Results: Compared with the conventional approach of using only fixed predictors, joint modelling prediction models showed significantly better sensitivity, specificity and likelihood ratios.
Discussion: Joint modelling is a useful statistical tool which can improve the prediction of the onset of psychosis and has the potential in guiding the provision of timely and personalized treatment to patients concerned.

S137. DO HALLUCINATIONS PREDICT THE TRANSITION FROM SUICIDAL THOUGHTS TO ATTEMPTS? RESULTS FROM AN AUSTRALIAN LONGITUDINAL COHORT STUDY

Emily Hielscher*[,1], Jordan DeVylder[2], Melissa Connell[1], Penelope Hasking[3], Graham Martin[1], James Scott[1]
[1]The University of Queensland; [2]Fordham University; [3]Curtin University

Background: Although suicidal ideation is a well-documented risk factor for suicidal behaviour, the majority of those with suicidal thoughts do not go on to make an attempt. Therefore, it is important to improve prediction of which individuals are more likely to act on their suicidal thoughts, as highlighted in Klonsky and May's (2015) ideation-to-action framework. Auditory hallucinations (AH) and psychological distress (PD) are strongly associated with both suicidal thoughts and behaviour, but their role in the ideation-to-attempt transition has not been investigated in a longitudinal dataset.
Methods: Participants were from an Australian longitudinal cohort of 1793 adolescents (12–17 years). Suicidal thoughts and behaviours were measured using the Self-Harm Behaviour Questionnaire. The Diagnostic Interview Schedule for Children was used to assess AH. PD was categorised using the General Health Questionnaire (GHQ) clinical cut-off. Those reporting suicidal ideation were stratified into four groups: (i) Those who did not have PD or AH (reference group), (ii) AH only, (iii) PD only, and (iv) PD and AH. Using logistic regression, we examined associations between baseline suicidal ideation, and incident suicide attempts during the 12-month follow-up, stratified by the four comparison groups. All analyses were adjusted for age and sex.
Results: AH were strongly and independently associated with baseline suicidal ideation (OR=3.84; 95%CI=2.46–6.02) and suicide attempts in the following 12 months (OR=3.21; 95%CI=1.18–8.76). Among adolescents with baseline suicidal ideation (n=235; 13.1%), 14 or 6.0% attempted suicide at follow-up. Those with AH only were not at significantly increased risk of transition from suicidal thoughts to attempts (OR=2.97; 95%CI=0.26–34.59). Similarly, adolescents with PD only did not have a significant increase in transition from ideation to attempts (OR=4.48; 95%CI=0.91–22.14). Adolescents who had both PD and AH had an eight-fold increased risk (OR=8.42; 95%CI=1.46–48.67) of acting on their suicidal thoughts.
Discussion: Adolescents with both PD and AH had the greatest likelihood of acting on their suicidal thoughts. AH alone did not significantly predict the transition from suicidal thoughts to attempts despite high odds ratios, possibly due to the low prevalence of suicide attempts among ideators and consequently limited statistical power. Future studies examining for negative and distressing content of hallucinations may assist in explaining their role in the ideation-to-attempt transition. Screening adolescents who are distressed and have hallucinations may assist with predicting those at greatest risk of future suicide attempts.

S138. AN INVESTIGATION INTO THE ASSOCIATION BETWEEN EXPOSURE TO PRENATAL STRESS AND RISK OF PSYCHOSIS IN OFFSPRING

Ross Brannigan*[,1], Antti Tanskanen[2], Matti O. Hunnunen[3], Mary Cannon[1], Finbarr Leacy[1], Mary Clarke[1]
[1]Royal College of Surgeons in Ireland; [2]Karolinska Institutet; [3]National Institute for Health and Welfare

Background: Existing literature suggests that prenatal stress may be a risk factor for offspring psychiatric disorders. For example, large ecological studies have found that those exposed to stressors during gestation, such as war and famine, have a twofold increase risk of schizophrenia, as well as an increased risk for other affective disorders. Similarly, it was found that exposure to stressful events during pregnancy, such as the death of a relative during first trimester, increases the odds of the offspring developing schizophrenia in adulthood. In this study, our aim was to assess in a birth cohort, whether those who were exposed to prenatal stress were at higher odds for developing psychosis and other psychiatric disorders.
Methods: Using the Helsinki temperament cohort, a yearlong birth cohort with data collected from pregnancy onwards, logistic regressions were run examining perceived prenatal stress as a risk factor for psychosis and other psychiatric disorders. The exposure (prenatal stress) was measured using prenatal questionnaires which were given to pregnant women at antenatal clinic visits if birth was expected between 1st July 1975 and 30th June 1976. Psychiatric outcomes were assessed using linkage between the Finnish population register and the Finnish hospital discharge register in 2005.
Results: In total, 3660 pregnant women submitted at least one prenatal questionnaire with the mean number of prenatal questionnaires submitted per woman being 6. At the point of register access, 226 individuals had either an ICD 8, 9 or 10 diagnoses, 72 diagnosed with a psychosis disorder. It was found that those exposed to prenatal stress were at a greater risk of developing psychosis (OR = 1.54, 95% CI = 0.78 – 3.05).
Discussion: Our findings are in line with the current literature indicating a higher risk of psychosis among those exposed to perceived prenatal stress.

