S18. STRUCTURAL COVARIANCE PREDICTORS OF CLINICAL IMPROVEMENT AT 2-YEAR FOLLOW-UP IN FIRST-EPISTEME PSYCHOSIS

Cristina Suárez-Masvidal*, Carles Soriano-Mas1, Fernando Contreras2, Gisela Mezquida3, Antonia Lobo4, Ana González-Pinto5, Laura Pina-Camacho6, Mara Parelleda7, Bernardo Miguel8

1Bellvitge Biomedical Research Institute - IDIBELL; 2University Hospital of Bellvitge; 3Hosp.Clinic Barcel/Instituc Clinic Neuro; 4Instituto Investigación Sanitaria Aragón; University of Zaragoza; CIBERSAM; 5Hospital Santiago Apóstol de Vitoria. Centro de Investigación Biomédica en Red de Salud Mental, CIBERSAM; 6Hospital General Universitario Gregorio Marañón, CIBERSAM, IISGAM, School of Medicine, Universidad Complutense Madrid; 7CIBERSAM; 8Hospital General Universitario Gregorio Marañón, Universidad Complutense de Madrid; 9Barcelona Clinic Schizophrenia Unit (BCSU). Hospital Clinic Barcelona. Universitat Barcelona. IDIBAPS. CIBERSAM. Barcelona

Background: Neural correlates of psychotic disorders encompass multiple brain regions in many brain circuits, even at early stages. Previous research has characterized structural brain alterations in first-episode psychosis (FEP), but few studies have focused on the relationship between brain alterations and disease trajectories. First psychotic episodes typically evolve into a chronic course, affecting quality of life of patients and their families, with huge societal costs. Importantly, up to 80% of the patients relapse in the next five years after a first psychotic episode, with a significant risk of developing treatment resistance. Here, we investigated whether disease course may be predicted from brain structural assessments. Specifically, we measured structural covariance, a well-established approach to identify abnormal patterns of volumetric correlation across distant brain regions, which allows to incorporate network-level information to structural assessments. We performed a whole-brain structural covariance assessment of three bilateral regions form to three different cortical networks - dorosateral prefrontal cortex (dlPFC) for the executive network, posterior cingulate cortex for the default mode network and insulae for the salience network - and subcortical structures (hippocampi, amygdalae and dorsomedial nucleus of the thalamus) that have shown to play a key role in schizophrenia.

Methods: We assessed a sample of 74 subjects from a multicenter, naturalistic, prospective and longitudinal study designed to evaluate clinical, neuropsychological, neuroimaging, biochemical, environmental and pharmacogenetic variables in first episode psychotic patients (PEPs project). Magnetic resonance imaging (MRI) scans were acquired at baseline and at 2-year follow-up, as well as clinical assessments. Psychotic symptoms were assessed using the Positive and Negative Symptom Scale (PANSS) due its widespread use in clinical studies and its reliability in assessing psychopathology across a range of patient populations. The sample was split in two groups as a function of the clinical improvement at 2-year follow-up: responders (i.e. 40% reduction in PANSS global score from baseline; n=29) and non-responders (n=45).

Results: Responder patients showed increase structural covariance between the left dlPFC and the left middle frontal gyrus, and between the right dlPFC and the right middle and superior gyrus, the left rectus and inferior frontal gyrus, the right hippocampus, and the vermis of the cerebellum. In addition, they showed increased structural covariance between the left anterior hippocampus and the ipsilateral middle occipital gyrus and the contralateral postcentral gyrus. Likewise, the structural covariance of right anterior hippocampus with right superior occipital gyrus and precentral gyrus was also increased in responder patients.

Discussion: This study shows, for the first time in the literature, that increased structural covariance at baseline within the executive network and between the hippocampi and posterior brain regions was associated with a superior treatment response at two-year follow-up. These results indicate that the integrity of structural networks should be taken into account to predict treatment outcome in FEP patients.

S19. THE ROLE OF ACE AS POSSIBLE BIOMARKER FOR TREATMENT RESISTANCE TO ANTI-PYSCHOTICS IN FIRST EPISODE OF PSYCHOSIS

Longo Luisa*, Akira Sawa

1University of Bari; 2John Hopkins University School of Medicine and Bloomberg School of Public Health

Background: Angiotensin I–converting enzyme (ACE) is a peptidase that converts angiotensin I into the vasoactive and aldosterone-stimulating peptide angiotensin II, a key protein in controlling blood pressure. Recently, several evidences have shown a role of ACE in psychosis. However, the role of ACE in psychosis is poorly characterized, and at last unknown. In this study we hypothesized that ACE blood and CSF levels are lower in patients at first episode of psychosis (FEP) compared to controls; that blood ACE levels can predict the response to antipsychotics; that low plasma ACE levels correlate with both severity of symptoms and cognitive performance.

