

Impact of different stress intensities on cognition and emotion: A focus on endocannabinoids

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The activation of neuromodulatory systems by stress and emotional arousal within limbic brain regions plays a key role in the modulation of learning and memory for emotionally significant experiences. Cannabinoid type 1 (CB1) receptors are abundantly expressed within these brain regions, where they regulate emotional responses. Emerging evidence indicates that cannabinoid drugs can induce distinct and often opposite effects on anxiety, cognition, and several other behaviors, depending on the stress level and the aversiveness of the environmental context. Indeed, deliberate variations in environmental conditions result in marked changes in the effects of the same manipulations within the same series of experiments.

Findings will be presented on how increasing intensity of stressors or states of high and low emotional arousal at the time of training or testing influence endocannabinoid release in different limbic brain regions leading to differential effects on memory and emotionality. Data will show that CB1 antagonism induces opposite effects on recognition memory consolidation depending on the level of emotional arousal at the time of training and that the endocannabinoid anandamide in the amygdala, hippocampus and prefrontal cortex enhances memory formation under stressful situations. Conversely, the endocannabinoid 2-arachidonoylglycerol, in the hippocampus, is involved in the selective regulation of memory retrieval of stressful experiences. Furthermore, data will be presented on how increasing endocannabinoid anandamide and 2-arachidonoylglycerol levels in the amygdala selectively decreases anxiety when animals are tested under conditions of low emotional arousal.

Collectively, these findings help to elucidate the neural underpinnings of the fine-tuned regulation of limbic neurocircuitry involved in modulating the impact of stress and emotional arousal on memory processes and emotionality, thus facilitating our understanding of the state-dependency of many drug interventions on psychiatric disorders.