

## **The Endocannabinoid Hypothesis of Schizophrenia: From Risk Factor to Therapy**

Cannabis intake has been long recognized to exacerbate psychosis in vulnerable individuals and to be a risk factor for the development of schizophrenia. The mechanism by which cannabinoids produce transient psychotic symptoms remains unclear. Nevertheless, recent advances in the neurobiology of the endocannabinoid system have provided an opportunity to revisit the association between cannabinoids and schizophrenia. While over-activity of cannabinoid CB1 receptors may contribute to the disease manifestations, other studies have shown that the endocannabinoid anandamide is elevated in the cerebrospinal fluid of drug-naïve schizophrenics and inversely correlated with both positive and negative schizophrenic symptoms, suggesting a protective role for endocannabinoids. In this talk I will present recent data on the ability of endocannabinoid-enhancing drugs to normalize dopamine dysregulation and reverse behavioral deficits in the phencyclidine rat model of schizophrenia, and provide a new frame to discuss the role played by natural and endogenous cannabinoids in schizophrenia.

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