Studying pain transmission with BOLD fMRI: thermal vs. electrical stimulation

A. P. Wunderlich[1], G. Stuber[2], R. Klug[3], and W. Freund[2]

[1]Diagnostic and Interventional Radiology, Univ.-Clinic Ulm, Ulm, Baden-Württemberg, Germany, [2]Diagnostic and Interventional Radiology, Univ.-Clinic Ulm, Ulm, Germany, [3]Neurology, Rehabilitation Clinic Ulm, Ulm, Germany

Introduction. Regarding transmission of pain in the human nervous system, usually the medial and lateral pathways are discerned. Because of receptor type properties, electrical and thermal stimulation tend to be transmitted differentially (1): Thermal stimulation results in transduction via c-fibres to the medial thalamus, whereas low level electrical stimulation will activate the lateral thalamus via Aα and Aβ fibres. The purpose of this work is to study the feasibility to distinguish these mechanisms by fMRI, comparing activation due to thermal and electrical stimulation.

Methods. After approval of the local ethics committee, 15 right handed healthy volunteers without acute pain, current or prior chronic pain-syndromes, or MRI contraindications were recruited for each arm of the study. fMRI data were acquired at 1.5 T using a BOLD-EPI sequence with 28 axial slices of 5mm thickness, 10% gap, and field of view 230 mm. TR was 2600 ms, TE 60 ms, FA 90°, and matrix size 64 x 64. Anatomical data were acquired using a sagittal T1w 3D MP-RAGE sequence in isotropic 1mm³ resolution and a T2w TSE sequence (TR 2530ms, TE 99ms, FOV 230mm, matrix 256) with the same slice orientation as the BOLD sequence.
The subjects were stimulated at the index finger of both sides subsequently in 4 different, individually adjusted intensities, ranging from no stimulation to the strongest painful sensation the subject was willing to bear. For fMRI, the stimulation was applied in blocks of 21 s length in pseudorandomized order, and each stimulus intensity was presented the same number of times.
Electrical stimulation was administered via 2 MRI-compatible adhesive ECG skin electrodes by an electroneurograph, whereas thermal stimulation was applied by an MRI-compatible Peltier thermode .
Data were analysed with SPM. Contrasts between each stimulus intensity and rest were calculated for individuals, and both stimulation modalities were compared in a second level analysis.

Results. During electric stimulation, activation of the contralateral posterior insula as well as bilateral dorso-lateral prefrontal cortex and ventral posterior anterior cingulate cortex (ACC) was more prominent than with thermal stimulation in all stimulus intensities.
The reverse contrast, which reveals areas that are more activated during thermal stimulation compared to electric stimulation, showed significant activation of ipsilateral primary motor and sensory areas, dorsal posterior ACC and thalamus in all intensities but the weakest stimulus.

Discussion. Our results suggest that cortical and subcortical activation due to different pathways of pain perception, employed mainly by one of the stimulation modalities, can be visualized by fMRI using thermal or electric stimulation, resp.
Electrical stimulation resulted in activation of the contralateral dorsal insula, which mostly is equated to secondary sensory areas and assumed to belong to the lateral pathway.
Thermal stimulation activated the thalamus, which is an integral part of both medial and lateral pathways, and also primary and secondary ipsilateral motor and sensory areas. These activations may be task related in the sense that thermal stimuli needed a longer amount of time to reach the correct intensity. Therefore, significantly more corrections of the rating answers in the thermal vs. the electrical stimulation task have been observed.
While in electrostimulation the ventral posterior ACC was activated, during thermal stimulation the dorsal posterior ACC was activated, suggesting a modality specific activation pattern for parts of the ACC. This has not been reported before.

References. 1. Rainville, P., et al., A psychophysical comparison of sensory and affective responses to four modalities of experimental pain. Somatosens Mot Res, 1992. 9(4): p. 265-77