Abstracts for the Sixth Biennial SIRS Conference

T166. SPATIAL INCOHERENCE OF LARGE-SCALE CORTICAL NETWORKS RELATES TO NORMAL THOUGHT DISORDER IN SCHIZOPHRENIA: A 7T MRI-BASED THICKNESS STUDY

Lena Palaniyappan*,1, Ali Al-Radaideh2, Penny Gowlan1, Peter Liddle3
1University of Western Ontario; 2The Hashemite University; 3University of Nottingham.

Background: The thickness of cerebral cortex varies across individuals as well as across different regions within an individual. Shared trophic or plastic influences such as repeated task-related recruitment of extant brain regions results in morphological covariance within large-scale brain networks. Pathological processes disrupting functional co-activation can result in higher than expected degree of variability within large-scale networks in an individual level, resulting in spatial incoherence. We studied spatial incoherence of cortical thickness in 17 cortical networks identified on the basis of well-known patterns of intrinsic connectivity, to identify the spatially incoherent networks and relate them to differences in severity of thought disorder among patients with schizophrenia.

Methods: Ultra-high field 7T anatomical MRI scans (MPRAGE) were obtained from 20 subjects in a clinically stable, medicated early stage of schizophrenia. We used ultra-high resolution (7 Tesla) MTI in 17 patients with schizophrenia and 20 controls, to evaluate the macromolecular (predominantly myelin) content of the brain. Immediately after the 7T scanning, we also used a 3T diffusion tensor imaging (DTI) and undertook probabilistic tractography using FSL software (AutoPtx, ProbTrackX) to delineate anterior cingulum bilaterally. Unpaired t tests were used for group comparisons along with estimates of Cohen's d for effect sizes.

Results: Patients had a significant reduction in GMV in left fusiform gyrus (Hedge's g = 1.98, T = 6.7), and increased GMV in the right precuneus (Hedge's g = 1.63, T = 5.5) and lingual cortex (Hedge's g = 1.19, T = 4.0). We did not find any other areas of significant GMV change. Of these 3 circumscribed GMV changes, reduced fusiform GMV was found among FEP patients with lower processing speed (t0=0.45, p=0.04), higher severity of delusions (t0=0.43, p=0.049) and unusual thought content (t0=0.59, p=0.01). Increased precuneus GMV was found among FEP patients with higher severity of delusions (t0=0.62, p=0.008) and unusual thought content (t0=0.50, p=0.03). Right lingual changes were not related to the severity of delusions or processing speed scores.

Discussion: Our findings suggest that (1) GMV deficits are minimal in drug-naive FEP subjects, with large effect-size changes concentrated around face processing (fusiform) region (2) GMV increases co-occur with GMV reduction especially in those with most severe delusions and cognitive deficits indicating a role for compensatory plasticity. Subtle early brain structural changes appear to predict symptom burden and cognitive deficits at the time of first clinical presentation with psychosis. Focusing on treatments that manipulate the structure of fusiform cortex could potentially reduce the severity of some of the early symptoms in FEP.

T167. ABERRANT MYELINATION OF THE CINGULUM BUNDLE IN PATIENTS WITH SCHIZOPHRENIA: A 7T MTI/DTI STUDY

Lena Palaniyappan*,1, Ali Radaideh*, Olivier Mougin1, Penny Gowlan1, Peter Liddle2
1University of Western Ontario; 2The Hashemite University; 3University of Nottingham

Background: The structural integrity of the anterior cingulum has been repeatedly observed to be abnormal in patients with schizophrenia. Reduced glutathione levels, indicating oxidative stress, is associated with reduced structural integrity of cingulum bundle in patients with schizophrenia. Variations in neuregulin-1, a well-established candidate marker for schizophrenia, results in oligodendrocyte dysfunction and defective myelination, and is shown to affect the structural integrity of the anterior cingulum in patients with schizophrenia. While the evidence to date has been obtained using diffusion tensor imaging, abnormal tract-specific changes in myelin content can be more directly inferred by combining multiple modalities of WM imaging such as diffusion tensor (DTI) and magnetization transfer imaging (MTI) in parallel.