S139. INVESTIGATING THE GENETIC ARCHITECTURE OF GENERAL AND SPECIFIC PSYCHOPATHOLOGY IN ADOLESCENCE USING SCHIZOPHRENIA POLYGENIC SCORES

Hannah Jones*[,1], Jon Heron[1], Gemma Hammerton[1], Jan Stochl[2], Peter B. Jones[2], Mary Cannon[3], George Davey Smith[1], Peter Holmans[4], Glyn Lewis[5], David EJ. Linden[4], Michael C. O'Donovan[4], Michael J. Owen[4], James Walters[4], Stanley Zammit[6]
[1]University of Bristol; [2]University of Cambridge; [3]Royal College of Surgeons in Ireland; [4]Cardiff University; [5]University College London; [6]University of Bristol, Cardiff University

Background: Whilst associations between polygenic risk scores (PRSs) for schizophrenia and various phenotypic outcomes have been reported, an understanding of developmental pathways can only be gained by modelling comorbidity across psychopathology, something no studies have done to date. We examine how genetic risk for schizophrenia relates to a broad range of adolescent psychopathology using a latent modelling approach, and compare this to genetic risk for other psychiatric disorders, to gain a more comprehensive understanding of development pathways at this age.
Methods: PRSs for schizophrenia, major depressive disorder, neuroticism and bipolar disorder were generated for individuals in the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort. Multivariate linear regression was used to examine relationships of these PRSs with psychopathology factors modelled within i) a correlated factors structure, and ii) a bifactor structure.
Results: The schizophrenia PRS was associated with an increase in factors describing psychotic experiences, negative dimension, depression, and anxiety, but once modelling a general psychopathology factor specific effects above this persisted only for the negative dimension. Similar factor

relationships were observed for the neuroticism PRS, with a (weak) specific effect only for anxiety once modelling general psychopathology.
Discussion: Psychopathology during adolescence can be described by a general psychopathology construct that captures common variance as well as by specific constructs capturing remaining non-shared variance. Schizophrenia risk genetic variants identified through genome-wide association studies mainly index negative rather than positive symptom psychopathology during adolescence. This has potentially important implications both for research and risk prediction in high-risk samples.

S140. VOICE-SELECTIVE FORWARD MODEL ABNORMALITIES IN NONCLINICAL VOICE HEARERS

Ana Pinheiro*[,1], Michael Schwartze[2], Sonja Kotz[2]
[1]University of Lisbon; [2]Maastricht University

Background: Auditory verbal hallucinations (AVH) are one of the cardinal symptoms of psychosis but they are also present in 6–13% of individuals in the general population. Impaired predictive internal forward modelling has been proposed to underlie the experience of AVH in psychotic patients, but it remains unclear whether similar abnormalities are also present in nonclinical voice hearers. The current study sought to answer the question of whether and how hallucination predisposition modulates sensory prediction of tones and voices using event-related potentials (ERP) of the electroencephalogram (EEG).
Methods: Participants with low (n=15) and high (n=17) hallucination predisposition, classified based on their Launay-Slade Hallucination Scale (LSHS) scores, were tested in an auditory task involving presentation of self-triggered and externally triggered tonal or own voice stimuli.
Results: Participants with low and high hallucination predisposition displayed comparable N1 suppression effects to self-triggered tones (no significant group effect – $p>.05$) but the latter displayed enhanced N1 (group x condition x ROI interaction - $F(4, 120)=7.971$, $p<.001$) and reduced P2 (group x condition x ROI interaction - $F(4, 120)=5.626$, $p<.001$) responses to their self-triggered voice. Further, pre-stimulus alpha power was enhanced for self-triggered voices compared to tones in individuals with high hallucination predisposition (group x stimulus type interaction - $F(1, 30)=4.479$, $p=.043$). Anomalies in forward modelling were specifically associated with LSHS auditory hallucination scores ($r=-471$, $p=.003$).
Discussion: Together, these findings suggest that altered forward modelling of one's own voice is core to AVH. These results also provide partial support for the continuum model of psychosis, suggesting that psychotic symptoms form a continuum in the general population. A voice-specific, rather than a generalized, forward model dysfunction may explain why hallucinated voices are the most common type of auditory hallucinations.

