

ALTERED ENDOCANNABINOID-MEDIATED SYNAPTIC PLASTICITY IN HIPPOCAMPAL NEURONS IN OBESITY

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Recently developed therapeutics against obesity target the cannabinoid receptor type 1 (CB1 receptor), resulting in decreased appetite, sustained weight loss, increased insulin sensitivity, and several other metabolic changes, alleviating the metabolic syndrome. On the other hand, agonists for CB1 receptors stimulate feeding and enhance the reward aspects of eating. Moreover, enhanced levels of endocannabinoids were found in various tissues of obese patients and rodents treated with high-fat diet. These tissues include hypothalamus, liver and adipocytes. Thus, the hypothesis has been put forward that the endocannabinoid system is overactive in obesity. Hippocampal circuits are not directly involved in the neuronal control of food intake and appetite, but they play an important role in the hedonic aspects of eating. We investigated the possibility that high-fat diet might alter endocannabinoid-mediated synaptic plasticity. Here we show that in the CA1 region of the hippocampus depolarization-induced suppression of inhibition (DSI) and paired-pulse facilitation, two forms of presynaptic short-term plasticity mediated by endocannabinoids, are enhanced in high-fat diet mice as compared to mice under standard diet. Our data provide direct electrophysiological evidences for the involvement of the endocannabinoid system as modulator of synaptic plasticity in obese mice and point to the possibility of the presence of an overactive endocannabinoid system under obesity also in the hippocampus.