S159. SUBCORTICAL GRAY MATTER VOLUME IS ASSOCIATED WITH SCHIZOPHRENIA AND WITH BOTH ITS FAMILIAL AND CLINICAL RISK

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Background: The association of white matter (WM) abnormalities with clinical variables in schizophrenia (SCZ) is poorly understood. We investigated the clinical correlates of WM impairments using imaging data of 597 patients with SCZ and 490 healthy controls (HC). We focused on lifelong changes of WM (measured by Fractional Anisotropy [FA]) in SCZ and compared it to that of HC. We investigated how age, duration of illness, and medication influence WM trajectories, and examined how structural impairments are related to symptoms and cognition. Last, we tested for the role of sex in structure-function interactions.
Methods: Diffusion-weighted images and clinical measurements were collected as part of 13 independent studies, and data was harmonized across all sites. We registered images to the IIT Human Brain Atlas and averaged FA for forceps major, forceps minor, cingulum, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus (SLF) and uncinate fasciculus.
First, we modeled the FA age trajectory of each tract in HC and used it to regress out the effect of age in patients. The residuals in the FA values were utilized for further analyses.
We conducted mediator regression analyses with FA as the dependent variable, sex as a covariate, and age and duration of illness as the independent variables. Next, patients were grouped based on Chlorpromazine equivalent dosage (CPZ) and CPZ group was added to the regression model. To examine the association between structure and function, a structural equation model (SEM) was used, with cognition as a mediator. Last, all analyses were repeated for males and females separately.
Results: Regression analyses revealed a significant influence of duration of illness on the forceps major (T=3.24, p<.001), forceps minor (T=3.40, p<.001), and SLF (T=3.83, p<.0001). When adding both age and duration of illness, duration of illness mediated the influence of age on FA.
Adding CPZ to the model displayed a significant effect of medication on forceps major (T=3.93, p<.0001).
For SEM, FA of all tracts was used to represent structural impairment, and symptom scores were used to reflect functional impairment. All data paths were calculated with an asymptotically distribution-free model. The overall model fit was acceptable (RMSEA =.09) with a medium-strong effect of structural impairment on functional impairment (standardized estimate=.44).
When separating sexes, males showed a significant association of duration of illness and FA. Females displayed a stronger influence of structural impairment on functional impairment (standardized estimate: males = .29, females =.52), and cognition had an impact on this relationship for females only.
Discussion: The effect of duration of illness on specific WM tracts suggests a progressive, neurodegenerative pathology, which might contribute to the devastating effects of chronicity. Medication seems to have only a small, localized effect on corpus callosum WM integrity. However, since our analysis used cross-sectional CPZ measures, future studies should include measurements of lifetime dosage. The observed impact of WM abnormalities on function further highlights the importance of WM for SCZ pathology.
The association of structure and function seems sex-specific. Men show a stronger effect of chronicity. For females, cognition mediates the effect of structure on function, suggesting the role of cognitive reserve.
Our approach provides the first step towards evidence-based medicine, by demonstrating the apparent relationship between structural pathology and functional outcome and suggesting possible mediators of this relationship, including duration of illness, cognition, medication, and sex.

