



Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

Cognitive and affective mechanisms of pain modulation and their neuronal and neurochemical correlates

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This dissertation presents two studies investigating stress-induced analgesia (SIA, study 1) and control-induced analgesia (study 2) as two endogenous mechanisms of pain control. In study 1 SIA was induced in 19 healthy volunteers after administration of Tetrahydrocannabinol (THC), Cannabidiol (CBD) and placebo. The SIA effect was evaluated by pain ratings and blood oxygen level dependent (BOLD) responses to suprathreshold painful stimulation, pain thresholds, BOLD responses and psychophysiological measures. The aim was to determine whether cannabinoids are involved in human descending pain control. The main result was that SIA, although successfully induced in all conditions, was not modulated by an exogenously administered cannabinoid receptor agonist or inverse agonist. However, after THC administration the habituation to painful stimulation was attenuated. This was accompanied by altered brain activation in the middle frontal gyrus and middle temporal gyrus. The results suggest that in humans, cannabinoids are involved in habituation to pain, but not in SIA.

In study 2, 26 healthy volunteers were given painful stimulation in a controllable and an uncontrollable condition. The control-induced pain relief was assessed with ratings of pain intensity, pain unpleasantness and pain-related suffering. The aim of the study was to determine which pain dimension is affected by controllability of pain stimulation. The main result was that the exertion of control over pain reduced the experience of pain-related suffering while pain intensity and pain unpleasantness were not affected. Moreover, the effect on pain-related suffering was more pronounced in individuals with a higher general belief that their environment is determined by chance. The results suggest that control over a painful stimulus does not affect the classical pain dimensions of intensity and unpleasantness, but rather the suffering that is associated with them.

The results of study 1 indicate that SIA induced by mental arithmetic tasks is not mediated via endocannabinoid pathways, whereas these pathways seem to be involved in other inhibitory pain systems. Study 2 demonstrates that control over pain alleviates the suffering rather than the pain itself. It therefore offers a therapeutic target in cases of terminally ill, where suffering but not pain can be avoided. A better understanding of behavioral, physiological and neuronal mechanisms underlying healthy human pain inhibition offers new targets for pain inhibition in chronic pain.