Methods: 44 healthy controls (HC), 63 at-risk mental state (ARMS) subjects without later transition to psychosis (ARMS-NT), 16 ARMS subjects with later transition (ARMS-T), and 38 antipsychotic-free patients with FEP were recruited from the specialized clinic for the early detection of psychosis at the Department of Psychiatry, University of Basel, Basel, Switzerland. Gyrification-based structural covariance networks (connectomes) were constructed to quantify global integration, segregation and small-worldness. Extremely randomized trees with repeated, nested cross-validation was performed to differentiate ARMS-T from ARMS-NT individuals. Permutation testing was used to assess the significance of classification performance measures.
Results: Small-worldness is reduced in both ARMS-T and FEP patients, secondary to reduced integration and increased segregation in both groups. In addition, we also found that transitivity (segregation) was significantly higher in ARMS-T and FEP groups compared to both ARMS-NT and healthy controls. Using the connectome properties as features, we obtained a high classification accuracy of 90% (balanced accuracy: 81%, positive predictive value: 85%, negative predictive value: 92%.) All performance measures were highly significant as indicated by permutation tests (all $p < 0.01$).
Discussion: Our findings suggest that there is poor integration in the coordinated development of cortical folding in patients who develop psychosis. This study further indicates that gyrification-based connectomes might be a promising means to generate systems-based measures from anatomical data that improves individual prediction of psychosis transition in CHR subjects.

O10.2. PSYCHOTIC EXPERIENCES ARE ASSOCIATED WITH HEALTH ANXIETY AND FUNCTIONAL SOMATIC SYMPTOMS IN PRE-ADOLESCENCE

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Background: Psychotic experiences (PE) in children and adolescents include hallucinations, delusions and thought-disturbances in the absence of psychotic disorders. Psychosis can be viewed on a continuum ranging from subclinical PE throughout the life span, to clinical psychosis syndromes. Psychosis and PE often co-occur with anxiety and depression, and several studies point towards an affective pathway to psychosis.
Health anxiety (HA) is a relatively new concept in child and adolescent psychiatry, characterized by obsessive rumination, with thoughts about suffering from a disease and misinterpretation of benign bodily sensations and changes. HA at age 11–12 years are associated with emotional disorders and functional somatic symptoms (FSS). In adolescence extensive physical changes occur, and it has been suggested that increased bodily awareness in some cases is accompanied aberrantly by anxiety regarding somatic sensations and somatic health.
We hypothesized that PE would be associated with HA and FSS, and that the associations would remain significant after adjustment for general psychopathology, suggesting a particularly strong specific link between these specific psychopathologies over and above the general multidimensionality of psychopathology.
Methods: The study population consists of 1572 children from the general population who participated in the 11–12 year follow-up of the Copenhagen Child Cohort 2000 (CCC2000). PE were assessed face-to-face by the Kiddie Schedule for Affective Disorders and Schizophrenia present and life-time version, and were rated dichotomously as either present (likely or definitely) or not present. HA was self-reported using the Childhood Illness Attitude Scale and FSS were self-reported using the Children's Somatization Inventory, Child Report Form, revised. HA and FSS were scored dichotomously into high (high 10%) and low (bottom 90%) scores. The associations between PE and HA + FSS were adjusted for i) general psychopathology, rated by parents, using the Strengths and Difficulties Questionnaire total score, ii) chronic physical conditions assessed by parent report, iii) onset of puberty onset defined by Tanner-stage I vs II-IV and iv) sex.
Results: PE were associated with HA (OR 2.91 (CI95% 1.86–4.57)) and FSS (OR 4.61 (CI95% 3.08–6.89)) in univariate analyses. In a mutually adjusted multivariate model which was further adjusted for general psychopathology, puberty, chronic physical conditions and sex, the associations still held significance for both HA (OR 1.73 (CI95% 1.03–2.90)) and FSS (OR 3.39 (CI95% 2.15–5.35)).
Discussion: Our study is, to our knowledge, the first to estimate the role of HA and FSS with regard to PE. Our hypothesis, that PE are associated with HA and FSS in pre-adolescence, was confirmed. The statistical effects were reduced, but remained significant after mutual adjustment and adjustment for general psychopathology. This shows that part of the association is confounded by a general load of psychopathology, but also indicates that HA and FSS contribute to PE over and above general psychopathology. Our study warrants further longitudinal studies, exploring if HA and FSS might constitute a specific pathway in psychosis development.