Methods: This research used data from a longitudinal cohort study of FEP (N = 138) and controls (N = 115). First of all, we conducted a two-group comparison analyses to assess the differences between patients and controls in terms of ACE levels in both blood and CSF. As a second step, we divided our patients into treatment resistant (TR) and not treatment resistant (non-TR) to investigate ACE blood levels in these two group. Finally, we evaluated the association between ACE blood levels and clinical phenotype and neurocognition.

Results: Two-group analyses showed lower levels of ACE in patients than controls, both in blood and CSF (p values< 0.05). The two-group analyses between TR and non-TR showed lower ACE blood levels in TRs compared to non-TRs (p value< 0.05). Finally, multiple regressions showed a continuous relationship between cognitive performance and ACE blood levels (p values < 0.05).

Discussion: In conclusion, these findings showed that those FEP with lower ACE blood levels were not only more likely to develop TR conditions, but they also had greater cognitive impairment. These results are very promising, as they suggest that ACE levels can be used as a peripheral biomarker to stratify patients at first episode of psychosis.

S20. LIFETIME PSYCHOPATHOLOGY IN CHILD AND ADOLESCENT OFFSPRING OF PARENTS DIAGNOSED WITH SCHIZOPHRENIA OR BIPOLAR DISORDER

Elena De la Serna*, Daniel Ilzarbe2, Gisela Sugranyes3, Inmaculada Baesa4, Dolores Moreno5, Elisa Rodriguez1, Ana Espelio5, Miriam Ayora1, Soledad Romero1, Josefina Castro-Fornieles2

1Hospital General Universitario de Elche; 2University of Vigo; 3University of Málaga; 4University of Alicante; 5University of Granada

Background: Schizophrenia and bipolar disorder are severe and complex mental disorders with a high lifetime prevalence, and a poor treatment response. Even for those who do benefit from treatment, relapse is common. The reasons are still unknown. However, a growing field of research is focusing on the role of lifetime childhood psychopathology in the aetiology and course of schizophrenia and bipolar disorder.

Methods: This study is part of a longitudinal study of offspring of parents diagnosed with schizophrenia or bipolar disorder. The objective of the study is to evaluate the lifetime prevalence of childhood psychopathology in this cohort and to explore possible associations with later development of psychotic symptoms and bipolar disorder.

Results: The lifetime prevalence of childhood psychopathology in offspring of parents with schizophrenia or bipolar disorder is significantly higher than in the general population. Moreover, the prevalence of childhood psychopathology is associated with a higher risk of later development of psychotic symptoms and bipolar disorder.

Discussion: These findings highlight the importance of childhood psychopathology in the aetiology and course of schizophrenia and bipolar disorder. Further research is needed to explore the mechanisms underlying these associations and to develop effective interventions to prevent the development of these disorders.
Background: Having one parent diagnosed with a severe mental disorder is considered one of the main risk factors for developing that disorder in adulthood and it also increases the risk of a wide range of mental disorders in the offspring from early childhood and adolescence. The aim of this study is to analyze the prevalence of several psychopathological diagnoses, the presence of prodromal symptoms and global functioning in schizophrenia offspring (SZoff) or bipolar offspring (BDoff) compared to community control offspring (CCoff) at baseline and 2-year follow-up.

Methods: 41 SZoff, 97 BDoff and 107 CCoff between 7 and 17 years were included. Clinical assessment consisted of a clinical evaluation using the following instruments: structured interview KSADS-PL or SCID-I, semi-structured Interview for Prodromal Syndromes (SIPS) and the Children’s Global Assessment Scale (CGAS). To test between-group differences in DSM-IV diagnoses multilevel mixed-effect logistic regression models (categorical variables) or linear (continuous variables) regression models were conducted with group (SZoff, BDoff and CCoff), time (baseline or 2-year follow-up), interaction time x group, age, gender and socio-economic status as fixed variables.

Results: Significant differences between groups were found in any lifetime axis I disorder (F=8.720; p<0.001), mood disorders (F=4.774; p=0.009), anxiety disorders (F=4.368; p=0.013), ADHD (F=21.593; p<0.001), disruptive behavioral disorders (F=10.788; p<0.001) and comorbidity (F=5.588; p=0.004). Significant differences between groups were also found in the positive (F=6.088; p=0.003), negative (F=4.423; p=0.015), disorganized (F=3.866; p=0.024) and total (F=6.394; p=0.002) sub-scales of the SOPS and CGAS (F=11.613; p<0.001). Interestingly, mood disorders were more prevalent in BDoff and disruptive disorders were more prevalent in SZoff. Prodromal symptoms were higher in SZoff compared to CCoff, while the BDoff group showed an intermediate pattern. Finally, global functioning was lower in the SZoff group compared to BDoff and CCoff.

Discussion: Screening patients’ children is clinically relevant since, as a group, they have an elevated risk of developing a psychiatric disorder and of experiencing their first symptoms during childhood and adolescence.