S141. TRANSGENIC OVEREXPRESSION OF THE TYPE III ISOFORM OF NEUREGULIN 1 IN MICE INDUCES ABNORMALITIES ON AUDITORY EVENT RELATED EEG BIOMARKERS RELATED TO SCHIZOPHRENIA

Holger Rosenbrock*[,1], Wiebke Nissen[2], Roberto Arban[2], Rossner Moritz[3], Schwab Markus[4], Cornelia Dorner-Ciossek[2], Niklas Schülert[2]
[1]Boehringer Ingelheim Pharma GmbH & Co KG; [2]CNS Diseases Research, Boehringer Ingelheim Pharma GmbH & Co KG; [3]Ludwig-Maximilians-Universität München; [4]Hannover Medical School

Background: Genetic, post-mortem and preclinical studies in transgenic mice repeatedly implicate neuregulin 1 (NRG1) as a critical component in the pathophysiology of schizophrenia. Its predominant neuronal receptor, ErbB4, is primarily expressed in fast-spiking interneurons enabling the maintenance of normal excitatory/inhibitory balance (E/I balance) of neuronal networks. Changes in E/I balance can be assessed in-vivo via special electroencephalography (EEG) techniques and have become an important preclinical and clinical readout to investigate the underlying mechanisms of psychiatric disorders. In fact, patients with schizophrenia show aberrant processing of sensory information leading to deficits in auditory event-related potentials (AERP), the detection of deviant auditory stimuli (mismatch negativity, MMN) and the 40Hz auditory steady-state response (ASSR) as well as to increased basal gamma oscillation.
Patients with Schizophrenia carrying NRG1 HapICE risk alleles appear to overproduce the NRG1 type III isoform in their brain. In the transgenic mouse, NRG1 type III overexpression (HANI mice; Velanac et al., 2012) results in altered synaptic activity and in behavioural changes like reduced prepulse inhibition and impaired cognition compatible with a schizophrenia-related phenotype (Agarwal et al, 2014). In the present study, the potential disruption of the E/I balance in HANI mice has been investigate via EEG recording.
Methods: Superficial electrodes were implanted above the auditory cortex and the frontal cortex. We used a novel wireless neurologger system for the recording of EEG data in awake freely moving mice. Data analysis was performed with commercially available software which is also used in clinical setting.
Results: Overexpression of NRG1 abolished MMN, significantly increased the P1 and N1 amplitude of AERP, increased basal gamma oscillation and reduced phase-lock coherence in the 40 Hz ASSR compared to the wildtype littermates.
Discussion: In this study we showed for the first time that overexpression of NRG1 leads to deficits in event-related EEG biomarkers supporting the notion that the NRG1-ErbB4 pathway is involved in maintaining the E/I balance, sensory stimulus processing and ultimately cognitive function. Our results indicate that the NRG1 III tg mouse model represents a tool with high translational potential to investigate pathological mechanisms related to schizophrenia.

S142. RESTING STATE NETWORKS ALTERATION IN BIPOLAR DEPRESSION

Gianluca Mingoia*[,1], Igor Nenadic[2]
[1]Aachen University; [2]Jena University Hospital

Background: While functional MRI and PET studies have shown altered task-related brain activity in bipolar depression, recent studies suggest that such differences might also be found in the resting state (RS). Here we used ICA based analysis to investigate RS fMRI data to compare connectivity of 11 well known networks (Auditory, Cerebellum, DMN, Exectutive Control, Fronto-parietal 1, Fronto-parietal 2, Salience, Sensorimotor, Visual1, Visual2, Visual3 network) between patients with bipolar depression and healthy controls suggesting deficits in related neuropsychological functions.
Methods: We obtained RS fMRI series (3T, 3x3x3mm resolution, 45 slices, TR 2.55s, 210 volumes) in 22 bipolar patients (mean age 38.4a±11.3), on stable medication and 22 matched healthy controls (36.8a±11.7).
Subjects were asked to lie in the scanner keeping eyes closed with no further specific instructions. Data were pre-processed; we applied FSL MELODIC (pICA) yielding IC, we used FIX to auto-classify ICA components which represent artifacts and an automated routine to select for each subject the component matching the anatomical definition of resting state networks.
SPM12 was used for second level analysis, we used two sample t-test to compare networks functional connectivity between groups.
Results: Our method reliably identified all networks in every controls and patients. We found significant differences in the anatomical pattern of areas. Patients showed decreased functional connectivity in comparison to healthy controls in portions Cerebellum, DMN, Fronto-parietal1,