Methods: We assessed the total expression and subcellular localization of proteins involved in ER export processing of GPI-APs from the DLPFC of 15 matched pairs of SCZ and comparison subjects. Specifically, we measured levels of PGAP1 and Tmp21 (p24). Additionally, we performed a Triton X-114 phase separation to distinguish between membrane-associated and cytosolic forms of protein substrates. We confirmed the sensitivity of each target GPI-AP to phosphatidylinositol-specific phospholipase C (PI-PLC), an enzyme that specifically cleaves GPI from GPI-APs.

Results: We found a significant decrease in p24 in total tissue homogenates and PGAP1 in an ER enriched fraction from subjects with SCZ. We also identified diminished sensitivity of the GPI-APs, GPC1 and NCAM, to PI-PLC treatment in SCZ.

Discussion: Decreased PGAP1 in an ER enriched fraction in consistent with reduced inositol deacylation and potential dysfunction as the gatekeeper of GPI-AP ER exit in SCZ. This also suggests that the GPI-anchor is not correctly modified. Decreased p24 levels suggest downregulation of transport between the Golgi and the ER in SCZ. Additionally, we observed unchanged total level of GPI-APs in Triton X-114 phase separation, but a significant decrease in the amount of NCAM and GPC1 that was sensitive to PI-PLC in SCZ. This finding may be consistent with abnormal GPI modification of these two candidate proteins. Together, these findings suggest dysregulation of the GPI-APs remodeling system in SCZ, which may impact the structure of the GPI-anchor for SCZ-relevant proteins like NCAM and GPC1.

F203. A META-ANALYSIS OF MINOR PHYSICAL ANOMALIES IN FIRST-DEGREE UNAFFECTED RELATIVES OF PATIENTS WITH SCHIZOPHRENIA

Ozte Akgul*, Emre Bora1, Berna Binur Akkede2, Köksal Alptekin1
1Dokuz Eylül University; 2Dokuz Eylül University School of Medicine

Background: Neurodevelopmental abnormalities are common in schizophrenia. Minor physical anomalies (MPAs) are associated with abnormalities in neural development. Previous studies clearly demonstrated that MPAs are significantly increased in schizophrenia. However, the available evidence in unaffected relatives of patients with schizophrenia is contradictory.

Methods: A literature search was conducted between 1 JAN 1980 and SEP 2017 in PUBLMED and SCOPUS. Random-effects model was used. Heterogeneity was tested with Q test and I2. The meta-analysis was conducted using OpenMetaAnalyst software.

Results: 16 studies were included in the meta-analysis. MPAs were significantly more common unaffected first-degree relatives of patients with schizophrenia (d=0.56, CI=0.40–0.73, p=0.001). There was a significant heterogeneity in distribution of effect sizes (Q=42.2, p<0.001). The level of this heterogeneity was medium in range (I2=64%). In meta-regression analyses, demographic variables were not significantly related with magnitude of the effect size.

Discussion: MPAs are associated with risk of schizophrenia. However, the level of heterogeneity suggests that risk of psychosis is associated with neurodevelopmental abnormalities in some but not all individuals. Findings also emphasize that resilience factors might be protecting many neurodevelopmentally impaired relatives of schizophrenia against having a full-blown psychotic disorder.

F204. THE DANISH HIGH-RISK AND RESILIENCE STUDY - VIA 7 - A PROSPECTIVE COHORT STUDY OF 522 7 YEARS OLD CHILDREN BORN TO PARENTS DIAGNOSED WITH SCHIZOPHRENIA OR BIPOLAR DISORDER - RESULTS ON PSYCHOPATHOLOGY, COGNITION AND LIVING CONDITIONS

Anne Amalie Thorup*, Nicoline Hemager1, Ditte V. Ellersgaard2, Camilla Jerlang Christiani2, Kerstin von Plessen1, Merete Nordentoft2
1Child and Adolescent Mental Health Center Capital Region of Denmark; 2Mental Health Center, Capital Region of Denmark, The Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH); 3Aarhus University Hospital, The Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH); 4Center for Neuropsychiatric Schizophrenia Research, Child and Adolescent Mental Health Center, Mental Health Services, Capital Region of Denmark; 5University Hospital Lausanne

Background: For decades familial high-risk studies have informed us about genetic and environmental risk factors for schizophrenia and recently also bipolar disorder. Familial high-risk studies are important and relevant and may represent a possible shortcut to learning more about early markers of illness, mental vulnerability and resilience.

Methods: The Danish High Risk and Resilience Study – VIA 7 is a prospective cohort study of 522 7-year old children, 202 of them born to at least one parent diagnosed with schizophrenia in the Danish registries, 120 of them born to at least one parent diagnosed with bipolar disorder and 200 of them born to parents without any of these diagnoses. A comprehensive battery has been used combining assessments from several domains for both parents and children.