S158. URBANICITY INDEX AND CORTICAL GYRIFICATION IN SCHIZOPHRENIA

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Background: Urban birth and upbringing are considered to be risk factors for schizophrenia, but recent studies do not support the same. While several hypotheses are suggested, the pathogenic mechanisms are not known. Notably, no study has examined brain changes, if any, associated with an urban upbringing in schizophrenia. Hence, in this study, we examined the effect of urban upbringing on the cortical gyrification in schizophrenic patients.
Methods: We recruited 108 persons with DSM-IV schizophrenia and 74 healthy volunteers. Study participants underwent clinical assessments using Positive and negative syndrome scale, Calgary depression scale to measure severity of clinical symptoms. All participants were scanned using 3T MRI scanner and a high resolution T1 structural scan was obtained. Cortical gyrification measurements were conducted on these images using Freesurfer software. Statistical maps were generated in Query, design, Estimate, Contrast (QDEC) interface. A Monte Carlo Simulation (MCS) was run for FWE correction with the threshold 1.3 ($p<0.05$) in QDEC. Participants upbringing place was noted with respect to the place where they lived for the first 15 years of life. Based on Census India of 2011, the places were categorized into 1) rural 2) statutory town and 3) census town. These 3 groups and assigned values 1,2 and 3, respectively, which were then rated for each year of life (1–15) and urbanicity index was calculated using a previously used method (range from 15 to 45). A regression analysis was implemented in QDEC with age, sex, education and demean ICV as covariates to examine the relation between Urban upbringing and cortical gyrification index.
Results: In the overall population, HV had higher gyrification index in the left superior parietal cortex ($p<0.008$) than SCZ. There was a significant negative correlations between gyrification index and urbanicity index in left postcentral ($p<0.0001$), left insula ($p<0.0001$), left fusiform ($p<0.0005$), left rostral middle frontal ($p<0.01$), right supramarginal ($p<0.0001$), right fusiform ($p<0.0001$), and right superior temporal ($p<0.005$) cortices.
Discussion: The results indicate a significant effect of urbanicity on cortical gyrification in patients with SCZ as well as HV. The presence of deficits in frontal areas indicate the likely effect of urban upbringing on growth and maturation of the frontal cortex. Interestingly, the presence of difference in areas implicated in schizophrenia provides support to the possible increased risk of urban upbringing on schizophrenia. The preliminary evidence from this analysis provides the necessary rationale to further examine the impact of urban upbringing on brain structure/ function and the risk of developing schizophrenia.

S159. SUBCORTICAL GRAY MATTER VOLUME IS ASSOCIATED WITH SCHIZOPHRENIA AND WITH BOTH ITS FAMILIAL AND CLINICAL RISK

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Background: Patients with schizophrenia (SCZ) show lower volumetric estimates of gray matter (GM) than healthy controls (HC). Similar results have been reported in healthy siblings of patients (SIB). However, it is unclear whether this phenotype is also present in individuals at clinical high-risk (CHR), characterized by sub-threshold symptoms and loss of

functioning. We hypothesized that GM volumetric differences are associated with both familial and clinical risk for schizophrenia
Methods: We processed the T1-weighted MRI scans acquired at 3 Tesla of 544 HC, 63 SIB, 20 CHR and 120 SCZ using CAT12. We used ANCOVA to assess group differences (HC vs. CHR vs. SIB vs. SCZ), with linear and quadratic age, gender and total intracranial volume as nuisance covariates. We assessed the reproducibility of our case/control findings in an independent sample of 127 HC and 36 SCZ. Group differences were tested post hoc through Fisher's test.
Results: We found significant group effects in the bilateral thalamus, bilateral hippocampus and anterior cingulate (FWE<0.05). Specifically, SCZ presented the lowest GM volume in these regions compared to the other three groups, with SIB and CHR's GM estimates intermediate between HC and SCZ ($p<0.05$). The associations with schizophrenia were replicated in the independent validation sample.
Discussion: Individuals with familial or clinical risk for schizophrenia have lower GM estimates in the same brain regions. These findings, suggest that these structural features are not only associated with familial risk for schizophrenia but that they are also associated with its sub-threshold symptoms.