S21. CORRELATES AND TRANSITION RATE OF CHILDREN AND ADOLESCENTS WITH ATTENUATED PSYCHOTIC SYMPTOMS: FINDINGS FROM A LONGITUDINAL STUDY

Silvia Molteni1, Giulia Spada2, Eleonora Filosi3, Martina Maria Mensi1, Elena Ballante1, Federica Ferro1, Chiara Morabito1, Melanie Iorio1, Umberto Balottin1

1University of Pavia; 2King’s College of London; 3IRCCS Mondino Foundation; 4IRCCS Mondino Foundation, University of Pavia; BioData Science Center, IRCCS Mondino Foundation; 6University of Pavia, IRCCS Mondino Foundation

Background: The identification of people at high risk of developing psychosis is one of the most promising strategies to improve outcomes. However, in children and adolescents research on the high risk state and attenuated psychotic symptoms is still in its infancy and the clinical validity of at risk criteria appears understudied in this population (Tor et al. 2018). Thus, in this longitudinal cohort study, we aimed to: (1) characterize the clinical profile of APS adolescents, adolescents suffering from early onset psychosis (EOP) and adolescents with psychiatric disorders other than APS and EOP (non-APS) and (2) to calculate the cumulative transition rate to psychosis at follow-ups and investigate predictors of conversion to psychosis.

Methods: Help-seeking adolescents (aged 12–18 years) consecutively admitted to Child and Adolescent Neuropsychiatric inpatient and outpatient units of the IRCCS Mondino Foundation (Pavia, Italy) were recruited. The Comprehensive Assessment of At-Risk Mental State (CAARMS) was used in order to evaluate the presence of attenuated or full-blown psychotic symptoms. The final sample consisted of 31 EOP, 110 APS and 102 non-APS adolescents. At baseline patients underwent an extensive clinical and, in a subset, also neuropsychological assessment using standardized semi-structured interviews and instruments. All APS patients recruited until March 2019 were followed up for a median period of 33 months (range 4–81 months) and baseline measures were repeated (every 12 months). Transition to psychosis was defined according to the CAARMS criteria.

Results: At baseline, APS status was associated with poor socio-occupational functioning, especially social functioning (p<0.0001), as well as clinical severity (p<0.0001) as assessed by clinicians. APS adolescents reported a higher level of suicidality compared to non-APS (p=0.0003). The APS group displayed a higher number of comorbid disorders compared to the EOP and non-APS (p<0.0001) and was related to a wide range of disorders. APS and non-APS adolescents did not significantly differ in any of the neuropsychological test administered, although a worsening trend was observed between the two groups with lower scores in APS adolescents. The cumulative proportion of psychosis transition in the APS group was 13%, 17%, 24.2% and 26.8% at 1.23 and 4-year follow-ups, respectively. A high percentage of APS patients received at least one psychotropic medication (62.1%) during the follow-up period, especially antipsychotics (43.7%). Baseline lower global and social functioning (p=0.0092), higher clinical severity (p<0.0001), negative symptoms, lower Total IQ (p=0.02) and Processing Speed Index (p=0.03) were associated with transitioning to psychosis at follow-ups.

Discussion: Our findings support the importance of clinical relevance of the identification of APS in children and adolescents. Indeed, in our sample APS adolescents suffer from a variety of comorbidities and non-psychotic symptoms, present higher suicidality and are markedly impaired compared to non-psychotic adolescents not fulfilling APS criteria. Moreover, they show a cumulative transition risk to psychosis of 26.8% at 4 years that, although being lower than that found in adult samples, is still comparable to that of other conditions in preventive medicine.

S22. SPECIFIC PSYCHOTIC EXPERIENCES AND DEPRESSIVE SYMPTOMS IN CHILEAN ADOLESCENTS: A MULTIPLE MEDIATION MODEL OF THEIR IMPACT ON SUICIDAL IDEATION

Daniel Nunez1, Susana Campos1, Rosario Spencer1, María Faúndez1, Andrés Fresno1, Patricia Bravo1

1Universidad de Talca, Chile

Background: Adolescence is a critical period for the emergence of psychopathology and risk behaviors, including psychotic symptoms and suicidal behavior. Literature has shown that psychotic experiences (PE) are associated with increased odds of suicidal ideation (SI) and attempts in young people. PE are normally regarded as subthreshold positive symptoms, and have been clustered in three domains: persecutory ideation (PI), bizarre experiences (BE) and perceptual abnormalities (PA). All of these domains have been linked to depression, and recent studies demonstrated that, in young people, perceptual abnormalities and persecutory ideation are associated with a higher risk of suicidality, instead, while bizarre experiences were not. Nevertheless, how specific PEs are associated to suicidal is not clearly understood, and the role of common risk factors in this link, such as depressive symptoms (DS), remains controversial. Thus, the aim of