general population.[3] Little is known though about the contribution of the PRS in the risk prediction in children at genetic risk.

Our group and others have shown that the risk trajectory of high-risk children (HR) born to an affected parent can be characterized by their risk endophenotypes, i.e. specific cognitive deficits and psychotic-like or mood-like experiences in childhood that flag the neurodevelopmental origin of the illness. Children at risk accumulate these risk endophenotypes along their developmental trajectory and this aggregation is a predictor of later transition to illness.[4,5]

We hypothesized that since the PRS is a reflection of the genomic liability to illness, it would consequently relate to risk endophenotypes and their aggregation in children at risk. Our objectives were to evaluate i) the power of PRS to discriminate children at risk from healthy controls and, ii) the association of SZ and BP PRS to early risk endophenotypes in these children.

**Methods:** The sample comprised 70 HR from the Eastern Quebec Kindred Study of multigenerational families densely affected by SZ and BD and 894 healthy controls from the CARTaGENE project. Whole genome SNP genotyping was performed from blood samples. Calculation of PRS was made according to our previous report.[1] All HR were characterized using 4 established risk indicators[4]: cognitive impairments, psychotic-like experiences, childhood non-psychotic Axis 1 DSM diagnoses and episodes of poor functioning. Stratification of the HR by the presence of childhood trauma was also performed.

**Results:** PRS distinguished HR from healthy controls ($p<.05$). Significant associations of SZ PRS and risk endophenotypes were detected for psychotic-like experiences (relative risk RR=1.4, p=.034) and, when stratifying for trauma, for the speed of processing cognitive domain (p=.049). Importantly, PRS was significantly higher in HR who aggregated psychotic-like experiences and axis 1 diagnoses (RR=3, p=.01), and a trend was detected with the aggregation of cognitive deficits, psychotic-like experiences and axis 1 diagnoses (p=.08).

**Discussion:** PRS were associated with individual risk endophenotypes and with the aggregation of risk endophenotypes in children born to an affected parent. These results call for further study on the exact contribution to the childhood risk status of the genomic susceptibility indexed by PRS and the combination of risk endophenotypes. Considering that the clinically high-risk (CHR) status can be defined as a late phase of risk,[6] the accumulation of risk indicators in childhood, including PRS and risk endophenotypes, document this early life period as the optimal timing for early intervention approaches.

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## F32. DIFFERENCES BETWEEN YOUTH AT CLINICAL HIGH-RISK FOR PSYCHOSIS WHO DO NOT TRANSITION TO PSYCHOSIS: THE NORTH AMERICAN PRODROME LONGITUDINAL STUDY (NAPLS-2)

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**Background:** In the clinical high risk (CHR) for psychosis literature, typically, the focus is on determining the risk of conversion to psychosis. However, between 70% and 85% of youth who meet CHR criteria do not develop psychosis during the follow-up period of the study in which they participate. The aim of this study is to focus on CHR youth who did not transition to psychosis and to determine whether there are differences amongst them.

**Methods:** The North American Prodrome Longitudinal Study (NAPLS-2) is an 8-site prospective, longitudinal study including 764 help-seeking youth, age 12–35, meeting criteria for a psychosis risk syndrome based on the Structured Interview for Psychosis-risk Syndromes (SIPS), and 279 healthy controls (HC). For this analysis, only youth who did not make a transition to psychosis and completed 2 years of follow-up (n=278, 154 males, 124 females; mean age 18.8) were included. At the 24-month final assessment, the sample was divided into 3 groups: 1) those in remission, determined by scores ≤2 on all 5 attenuated psychotic symptoms on The Scale of Psychosis-risk Symptoms (SOPS); 2) symptomatic, determined by still having a rating of 3–5 on any one of the 5 attenuated psychotic symptoms on the SOPS; 3) prodromal progression, determined by continuing to meet the Criteria of Psychosis-risk Syndromes (COPS). The groups were compared at baseline and at 24-month follow-up on: age, gender, the presence of a current and lifetime psychiatric diagnosis, and social and role functioning. The use of antipsychotic medication was examined across all assessments (baseline, 6-, 12-, 18- & 24 months) using Generalized Linear Models to examine differences among the 3 groups.

