approach to identify latent trajectory classes to account for heterogeneity in patterns of change in psychotic symptoms over time and characterize these trajectories with the WHO classification, baseline demographic characteristics and diagnoses. Ulrich Reininghaus will present novel data from the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) consortium to investigate whether there is a transdiagnostic dimension cutting across symptoms of schizophrenia, schizoaffective disorder and psychotic bipolar I disorder. Diego Quattrone will report recent findings from EU-GEI Functional Enviromics Study on genetic and socio-environmental factors associated with transdiagnostic and specific symptom dimensions of non-affective and affective psychosis. Robin Murray will discuss these findings in the context of new challenges in the field and directions for future research.

5.1 DIMENSIONS OF PSYCHOSIS AND THEIR TRAJECTORIES DURING TWO DECADES AFTER FIRST HOSPITALIZATION

Roman Kotov*[,1]
[1]*Stony Brook University*

Background: Heterogeneity of psychosis presents significant challenges for classification. Between two and 12 symptom dimensions have been proposed, and consensus is lacking. The present study sought to identify uniquely informative models by comparing the validity of these alternatives. A critical validator is future course, and we examined trajectory of each dimension.
Methods: We investigated this question in the first U.S. study to follow an epidemiological cohort with psychotic disorders for 20 years after first hospitalization. Participants were assessed in person 6 times over 2 decades on Global Assessment of Functioning (GAF), psychotic symptoms, and mood symptoms, and 373 completed 20-year follow-up (68% of survivors) including an electrophysiological assessment of error processing. We first analyzed a comprehensive set of 49 symptoms rated by interviewers at baseline, progressively extracting from one to 12 factors. Next, we compared the ability of resulting factor solutions to (a) account for concurrent neural dysfunction and (b) predict 20-year role, social, residential, and global functioning, and life satisfaction.
Results: A four-factor model showed incremental validity with all outcomes, and more complex models did not improve explanatory power. The four dimensions—reality distortion, disorganization, inexpressivity, and apathy/asociality—were replicable in 5 follow-ups, internally consistent, stable across assessments, and showed strong discriminant validity. On all of these measures schizophrenia exhibited a decline that began between years 5 and 10. Correspondingly, GAF scores dropped from 49 (Year 4) to 36 (Year 20). Neither aging nor changes in antipsychotic treatment accounted for the declines.
Discussion: These results reaffirm the value of separating disorganization and reality distortion, are consistent with recent findings distinguishing inexpressivity and apathy/asociality, and suggest that these four dimensions are fundamental to understanding neural abnormalities and long-term outcomes in psychosis. They also revealed a substantial symptom burden across psychotic disorders that increased with time and ultimately may undo initial treatment gains. Additional research is needed, but previous studies suggest sociocultural factors and different care models may preempt this decline.

5.2 RETHINKING THE COURSE OF PSYCHOTIC DISORDERS: IDENTIFYING LATENT TRAJECTORIES

Craig Morgan*[,1], Paola Dazzan[1], Julia Lappin[2], Margaret Heslin[1], Gillian Doody[3], Robin Murray[1], Peter B. Jones[4], Ulrich Reininghaus[5]
[1]*Institute of Psychiatry, Psychology & Neuroscience, King's College London;* [2]*University of New South Wales;* [3]*University of Nottingham;* [4]*University of Cambridge;* [5]*Maastricht University*

