treatment outcome and may even prevent transition to illness. Based on abundant evidence that SZ and BD are associated with structural brain abnormalities, we investigated whether MRI brain-scans can be used to detect individual risk of developing SZ or BD in adolescents.
Methods: Structural MRI brain-scans were acquired in adolescent offspring (8–19 year) of parents with schizophrenia (oSZ;N=50), bipolar disorder (oBD;N=82), and without a mood or psychotic DSM-IV disorder (oHC;N=53), as part of the Dutch Bipolar and Schizophrenia Offspring Study (DBSOS). Support vector machine (SVM) models were trained on the gray matter tissue density maps to predict to which offspring class (oHC/oBD/oSZ) an individual belonged. Prediction accuracy was assessed using cross-validation. To validate our prediction models, we applied them to the tissue maps from subjects from a sample of unrelated HC/BD/SZ adults. Secondly, validated prediction models built from the adult subjects' MRI scans were applied to the tissue maps of the adolescents to predict illness class (HC/BD/SZ).
Results: The offspring-based model separated oHC/oSZ individuals with 77% accuracy ($p<0.001$), oHC/oBD with 68% accuracy ($p<0.001$), and oBD/oSZ with 64% accuracy ($p<0.01$). The adult-based models could separate the patients' offspring from the healthy offspring with 66–70% accuracy, but oBD from oSZ with lower accuracy (59%). In addition, the offspring models could separate adult patients from control subjects with comparable accuracy (66–68%) and separate the two patient groups with moderate accuracy (69%).
Discussion: The familial high-risk adolescents could be separated from controls with moderate to high accuracy (up to 77%), based on their MRI-scans. Moreover, the brain tissue patterns based on risk (adolescents) or illness (adults) were able to predict (risk) class in the other stage group. These results show (1) that high-risk individuals already show brain abnormalities, and (2) display similarities with abnormalities in ill adults, and (3) which can be used to detect (risk of) the disorder at the individual level. This suggests that MRI-scans, after further improvement and independent validation, may be of added value in the risk profiling of BD and SZ.

F173. PITCH AND DURATION MISMATCH NEGATIVITY, AUDITORY CORTEX GRAY MATTER, AND PRODROMAL ROLE FUNCTIONING IN THE FIRST EPISODE SCHIZOPHRENIA SPECTRUM

Dean Salisbury*[,1], Anna Shafer[2], Brian Coffman[2], Timothy Murphy[2]
[1]University of Pittsburgh School of Medicine; [2]University of Pittsburgh

Background: Primary auditory cortex, contained within Heschl's gyrus, is implicated auditory processing deficits and auditory verbal hallucinations in schizophrenia. Previously we showed a pathological correlation between the magnitude of the pitch-deviant mismatch negativity (pMMN) response during a passive auditory task and reductions in gray matter volume in Heschl's gyrus in subjects with first hospitalized for schizophrenia. The aim of this study was to replicate this finding, examine duration-deviant mismatch negativity (dMMN) and gray matter correlations, and to examine pre-psychosis role functioning, in a first episode psychosis sample within the schizophrenia-spectrum.
Methods: Participants included 40 first episode schizophrenia subjects (FESz) and 40 healthy controls (HC) matched for age, parental socioeconomic status, IQ, sex, and handedness. For MMN extracted from the EEG, standard tones were presented repeatedly (1 kHz, 75 dB, 50 ms pips, 5 ms rise/fall times, 330 ms SOA) with an occasional pitch deviant (1.2 kHz, 10% of trials) or duration deviant (100 ms, 10% of trials) interspersed. pMMN and dMMN were measured from subtraction waveforms as the average voltage within a 100-ms group averaged peak window at Fz. Role functioning was measured with the Cornblatt Global Functioning: Role scale. A subset of 28 FESz and 28 matched HC underwent structural MRI. High-resolution T1-weighted structural MRI data (3T) were acquired for each subject. Freesurfer was used to segment white matter, gray matter, and pial surfaces. Left and right Heschl's gyri were manually edited regions of interest, and gray matter volumes determined.
Results: Despite a lack of pMMN or dMMN reduction at the group level in FESz, both measures were pathologically correlated with role functioning in the year prior to hospitalization. In FESz, smaller pMMN at Fz was associated with poorer role functioning in the year prior to psychosis ($rho= -.35$, $p =.03$). Similar associations were observed for dMMN ($rho= -.41$, $p <.01$). Furthermore, in the subset of FESz with sMRI, smaller pMMN at Fz was associated with less total gray matter volume in left Heschl's gyrus (TGMV) ($rho= -.40$, $p =.03$) but not right. Similar associations were observed for dMMN ($rho= -.47$, p .01). As well, role functioning and auditory cortex gray matter volumes were not correlated in FESz. There were no significant correlations within HC.
Discussion: Although pMMN and dMMN are not reduced at the group level, the size of both are associated with impaired functioning prior to psychosis and reduced gray matter volume of left hemisphere Heschl's gyrus, containing primary and secondary auditory cortices. Thus, pMMN and dMMN although not sufficient as biomarkers of disease presence, are suitable as reliable biomarkers of disease progression. Presumably, poorer role functioning and less gray matter reflect more of the pre-psychosis progressive pathological process thought to occur in the prodromal phase of psychosis. Hence, pMMN and dMMN are likely to serve as sensitive and robust outcome measures for therapeutic interventions and to guide treatment strategies in the prodrome and during early psychosis.

