

Poster: computer assisted procedures

New animal model for objective pain research: non-invasive functional imaging in anesthetized animals by BOLD fMRI to study initial processes of chronic pain

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The experience of acute pain is an elementary sensation necessary for maintaining individual integrity and well-being in interaction with the environment. However, repetitive noxious input can induce chronic pain states without any biological advantage. Long-term changes in the excitability of neurons have been shown at the peripheral and spinal cord levels. Maladaptive supraspinal reorganization is thought to play an important role in central sensitization, reconfiguring the central pain-processing matrix through learning, extinction, and memory processes. But it is a major challenge to investigate cerebral mechanisms and structures that contribute to sensitization of pain.

Traditional behavioural pain examinations in animals are highly stressful and subjective. Contributing to the 3R's non-invasive imaging approaches like fMRI in anesthetized animals would significantly reduce the stress for animals and simultaneously refine and improve objective measurements of chronic pain. Moreover, a model which would allow the investigation of chronic pain processes would open a new avenue in pain research.

Having established a model for acute heat pain in fully anesthetized animals we now seek to identify brain areas that may be involved in initial processes of chronic pain using an experimental model of repetitive pain exposure in healthy rats which results in reliable and quantifiable BOLD responses in pain related brain areas.

fMRI data were acquired in slightly anesthetized rats with mild noxious heat stimulation (max. 48°C, 12 repetitions over 1h) every second day over 6 days. Highly specific activity of the pain pathway was found (e. g. thalamus, primary and secondary somatosensory cortex, cingulate cortex, insular cortex, frontal cortex and parietal cortex). The comparison of fMRI data of the first *versus* the last stimulation indicated increased activation in terms of increased stimulus coupling in cingulate cortex, entorhinal cortex and hippocampus. This finding nicely compares to a human study (Valet et al., 2006) suggesting that in these structures first processes of pain chronification take place. Interestingly, no significant increases for response amplitudes in these structures could be found. Structures reported to be involved in pronounced chronic pain like parietal cortex and structures of the medial prefrontal cortex (Baliki et al., 2006) also showed increased stimulus coupling between the first *versus* last session. These results could neither be found comparing the first versus earlier days nor during innocuous heat stimulation. Moreover, optimized data-analysis strategies reduced the number of experiments needed to obtain statistically significant results.

In conclusion, our topical heat stimulation of the rat hind paw is a robust paradigm leading to reliable BOLD signals well suited for repetitive stimulations. This non-invasive animal pain model at minimal animal stress level due to the anaesthesia of the animal is highly objective and well qualified for studying chronification of pain responses.

References

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