Exploring psychotic experiences in the context of multidimensional psychopathology

CHAPTER7

Summary

In **Chapter 1,** a background was provided on the conceptualization of psychosis as laid out in current classification systems. In addition, the concept of an extended psychosis phenotype in the general population was described, as was the notion that there is a distribution or spectrum of psychosis across current psychiatric nosology. Evidence on the transdiagnostic nature of the psychosis spectrum was discussed, and a multidimensional view of psychosis was introduced. Research describing a network of overlapping and interacting dimensions across the psychosis spectrum was reviewed. Finally, the aims and the outlines of the thesis were described.

In **Chapter 2**, the design of the TurkSch study was presented. This included the assessment of the different dimensions of the extended and transdiagnostic psychosis phenotype, as well as the description of the multilevel data collection including socio-environmental exposures and blood sampling in a representative community-based population. Outcomes of household visits and analysis of attrition, based on noncontacts and refusals in the longitudinal arm were introduced. Finally, dynamic transitions over time, within the spectrum of the extended psychosis phenotype, were demonstrated. Results showed that attrition over time showed no large differential effect sizes as a function of important variables. Furthermore, increasing severity of subthreshold psychosis at baseline was associated with increasing rates of persistence and psychotic disorder outcomes over the follow-up period. However, an even higher proportion of clinically relevant subthreshold psychosis did not persist over time.

In **Chapter 3,** longitudinal bidirectional associations between the spectrum of the positive psychosis domain and affective psychopathology were evaluated, accounting for other possible influences. The analyses revealed reciprocal sub-additive longitudinal associations between these domains, as well as similar cross-lagged correlations over time. Finally, there was considerable sharing of socio-environmental and familial risk factors

across these domains. These results suggest mutually causal connections between the affective and positive domains.

In **Chapter 4**, clinician-based longitudinal diagnoses of clinically relevant subthreshold psychosis were presented as well as moderating factors. Results showed that the psychotic disorder diagnosis rate at follow up was 7.0%. This is much lower than the rates of mood disorders without psychotic features (42.8%) and other non-psychotic disorders (24.1%). Female sex, lower socio-economic status, co-occurrence of mood disorders, family history of a mental disorder, and persistence of psychotic experiences predicted any follow-up DSM diagnosis. Furthermore, follow-up psychotic versus non-psychotic disorder outcome was predicted by younger age (15–30 years), co-presence of delusional and hallucinatory PE and family history of severe mental illness. The results demonstrated the importance of subthreshold psychosis as a marker of transdiagnostic risk.

In **Chapter 5**, the association of a priori hypothesized SNP (rs6265) with a longitudinally assessed dimensional phenotype covering subthreshold and threshold levels of the positive psychosis domain was investigated. The SNP was significantly associated with the positive spectrum of psychosis. The pattern of the association was that the SNP impacted in a dose-response but extra-linear fashion, with stronger impact at the threshold end. Associations were still significant when adjusted for sociodemographic factors and environmental exposures including life events, childhood adversity, socioeconomic status, urbanicity, and cannabis use. The results potentially indicate the relevance of dimensional risk assessment in relation to genetic association.

In **Chapter 6**, the results of the studies in this thesis were summarized, discussed and integrated in light of the current literature. Strengths and limitations were stated. Finally, future directions were provided.