**Results:** Among the participants, 110 (39.57%) were in-remission, 93 (33.45%) symptomatic, and 75 (26.98%) prodromal progression. At baseline there were no significant differences in age, gender, social and role functioning, or SCID diagnoses except on current PTSD (p=.001) with most cases in the prodromal progression group, and on current anxiety disorder (p=≤.0001) with most cases in the symptomatic group. The prodromal progression had significantly higher ratings on unusual thought content compared to the in-remission group and significantly higher ratings on suspiciousness than the symptomatic group. At 24-month follow-up there were significant differences in negative symptoms (p=≤.0001) between prodromal progression (M=9.19), symptomatic (M=8.84), and in remission (M=5.99) groups; and social functioning (p=≤.005; M=6.56, M=6.68, M=7.20 respectively). Although the in-remission group had the highest ratings on social functioning these were significantly lower in social (M=7.20) and role (M=6.68) functioning than HC (M=8.73, M=8.62 respectively). The groups did not differ on their use of antipsychotics over the course of their 2 years in the study.

**Discussion:** There were very few differences on baseline measures amongst the different two-year outcome groups. At 2 years, even though those in remission had improved social and role functioning relative to the other 2 groups, they still had lower social and role functioning than HC.

## F33. MATERNAL AND PATERNAL CANNABIS USE DURING PREGNANCY AND RISK OF PSYCHOTIC SYMPTOMS IN THE OFFSPRING

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**Background:** Cannabis use has repeatedly been associated with psychotic symptoms, with persistent risks beyond the direct effects of exogenous cannabinoids. However, it remains unknown whether cannabis use during

pregnancy is a causal risk factor for psychotic symptoms in the offspring, or whether this relationship is explained by shared etiological factors, such as genetic and environmental vulnerabilities. More innovative study designs are needed to address this question. Here, we examined the adverse effects of cannabis exposure during pregnancy on psychotic symptoms in pre-adolescent offspring. Such a method would help causal inference as comparisons can be made between the observed associations of maternal versus paternal cannabis use during pregnancy and the risk of psychotic symptoms in the offspring. If the association between cannabis use and psychotic symptoms is causal, early intra-uterine exposure to cannabis could potentially affect neurodevelopment and, hence, contribute to the pathogenesis of psychotic phenomena in children who have not yet used cannabis themselves.

**Methods:** This study used data from the Generation R Study, a prospective population-based birth cohort from Rotterdam, the Netherlands. Participants were included if data on maternal cannabis use during pregnancy of offspring psychotic-like symptoms at age ten years were available (N = 3692). To determine cannabis exposure, we used prospective maternal self-reports during pregnancy and cannabis metabolite levels from urine. Paternal cannabis use during pregnancy was obtained through maternal report. At age ten years, children were queried regarding psychotic symptoms. Ordinal logistic regression was conducted to investigate whether maternal and paternal cannabis use were associated with offspring psychotic symptoms. In a secondary analysis, a distinction was made between maternal cannabis use exclusively before versus continued maternal cannabis use during pregnancy. All models were adjusted for covariates that were previously associated with cannabis use in this cohort.

**Results:** Maternal cannabis use was associated with an increased risk for psychotic symptoms in their offspring (n = 183, ORadjusted=1.38 [95% CI 1.03–1.85]). Estimates were comparable for cannabis use exclusively before pregnancy versus continued cannabis during pregnancy (cannabis use before pregnancy: n = 98, ORadjusted=1.39 [95% CI 0.94–2.06]; continued cannabis use during pregnancy: n = 85, ORadjusted=1.37 [95% CI 0.90–2.08]). Paternal cannabis use was significantly associated with offspring psychotic symptoms (n = 297, ORadjusted=1.44 [95% CI 1.14–1.82]).

