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371. Endogenous Cannabinoids and Their Neurobiological and Functional Role in Schizophrenia Spectrum Disorders

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Background: Activation of cannabinoid CB1 receptors produces intense emotional and cognitive responses, suggesting that dysfunction in the endocannabinoid system may contribute to the pathogenesis of mental disorders.

Methods: We have examined the role of endocannabinoid signaling in psychotic states by measuring levels of the endocannabinoid anandamide in cerebrospinal fluid (CSF) and serum of various groups of healthy volunteers (n=84) and patients suffering from acute psychiatric disorders (n=187) by HPLC/MS.

Results: The level of anandamide in CSF is significantly elevated in acute, antipsychotic-naive, first-episode schizophrenic patients (n=47) when compared

to controls. This is reversed by the administration of antipsychotics, which antagonize dopamine D2-like receptors (n=37), but not by those, which preferentially antagonize 5HT2A receptors (n=34). Furthermore, we found that, in antipsychotic-naïve, acute schizophrenics, CSF anandamide is negatively correlated with psychotic symptoms. Our findings were specific for schizophrenia spectrum disorders.

Conclusions: Our results suggest that anandamide elevation in schizophrenia may reflect a compensatory adaptation to dopaminergic hyperactivity revealing an unexpected protective role for this endocannabinoid lipid in psychotic states.