SP022

Multivariate Patterns of Cognitive and Socio-Cognitive Deficits in Schizophrenia, Bipolar Disorder, and related risk

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Abstract: Alterations in cognition and social cognition in bipolar disorder and schizophrenia have been largely documented. However, to which extent these alterations overlap between the disorders and how they are relevant to early stages as well as to risk conditions remains unclear. To shed light on this topic, 59 patients with Bipolar Disorder (BD), 118 patients with schizophrenia (SCZ), two independent cohorts of Healthy Controls (HC1=95, HC2=195), as well as individuals at Clinical High Risk (CHR=35) and at First Episode of Psychosis (FEP=29) were characterized for a series of cognitive and socio-cognitive features, which were entered in a machine learning analysis as a cognitive, a socio-cognitive, and a combined cognitive and socio-cognitive (stacking) classifier. Such classifiers were probed to discriminate at the single subject level BD vs. HC1 and SCZ vs. HC2. Then, those with the greatest diagnostic power in categorizing BD vs. HC1 were challenged to predict discrimination between SCZ vs. HC2, and vice-versa. Thus, decision scores for such models were compared with those obtained when they were applied to FEP and CHR. Results indicated that stacking classifiers were the best in discriminating HC1 vs. BD (Balanced Accuracy - BAC = 80%) and HC2-SCZ (BAC = 84%). Furthermore, the HC1-BD staking classifier successfully discriminated HC2 from SCZ (BAC=77.4%), and vice-versa (BAC=83.1%). Decision scores for SCZ and BD overlapped with those obtained when stacking models were applied to FEP, identifying a "patient-like" pattern. Differently, when such combined signatures were applied to CHR individuals, they were classified neither as patients nor as HC. Findings suggest an overall overlap of cognitive and socio-cognitive anomalies classifying schizophrenia and bipolar disorder, which is also relevant to early stages of disease. In this general context, disease-specific core abnormalities characterize SCZ and BD. Personalized rehabilitative programs may be oriented to primarily manage disease-related cognitive and socio-cognitive "hub" alterations, but always within a broader assessment.

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SP023

Genetics and other biomarkers of treatment resistance in depression

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Abstract: Major depressive disorder (MDD) is the most heterogeneous psychiatric disorder, as over 1400 combinations of symptoms can satisfy DSM diagnostic criteria, and understanding the underlying biological heterogeneity is fundamental in the perspective of precision psychiatry. Genetic variants are responsible for part of this heterogeneity and contribute to inter-individual differences in treatment effects. Therefore, pharmacogenetic studies can identify predictors of poor treatment response and treatment-resistant depression (TRD), aid the prescription and development of targeted treatments or the prescription of early intensive treatments in patients at risk of TRD. Previous genome-wide association studies (GWASs) had limited power to identify specific variants/genes involved in TRD, but polygenic overlap between poor antidepressant response/TRD and several other traits was demonstrated, e.g., schizophrenia, attention deficit hyperactivity disorder (ADHD), and cognitive traits. As suggested by the high clinical heterogeneity of MDD, considering specific symptom profiles can improve the power to identify genetic signals associated with TRD. Other promising strategies to identify the biological mechanisms involved in TRD include the study of large population cohorts, using proxies of TRD defined from electronic health records (EHRs), and the integration of biomarkers reflecting also environmental factors, such as proteomics. These strategies and ongoing studies will be discussed during this talk, with reference to Psych-STRATA, a project within the Horizon Europe research and innovation programme (101057454; https://psych-strata.eu).

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SP024

Definition and neurobiological underpinnings of treatment resistance in bipolar disorder

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Abstract: The pharmacological treatment strategies for bipolar disorders include both acute and maintenance treatments. However, a substantial number of patients do not respond sufficiently to pharmacotherapy. Thus far, there has been no standardized definition for treatment resistance in bipolar disorder. Studies have been using different definitions, possibly due to the clinical complexity including the episodic nature of bipolar disorder and various subtypes. The talk will discuss the definitions, neurobiological, and genetic aspects as well as ongoing initiatives to identify markers for treatment resistance in bipolar disorder.

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