Convergent molecular, cellular, and neuroimaging signatures of major depression

Major depressive disorder (MDD) emerges from complex interactions of biological systems that span from genes and molecules through cells, circuits, networks, and behavior. Establishing how neurobiological processes coalesce to contribute to the onset and maintenance of MDD requires a multi-scale approach, encompassing measures of brain structure and function as well as genetic and cell-specific genomic data.

Presenter

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The relevance of transdiagnostic shared networks to symptoms and cognition in schizophrenia

Schizophrenia (SZ) is frequently concurrent with substance use (SU), depressive symptoms (DEP), social communication and attention deficits. However, little work has been done to evaluate the shared multimodal brain regions between SZ and these various factors.
Hallucinations and Delusions Relate to Distinct Hierarchical Alterations in Neural Timescales

Hallucinations and delusions are burdensome symptoms that typically co-occur and comprise the psychotic syndrome of schizophrenia. Hierarchical Bayesian inference may provide a unifying model for these symptoms. Evidence suggests that abnormalities at low versus high hierarchical levels are related to hallucinations versus delusions, respectively. Intrinsic neural timescales (INT) are organized hierarchically and can be measured using resting-state fMRI (rfMRI). Here, for the first time, we investigated differential hierarchical relationships of INT to hallucinations and delusions in schizophrenia.

Uncoupling of Energy Consumption and Functional Connectivity in Psychotic Disorders

Schizophrenia (SZ) and bipolar disorders (BD) are often conceptualized as disconnection syndromes, with the evidence of decreased anticorrelation of the neural activities between the default mode network (DMN) and other task-positive networks (TPN). Abnormal bioenergetics, which can be quantified by the in vivo 31P magnetization transfer spectroscopy (31P-MT-MRS) [1-3], has been suggested to be underlying biological mechanism for the altered functional connectivity (FC) [4]. ATP is the primary energy source which can be directly used by brain cells. Besides oxidative phosphorylation in mitochondria, ATP can also be generated locally via the reversible enzyme creatine kinase (CK) reaction when energy is in high demand. To date, no study has directly linked regional energy metabolism to FC in SZ or BD. We hypothesize that abnormal FC may be associated with altered regional bioenergetic activity in psychiatric disorders.

Brain Age and Epigenetic Age Acceleration During Conversion to Psychosis.

Schizophrenia is a chronic progressive disease starting during adolescence in at-risk individuals. These subjects can be clinically screened for at-risk symptoms but only one third of them will develop a psychotic episode in three
years. The determinants leading to this differential outcome are yet to be understood (Fusar-Poli et al. 2013). Inflammation and oxidative stress were postulated to be some of the biological mechanisms involved in the emergence of psychosis on the one hand (Hardingham and Do 2016; Kebir et al. 2017), while on the other, these mechanisms were strongly associated with physiological aging (Campisi et al. 2019). The emergence of psychosis might thus entail an acceleration in aging. Therefore, we used epigenetic and brain imaging data from at-risk subjects who have been longitudinally followed (the ICAAR cohort) to test the hypothesis that subjects converting to psychosis ("converters") age faster than those not converting ("non-converters").

Presenter

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Psychopathology phenotypes explain individuals’ unique deviations from normative neurodevelopment

Throughout childhood and adolescence, the brain undergoes major structural changes that facilitate the emergence of complex behaviors and cognitive functions (Blakemore & Choudhury, 2006). Mental disorders often emerge during childhood, adolescence, and young adulthood (Paus, Keshavan, & Giedd, 2008), and are increasingly understood as disruptions to normative brain maturation (Bassett, Xia, & Satterthwaite, 2018). However, while maturational changes are stereotyped at the population level, large amounts of individual variation are also present (Foulkes & Blakemore, 2018). The extent to which this individual variation in neurodevelopmental abnormalities may explain psychopathology remains unclear. Linking individual variation in neurodevelopment to psychopathology has so far been challenged by current diagnostic nosologies that assign individuals with heterogenous symptom profiles to the same clinical diagnosis. Moreover, much of the extant literature has adopted case-control designs that reveal only abnormalities associated with the 'average' patient, thereby ignoring the dimensional nature of psychopathology (Lahey et al., 2012). Here, we evaluate whether dimensions of psychopathology explain deviations from normative neurodevelopment.

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