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FUNCTIONAL ASPECTS OF THE ENDOCANNABINOID SYSTEM IN SCHIZOPHRENIA

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Introduction: The endocannabinoid system represents the target for the hallucinogenic Δ^9 -Tetrahydrocannabinol. It consists of naturally occurring endocannabinoid lipids (eCBs) - of which anandamide is the first characterized example - and their attending CB₁ cannabinoid receptors. Activation of CB₁ receptors produces intense emotional and cognitive responses, suggesting that dysfunction in the eCB system may contribute to the pathogenesis of mental disorders.

Methods: We examined levels of anandamide in cerebrospinal fluid (CSF) and serum of healthy volunteers (n=84) and various groups of patients suffering from acute psychiatric disorders (n=180).

Results: Compared to controls, the levels of anandamide in CSF were significantly elevated in acute, antipsychotic-naïve, first-episode schizophrenic patients (n=47) and negatively correlated with psychotic symptoms. This was reversed by the administration of antipsychotics, which antagonize dopamine D₂-like receptors (n=37), but not by those, which preferentially antagonize 5HT_{2A} receptors (n=34). In addition, a significant elevation of anandamide was already apparent in a sample of persons clinically at high risk for developing psychosis (prodromal states, n=27). Furthermore, the levels of anandamide in CSF were found significantly lower in antipsychotic-naïve schizophrenic patients reporting more than 20 times of cannabis use in life when compared to those with no more than 5 times.

Conclusion: Our results suggest that anandamide release in the central nervous system (CNS) may serve as an adaptive mechanism countering neurotransmitter abnormalities in acute schizophrenia. They indicate that frequent cannabis exposure may down-regulate CNS anandamide signaling in schizophrenia and thereby further impact the course of the disease.