**Discussion:** Using data from a large population-based birth cohort, we demonstrated that maternal and paternal cannabis use were each associated with offspring psychotic symptoms at age ten years, well before the risk period of adolescent cannabis use initiation. Notably, estimates were similar for maternal cannabis use exclusively before pregnancy versus continued cannabis use during pregnancy. Moreover, estimates were comparable for maternal versus paternal cannabis use during pregnancy. This suggests that common etiologies, rather than solely causal intra-uterine mechanisms, underlie the association between parental cannabis use and offspring psychotic symptoms, shedding potential new light on the debated causal path from cannabis use to psychosis. Our findings indicate that diagnostic screening and preventative measures need to be adapted for young people at risk for severe mental illness, and that these programs need to offer a family-focused approach.

## F34. AUDITORY SENSORY GATING IN YOUNG ADOLESCENTS WITH EARLY-ONSET PSYCHOSIS: A COMPARISON WITH ADHD

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**Background:** Numerous studies have demonstrated impaired sensory gating in schizophrenia and this phenomenon has been proposed as a candidate biomarker for the disorder. Sensory gating is typically assessed during an auditory paired-click test commonly referred to as a P50 suppression paradigm. When two identical stimuli are presented, healthy subjects show a decrease in their neural response to the second stimulus, reflected in a decreased P50 amplitude, whereas schizophrenia patients on average show a much smaller decrease. So far, sensory gating has primarily been investigated in adult patients with schizophrenia, but gating disturbances have also been demonstrated in other illnesses, e.g. in schizotypal personality disorder, albeit less marked. Although the typical age of onset for schizophrenia is late adolescence to early adulthood, a sizable group of patients presents with psychotic symptoms during childhood or early adolescence. Manifestation of psychotic symptoms before the age of 18 is commonly referred to as early-onset psychosis (EOP). Various studies have reported a more severe course of illness and a poorer outcome in EOP compared to the adult-onset form of the disorder. In parallel, we expect more pronounced sensory gating deficits in EOP.

Impaired sensory gating may not be specific to psychosis, but rather a shared disturbance of neuropsychiatric disorders. Although symptoms of attention deficit hyperactivity disorder (ADHD) differ in many ways from those found in schizophrenia, there are common characteristics. Compared to schizophrenia, relatively few studies have investigated sensory gating in ADHD, and some report P50 gating deficits similar to those frequently found in patients with schizophrenia.

**Methods:** We investigated P50 suppression in a large cohort of adolescents (12–17 years old) consisting of patients with either EOP (N=56) or ADHD (N=28) as well as age and gender matched healthy controls (N=72). In our paradigm two identical sounds (clicks) were presented separated by a 500ms interval. The amount of suppression was expressed as the ratio between the P50 amplitude of a subject's response to the first click and his/her amplitude in response to the second click.

**Results:** The EOP patients scored significantly higher on PANSS (positive, negative, general, and total PANSS scores) compared to both ADHD patients and healthy controls. However, there were neither significant group differences in raw P50 amplitude, nor in the gating ratios between young adolescents with EOP, ADHD and healthy controls.

**Discussion:** This is the first study to investigate sensory gating in young adolescents with EOP. We found no P50 suppression deficits in these patients which, given the relatively large sample size in our study, cannot merely be ascribed to power issues. The results are in contrast with the majority of studies investigating sensory gating in schizophrenia and ADHD. However, the results are in agreement with earlier studies from our lab showing evidence of inconsistent P50 suppression deficits in two separate cohorts of adult, antipsychotic naïve, first-episode patients with schizophrenia. Based on our findings, P50 sensory gating cannot differentiate between young adolescents with EOP or ADHD, and deficient P50 suppression does not seem to be a valid biomarker for EOP.

## F35. PRESCRIPTION PATTERN OF ANTIPSYCHOTICS FOR CHILDREN AND ADOLESCENTS WITH SCHIZOPHRENIA IN KOREA BASED ON NATIONWIDE DATA

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**Background:** This study aimed to analyze the extent and pattern of antipsychotic prescription for Korean children and adolescents with schizophrenia using population-based data.

**Methods:** Our data was retrieved from the Korean National Health Insurance Review & Assessment Service-National Sample for 2013, which was a stratified sampling from the entire population under the Korean national health insurance program. Among 0.2 million children and adolescents aged 6–18 years from data, subjects who had received any