Methods: We used ultra-high resolution (7 Tesla) MTI in 17 patients with schizophrenia and 20 controls, to evaluate the macromolecular (predominantly myelin) content of the brain. Immediately after the 7T scanning, we also obtained a 3T diffusion tensor image (DTI) and undertook probabilistic tractography using FSL software (AutoPtx, ProbTrackX) to delineate anterior cingulum bilaterally. Unpaired t tests were used for group comparisons along with estimates of Cohen's d or Hedge's g for effect sizes.

Results: Patients had a significant reduction in magnetization transfer ratio (MTR) in right (Cohen's d=0.91, p=0.007) but not left (d=0.03, p=0.92) cingulum bundle. There was also a trend level reduction in fractional anisotropy of right (d=0.60, p=0.07) but not left (d=0.47, p=0.17) cingulum bundle. We did not find any significant relationship between the 3 major symptom dimensions of schizophrenia (Reality Distortion, Disorganization, Psychomotor Poverty) and Cingulum MTR. Patients with Schneiderian delusions (n=5) showed a significantly reduced MTR of left cingulum compared to patients (n=12) with no Schneiderian delusions (Hedges' g=1.36, p=0.02).

Discussion: Our findings suggest that MTR changes in anterior cingulum, resulting from either dysmyelination or neuroinflammation, is present in schizophrenia. Reduced glutathione levels, indicating oxidative stress, is associated with reduced structural integrity of cingulum bundle in patients with schizophrenia. Variations in neuregulin-1, a well-established candidate marker for schizophrenia, results in oligodendrocyte dysfunction and defective myelination, and is shown to affect the structural integrity of the anterior cingulum in patients with schizophrenia. While the evidence to date has been obtained using diffusion tensor imaging, abnormal tract-specific changes in myelin content can be more directly inferred by combining multiple modalities of WM imaging such as diffusion tensor (DTI) and magnetization transfer imaging (MTI) in parallel.

T168. STRUCTURAL COVARIANCE AND CORTICAL REORGANIZATION IN SCHIZOPHRENIA: AN MRI-BASED MORPHOMETRIC STUDY

Lena Palaniyappan*,1, Peter Liddle2
1University of Western Ontario; 2University of Nottingham

Background: Structural aberrations of the anterior cingulum and thalamus have been repeatedly observed to be abnormal in patients with schizophrenia. Reduced glutathione levels, indicating oxidative stress, is associated with reduced structural integrity of cingulum bundle in patients with schizophrenia. Variations in neuregulin-1, a well-established candidate marker for schizophrenia, results in oligodendrocyte dysfunction and defective myelination, and is shown to affect the structural integrity of the anterior cingulum in patients with schizophrenia. While the evidence to date has been obtained using diffusion tensor imaging, abnormal tract-specific changes in myelin content can be more directly inferred by combining multiple modalities of WM imaging such as diffusion tensor (DTI) and magnetization transfer imaging (MTI) in parallel.

Methods: We used ultra-high resolution (7 Tesla) MTI in 17 patients with schizophrenia and 20 controls, to evaluate the macromolecular (predominantly myelin) content of the brain. Immediately after the 7T scanning, we also obtained a 3T diffusion tensor image (DTI) and undertook probabilistic tractography using FSL software (AutoPtx, ProbTrackX) to delineate anterior cingulum bilaterally. Unpaired t tests were used for group comparisons along with estimates of Cohen's d or Hedge's g for effect sizes.

Results: Patients had a significant reduction in magnetization transfer ratio (MTR) in right (Cohen's d=0.91, p=0.007) but not left (d=0.03, p=0.92) cingulum bundle. There was also a trend level reduction in fractional anisotropy of right (d=0.60, p=0.07) but not left (d=0.47, p=0.17) cingulum bundle. We did not find any significant relationship between the 3 major symptom dimensions of schizophrenia (Reality Distortion, Disorganization, Psychomotor Poverty) and Cingulum MTR. Patients with Schneiderian delusions (n=5) showed a significantly reduced MTR of left cingulum compared to patients (n=12) with no Schneiderian delusions (Hedges' g=1.36, p=0.02).

