Optimized fMRI protocol for fear conditioning experiments at 3 Tesla using parallel acquisition technique

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Introduction:

The prefrontal cortex, especially the orbito-frontal cortex and subcortical limbic structures such as the amygdala are of primary interest when studying neuronal activation of conditioned fear extinction [1]. As the detected BOLD-contrast is increased, fMRI benefits of high magnetic field strength of 3 Tesla, but susceptibility artefacts in these regions become increasingly worse, causing strong image distortion and signal dropout [2]. In a fear conditioning study an echo-planar imaging (EPI) BOLD protocol with parallel acquisition technique was compared to a standard EPI-BOLD protocol.

Method:

The experimental procedure consisted of a habituation, an acquisition, and an extinction phase. In all phases, four neutral faces were used as conditioned stimuli (CS). During acquisition, two of the CS (=CS+) were followed by an aversive unconditioned stimulus US (unpleasant electrical shock), whereas the two other CS (=CS-) were not paired with the US. During extinction, no further presentation of the US occurred.

The functional experiments were conducted on a 3 T whole body scanner (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) with a twelve-channel head coil. The first group (4 healthy subjects) was imaged using a standard EPI-BOLD protocol with the following parameters: TR=2700ms, flip angle=90°, TE=34ms, FOV=220mm, matrix=64x64, receiver bandwidth=1270Hz/pixel, 35 slices, slice thickness=3mm, slice gap=1mm. The data acquisition of the second group (4 healthy subjects) was performed using GRAPPA-technique [3] (acceleration factor 2), increased matrix size (96x96) and the parameters mentioned above.

Pre-processing of the functional datasets and subsequent random effects analysis for each group was performed with SPM2 (http://www.fil.ion.ucl.ac.uk/spm/). All datasets were normalized to a MNI-template with identical resolutions (2x2x3mm^3). Both protocols were compared based on the t-test for the contrast CS+>CS- during extinction phase.

Results:

Fig.1 shows functional EPI-images taken from one subject acquired without parallel imaging and with a matrix size of 64x64, Fig.2 shows data taken with GRAPPA-technique and higher resolution (96x96 matrix). The arrows indicate the left amygdala and orbito-frontal cortex. With the latter protocol, signal dephasing from field inhomogenities was reduced significantly, especially in the amygdala.

Results from the random effects analysis of the data acquired during extinction phase are summarized in Table 1. The statistical maps were thresholded using a small-volume corrected significance threshold of p=0.05. Cluster size was calculated with a cluster-level statistics. Contrary to the data acquired with the standard protocol, the data acquired using GRAPPA-technique shows a significant cluster in the left amygdala and one additional significant cluster in the orbito-frontal cortex.

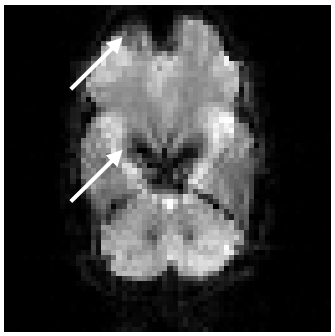

Fig.1: Functional EPI image taken from one subject. The arrows indicate the left amygdala and the orbito-frontal cortex.

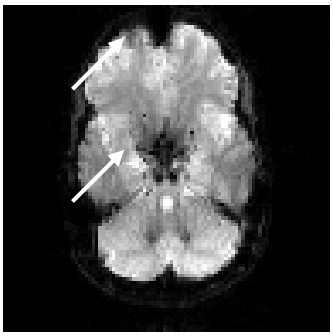

Fig.2: Functional EPI image acquired with GRAPPA-technique and higher resolution.

Tab.1: Cluster sizes and corresponing p-values in the left amygdala and the orbito-frontal cortex using different protocols.

cluster size / $p_{uncorrected}$	GRAPPA protocol, matrix 96x96	standard protocol, matrix 64x64
left amygdala	134 voxels / 0.050	no significant cluster
orbito-frontal cortex	373 voxels / 0.003 357 voxels / 0.004	485 voxels / 0.049

Discussion:

Our results suggest that standard EPI-BOLD protocols are not optimal when studying the activation of prefrontal areas and limbic structures involved in cognitive-emotional processes using fMRI at 3 Tesla. Using our protocol with GRAPPA-technique, susceptibility-related image distortions in these regions were significantly reduced due to faster k-space acquisition. Additionally it is possible to increase resolution of the functional images. In fear conditioning fMRI experiments at 3 Tesla, our optimized protocol leads to more significant clusters in regions of interest such as the amygdala and the orbito-frontal cortex.

References:

[1] Phelps E.A., Delgado M.R., Nearing K.I., LeDoux J.E. Extinction Learning in Humans: Role of the amygdala and vmPFC. Neuron 43 (2004), 897-905

[2] Schmidt C.F., Degonda N., Luechinger R., Henke K., Boesiger P., Sensitivity-encoded (SENSE) echo planar fMRI at 3T in the medial temporal lobe. NeuroImage 25 (2005), 625-641

[3] Grisworld M.A., Jakob P.M., Heidemann R.M., Nittka M., Jellus V., Wang J. et al. Generalized autocalibrating partially parallel acquisitions (GRAPPA). Magn Reson Med 47 (2002), 1202-1210