Background: The clinical course of psychotic disorders is highly variable. Typically, researchers have captured course types using broad categories, e.g. the WHO instruments to assess course and outcome distinguish three categories: episodic (i.e., no episode > 6 months), continuous (i.e., no remission > 6 months), and neither (i.e., an episode and a remission > 6 months). However, whether these adequately capture symptom trajectories of psychotic disorders has not been assessed. Using AESOP-10 data, we sought to identify classes of individuals with specific symptom trajectories over a 10 year follow up and to, then, compare trajectories with WHO categories and examine associations between trajectories and baseline demographic characteristics and diagnoses.
Methods: AESOP-10 is a follow-up, at 10 years, of a cohort of 552 patients with a first episode psychosis identified in south-east London and Nottingham, UK. At follow-up, we collated detailed information on clinical and social course and outcome. This included collating extensive information on month by month fluctuations in presence of psychotic symptoms. Using this data, we fitted growth mixture models to identify latent trajectory classes that accounted for heterogeneity in patterns of change in psychotic symptoms over time.
Results: We had sufficient data on occurrence of psychotic symptoms throughout the follow up on 326 (~ 60%) patients.
A four-class quadratic growth mixture model best fit the data, with four trajectories defined by variations in the mean number of months psychotic per year during the follow-up period: (1) low and reducing [intermittent] (58.5%); (2) persistently high [persistent] (30.6%); (3) high, followed by gradual reduction [late improvement] (5.6%); and (4) intermediate, followed by gradual increase [late decline] (5.4%). When compared with the usual classification of course types (episodic, continuous, neither), the intermittent class included all those in the episodic category (n 94 of 94; 100%) and the persistent class included almost all those in the continuous category (n 72 of 78 persistent; 92%). A majority of those in the neither category had an intermittent trajectory (i.e., n 90 of 145; 62%), with the remainder spread across the other three classes (i.e., n 25, 17% persistent; n 14, 10% late decline; n 16, 11% late improvement).
Compared with those with an intermittent trajectory, patients with a persistent trajectory were less often women (OR 0.6, 95% CI 0.4–0.9), more often of black Caribbean ethnicity (OR 2.3, 95% CI 1.2–4.1), and less often had a diagnosis of affective psychosis (OR 0.2, 95% CI 0.1–0.4). There were no differences by age. Numbers were small, but there were indications that those with a late decline trajectory more closely resembled those with a persistent trajectory (i.e., less often women, more often of black Caribbean ethnicity, less often diagnosis of affective psychosis) than did those with a late improvement trajectory.
Discussion: Our current approach to classifying course of psychotic disorders may be flawed, particularly in specifying a group as neither episodic nor continuous. Our findings suggest this group is heterogeneous and includes patients whose outcomes more closely resemble one of the two main trajectories, intermittent or persistent. Only a small proportion of patients fit neither. These patients constitute clinically important sub-groups whose trajectories appear to change, either from an initially positive or initially negative course, some years after first contact with mental health services. Our failure to fully characterise trajectories of psychosis may confound efforts to elucidate predictors of long-term outcome.

5.3 EVIDENCE ON A TRANSDIAGNOSTIC PSYCHOSIS SPECTRUM OF SCHIZOPHRENIA, SCHIZOAFFECTIVE AND PSYCHOTIC BIPOLAR DISORDER IN THE BIPOLAR-SCHIZOPHRENIA NETWORK ON INTERMEDIATE PHENOTYPES (B-SNIP)

Ulrich Reininghaus*[,1], Jan Boehnke[2], UnYoung Chavez-Baldini[1], Brett Clementz[3], Godfrey Pearlson[4], Matcheri Keshavan[5], John Sweeney[6], Carol Tamminga[7]

[1]Maastricht University; [2]University of Dundee; [3]University of Georgia; [4]Yale University; [5]Harvard University; [6]University of Texas Southwestern; [7]The University of Texas Southwestern Medical Center

Background: The validity of the classification of non-affective and affective psychoses as distinct entities has recently been disputed in light of calls for a dimensional and transdiagnostic approach to diagnostic classification and evidence on shared aetiological factors. Despite the shifts in view, there remains a dearth of empirical efforts to clarify and identify a transdiagnostic spectrum of psychosis. Our recent research has demonstrated evidence for a transdiagnostic psychosis spectrum as detailed in a bifactor model with one transdiagnostic symptom dimension and five specific symptom dimensions of positive symptoms, negative symptoms, disorganization, mania, and depression in patients with schizophrenia, schizoaffective and bipolar disorder. The aim of the current study was to investigate whether there is a transdiagnostic dimension cutting across symptoms of schizophrenia, schizoaffective disorder and psychotic bipolar I disorder using widely established measures for assessing psychosis, mania and depression in the large multi-centre Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) consortium in the United States.
Methods: This study analysed data from the B-SNIP Phenotyping Consortium, which included 933 patients with a diagnosis of schizophrenia (n=397), schizoaffective disorder (n=224), and bipolar disorder (n=312). Multidimensional item-response modelling was conducted on symptom ratings of the Positive and Negative Syndrome Scale (PANSS), the Young Mania Rating Scale (YMRS), and the Montgomery-Åsberg Depression Rating Scale (MADRS) using the mirt package of the R environment.
Results: A bifactor model with 1 transdiagnostic symptom dimension and 5 specific symptom dimensions of positive symptoms, negative symptoms, cognitive disorganization, mania, and depression best matched the B-SNIP sample data. The bifactor model with 1 transdiagnostic factor and 5 specific factors based on the PANSS 5-factor solution by Emsley et al. (2003) provided the best model fit (AIC=53209.8, BIC=53920.0, aBIC=53443.7), as compared with a unidimensional model (AIC=55583.1, BIC=56151.3, aBIC=55770.2), a pentagonal model based on the PANSS 5-factor solution by Emsley et al.3 (AIC=53452.6, BIC=54068.1, aBIC=53655.3) as well as pentagonal and bifactor models of other previously reported factor solutions. When we extended analyses to include YMRS and MADRS, again, the bifactor model with 1 transdiagnostic factor and 5 specific factors, again, provided the best model fit.
Discussion: Consistent with our previous findings, this study provides evidence on a transdiagnostic symptom dimension that cuts across traditional diagnostic boundaries of schizophrenia, schizoaffective disorder and psychotic bipolar disorder using three widely established measures for assessing psychosis, mania and depression. The best-fitting, bifactor model also included 5 specific symptom dimensions based on the PANSS 5-factor solution by Emsley et al. (2003), which reflects a direct replication of our previous findings on the dimensionality of the PANSS. Overall, our findings lend further support to a transdiagnostic psychosis spectrum encompassing schizophrenia, schizoaffective and bipolar disorder as we have previously proposed.