O10.3. EARLY BRAIN AND COGNITIVE DEVELOPMENT IN CHILDREN AT RISK FOR SCHIZOPHRENIA

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Background: Currently, most attempts at early identification and intervention for individuals at risk for schizophrenia focus on the prodromal phase of the illness during adolescence. However, cognitive and other deficits likely arise well before the prodromal phase. Many risk genes for schizophrenia play a role in early brain development, and recent studies indicate that the basic structural and functional networks of the brain are in place by the second year of life. This suggests that schizophrenia likely has origins in prenatal and early childhood brain development, and that early identification and intervention may need to be shifted to this developmental period to have a real impact on the incidence and severity of schizophrenia.
Methods: We studied early childhood brain development 25 children of mothers with schizophrenia and 178 control children. Children had a 3T MRI after birth and at 1 and 2 years of age, and global tissue volumes (gray matter, white matter, CSF), ventricle volumes, and cortical thickness and surface area were determined. Children were also assessed with the Mullen Scales of Early Learning at 1 and 2 years.
Results: Children at risk for schizophrenia had significantly lower Mullen Composite scores at both age 1 ($p=0.0078$) and 2 years ($p=0.0001$) compared to control children. Reductions were present in fine motor, expressive and receptive language scales at both ages. Overall, high-risk children did not differ from controls in global tissue volumes, though there was evidence of a gender effect. Female high-risk children tended to have reduced gray matter volumes after birth and at age 1 year (significant reduction after birth, $p =0.018$), while males tended have increased gray matter volumes at age 1 and 2 years (significant at 1 year, $p = 0.037$). Cortical thickness and surface area results tended to reflect the gray matter volume findings. Females had regions of significant cortical surface area reduction after birth, while males had several regions of significant of cortical surface area expansion at 1 year. Males had a few regions of significant changes of cortical thickness after birth.
Discussion: In the context of its limitations, this study confirms previous studies that find alterations of very early childhood development in children at risk for schizophrenia. It also indicates that alterations of cortical gray matter are evident in very early childhood, and that there is a gender difference in these alterations, with females having reduced gray matter volumes and males having increased gray matter volumes. Brain structure and

cognitive abnormalities associated with risk for schizophrenia are present shortly after birth; future studies may be able to identify very early biomarkers of risk that will not only improve our understanding of how brain abnormalities associated with schizophrenia develop, but also define periods of childhood development that can be targeted with early intervention.

O10.4. INCREASED RISKS FOR NON-AFFECTIVE PSYCHOTIC DISORDER AND BIPOLAR DISORDER IN AUTISM SPECTRUM DISORDER

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Background: Young adults with autism spectrum disorder (ASD) appear to be at increased risk for non-affective psychotic disorder (NAPD) and bipolar disorder (BD). However, previous studies have mostly examined the co-occurrence of ASD with NAPD and BD, which is problematic given substantial overlap in symptoms between these disorders. As such, previous risk estimates may have been influenced by diagnostic bias (i.e. NAPD/BD symptoms being mistakenly diagnosed as ASD) or selection bias (i.e. individuals being recognized and/or registered with ASD due to the development of NAPD/BD). In the present study, we used longitudinal data from two Dutch psychiatric case registers to obtain more reliable risk estimates for NAPD and BD among young adults with ASD.
Methods: ASD cases were followed between ages 16 and 35 (n = 17,234). Kaplan-Meier estimates were used to calculate risks for NAPD and BD. We conducted separate analyses to reduce possible bias, taking into account the age of ASD diagnosis (ASD diagnosed before or after age 16) and sequence of diagnoses (ASD before or after NAPD/BD). We conducted prognostic analyses using Cox regression to examine possible risk factors for NAPD and BD in ASD.
Results: ASD cases were at an increased risk for NAPD and BD compared to previously-reported risks in the general population, even when ASD had already been diagnosed at an early age, before a diagnosis of NAPD or BD. Among cases who were diagnosed with ASD at least one year before a diagnosis of NAPD or BD, an estimated 7.90% (95% CI, 6.70–9.31) developed NAPD, whereas 1.35% (95% CI, 0.89–2.04) developed BD, prior to age 36. Prognostic analyses showed that men with ASD were at a relatively greater risk for NAPD, whereas women with ASD were at a greater risk for BD.
Discussion: Young adults with ASD are at an increased risk to develop NAPD and BD, which is not only the result of diagnostic or selection bias. More research is necessary to examine possible mechanisms underlying these risks.