Discussion: Our findings suggest that MTR changes in anterior cingulum, resulting from either dysmyelination or neuroinflammation, is present in schizophrenia. Reduced glutathione levels, indicating oxidative stress, is associated with reduced structural integrity of cingulum bundle in patients with schizophrenia. Variations in neuregulin-1, a well-established candidate marker for schizophrenia, results in oligodendrocyte dysfunction and defective myelination, and is shown to affect the structural integrity of the anterior cingulum in patients with schizophrenia. While the evidence to date has been obtained using diffusion tensor imaging, abnormal tract-specific changes in myelin content can be more directly inferred by combining multiple modalities of WM imaging such as diffusion tensor (DTI) and magnetization transfer imaging (MTI) in parallel.
Background: In patients with schizophrenia, distributed abnormalities are observed in grey matter volume. A recent hypothesis posits that these distributed changes are indicative of a plastic reorganization process occurring in response to a functional defect in neuronal information transmission. We investigated the structural covariance across various brain regions in early-stage schizophrenia to determine if indeed the observed patterns of volumetric loss conformed to a coordinated pattern of structural reorganization.

Methods: Structural MRI scans were obtained from 40 healthy adults and 41 age, gender and parental socioeconomic status matched patients with schizophrenia. Volumes of grey matter tissue were estimated at regional level across 90 atlas-based parcellations. Group level structural covariance was studied using a graph theoretical framework.

Results: Patients had distributed reduction in grey matter volume, with high degree of localized covariance (clustering) compared to controls. Patients with schizophrenia had reduced centrality of anterior cingulate and insula but increased centrality of the fusiform cortex, compared to controls. Simulating targeted removal of highly central nodes resulted in significant loss of the overall covariance patterns in patients compared to controls.

Discussion: Regional volumetric deficits in schizophrenia are not a result of random, mutually independent processes. Our observations support the occurrence of a spatially interconnected reorganization with systematic de-escalation of conventional ‘hub’ regions. The resulting morphological architecture may be primed for compensatory functions, albeit with a high risk of inefficiency.

T169. COGNITIVE INSIGHT AND CORTICAL THICKNESS IN SCHIZOPHRENIA
Arpitha Jacob¹, Mariamanna Philip², Rose Bharathi³, Shivarama Varambally³, Ganesan Venkatasubramaniam⁴, Gopikrishna Deshpande⁵, Naren Rao*¹, Ayushi Shukla¹
¹National Institute of Mental Health and Neurosciences; ²Auburn University

Background: Diminished cognitive insight is exhibited by substantial proportion of patients suffering from schizophrenia and is an important determinant of poor treatment adherence. While the clinical correlates of cognitive insight are well examined the neural correlates of cognitive insight are less explored. We examined relation between cortical thickness and cognitive insight are in schizophrenia patients.

Methods: We examined 37 schizophrenia patients in comparison with 19 healthy volunteers. We measured cortical thickness using a high resolution anatomical magnetic resonance image and cognitive insight using Beck’s Cognitive Insight Scale (BCIS). We measured the difference between schizophrenia patients and healthy volunteers using Analysis of covariance and relation between cortical thickness and BCIS scores in schizophrenia patients using stepwise regression analysis.

Results: Patients had significantly thinner cortices than healthy volunteers in orbitofrontal cortex, superior temporal gyrus, occipital cortex, dorsomedial prefrontal cortex and posterior cingulate cortex. Significant positive correlations were found between self-reflection and cortical thickness in posterior cingulate cortex, dorso-medial frontal gyrus, occipital lobe. Significant negative correlations were observed between self-certainty scores and bilateral Posterior cingulate and orbitofrontal cortex.

Discussion: We found significant differences in cortical thickness between SCZ and HV in brain regions implicated in cognitive insight. Our findings also suggest higher self-certainty to be associated with thinner cortices in bilateral PCC and OFC. Significant relations between cortical thickness and cortical midline structures supports the critical role of these self-evaluative brain regions in cognitive insight in schizophrenia.

