adverse life events, and insecure attachment styles. Earlier studies have shown that PEs during childhood are predictive of later psychotic disorders, especially if they persist over time. We expect the possible risk factors to have a cumulative effect.

**Methods:** The Danish High Risk and Resilience Study, Via 11, is the first follow-up of a cohort of 522 children and their parents. The cohort consists of children where one or both parents have been diagnosed with a schizophrenia spectrum disorder (N=202), children where one or both parents have been diagnosed with bipolar affective disorder (N=120) and children where neither of the parents have been diagnosed with these disorders (N=200). The children and their parents were assessed with a comprehensive assessment battery e.g. social- and neurocognitive tests and diagnostic interviews when the children were seven years old, and they will now be reassessed for the first time at age 11. Data for this study is currently being collected as a part of the VIA 11. Psychotic experiences will be assessed on the Scale of Prodromal Symptoms based on K-SADS interviews and with the Magical Thinking Questionnaire. Social cognitive skills will be assessed with Frith-Happe Animated Triangles and Theory-of-Mind Storybook Frederik. Cognitive bias i.e. jumping to conclusions will be assessed with the Beads task. Adverse life events will be assessed with the K-SADS interviews, the Child Trauma Screening Questionnaire, and with a questionnaire about bullying based on the Olweus Bully/Victim Questionnaire. Measures of neurocognitive and attentional deficits will also be included. Child attachment style was assessed with the Story Stem Assessment Protocol and emotion recognition with the ERT from Cantab.

**Hypotheses:**
- Age seven: Children in the two high risk groups will have higher rates of insecure or disorganized attachment styles compared with children in the control group. We expect insecure and disorganized attachment to be associated with poorer social cognition (theory of mind and emotion recognition) and with worse general psychopathology and PEs.
- Age 11: We expect children born to parents with schizophrenia spectrum disorders to report higher frequencies of PEs than children born to parents without these disorders. We expect children with PEs to have higher levels of general psychopathology and poorer levels of daily functioning than children without PEs. We expect children in the two high risk groups to have poorer theory of mind than children in the control group.
- Age 11: We expect PEs to be associated with poor social cognition, particularly hyper theory-of-mind, higher rates of cognitive bias, adverse life events, neurocognitive and attentional impairments, and to be predicted by insecure and disorganized attachment styles.

**Results:** The data collection started in March 2017. Results from the 11-year-follow-up are expected in 2020.

**Discussion:** Examining PEs over time during childhood is important since it may improve our ability to identify children who are at a particularly high risk of developing psychotic disorders and other psychopathology later in life and thus to identify a particularly vulnerable subgroup towards whom early interventions should be targeted.

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**S35. NEURORADIOLOGICAL FINDINGS IN CHILD AND ADOLESCENT PATIENTS WITH PSYCHOTIC DISORDERS**

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**Background:** A 22 - 31% prevalence of abnormal radiological findings (RF) has been reported among patients with first episode of psychosis (FEP), ranging from clinically non-significant findings to overt neurological pathology. While one study (Borgwardt et al., 2006) found a higher proportion of RF in adult subjects at high risk for psychosis (35%) and FEP patients (40%) than in patients with depression (18%) or healthy controls (12%), another found a similar increase in RF in patients with affective and psychotic disorders (Landin et al., 2016). This suggests that macroscopic brain anomalies may be characteristic of at least a subset of patients in the early stages of psychosis, and these RF may not be specific to schizophrenia, but also to psychosis with affective symptoms.

To this day, all published research studies have been done in primarily adult samples. Psychosis with onset before age 18 may be associated with more salient biological features linked with greater genetic load and neurodevelopmental antecedents (Arango, 2014).

**Aims:** To assess the prevalence of neuroradiological abnormalities in a population with early-onset psychosis (EOP) in comparison to a sample of community controls, and to evaluate the association of these findings with the type of psychotic disorder of the patients.

**Methods:** Design: Naturalistic, observational, retrospective, single-center controlled study.

A chart review of individuals admitted to the Inpatient unit of the Dept. of Child and Adolescent Psychiatry and Psychology from January 2013 to December 2016 was done. Patients were 6 to 17 years old, fulfilled DSM-IV-TR criteria for a psychotic disorder (PD), and had a radiology report of a brain MRI. The community control (CC) group had a similar age and gender distribution and no current diagnosis of any psychotic disorder. Any neurological or severe medical condition or head trauma with loss of consciousness were exclusion criteria for both groups. Sociodemographic, clinical, and radiological variables were recorded for both groups. Given the association of abnormal RF with prematurity, perinatal complications and neurodevelopmental disorders, these data were collected and sorted dichotomously.

