Background: Schizophrenia is a disorder with a heterogeneous genetic and neurobiological background that influences early brain development. The symptoms is the behavioural outcome of deviations in early neurodevelopment, including prenatal insults such as obstetric complications (OC). OC have been linked to an increased risk for schizophrenia in offspring, especially in early-onset schizophrenia (EOS). Extensive cognitive deficits occur in EOS, whereof executive function is one of the best documented. Cognitive dysfunction reflects underlying abnormalities in the brain neurodevelopment, and is considered to be an intermediate variable between OC and schizophrenia. Our research group (Teigset et al, 2016) is the only study that has investigated the relationship between OC and cognition in EOS. This study aimed to examine the frequency of OC in EOS compared to controls, and also investigate the relationship between OC and neurocognitive dysfunction. In the present presentation we will focus upon executive function and report the findings when comparing the same sample of patients and controls as in the Teigset et al study.
Methods: Nineteen EOS patients and 53 healthy controls were tested with the MATRICS Consensus Cognitive Battery(MCCB), and two tests for assessment of executive functioning. The selected subtests for measuring executive function were the D-KEFS Color Word Interference Test (Stroop) and the Wisconsin Card Sorting Test. WCST assesses perseverative responses and failure to maintain set, and the Stroop assesses time in seconds for completing the Inhibition and Switching conditions. The cognitive measures were combined with data from the Norwegian Birth Registry (NMBR). Information on OC was collected from the NMBR containing information about all births in Norway, including information about maternal health before and during pregnancy, and any complications arising during pregnancy or birth. The registry includes information about medication during pregnancy, labor interventions, birth complications, maternal complications after birth, whether this was a live birth, any diagnoses in the child or evidence of congenital abnormalities.
Results: Group differences in OC were studied with Student's t-tests and Chi-square tests. The association between OC and cognitive function were studied using linear regression analyses. The results indicated no group differences in OC in EOS and healthy controls. However, a shorter gestational length in the EOS group led to significant decreases in the overall neurocognitive composite score (MCCB), in processing speed and in the two executive function tasks.
Discussion: Our findings indicate that a shorter gestational length did not increase the risk for developing EOS, but was significantly associated with the cognitive difficulties in this group. In particular, executive functioning were affected, a finding in line with those of Brown et al (2009), showing that prenatal infections were associated with impaired executive function. Interestingly, reductions in neurocognitive performance among those exposed to OC was less extensive in the healthy control group with the same labor-conditions, which may indicate a greater effect of OC on neuropsychological development in schizophrenia. In conclusion, gestational length does not increase the risk for developing EOS, but significantly affects the cognitive difficulties - particularly executive function - seen among cases.
References:
1. Brown et al. (2009) Am J Psych, 166: 683–690.
2. Teigset et al. (2016). Psych Res, 244: 78–85.

S198. PRE-ADOLESCENT BRAIN STRUCTURE: THE INTERPLAY BETWEEN GENETIC VULNERABILITY FOR SCHIZOPHRENIA AND CORTISOL LEVELS

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Background: Schizophrenia is a highly heritable disease, mediated through a combination of common and rare genetic variants. In addition to genetic risk, several putative environmental risk factors have been studied in the context of schizophrenia. It has been suggested that the genetic effects on the etiology of schizophrenia may be of limited explanatory power if not viewed in the context of interaction with environmental stressors. Here, in a pre-adolescent population-based sample, we used polygenic risk scores from a case-control discovery sample of the Psychiatric Genomics Consortium as indicators of genetic vulnerability to schizophrenia. In addition, hair cortisol levels were obtained as a naturalistic quantitative metric of long-term physiological stress. We examined whether cortisol levels moderated the relationship between schizophrenia polygenic risks scores and pre-adolescent brain structure.
Methods: This study was embedded in the Generation R Study, a prospective birth cohort from the Netherlands. Polygenic risk scores for schizophrenia were calculated in children of European ancestry only. P-value thresholds for inclusion of genetic variants in the polygenic risk score varied between $P < 0.001$ and $P < 1$. Hair cortisol was collected when the children were approximately 6 years old. At age 9 years, children underwent a magnetic resonance imaging (MRI) procedure to assess volumetric brain measures. After genetic and neuroimaging quality control procedures, the final sample consisted of 522 participants. Linear regression models were conducted to examine the associations between schizophrenia polygenic risk scores, hair cortisol levels, and brain volumes. All analyses were adjusted for age, sex, hair color, hair product use and four genetic principal components.
Results: Schizophrenia polygenic risk scores were not associated with hair cortisol levels (P-value threshold [PT] < 0.001, $\beta = -0.03$, 95% confidence interval [CI] -0.11 – 0.05, $P = 0.441$), cortical grey matter volume ($PT < 0.001$, $\beta = -0.03$, 95% CI -0.11 – 0.05, $P = 0.457$) or cerebral white matter volume ($PT < 0.001$, $\beta = -0.04$, 95% CI -0.12 – 0.04, $P = 0.356$). Higher schizophrenia polygenic risk scores were associated with lower total ventricle volume ($PT < 0.001$, $\beta = -0.10$, 95% CI -0.19 – -0.02, $P = 0.022$), including when mutually adjusted for total brain volume. Notably however, hair cortisol exhibited a positive interaction with schizophrenia risk scores in predicting total ventricle volume ($PT < 0.001$, $\beta = 0.10$, 95% CI 0.01 – 0.18, $P = 0.027$), i.e. higher schizophrenia polygenic risk score and higher hair cortisol levels were associated with increased ventricle volumes. Hair cortisol was not independently associated with total ventricle volume ($PT < 0.001$, $\beta = -0.05$, 95% CI -0.14 – 0.03, $P = 0.215$).
Discussion: Elevated hair cortisol levels, a biological index of long-term stress, moderated the association between genetic vulnerability to schizophrenia and total cerebral ventricle volume among pre-adolescents. These findings underscore the importance of the interplay between genes and environment in shaping brain development. Using a polygenic risk score for schizophrenia, we provide novel, albeit preliminary, evidence for gene-environment interaction between genetic risk for schizophrenia and environmental stressors in the general pre-adolescent population. This may help to elucidate underlying etiologies and possible early interventions for the psychosis spectrum.

S199. ENHANCED OLFACTORY IDENTIFICATION IN ADOLESCENTS WITH PSYCHOTIC EXPERIENCES

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Background: The olfactory system has a widely distributed anatomical network reaching both cortical and subcortical structures (Milardi et al., 2017). Olfactory dysfunction has been associated with schizophrenia (Moberg & Turetsky, 2003), where deficits in odour identification (Seidman et al., 1997), odor detection threshold sensitivity (Serby et al., 1990) and odour memory (Wu et al., 1993) can be seen early in the course of the disorder