Results: Results show that children born to parents with schizophrenia or bipolar disorder have higher frequencies of early mental problems. Further there are marked differences between the three groups concerning neuro cognition, motor functioning and living conditions including socioeconomic status, early risk factors and home environment - all factors that are known to be important with regard to healthy child development.

Discussion: First results from the VIA 7-study indicate that many children and families have unmet needs and problems. Perspectives are two-fold: we aim to follow the cohort and conduct a new assessment before puberty (at age 11). Simultaneously, we are evolving an early, integrated, specialized and family based intervention, called VIA Family, to prevent or ameliorate development of severe mental illness in individuals born to parents with schizophrenia or bipolar disorder.

F205. OLFACTORY IDENTIFICATION IN 7-YEAR OLD CHILDREN AT FAMILIAL RISK TO DEVELOP SCHIZOPHRENIA

Anna Hester Ver Loren van Themaat*, Jens Richardt Mollegaard Jepsen2, Camilla Christiani1, Merete Nordentoft3
1University of Copenhagen; 2Mental Health Services – Capital Region of Denmark, Child and Adolescent Mental Health Centre, The Lundbeck Foundation Initiative for Integrative Psychiatric Research, Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research; 3Mental Health Centre Copenhagen

Background: Olfactory dysfunction has repeatedly been observed in individuals diagnosed with schizophrenia. The most stable and consistent finding on the behavioral level is that of smell identification deficits. However, the nature of olfactory identification abnormalities seems to extend to structural abnormalities in the underlying neurobiology of the olfactory system. Furthermore, smell identification deficits are also documented in first-episode patients and non-psychotic first-degree relatives of schizophrenia patients. Family members of schizophrenia patients also show structural abnormalities of the olfactory system, suggesting that these may serve as an endophenotype for the development of schizophrenia.
Only a few studies examined the olfactory identification ability in adolescents at-risk for schizophrenia and suggested smell identification deficits as a risk marker for schizophrenia. These studies included adolescents at clinical as well as at genetic risk for schizophrenia. None of these studies focused on children at genetic risk for schizophrenia. Therefore, we investigated the olfactory identification ability in children of parents with schizophrenia in comparison to children of parents without a psychotic disorder. As we are also interested in the specificity of the olfactory impairments to schizophrenia, we included children of parents with bipolar disorder. We hypothesize that children at genetic risk for schizophrenia would have the most severe smell identification deficits and that children of bipolar disorder patients would have less severe deficits than the at-risk for schizophrenia group but more severe than the group of children without a psychotic parent.

Methods: Participants - The olfactory identification ability was assessed in 202 children of schizophrenia patients (‘children at familial risk for schizophrenia’) in relation to that of 200 children of parents without a psychotic disorder (‘controls’). In addition, we also assessed the B-SIT in 120 children of bipolar disorder patients (‘children at familial risk for bipolar disorder’). All children were 7 years of age at the time of assessment and they were part of the Danish High Risk and Resilience Study – VIA7.

Brief Smell Identification Test - The Brief Smell Identification Test (B-SIT) contains 12 items that need to be scratched and sniffed. The test has excellent reliability (> 0.80) and demonstrates agreement for abnormal olfaction comparing B-SIT with the San Diego Odor Identification Test (SDOIT). A maximum score of 12 reflects intact olfactory identification functioning. B-SIT has been conducted in patients with neurodegenerative disorders (Parkinson’s disease and Alzheimer’s disease) and can be used for individuals above 5 years of age.

Statistics - We will use analysis of covariance (ANCOVA) for analysis of the B-SIT total scores with ‘diagnosis of parent’ as the independent variable and age and sex as covariates for the three groups.

Results: Analyses will be performed within the next 3 months so can be presented in April 2018.

Discussion: Conclusion and discussion cannot be drawn at this time.

F206. A TRANSLATIONAL STUDY OF BEHAVIOR, BRAIN STRUCTURE AND GENE PATHWAY IN ERBB4 KNOCKOUT MICE AND FIRST-EPISODE TREATMENT-NAÏVE PATIENTS WITH SCHIZOPHRENIA

Chengcheng Zhang*,1, Peiyan Ni2, Tao Li2
1West China Hospital Sichuan University; 2Mental Health Center, West China Hospital of Sichuan University

Background: The current study was to explore how disruption of specific molecular circuits in the cerebral cortex may cause large-scale brain structure deficits and behavior changes via a translational study in conditional Erbb4 mutant mice and patients with schizophrenia.

