BOLD Signal Changes in Tonic Pain

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Purpose.

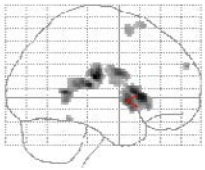
To study underlying neural correlates of tonic pain perception and supression. To check for signal changes missed in conventional block-design fMRI analysis in a study approved by our local ethics review board.

Methods.

Fifteen healthy volunteers (5 f, 10 m, 25-64 (35.5) yo) were scanned with fMRI using a block design. Subjects were stimulated electrically using a neurograph and MR compatible ECG electrodes. Stimulation intensity was adjusted to the maximum level of pain subjects were able to endure for 52 sec (total stimulation time). Stimulation phases were repeated six times with 26 sec rest periods in between. Subjects were advised to supress the pain sensation and to report subjective sensation levels. On a Siemens Magnetom Symphony MR scanner at 1.5 T, 28 slices (5 mm + 0.5 mm gap) covering the entire brain were acquired using a single-shot EPI sequence with cartesian readout at 64x64 matrix, FoV 230 mm and TE/TA/FA 60/2600 ms / 90°.
Data processing and analysis was performed with SPM 99. The stimulation block was divided into two regressors according to the reported subjective sensation level. The early phase covered the first 5 volumes (13 sec), the late phase the remaining 15 volumes. Both phases were contrasted separately against rest, and also the contrasts early minus late and vice versa were calculated for each subject. To simulate conventional block design analysis, early and late phase were contrasted together against rest. All results were combined to a group analysis.

Results.

Single subject analysis shows certain variability which reflects subjects' pain suppression strategies (not shown). The group analysis of stimulation of the left index finger reveals activation in the anterior insula during early stimulation (Fig. 1), where in the late phase activation shows up in the posterior insula and primary sensory areas SI (Fig. 2). The contrast early minus late phase shows the caudate nucleus as well as some parietal activity (Fig. 3). The reverse contrast late minus early is dominated by the posterior insula (not shown). Early and late phase together minus rest shows results similar to the late phase at comparable significance (not shown).



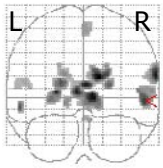


Fig. 1 Early phase minus rest, p<0.0001. Anterior insula and basal ganglia.

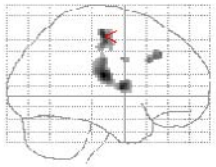


Fig. 2 Late phase minus rest, p<0.0001. Posterior insula and SI.

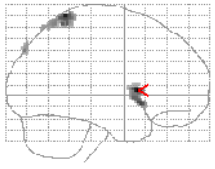


Fig. 3 Early minus late phase, p<0.0001. Caudate nucleus activation.

Discussion.

The pathway of pain perception is known [1] as two-fold: the lateral pathway with projections from the lemniscal tract to the primary sensory area SI, and the medial pathway, which passes from the spinothalamic tract via the thalamus to the secondary sensory area SII, anterior cingular cortex ACC and the posterior insula. Whereas the first represents sensory-discriminative aspects, the second is related to emotional-motivational aspects [2]. In our study, brain activation during sensation of tonic pain showed changes on a timescale of several seconds. In the early phase, subcortical structures activated besides the anterior insula, whereas in the later phase the endpoints of both pathways, namely SI and posterior insula, showed significant activation.
Modelling our long activation phase as two regressors, we were able to detect signal changes not adressed by the conventional block-design analysis. Remarkably, z-values of activated clusters in both evaluations early phase minus rest and late phase minus rest don't differ much. Evaluation of the late phase, however, should reveal higher significance levels since the ratio between sampled volumes of early and late phase is 1:3. A similar, also unexpected, effect are comparable z-values when contrasting both early and late phase together against rest. Both findings indicate marked changes in BOLD signal and therefore in brain activation as confirmed by robust z-values of contrasts between early and late activation phases (Fig. 3).

References. 1. Brodal P: The central nervous system. Structure and Function. Third Edition.Oxford University Press 2004, 162 ff
2. Treede R-D, Kenshalo DR et al: The Cortical Representation of Pain. Pain 79 (1999) 105-11