T170. THE SUPERIOR LONGITUDINAL FASCICULUS: CAN CSD BASED TRACT DELINEATION AND NODAL ANALYSIS CLARIFY THE PRESENCE OF TARGETED DIVERGENT DEVELOPMENTAL STRUCTURAL CONNECTIVITY IN ADOLESCENTS REPORTING PSYCHOTIC EXPERIENCES
Erik O’Hanlon*¹, Niamh Dooley¹, Colm Healy¹, Mary Cannon¹
¹Royal College of Surgeons in Ireland

Background: Superior Longitudinal Fasciculus (SLF) differences are consistently reported in psychotic disorders. The SLF is a complex large bundle of association white matter fibers that bidirectionally connect caudal, temporal cortex and inferior parietal cortex to locations in the frontal lobe. Advances in tractography methodologies detail four discrete subdivisions (SLF I, II, III and IV, more often referred to as the arcuate fasciculus (AF)). Greater specificity of the SLF subdivisions and associated cognitive networks may clarify the mechanisms of divergent tract developmental and functional aspects associated with psychotic experience symptomology in population based samples of adolescents within the extended psychosis continuum.

Methods: A case-control sample of 25 adolescents reporting psychotic experiences versus 25 controls (mean age 13.7 years). We employed High Angular Resolution Diffusion Imaging (HARDI) data based with constrained spherical de-convolution (CSD) based fibre tractography to delineate the discrete subdivisions of the SLF including the arcuate fasciculus. Following tract identification, standard diffusion metrics, (fractional anisotrophy (FA), and Diffusivity measures MD, AD and RD), were assessed. A secondary supportive ‘along-tract’ analysis to ascertain more subtle patterns of variation of tract integrity over the tract length was applied. White matter nodal analysis exploring the structural connectivity was applied to investigate additional functional networks recruited by and interconnected via the SLF. We investigate the ability of tractography of the SLF subdivisions and nodal analysis to identify possible differences between adolescents experiencing subclinical psychotic like experiences and those who don’t.

Results: Our results agree with recent studies of the SLF I and AF (Fernandes-Miranda et al 2015) revealing a pattern of asymmetry of these tracts with more extensive tract bundles being consistently identified in the left hemisphere compared to the right. Along-tract analysis revealed subtle patterns of change in discrete subdivisions of the SLF while nodal analysis shows promise in its ability to define precise organisational networks.

Discussion: Delineating the SLF subdivisions may clarify potential developmental trajectories between frontal and parieto-temporal speech-related areas contributing to the pathogenesis of psychotic like experiences. These results reveal the presence of aberrant structural connectivity in young adolescents with psychotic experiences.

T171. REDUCED FRONTAL CORTICAL THICKNESS AND SURFACE IN A 10 YEARS FOLLOW-UP OF EARLY ONSET PSYCHOSIS
Daniel Ilzarbe*¹, Elena de la Serna², Inmaculada Baiza³, Jose Pariente⁴, Adriana Fortea¹, Marina Redondo⁴, Nuria Bargallo⁵, Josefinia Castro-Fornieles³, Gisela Sugranyes³
¹Hospital Clinic de Barcelona; ²Hospital Clinic de Barcelona, Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM); ³Hospital Clinic de Barcelona, Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Institut d’Investigacions Biomèdiques Agustí Pi i Sunyer (IDIBAPS); ⁴Hospital Clinic de Barcelona, Institut d’Investigacions Biomèdiques Agustí Pi i Sunyer (IDIBAPS); ⁵Diagnostic and Interventional Imaging, Hospital Clinic de Barcelona, Institut d’Investigacions Biomèdiques Agustí Pi i Sunyer (IDIBAPS)

Background: In early-onset psychosis, distributed abnormalities are observed in grey matter volume. A recent hypothesis posits that these distributed changes are indicative of a plastic reorganization process occurring in response to a functional defect in neuronal information transmission. We investigated the structural covariance across various brain regions in early-stage schizophrenia to determine if indeed the observed patterns of volumetric loss conformed to a coordinated pattern of structural reorganization.