Temporal Changes of BOLD fMRI Activation in a Block Design

A. P. Wunderlich[1], G. Stuber[1], and W. Freund[1]
[1]Diagnostic and Interventional Radiology, Univ.-Clinic Ulm, Ulm, Baden-Württemberg, Germany

Purpose. To check for signal changes missed in conventional block-design fMRI analysis.

Methods. After obtaining the agreement of our local ethics committee, fifteen healthy, right-handed volunteers (5 f, 10 m, 25-64 (35.5) yo) gave informed written consent and were scanned with fMRI using a block design. Subjects were electrically stimulated at the left index finger 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, the duration of the stimulation. Stimulation blocks were repeated six times, each time followed by a 26 sec rest period, and subjects were advised to suppress pain sensation. Data acquisition started 26 sec before the first stimulation. 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/TR/FA 60/2600 ms/90°.
Data processing and analysis was performed with statistic parametric mapping (SPM). The paradigm was modeled as one regressor per acquired volume averaged over the repetitions in the stimulation-rest-cycle (e.g. the first volume acquired in each stimulation block, the second vol. etc., as well as the 1st, 2nd … vol. of rest). This allows a time-resolved activation analysis. As reference for BOLD signal changes, the rest phase before the first stimulation was chosen. All averaged volumes were contrasted separately against the reference, and a group analysis was performed for all time points. Significance threshold level was set to $p<0.00001$.

Results. Figure 1 shows axial glass brain views of the group analysis time series (the 3rd, 6th, 9th, 12th, 15th, 18th, 20th volume after stimulation onset, as well as the 5th and 10th volume during rest after stimulation). The added red circle covers the most intense activation and shifts backwards during the time course. Activation is revealed in the contralateral primary sensory area S1 as well as bilateral activation of the insula in the 3rd volume after stimulus onset (cf. Fig. 1). Activity decreases and rises again until a second maximum is reached in the 18th volume at 45 s after stimulus onset. The right hemispheric activation of the volumes 12 to 20 shows an overlay of DLPFC (dorsolateral prefrontal cortex) areas and posterior insular activations which are not present in the first volumes. After the end of the stimulation, activation first sustains at the level of volume 20 before fading and vanishing completely. Volume 9p shows no suprathreshold clusters and volume 10p is also nearly blank. Note that not only the level of the activation does change, but also the location of the local maxima.

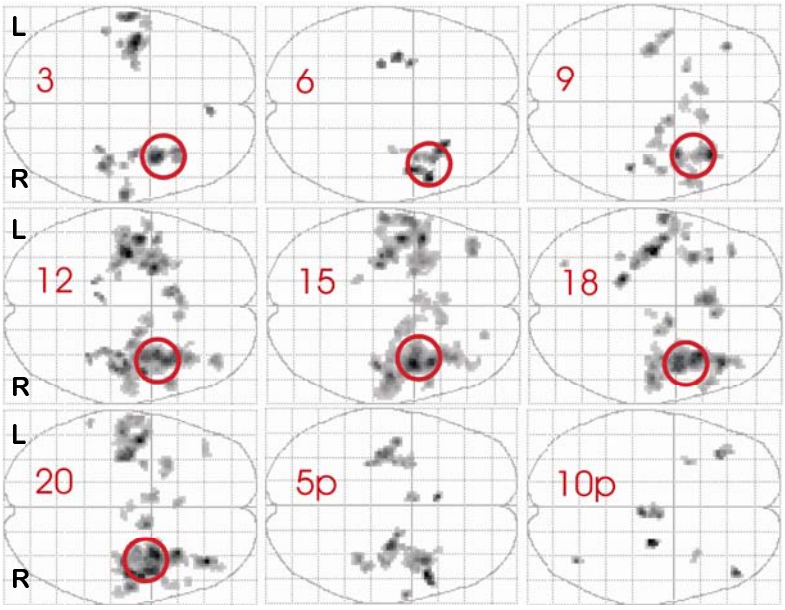

Figure 1. Time series of axial glass brain views showing the third to twentieth volume (2.6 seconds each) during stimulation numbered 3 to 20 and the fifth and tenth volume post stimulation (5p and 10p).

Discussion. According to the task to suppress the feeling of pain, subjects were able to suppress the feeling of pain. During that process, insular activation slowly changed its focus from anterior insula (supposed to correlate to aversive components of pain) to dorsal posterior insula (probably corresponding to SII), correlated to the still perceived stimulus that was rated not so painful anymore despite identical parameters. Modeling the repeated blocks in our study design as multiple regressors, each for one volume, gave the chance to detect signal changes not addressed by the conventional block-design analysis. Our results indicate that there was more variability in activations in our block-design study than expected. Activity tends to fluctuate between areas known as being involved in pain processing [1], also found in previous studies [2].
Furthermore, our results demonstrate that the rest period between stimulation is not suited as a reference ('off'-condition) for block design analysis, since activation observed during stimulation ('on'-condition) does not vanish in the amount of time expected from the hemodynamic response function, but sustains for 16 s before fading.
BOLD signal changes have been reported before and are addressed on a sub second timescale in event related fMRI. To our knowledge, however, this is the first study which describes signal changes on a timescale of seconds in a paradigm using noxious stimuli.

References. 1. Treede R-D, Kenshalo DR et al: The Cortical Representation of Pain. Pain 79 (1999) 105-11
2. Wunderlich et al.: BOLD Signal Changes in Tonic Pain. Proc. ISMRM 13 (2006), 3285