5.4 BIOLOGICAL AND EPIDEMIOLOGICAL EXAMINATION OF TRANSDIAGNOSTIC AND SPECIFIC SYMPTOM DIMENSIONS AT PSYCHOSIS ONSET: FINDINGS FROM THE EUGEI STUDY

Diego Quattrone*[,1], Pak Sham[2], Evangelos Vassos[1], Charlotte Gayer-Anderson[1], Giada Tripoli[1], Laura Ferraro[3], Michael O'Donovan[4], Alex Richards[4], Jim van Os[5], Craig Morgan[1], Ulrich Reininghaus[5], Robin Murray[1], Marta Di Forti[1], Cathryn Lewis[1]
[1]Institute of Psychiatry, Psychology & Neuroscience, King's College London; [2]Centre for Genomic Sciences, The University of Hong Kong; [3]University of Palermo; [4]MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University; [5]School of Mental Health and Neuroscience, Maastricht University

Background: Current diagnostic models of psychosis have been questioned since Kraepelin's original dichotomy of dementia praecox and manic depression. Indeed, increasing evidence has suggested that a dimensional approach might be a valid alternative platform for research. However, while an increasing number of studies have investigated how environmental risk factors for affective and non-affective psychosis map onto symptom dimensions, only a few have examined these dimensions in relation to genetic variants as summarised by Polygenic Risk Score (PRS). Furthermore, no studies have examined the putative effect of PRS for Schizophrenia (SZ), Bipolar Disorder (BP), and Major Depressive Disorder (MDD) on previously identified general and specific symptom dimensions. At the same time, only one study has investigated how symptoms vary according to epidemiological factors such as living in urban neighbourhoods. The objectives of this study were to: 1) test whether a bi-factor model statistically fits the conceptualization of psychosis as composed of general and specific dimensions; 2) examine the extent to which SZ, BP, and MDD PRSs explain the phenotypic variance due to general and specific dimensions; 3) test the hypothesis that the general psychosis dimension would be more severe in highly urban environments.
Methods: We used clinical and epidemiological data from the EUropean network of national schizophrenia networks studying Gene-Environment Interactions (EUGEI) study, including 2322 First Episode Psychosis (FEP) patients recruited in 17 sites across 6 countries. Genetic variants were collectively analyzed for 800 individuals.
The following analysis steps were performed:

1) Psychopathology items were analysed using multidimensional item response modelling in MPlus to estimate unidimensional, multidimensional, and bi-factor models of psychosis. Model fit statistics included Log-Likelihood, and Akaike and Bayesian Information Criteria to compare these models.
2) SZ, BP, and MDD PRSs for general and specific dimensions were built using PRSice. Summary statistics from large case-control mega-analyses from the Psychiatric Genomics Consortium were used as base data sets and general and specific dimension scores were used as discovery data sets. Individuals' number of risk alleles in the discovery sample was weighted by the log odds ratio from the base samples, accounting for population stratification, and summed into the three PRSs.
3) Multilevel regression analysis was used in STATA 14 to examine the variance in general dimension due to the population density levels across the sites.

Results: A bi-factor solution, composed of one general and five specific symptom dimensions, showed the best model fit statistics.
Higher SZ PRS score was associated with higher scores on positive dimensions (β= 0.27, t=2.11, p<0.05); higher BP PRS was associated with higher scores on mania dimension (β= 0.17, t=2.11, p<0.05); higher MDD PRS was associated with lower scores on negative dimension (β= -0.31, t=-2.25, p<0.05). No trends of association were found for SZ, BP, or MDD PRSs and the general psychosis dimension.
The transdiagnostic symptom dimension score was elevated in people living in more densely populated sites (η2=0.077, 95% CI 0.057–0.098).
Discussion: Our results suggest that a) symptom dimension structure at FEP is best represented by the bi-factor model; b) in FEP patients, there is a trend of associations between SZ PRS and positive dimension, and between BP PRS and mania dimension; and c) elevated level of transdiagnostic symptomatology was observed in more densely populated sites.