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Psychobiological mechanisms of endogenous pain modulation by pain relief as reward

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Pain is much more than a sensory experience. Pain has strong emotional and motivational components that fulfill crucial functions for survival and well-being, because they drive behavior to avoid and escape from pain. This motivation is also reflected in the opposite and rewarding nature of the pleasure of pain relief. Both endogenous modulation of the perception of pain and pain relief are thought to promote the motivational drive and with that behavior that serves homeostatic needs. In contrast to pain and despite this crucial role of pain relief as reward, the psychobiological mechanisms underlying pain relief perception as well as related learning remain poorly understood. The aim of this dissertation was to deepen our understanding of psychological and neurobiological mechanisms of pain relief in healthy humans and possible alterations of these mechanisms in patients suffering from chronic pain.

In a first experimental study, the role of the neurotransmitters dopamine and endogenous opioids in pain modulation and reinforcement learning were investigated using a probabilistic relief seeking task in healthy volunteers. The results showed that the informational value of pain and pain relief was endogenously enhanced in states of active decision making compared to passive states. This endogenous pain modulation scaled with perceived uncertainty of expected outcomes. Dopamine increased endogenous pain and pain relief modulation, while no evidence for the involvement of endogenous opioids was found. Successful reinforcement learning as found in the placebo condition was impaired by dopamine and endogenous opioids.

The same probabilistic relief seeking task was used in a second study to investigate neural correlates of learning driven by pain and pain relief using functional magnetic resonance imaging in patients with chronic pain and healthy controls. This study replicated the effects of endogenous pain modulation by its informational value, while no alterations in patients with chronic pain were found compared to healthy controls. This result suggests that motivationally driven enhancement of pain relief perception is a robust phenomenon that appears to be spared by maladaptive changes during pain chronification. However, compared to healthy controls patients with fibromyalgia showed a stronger bias towards relief related cues during learning, but a weaker association of activation in the pregenual anterior cingulate cortex with relief prediction errors. These findings suggest that although the informational content of pain relief seems to be preserved in patients with chronic pain, subtle differences in the underlying mechanisms may reflect altered reward processing in chronic pain, which have been discussed before.

In sum, the results highlight the important role of motivation and prospective control of behavior for endogenous modulation of pain and pain relief and provide insights in underlying psychobiological mechanisms in healthy states and in chronic pain.