Cannabinergic signalling in serotonergic and noradrenergic neurons

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The endocannabinoid system constitutes a widely distributed lipid signalling system in the brain and also in peripheral organs. The cannabinoid receptors (CB) are the major components of signal perception, and enzymes for endocannabinoid synthesis and degradation are involved in the signal initiation and termination. Numerous pharmacological agents have been developed in order to stimulate or dampen endocannabinoid signalling in the view that disregulations of endocannabinoid signalling is proposed to be disregulated. Indeed, such pharmacological modulations have been successful in influencing different behaviors, such as anxiety, fear extinction, depression-like behaviors, feeding, etc. A lot of attention has been drawn on CB1 receptors in central glutamatergic and GABAergic neurons. However, endocannabinoid signalling via CB1 receptors are also observed in other neurotransmitter systems, such as serotonergic and noradrenergic system. Such neurotransmitter system specific functions of the endocannabinoid system have been investigated using mutant mouse lines with specific CB1 receptor deficiencies in the respective neurotransmitter system, using the Cre/loxP system. To this end, the serotonergic endocannabinoid system is involved in anxiety and sociability. Recent investigations also revealed an involvement of CB1 receptor in this neuronal subpopulation in energy balance and in response to THC (tetrahydrocannabinol)-induced food intake. Furthermore, CB1 receptors in noradrenergic neurons are involved in consolidation of non-emotional episodic memory after stress, but also in various aspects of stress response and, interestingly, again in the regulation of energy balance. Using these genetic tools, our investigations reveal a very high complexity of cell type-specific functions of the endocannabinoid system regarding fine-tuned regulations of many neural processes.

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