Descriptive statistical analysis consisted of a means and standard deviation for quantitative variables and percentages for qualitative variables. Between-group differences were calculated with chi-square test or Fisher's test using IBM SPSS v23.

**Results:** A total of 191 individuals were included (127 PD vs 64 CC, mean ages: 14.7 ± 1.8 vs 13.8 ± 2.3, t=3.0, p=.01; %females: 55.9.0% vs 60.9%, χ²=44, p=.50). Main diagnoses in PD were psychosis not otherwise specified (PNOS) (59.1%), schizoaffective disorder (SAD) (12.6%), schizophrenia (SCZ) (11.0%), bipolar disorder (BD) (8.7%) and major depression with psychotic features (MDD) (8.7%).

The PD group presented with a significantly higher prevalence of qualitative neuroimaging abnormalities in comparison to CC (21.3% (n=27) vs 6.2% (n=4), χ²=7.1, p=0.008). These included arachnoid cysts, dilated perivascular space or white matter intensity anomalies. The prevalence of abnormal RF was 25.3% in PNOS, 21.4% in SCZ, 18.2% in MDD 12.5% in SAD and 9.1% in BD.

**Discussion:** A significantly higher prevalence of RF was found in youth with both affective and non-affective psychosis compared to similar-aged controls, concuring with some (Borgwardt et al., 2006; Landin et al., 2016), yet not with other (Sommer et al., 2013) observations in adult samples. These findings may reflect an impact of subtle biological alterations associated with psychosis on brain development, which may be more salient in early-onset cases.

Our data highlight the need to continue assessing the significance of abnormal RF in patients with EOP.

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**S36. DIFFERENTIAL ENCODING OF SENSITIZATION AND CROSS SENSITIZATION TO PSYCHOSTIMULANTS AND ANTIPSYCHOTICS IN NUCLEUS ACCUMBENS D1- AND D2-RECEPTOR EXPRESSING MEDIUM SPINY NEURONS**

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**Background:** Nearly half of all individuals diagnosed with schizophrenia abuse addictive substances such as cocaine. Currently, the neurobiological mechanisms in patients with schizophrenia that lead to cocaine abuse are...
unknown. A possible explanation for the co-morbidity between schizophrenia and addiction is that the rewarding properties of cocaine reverse the diminished motivational drive caused by chronic antipsychotic regimens. Moreover, chronic antipsychotic treatment can sensitize and amplify cocaine rewarding effects and exacerbate psychoses.

Methods: The rewarding properties of cocaine are attributed to the differential effects of dopamine on D1 and D2 receptor-expressing medium spiny neurons (MSNs) in the nucleus accumbens (NAC). Using in vivo Ca2+ miniature microscopic imaging, we characterize the role of D1 and D2 MSN in mono- and a cross-sensitization paradigms. D1- and D2-Cre mice were injected with a Cre dependent calcium indicator (gCaMP6f) and implanted with a gradient index (GRIN) lens above the nucleus accumbens and calcium activity was recorded using a head mounted miniature microscope. Cocaine sensitization was measured after a classic repeated cocaine regimen and antipsychotic and psychostimulant cross-sensitization was measured by a single cocaine injection after chronic pre-treatment with haloperidol.

Results: We found that both D1-MSN and D2-MSN populations are modulated by initial cocaine experience and further modulated during the expression of cocaine sensitization. A subpopulation of D1-MSN displayed initial activation, but reduced activity during the expression of sensitization. By contrast, the majority of D2-MSNs were suppressed by initial cocaine experience, but became active during the expression of sensitization. Furthermore, activity of D1- and D2-MSNs bidirectionally related with the observed behavioral responses to cocaine. Cross-sensitization following haloperidol treatment led to increased behavioral responses to psychostimulants. Current experiments are set out to investigate the neuronal responses of D1 and D2-MSN during cross sensitization between haloperidol and cocaine.

Discussion: Cocaine sensitization leads to differential neuronal responses in D1- and D2-MSN and these responses are differentially correlated with the magnitude of the sensitized behavioral response. These results reveal important new insights in the neurobiological processes in the nucleus accumbens that underlie psychostimulant sensitization and provide an important new model for studying the pharmacology of antipsychotic effects on striatal function and its potential role in increasing the susceptibility of schizophrenic patients to developing drug addiction.