F174. OBESITY AND BRAIN INTEGRITY IN SCHIZOPHRENIA AND BIPOLAR DISORDER: DIVERGENT PATTERNS OF WHITE MATTER MICROSTRUCTURE DAMAGE IN A TRANSDIAGNOSTIC APPROACH

Ramiro Reckziegel[1], Raffael Massuda[2], Leticia Czepielewski[3], Monise Costanzi[4], Rodrigo Spinz[3], Isadora Remus[3], Clarissa Gama*[,3]
[1]Hospital de Clínicas de Porto Alegre - HCPA; [2]Universidade Federal do Parana - Brazil; [3] Federal University of Rio Grande do Sul; [4]Hospital Presidente Vargas - Brazil

Background: Obesity is associated with both structural and functional changes of the central nervous system, and is frequent in psychiatry settings. The increased prevalence of obesity in schizophrenia (SCZ) and bipolar disorder (BD) is associated with illness severity, functioning impairment and cognitive deficits. It cannot be attributed to biases inherent in treatment-seeking samples, given that this association is detectable even in drug-naïve patients. Diffusion tensor imaging (DTI) analyses of major brain fibers in both disorders show shared abnormalities of white matter. DTI has been employed as a highly sensitive tool to investigate microstructural changes in white matter structure. While gray matter alterations in obesity point to a consistent reduction with increasing body mass index (BMI), volumetric changes in white matter are more complex and less conclusive. Fractional anisotropy (FA) is the most commonly used parameter as it is the best estimate of fiber integrity as well as axonal and myelin degeneration, and has been reported an association with BMI in depressed BD patients, but not explored in SCZ nor in comparison with a control group (CTR). The aim of this study was to analyze the relationship between obesity and brain alterations assessed by DTI in SCZ, BD and CTR.
Methods: In one-hundred fifty (N=150) individuals (SCZ:49; BD:35; CTR:66) were administered clinical rating scales, collected sociodemographic data and submitted to magnetic resonance imaging (MRI) acquisition in a 1.5 T machine. Linear regression models were performed independently for each group in order to test the relationship of BMI on

each brain fiber FA, using gender, age and years of disease for the patients as covariates.
Results: The mean BMI was different among groups (F(143)6.533; P= .002), higher in BD group (BD 29.69 ± 6.55; CTR: 25.54 ± 4.25; SCZ: 26.42 ± 6.02). In BD, the model that predicted FA in the left cingulate gyrus endings was significant controlling for covariates (F(4,21)= 3.273; p = .031; Adj. R^2= .384), with a main effect of BMI (t=-2.870; p= .009; β=- .531). For SCZ and CTR groups, we did not find significant models to predict brain fiber FAs from BMI controlling for covariates.
Discussion: BMI was associated with reduced FA in cingulate gyrus in BD, implying that obesity may play a role in microstructure damage in the limbic system. These findings are in consonance with the literature and may be related with processing of emotional and cognitive responses disrupted in BD. Conversely, it did not predicted FA in SCZ or CTR connection bundles, possibly because of the lower BMI levels in these groups. Also, we were not able to control for treatment adherence, a variable correlated with both white matter integrity and weight gain. At last, obesity appears to be correlated with white matter microstructure in a heterogeneous and disease specific course depending on the underlying psychopathology, showing association with impairment in BD but not SCZ and CTR. Further studies are needed to explore the role of treatment in the interpretation of these findings.

F175. NEUROLOGICAL SOFT SIGNS (NSS) AND BRAIN MORPHOLOGY IN PATIENTS WITH CHRONIC SCHIZOPHRENIA AND HEALTHY CONTROLS

Christina Herold*[,1], Marc Lässer[2], Ulrich Seidl[3], Dusan Hirjak[4], Philipp Thomann[1], Marco Essig[5], Johannes Schröder[1]
[1]University of Heidelberg; [2]Rehabilitation Hospital Zihlschlacht; [3]Center for Mental Health; [4]Central Institute of Mental Health, Medical Faculty Mannheim; [5]German Cancer Research Center

