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S0063

From a Pathophysiological Concept to a New Drug

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Although antipsychotics were discovered over fifty years ago, it took another decade until dopamine antagonism was demonstrated as central to their clinical effectiveness. Since accumulated evidence implicates the dopamine system in the pathophysiology of schizophrenia, all licensed first-line treatments operate primarily via antagonism of the dopamine D2 receptor. However, dopamine D2 receptor blockade does not effectively treat negative, cognitive and affective symptoms and, in a significant proportion of patients, it does not improve positive symptoms either. Therefore, additional neurochemical targets were considered. The “revised dopamine hypothesis” proposes that positive symptoms emerge due to hyperactive dopamine transmission in mesolimbic areas, while hypoactive dopamine transmission via the mesocortical pathway in the prefrontal cortex is linked to negative, cognitive, and partly affective symptoms. In this context, the role of D3 receptors were recognised. However, there is also evidence for the involvement of other neurotransmitter systems, suggesting that dopamine signalling relies on a suite of receptors that are thought to either facilitate or inhibit neurotransmitter activity through several interconnected neural circuits. Furthermore, there seem to be clusters of symptoms that cross the boundaries of disorders. Symptoms having similar pathophysiology at neurotransmitter level can be treated with the same drug or class of drugs. Thus, one particular drug might be effective in more than one indication. This lecture aims to illustrate the process of a new drug development by explaining how the underlying pathophysiology on receptor level impacts clinical studies and vice versa.

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Transdiagnostic Psychiatry: The New Trend

S0064

Diagnostic Fluidity: Inter- and Intra-Disease Considerations

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Traditionally, psychopathology has been classified based on the publications of authoritative bodies, such as the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (APA’s DSM). Recently, researchers have expressed an interest in basing classification more on data, as opposed to authority. This movement led to the formation of the Hierarchical Taxonomy of Psychopathology (HiTOP) consortium. Working from data, the HiTOP approach emphasizes dimensions of human individual differences that are arranged hierarchically, as opposed to categories that are arranged based on traditional DSM chapter rubrics. In this talk, I will describe the origins and status of the HiTOP approach, as well as current and future HiTOP directions and priorities.

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Keywords: Nosology; Classification; Psychopathology; Comorbidity

Mental Health Policy

Discrimination and Its Impact on Mental Health: New Evidence from Research and Clinical Practice

S0065

Neural Basis of Societal Risk for Mental Illness: Focus on Ethnic Minority Position and Racial Prejudice

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Background Urban birth, urban living, and ethnic minority status are established risk factors for schizophrenia, but the mechanisms are unclear. Previous evidence suggests a causal role of social exposures and adverse experiences, but experimental evidence is scarce. Methods We combine multimodal neuroimaging with ecological momentary assessment, geolocation and geospatial analysis in an epidemiological longitudinal sample in Germany. Results We find that established risk factors converge on the perigenual cingulate-amygdala-ventral striatal pathway as shown by structural and functional imaging, supporting a role for the ventral-striatal system in psychosis risk. Using a combination of PET and fMRI data in migrants, we suggest a mechanistic link to psychosis by increased dopamine release and synthesis in striatum secondary to prefrontal dysregulation. Importantly, the regulatory system identified overlaps with that implicated in racial stereotyping and prejudice. Moreover, an experiment measuring information flow during an exchange between migrants and non-migrants indicates that during a trust interaction, cultural distance governs the exchange. Conclusions This work shows a convergent risk circuit related to minority position and migration that could guide primary prevention of schizophrenia through reduction of manifestation risk by contextual intervention.

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Keywords: migration; Dopamine; social exclusion; cingulate cortex