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Operant conditioning of the blood oxygenation level-dependent response in areas involved in the processing of pain

Autor: Mariela Rance
Institut / Klinik: Zentralinstitut für Seelische Gesundheit Mannheim (ZI)
Doktorvater: Prof. Dr. H. Flor

Using real time functional magnetic resonance imaging (rt-fMRI) to modulate brain activation is a well-established method associated with changes in behavior, emotional processing, and cognition. The aim of the present study was to investigate the effect of self-regulation of pain evoked brain activation in pain perception in areas involved in the processing of pain in healthy participants. In two studies we compared the controllability and the extent of the control learned with rt-fMRI over two regions similarly involved in the processing of a painful electric stimulus and the effect on pain intensity and unpleasantness ratings. In the first study 10 participants trained to up- and downregulate activation of the rostral anterior cingulate cortex (rACC) and the left posterior insula cortex (plnsL) in four separate conditions in a balanced training schedule over the course of four consecutive training days. In the second study 10 different participants trained to increase the activation difference in the rACC and the plnsL with either rACC activation (2 conditions) or plnsL activation (2 conditions) being higher in 4 distinct conditions. The participants were not informed about the function of the regulated brain areas or the connection with the painful stimulus. The participants described the strategy they employed to modulate activation.

In both studies the participants learned modulation of both regions, but not always all conditions. The ratings of pain intensity and pain unpleasantness were unrelated to both the magnitude of the modulation of brain activation and learning success. Success in one condition was not significantly correlated to success in another, i.e. learning control over one region or direction of modulation did not lead to success in the other region or direction. This finding was even more pronounced in the second study where both states were trained in two conditions and there was no significant correlation between success in learning to achieve one state between the two conditions. We found that the group as a whole (study 1) learned successful downregulation of both regions, upregulation was learned in the plnsL only.

This result was mirrored in the second study where both states in their respective two conditions were learned but without significant changes in the rACC, i.e. the increase in the activation difference was caused by changes in the plnsL activation. In our first study we saw that one influence on learning was the state of the network, with learning success being significantly positively correlated with higher dissociation between the target and non-target region. A higher mean dissociation between both regions was significantly positively correlated with higher unpleasantness ratings when the participants trained upregulation of the plnsL activation. When the participants trained to dissociate the regions in the second study, the conditions were learned with a higher success rate, i.e. more participants per condition learned to achieve one state successfully. In both studies, there was no preference for a specific strategy and the participants also chose strategies that were not related to the painful stimulation.

We conclude that single regions in the pain processing network and regions combined can be modulated without causing changes in the perception of the experimental pain. The extent to which the pain evoked activation in the regions can be modulated is comparable between the regions; the same was the case for the magnitude of the difference between the regions in the two trained states. Modulating activation of the rACC and plnsL either combined or alone is not sufficient to alter the perception of pain intensity or pain unpleasantness of the painful experimental electric stimulus. Since both regions are involved in processes other than pain processing, it is possible that automatization of the change in activation would free regions from dual tasking and thus might have an effect on the modulation of pain perception. Another approach to modify the perception of pain is to identify regions involved in the modulation of the perception of pain and to identify altered states of these regions in

chronic pain states. Once these components are identified, it may be feasible to modulate the communication between specific parts of the network and even correct altered states of the network in patients with chronic pain.