S37. STATE-DEPENDENT EFFECTS OF D2 PARTIAL AGONIST ARIPIPRAZOLE ON DOPAMINE NEURON ACTIVITY IN THE MAM NEURODEVELOPMENTAL MODEL OF SCHIZOPHRENIA

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Background: Aripiprazole is an antipsychotic drug characterized by partial agonist activity at D2 receptors that impacts both hyperdopaminergic and hypodopaminergic states. It is unclear whether aripiprazole reduces dopamine neuron activity via inhibition or by excitation-induced depolarization block, the latter being characteristic of D2 antagonist administration, and how aripiprazole interacts with D2 antagonist-induced reduction in dopamine neuron activity.

Methods: Adult offspring of saline and MAM-treated rats received aripiprazole (10 mg/kg), or vehicle, p.o. and dopamine neuron activity was examined 2h following acute treatment, or after 1d or 7d withdrawal from 21d repeated treatment. Dopamine neuron activity in the VTA was measured using in vivo extracellular recordings from anesthetized rats. After electrophysiological sampling, apomorphine (200 μg/kg i.p. or 20 μg/kg i.v.) was administered, followed by resampling the VTA to test for the presence of depolarization block. Additional recordings were conducted in MAM rats 1 h following acute haloperidol treatment (0.6 mg/kg, i.p.). After electrophysiological sampling, aripiprazole (1mg/kg, i.p.) was administered to examine its effect on haloperidol-induced depolarization block.

Results: Both acute and repeated administration of aripiprazole reversed the increased number of spontaneously active dopamine neurons in MAM rats without impacting control rats. The reduction in dopamine neuron activity persisted after 7d withdrawal from repeated aripiprazole treatment and was not impacted by administration of apomorphine. In contrast, aripiprazole increased dopamine neuron activity in haloperidol-treated MAM rats.

Discussion: This study establishes that aripiprazole rapidly reduces hyperdopaminergic activity in MAM rats, without impacting dopamine neuron population activity in normal rats. The reduction is not due to depolarization block and persists 1 week following withdrawal from repeated treatment. Aripiprazole also removes haloperidol-induced depolarization block in MAM rats, which may underlie the acute psychotic symptoms observed clinically following the switch from D2 antagonist to aripiprazole treatment.

S38. CHARACTERISING THE COGNITIVE CONSEQUENCES OF DISRUPTED BDNF-TRKB SIGNALLING AT PARVALBUMIN-EXPRESSING INTERNEURONS

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Background: Schizophrenia is a debilitating syndrome characterised by three main symptom categories: positive, negative and cognitive. Cognitive symptoms emerge first, and currently do not have appropriate treatments, despite being a strong predictor of the severity and progress of the illness. Cognitive deficits are thought to be partly attributed to impaired synchronization of gamma frequency oscillatory activity. Gamma oscillations are generated by a subclass of GABAergic interneuron that expresses the calcium binding protein, parvalbumin (PV). PV-interneurons are supported by Brain Derived Neurotrophic Factor (BDNF) and recent evidence has found that cessation of BDNF support in PV-interneurons impairs gamma oscillations. All of these factors have been demonstrated to have a role in cognitive processing, but their dynamic relationship is not completely understood.

Methods: The aims of this study were: 1) To generate transgenic mice where 50% of BDNF receptor (TrkB) gene is excised from PV-expressing neurons using the cre-lox recombination system and 2) To investigate the cognitive and behavioural consequences of disrupted BDNF signalling at inhibitory PV-expressing interneurons. Male and female mice underwent a battery of tests including: Y-Maze, Novel Object Recognition Task (NORT), Elevated Plus Maze, Locomotor and Cheeseboard Maze.

Results: Sex-specific spatial memory impairments were found in PV-Cre x TrkB floxed mice with only males showing no preference for the novel arm in the Y-maze paradigm. Furthermore, male PV-Cre x TrkB floxed mice displayed a lack of cognitive flexibility in the cheeseboard maze for long term spatial memory. No significant differences were observed in measures of anxiety and activity, indicating that these were not confounding variables for cognitive measures.

Discussion: This mouse line has not been cognitively characterised before and the results are of major interest. Subtle changes to cognition were observed and were sex-dependent. Interestingly, only males were observed to have changes in cognition, in line with human data. Human males with schizophrenia tend to exhibit more severe cognitive symptoms. Overall, the evidence from this study supports a role for BDNF-TrkB signalling at PV interneurons in regulating spatial memory performance. Future work will be investigating spatial search strategies of the Cheeseboard Maze, in order to elucidate further any cognitive differences between the genotypes. Additionally, future work will aim to specifically disrupt BDNF-TrkB signalling in the hippocampus and/or prefrontal cortex, as these two areas are highly implicated in both cognition and schizophrenia. It would also be of interest to use this genotype in a two-hit model, to further investigate the interaction of multiple factors and their impact on cognitive functions.