S160. ALTERATIONS IN SHORT-RANGE STRUCTURAL CONNECTIVITY ACROSS THE PSYCHOSIS SPECTRUM: FINDINGS FROM THE B-SNIP STUDY

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Background: Schizophrenia (SZ) and bipolar disorder (BD) have been increasingly viewed as psychotic mood disorders along a shared spectrum. Long-range and short-range structural connectivity have been implicated in both disorders, conceptualising them as "disconnection syndromes". There has been a rise in neuroimaging tools to understand the overlap and boundaries between the two disorders, which has shifted our focus towards appreciating traits in addition to diagnosis. Our recent pilot study examining short-range U-fibers found in superficial white matter (SWM) found shared and distinct traits among people with SZ and BD and we aimed to investigate SWM further using data from the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) consortium.
Methods: Using diffusion weighted imaging (DWI), we performed whole brain tractography in 113 people with SZ, 69 people with SA disorder, 49 people with psychotic BD and 77 healthy controls using BrainVISA and Connectomist 2.0. Segmentation and labelling of SWM tracts were performed using a comprehensive U-fiber atlas. ComBat was applied to remove site effects and principle components analysis was performed to identity networks of bundles used for comparative analyses.
Results: Principle component analysis revealed a network comprised of 8 short tracts in frontal, parietal, and temporal regions that had decreased anatomical connectivity in patients, regardless of diagnosis, relative to healthy controls. This network overlaps, in part, regions that differed between patients (SZ and BD) and healthy controls in our recent pilot study. However, we were unable to detect differences between people with SZ, SA disorder and psychotic BD.
Discussion: We demonstrate that short U-fibers are likely vulnerable to pathological processes in psychotic illnesses, encouraging further understanding of their anatomy and function. Our lack of findings between patient groups may reflect a more homogeneous population (three subgroups of psychosis) and may suggest that abnormalities in SWM are less likely due to mood disturbances.

S161. DYNAMIC FUNCTIONAL NETWORK CONNECTIVITY COMPARING AUDITORY VERBAL HALLUCINATIONS IN PSYCHOTIC AND NON-PSYCHOTIC SUBJECTS

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Background: Auditory verbal hallucinations (AVH) are often seen as a hallmark of schizophrenia, but can also occur in the general healthy population. While AVH in non-clinical populations might offer an opportunity to study them in isolation, it remains debatable whether the mechanisms underlying AVH are the same in clinical and non-clinical populations. For example, non-clinical populations are reported to attribute lower emotional valence to their AVH. Such differences in phenomenology are hypothesized to arise from differences on the neurobiological level. With the current study, we employ a data-driven approach to define brain networks involved in AVH in clinical and non-clinical subjects, and test whether dynamic differences in network connectivity exist between these groups.
Methods: Functional magnetic resonance imaging data of 21 non-psychotic individuals and 21 matched psychotic patients with frequent AVH were obtained. During scanning, subjects manually indicated the on- and offset of their AVH. Using independent component (IC) analysis, the data were split into 72 statistically independent spatial maps and their time courses. These time courses were regressed with the AVH time courses. With a one sample t-test on the beta weights, we selected those ICs that related to AVH in both groups for further dynamic functional network connectivity analysis. To identify functional connectivity states, k-means clustering was implemented on correlation matrices acquired using sliding windows. Group differences between these states were determined with two-sample t-tests.
Results: Both groups experienced AVH during scanning, with a mean number of 24.71 AVH episodes in the clinical and 17.14 episodes in the non-clinical group. We identified seven ICs with time courses significantly related to the occurrence of AVH in both groups. The auditory, sensorimotor, and posterior salience network were positively related to AVH occurrence. The ventral default mode network (DMN), anterior salience network and a network consisting of (para-)hippocampal areas were negatively related to AVH.
While in general, networks related to AVH were similar in both groups, a significant difference between the two groups was found in the mean dwell time in states characterized by varying connectivity between these networks. Psychotic patients spent more time in a state of low connectivity ($r < 0.055$) between all AVH-related networks. Non-psychotic patients dwelled longer in a different state, where some weak correlations between networks were present ($.15 > r \geq .10$). Specifically, networks positively related to AVH showed small negative correlations with each other, and a small negative relationship with the DMN. At the same time, the anterior salience network displayed a small positive relationship with the sensorimotor, auditory and posterior salience networks.
Discussion: Our findings suggest that similar brain networks underlie AVH in non-psychotic and psychotic individuals, but that the groups differ in terms of connectivity between those networks. Among the involved networks are those typically associated with AVH in psychotic patients, such as the DMN and auditory network. During the experience of AVH, psychotic individuals are more likely to show a state defined by segregation of the AVH-related networks. On the contrary, during AVH non-psychotic individuals are in a state defined by more connectivity between the networks. This suggests that a distinction between clinical and non-clinical AVH may have its neurobiological basis in the extend of disruption of involved network connectivity.