TRAINING-ASSOCIATED EMOTIONAL AROUSAL DIFFERENTIALLY MODULATES CANNABINOID EFFECTS ON OBJECT RECOGNITION MEMORY

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Growing evidence suggests that cannabinoid signalling may impair short-term memory performance. However, C*annabis sativa* derivates often induce biphasic behavioral effects, depending on the environmental context and influenced by emotional arousal. Therefore, the present experiments investigated, in male Sprague–Dawley rats, the effects of immediate posttraining systemic injections of the cannabinoid agonist WIN 55,212-2 on short-term object recognition memory under two conditions that differed with respect to their training-associated emotional arousal. In rats that were not previously habituated to the experimental context, WIN 55,212-2 (0.1-1 mg/kg, i.p.) administered immediately after a 3-min training trial, impaired 1-hr retention performance in an inverted-U shaped dose–response relationship ($F_{(3,44)}$=4.015, p=0.0131). In contrast, WIN 55,212-2 enhanced 1-hr object recognition retention when administered to rats that had received extensive prior habituation to the experimental context and, thus, had decreased novelty-induced emotional arousal during the training ($F_{(3,44)}$=4.98, p=0.005). As the cannabinoid system is known to interact with the adrenocortical axis and increase the expression of brain-derived neurotrophic factor (BDNF) in specific brain areas, in a second experiment we investigated whether the effects of WIN 55,212-2 on short-term memory performance could be linked to any alteration of plasma corticosterone levels or BDNF content in the hippocampus, amygdala or prefrontal cortex, three brain areas of crucial importance in the regulation of emotional memory and highly expressing cannabinoid receptors. WIN 55,212-2 administration did not alter corticosterone levels in either habituated or non-habituated rats. However, WIN 55,212-2 selectively increased amygdalar BDNF content of rats that were previously habituated to the context ($F_{(3,20)}$=8.132 p<0.001), which may account, at least in part, for the cannabinoid-induced memory enhancement. However, the memory impairment induced by cannabinoids under the high-arousing condition seems to be BDNF independent. In conclusion, this is the first evidence that cannabinoid effects on object recognition memory are biphasic and depend upon the level of emotional arousal at encoding.