Methods: We conducted prepulse inhibition (PPI) and brain structural and diffusion magnetic resonance imaging (MRI) scans in 27 mice with Erbb4 knockout in parvalbumin (PV) interneurons and 23 age, sex-matched controls. Real-time quantitative polymerase chain reaction was used to assess the levels of five GABA-related transcripts in brain regions. We also measured structural and diffusion MRI and cumulative contribution of risk alleles in the GABA pathway genes using polygenic risk scores (PRS) in first-episode treatment-naïve schizophrenic patients (N=117) and age, sex-matched healthy controls (N=86).

Results: Erbb4 knockout mice displayed behavioral deficit of PPI, as well as gray and white matter impairment in right sensorimotor cortical-lateral striatal networks. We found significant correlations between gray matter volumes (GMVs) of the somatosensory cortex and PPI as well as GAD1 mRNA expression in controls but not in knockout mice. These findings were confirmed in a human sample where we observed significantly decreased gray and white matter impairment in sensorimotor cortical-striatal networks in schizophrenics. The PRS of GABA-pathway genes also displayed a negative correlation with the GMVs of the somatosensory cortex in patients.

Discussion: Our study identified ErbB4 ablation induced prepulse inhibition deficits and GABAergic dysregulation in sensorimotor cortical-lateral striatal networks. We propose that ErbB4 signaling participates in sensorimotor gating dysfunction in schizophrenia by getting involved in somatosensory cortex deficits and GABAergic dysfunction.

F207. SCHIZOTYPY AND SENSORY GATING: A 6-MONTH-OLD EGG STUDY

Eleanor Smith*,1, Trevor Crawford1, Megan Thomas2, Vincent Reid1
1Lancaster University; 2Blackpool Victoria Teaching Hospital NHS Foundation Trust

Background: Schizotypal traits are present in the general population and are distributed along a continuum, with the clinical disorder schizophrenia found at its extremity (Claridge, 1997). Schizotypy is a dimension of personality that is often co-occurring with the general population, which has been found to be elevated among schizophrenia-spectrum patients (Brose y Woodward, 2015) and their first-degree relatives (Morenzo-Izzo et al., 2015). One hypothesis to account for the sensory deficits observed across the spectrum suggests a difficulty in the inhibition of irrelevant sensory input, such as the secondary beep in the paired-click paradigm.

Sensory gating describes the pre-attentional habituation of responses to repeated sensory input, for example, auditory tones. This gating mechanism is used to distinguish between important and irrelevant information (Hall et al., 2011) and is typically explored using the paired-click paradigm and analysed using the P50 event-related potential component. This can be observed approximately 50-milliseconds following the presentation of an auditory stimulus and is a highly established biological trait of schizophrenia, with abnormalities displayed in the P50 component all throughout the schizophrenia-spectrum.

Methods: This research aimed to observe whether the 6-month-old offspring of mothers with schizotypic traits display abnormalities in the P50 event-related component when explored using the paired-click paradigm. The paired-click paradigm was used to highlight the sensory-gating abilities of fifty-three 6-month-old infants during 15-minutes of continuous sleep. The mothers of the infants completed the Short Form of the Oxford and Liverpool Inventory of Feelings and Experiences, which was used to determine their personality dimension scores, and identify schizotypic traits. Participants were categorized into one of three groups: infants of controls, mothers, infants of intermediate mothers, and infants of schizotypic mothers.

Results: It was predicted that the 6-month-old infants of mothers who demonstrate schizotypy scores would demonstrate different amplitudes compared to those of control mothers. This research found a significant generalised difference between the P50 component for the paired-clicks in the right hemisphere of the brain (F(1,51)=5.34, p=.025), and a significant latency effect was observed in the frontal regions (F(1,51)=5.41, p=.024). A significant between-subjects effect was observed centrally (F(2,50)=3.71, p=.031); suggesting there are significant differences between the ways each group distinguished the paired-clicks. Infants of schizophrenic mothers showed an increase in activation compared to other groups. An interaction was observed in the left hemisphere between the paired-clicks and each identifiable group (F(2,50)=3.45, p = .039). In addition to the P50 a significant slow wave effect was also observed across the left (F(1,51)=8.38, p=.006) and right (F(1,51)=7.81, p=.007) posterior regions; a latency effect in the left (F(1,51)=5.47, p=.023), and a distinction in a mean amplitude in the right (F(1,51)=7.25, p=.010).

Discussion: Schizotypy is viewed as a risk factor for schizophrenia, which is present in the general population, and is present on the schizophrenia-spectrum. The 6-month-old infants of mothers showed an increase in activity centrally, demonstrating that the infants’ P50 amplitudes were influenced by their mothers’ schizotypy status. This finding is consistent with the developmental hypothesis of