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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

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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.