Abstracts for the Sixth Biennial SIRS Conference

O9.8. STRESS AND COGNITIVE FUNCTION AMONG INDIVIDUALS AT CLINICAL HIGH-RISK FOR PSYCHOSIS: FINDINGS FROM THE NAPLS COHORT

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Background: Accumulated evidence from non-human animal studies suggests that the prominent deficits in memory and executive function that characterize individuals with psychosis may, at least in part, be due to the effects of stress on the brain regions that support these functions. However, studies of patients with established psychosis have yielded inconsistent findings with regards to the relationship between stress and cognition, and research in high-risk populations is notably lacking. Utilising data from the North American Prodrome Longitudinal Study 2 (NAPLS 2), we aimed to further elucidate the relationship between stress (daily stressors, life events, and childhood trauma) and cognitive function in clinical high-risk (CHR) individuals and healthy controls (HC). We additionally explored the role of potential mediators [hypothalamic-pituitary-adrenal (HPA) axis function] and moderators (group status, sex, family history of illness).

Methods: The sample comprised 885 participants (CHR=646; HC=239) who completed measures of stress and cognitive function at the NAPLS 2 baseline assessment. Stress measures included the Daily Stress Inventory and a modified version of the Psychiatric Epidemiology Research Interview Life Events Scale, both of which provided continuous measures of stress exposure (number of events) and distress (subjective feelings of distress). Participants were also interviewed using the Childhood Trauma and Abuse Scale to determine any exposure to childhood trauma (abuse, neglect, and bullying occurring prior to age 16 years). Basal HPA axis activity was determined via salivary cortisol samples obtained at the baseline assessment and standardised scores from selected subtests from the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) were used to derive two cognitive domain scores (memory and executive function). To examine relationships between stress and cognitive domain scores, linear regression analyses were performed on standardised variables.

Results: Daily stressor exposure, daily stressor distress, and life event exposure exhibited negative quadratic (i.e., inverted U-shaped) associations with both memory and executive function (P < 0.01 for all). In contrast, the reverse pattern (i.e., a negative linear relationship and a positive quadratic relationship) was shown in the model for life event distress and memory domain scores (P < 0.01) whilst trauma history showed only a trend-level association with poorer memory performance (P = 0.084). These relationships, which did not differ across CHR and healthy control groups, were largely unchanged after adjusting for demographic factors and salivary cortisol. Exploratory analyses suggested that trauma exposure and a family history of psychosis may moderate the relationship between daily stressors/ life events and cognitive function.

Discussion: In this large sample of predominately CHR individuals, we observed that the association between stress and cognition is complex and differs across stressor types. The negative quadratic associations that we observed for daily stressor exposure, daily stressor distress, and life event exposure imply that whilst lower levels of stress may facilitate memory and executive function, there may be a negative impact on cognition when these stressors become more frequent and distressing. Interventions aiming to minimise stress exposure and promote effective coping strategies might feasibly improve cognition in CHR individuals.

O10. Oral Session: Prediction

O10.1. DISORGANIZED GYRIFICATION NETWORK PROPERTIES DURING THE TRANSITION TO PSYCHOSIS

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Background: There is urgent need to improve the limited prognostic accuracy of psychopathology-based classifications to predict the onset of psychosis in clinical high-risk (CHR) subjects for psychosis. However, as yet no reliable biological marker has been established to differentiate CHR subjects who will develop psychosis from those who will not. This study investigated abnormalities in graph-based gyrification connectivity in CHR subjects and patients with first-episode psychosis (FEP) and tested the accuracy of this systems-based approach to predict the transition to psychosis among CHR individuals.
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-worldliness 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 to 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 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