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Dissertations-Kurzfassung

Stress-induced analgesia in healthy controls and patients with chronic musculoskeletal pain

Autor: Pinar Kirsch (geb. Yilmaz)

Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)

Doktormutter: Prof. Dr. H. Flor

The phenomenon of pain suppression due to exposure to stressful stimuli is termed stress-induced analgesia (SIA), and is mediated by descending pain-inhibitory circuits. The opioid mediated form of SIA activates endogenous pain-inhibiting pathways from the periaquaductal gray (PAG) over the medulla to the spinal cord and a deficient SIA can be indicative of an overall deficient pain-inhibitory system. The present thesis focuses on brain mechanisms involved in mediating the stress-induced analgesia (SIA) effect in healthy humans as well as in patients with chronic musculoskeletal pain.

In the first study functional magnetic resonance imaging (fMRI) was used to assess brain activation in response to SIA in 21 healthy participants (HC). Using a block design series of painful pressure stimuli were applied to the left medial phalanx of the second digit during fMRI. A cognitive stressor, i.e. mental arithmetic combined with increasing levels of white noise was used to induce stress. To confirm the validity of stress induction verbal ratings, changes in blood pressure and heart rate were assessed. We found significantly increased pain thresholds and pain tolerance post stress compared to pre stress condition and in line with this subjective ratings of pain and unpleasantness significantly decreased compared to pre stress levels. SIA led to an increase of the blood-level dependent oxygenation response in the primary somatosensory cortex, bilaterally in the anterior insula, and secondary somatosensory cortex. The increase in pain tolerance from pre to post stress condition correlated significantly with activation in the rostral anterior cingulate cortex and the decrease in pain unpleasantness correlated significantly with activation in the dorsal anterior cingulate cortex.

The changes in central processes involved in stress-induced analgesia in chronic musculoskeletal pain (CMP) have not yet been explored. For CMP we expected a deficient descending pain inhibition, along with reduced activity in brain regions related to stress-induced analgesia with this effect being more pronounced the more widespread the pain is. In the second study the same experimental setup was used to investigate brain activation in response to SIA in 22 patients with CMP and 19 HC. Again verbal ratings, changes in blood pressure and heart rate confirmed that the stressor was perceived as stressful. We found pain thresholds as well as pain tolerance to be increased after stress induction in both, the HC and CMP group. Additionally for the HC we found subjective ratings of painfulness and unpleasantness to be lower after stress induction. In the CMP group pain ratings as well as unpleasantness ratings did not change from the pre to post stress condition. For the HC we found the SIA effect, as seen in an increase of pain threshold, to correlate with activation in the rACC and the SIA effect, as seen in an increase of the pain tolerance with activation in RVM. As we expected for the CMP we found no correlated activation in descending inhibition areas. Further in the CMP group we did not find the post higher pre contrast to correlate significantly with the number of pain locations.

From results of the first study we conclude that SIA seems to activate similar brain networks as placebo analgesia or analgesia mediated by diffuse noxious inhibitory controls and involves sensory, affective and cognitive modulatory circuits. Results of study two are pointing towards a deficient descending pain inhibition in patients with chronic musculoskeletal pain, as seen in the absence of a recruitment of descending inhibitory pathways in response to stress. A better understanding of the pathophysiology of chronic pain conditions can contribute to the development and validation of efficacious pharmacological and behavioral treatment.