Background: Subtle abnormalities in sensory integration, motor coordination and sequencing of complex motor acts or neurological soft signs (NSS) are a characteristic phenomenon in patients with schizophrenia at any stage of the illness. Previous MRI studies in schizophrenia have shown that NSS are associated with abnormal cortical, thalamic and cerebellar structure. However, these studies mainly focused on first-episode or recent onset schizophrenia and the respective correlates between brain structure and NSS in patients with a chronic course of the disorder remain rather unclear.
Methods: 49 middle-aged patients with chronic schizophrenia with a mean duration of illness of 20.3 ± 14.0 years and 29 healthy subjects matched for age and sex were included. NSS were examined on the Heidelberg Scale and correlated to grey matter by using whole brain high resolution magnetic resonance imaging (3 Tesla) with SPM12 analyses.
Results: As expected, NSS in patients were significantly elevated in contrast to healthy controls, a finding, which not only applied to NSS sumscore, but also to the respective subscores motor coordination, sensory integration, complex motor tasks, right/left and spatial orientation and hard signs (p≤0.001).
Patients and healthy controls differed referring to right inferior frontal gyrus and left parahippocampal gyrus, with patients showing significantly reduced gray matter volumes, respectively. Within the patient group NSS total score was significantly correlated to reduced grey matter in right occipital lobe, left parahippocampal gyrus, left superior temporal gyrus, left thalamus (medial dorsal nucleus) and left posterior lobe of the cerebellum (declive). The respective findings remained significant after FDR correction for multiple comparisons (k=100 voxels). These results were confirmed when chlorpromazine (CPZ)-equivalents were introduced as additional covariate; moreover, no significant correlates arose between NSS and CPZ-equivalents. In the control group, VBM revealed that higher NSS total scores were significantly correlated with volume of right lentiform nucleus (medial globus pallidus).
Discussion: Our study leads further support to the model of 'cognitive dysmetria' with a disrupted cortico-cerebellar-thalamic-cortical circuit in schizophrenia. This interpretation is also maintained by a different correlational pattern in our control group. Furthermore, the middle temporal/parahippocampal region may correspond to reduced mnestic functions, which are – besides elevated NSS – consistently reported to be impaired in patients with a chronic course of the disorder.

F176. CLINICAL CORRELATES OF CORTICAL STRUCTURE IN ANTIPSYCHOTIC-NAÏVE SCHIZOPHRENIA PATIENTS BEFORE AND AFTER SIX-WEEK TREATMENT WITH A DOPAMINE D2/3 RECEPTOR ANTAGONIST

Kasper Jessen*[,1], Egill Rostrup[1], Rene C. W. Mandl[2], Mette Ø. Nielsen[1], Nikolaj Bak[1], Birgitte Fagerlund[1], Birte Y. Glenthøj[1], Bjørn H. Ebdrup[1]
[1]Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research, Mental Health Centre Glostrup, University of Copenhagen; [2]Brain Center Rudolf Magnus, University Medical Center Utrecht

Background: Schizophrenia has been associated with changes in both cortical thickness and surface area, but antipsychotic exposure, illness progression, and substance use may confound the observations. We investigated cortical thickness and surface area, as well as mean curvature, before and after antipsychotic monotherapy with a relatively selective dopamine D2/3 antagonist (amisulpride), in antipsychotic-naïve schizophrenia patients.
Methods: Fifty-six patients and 59 matched healthy controls (HC) underwent T1-weighted 3T magnetic resonance imaging. Forty-one patients and 51 HCs were re-scanned. FreeSurfer-processed baseline values and symmetrized percentage changes (SPC) in cortical structures were analysed using univariate ANOVA. Clinical measures comprised psychopathology ratings, assessment of functioning, and tests of premorbid and current intelligence.
Results: At baseline, groups did not differ in cortical thickness or surface area, while left curvature was higher in patients (p=0.015). In the complete sample, a higher curvature was associated with lower premorbid- (p=0.009) and current intelligence (p<0.001). Also, a lower surface area was associated with lower premorbid intelligence (p=0.014) and, in patients, a higher PANSS total (p=0.037). Lifetime substance use was associated with reduced cortical thickness (p=0.043). After six weeks, groups did not differ in overall change in cortical structures. Amisulpride dose (275.0 mg/day) did not correlate with cortical structures (p>0.43). A decrease in cortical thickness SPC was associated with less symptom improvement (p=0.002) and increase in surface area SPC was associated with improvement in GAF (p=0.047).
Discussion: Our results indicate that schizophrenia may be associated with subtle aberrations in cortical structures and these changes appear clinically relevant. Mean curvature holds promise as a sensitive supplement to cortical thickness and surface area, to detect complex structural brain abnormalities.

F177. THALAMIC SUBREGION RESTING STATE CONNECTIVITY IN SCHIZOPHRENIA MEASURED AT 7T

Jun Hua[1], Ann Choe[2], Nicholas Blair[2], Anita Barber[1], Allison Brandt[2], James Pekar[1], Peter van Zijl[1], Christopher Ross[2], Issel Lim[1], Feng Xu[1], Russell Margolis*[,2]