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The therapeutic potential of the endocannabinoid system for the development of a novel class of antidepressants.

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Abstract

The endocannabinoid system is a neuromodulatory system which is known to regulate emotional, cognitive, neurovegetative and motivational processes. Substantial evidence has accumulated implicating a deficit in endocannabinoid in the etiology of depression; accordingly, pharmacological augmentation of endocannabinoid signaling could be a novel target for the pharmacotherapy of depression. Within preclinical models, facilitation of endocannabinoid neurotransmission evokes both antidepressant and anxiolytic effects. Similar to the actions of conventional antidepressants, enhancement of endocannabinoid signaling can enhance serotonergic and noradrenergic transmission; increase cellular plasticity and neurotrophin expression within the hippocampus; and dampen activity within the neuroendocrine stress axis. Furthermore, limbic endocannabinoid activity is increased by both pharmacological and somatic treatments for depression, and, in turn, appears to contribute to some of the neuroadaptive alterations elicited by these treatments. These preclinical findings support the rationale for the clinical development of agents which inhibit the cellular uptake and/or metabolism of endocannabinoids in the treatment of mood disorders.

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