectivity analyses revealed a complex pattern of ketamine related rCBF changes. Positive correlations between the anterior cingulate/ frontal pole and insula decreased. Negative correlations between the hippocampus and the dorsolateral prefrontal cortex as well as the putamen decreased. We also found that the increase in rCBF in the bilateral putamen and left hippocampus was positively correlated with psychosis severity during the ketamine challenge while change in anterior cingulate cortex rCBF was negatively correlated with change in hippocampal Glx.

Discussion: Here we find regionally selective patterns of rCBF changes and metabolic connectivity changes at the level of large-scale brain networks that are thought to be central to the schizophrenia psychopathology. Our study adds to the efforts to confirm putative links between an imbalance in glutamate metabolism and dysconnectivity of large-scale brain networks. Development of glutamatergic compounds that alleviate disease burden, possibly through normalizing glutamate excess related increased rCBF, are direly needed.

T97. PATTERNS OF COGNITIVE FUNCTION ARE UNICALLY ASSOCIATED WITH WHITE MATTER-MICROSTRUCTURE IN INDIVIDUALS AT ULTRA-HIGH RISK FOR PSYCHOSIS

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