O10.5. ABNORMAL MODULAR ORGANIZATION OF THE FUNCTIONAL CONNECTOME PREDICTS CONVERSION TO PSYCHOSIS IN CLINICAL HIGH-RISK YOUTH

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Background: The first episode of schizophrenia is typically preceded by a prodromal phase characterized by sub-threshold symptoms and declining functioning. Elucidating the neurobiological substrate of prodromal symptoms that progress into overt psychotic illness is crucial to the development of early detection and intervention strategies for schizophrenia. In this study, we performed a functional connectome analysis in a large group of adolescents and young adults at Clinical High Risk (CHR) for schizophrenia. We aim to assess whether, and if so how, baseline connectome organization distinguishes CHR youth that go on to develop psychosis.
Methods: This study comprises a total of 251 subjects, including 158 psychotropically-naïve CHR subjects (CHRs) and 93 healthy controls (HCs), who were matched to CHRs on age, gender, and level of education. Prodromal symptoms and cognition were assessed using the SIPS structured interview and MATRICS cognitive battery. Anatomical T1 MRI and resting-state fMRI scans were collected at baseline and processed using Freesurfer v6.0 and CONN v17.d software. For each subject, a functional connectome map was reconstructed consisting of 162 nodes representing 148 cortical regions from the Destrieux atlas and 14 subcortical structures. Functional connectomes were analyzed in terms of modular topology using the Louvain community detection method. Modular network partitions of individual CHRs were compared to a group-averaged HC network using the rand similarity coefficient (SR), providing a measure of the level of (ab)normality of the CHRs' modular partitions. Analysis of covariance (correcting for age- and gender) was used to compare SR levels between CHRs who developed psychosis during follow-up (CHR+; N = 23) as compared to CHRs who did not develop psychosis (CHR-; N = 135). Kaplan-Meier analysis was used to estimate psychosis-free survival functions for CHRs with below- versus above-average SR, which were compared using log-rank tests. Cox regression analysis was used to assess how baseline connectome organization and clinical measures (i.e., demographics, symptoms, IQ) predicted time to conversion.
Results: Modular community detection in HCs yielded five major modules including a posterior 'visual', central 'sensorimotor', medial frontoparietal 'default-mode', lateral frontoparietal 'central-executive', and inferior 'limbic' module. Modular connectome organization of CHR+ was significantly less similar to HCs than CHR- ($F(1,154) = 7.14$, $p = 0.008$). A region-specific analysis to identify which regions contributed most to aberrant modular connectome organization in CHR+ showed that superior temporal (including STG), medial temporal (including amygdala), and ventromedial prefrontal regions were most abnormal in terms of their modular assignment. Psychosis-free survival functions of CHRs with low versus high SR were significantly different ($z = 2.5$, $p = 0.013$), with a Hazard ratio of 3.3 indicating an over 3-fold relative event rate (i.e., conversion to psychosis) in CHRs with abnormal baseline connectome organization. Cox regression analysis indicated that baseline connectome organization ($z = -2.3$, $p = 0.019$), IQ ($z = -2.7$, $p = 0.007$), and gender ($z = 2.0$, $p = 0.048$) predicted time to conversion.
Discussion: This study indicates that abnormalities in functional connectome organization precede the first psychotic episode. Conversion to psychosis was found to be over three times more likely in CHRs with abnormal modular organization of the functional connectome at baseline. Our results suggest that functional connectome reorganization may underlie the gradual manifestation of prodromal symptoms. These findings may contribute to early diagnosis and intervention in schizophrenia.

O10.6. OLANZAPINE IMPAIRS CENTRAL INSULIN ACTION: EFFECTS ON BODY FUEL PREFERENCE IN RATS

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Background: Antipsychotics (APs) remain the cornerstone of treatment in schizophrenia, with increasing use on- and off- label. Olanzapine (OLZ)