Simultaneous fMRI and field potential measurements of epileptic seizures in rat using RASER pulse sequence

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Introduction

Echo planar imaging (EPI) is the most often used pulse sequence in fMRI studies. However, the inherent sensitivity of EPI to magnetic field inhomogeneities makes it difficult to use this technique in areas with large differences in magnetic susceptibility. A new fast magnetic resonance imaging technique, Rapid Acquisition by Sequential Excitation and Refocusing (RASER), is based on formation of pure spin echoes and time encoding instead of phase encoding: therefore RASER possesses dramatically better performance than EPI in areas of large magnetic field gradients (1). The aim of this study was to examine the feasibility of performing simultaneous fMRI and local field potential (LFP) measurements using a deep electrode inserted into the hippocampus in order to follow epileptic seizures after kainic acid (KA) injection.

Materials and Methods

A tungsten wire electrode was inserted into the right hippocampus (AP 3 mm and ML 2.5 mm from bregma, -2.5 mm from the cortical surface). The femoral artery was cannulated (5/7 animals) for monitoring blood gases and pH during the fMRI experiment. The animals were anesthetized with isoflurane during the surgery. After surgery, isoflurane anesthesia was discontinued, and animals were sedated with subcutaneous infusion of medetomidine (0.05 mg/kg bolus and 0.1 mg/kg/h infusion). The field potential (FP) signal was measured using a BrainAmp MR plus magnet compatible system. The signal from the electrode was low pass filtered at 1000 Hz (sampling rate 5000 Hz). The MRI experiments were performed in a 4.7 T horizontal scanner interfaced with a Varian UnityInova console. Functional MR data were acquired using a single shot RASER sequence (TR 2 s, TE 60 ms, slice thickness 1.5 mm, image matrix of 64 x 32, and FOV of 2.5 x 2.5 cm). Simultaneous field potential and fMRI measurements were performed consisting of 1000 images of baseline, thereafter, KA was injected intraperitoneally in a dose of 10 mg/kg. After KA injection, image acquisition was continued for 3000 images in each rat (total 4000 images). Model, which was based on observed seizures in field potential signal, was used to evaluate the BOLD fMRI activations. Functional MR data were analyzed with the SPM5-program (Wellcome Department of Imaging Neuroscience, University College London, UK).

Results

Figure 1 shows anatomical image of the functional slice, the spin-echo EPI image of the fMRI slice and the RASER image of the fMRI slice with (A) and without (B) the electrode from a representative rat. The image distortion caused by measuring electrode was clearly seen in EPI image, whereas no artefact was seen in the RASER image. After kainic acid injection, the field potential data showed recurrent epileptic seizure(s) lasting from 30 sec to 2 min in the hippocampus (Fig. 2). During this period, there were strong bilateral BOLD signal changes in the hippocampus. In all cases during kainic acid induced seizures, BOLD signals increased bilaterally in the hippocampus (Fig. 3). Increases were also present in cortical regions and amygdala (Rat # 1, 3, 4 and 7); however, substantial inter-animal variation in cortical activations was detected.

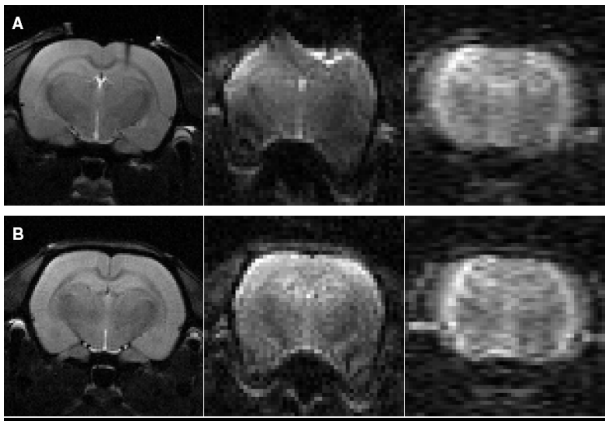

Fig 1. From left to right: anatomical, EPI and RASER image of functional slice with (A) and without (B) electrode.

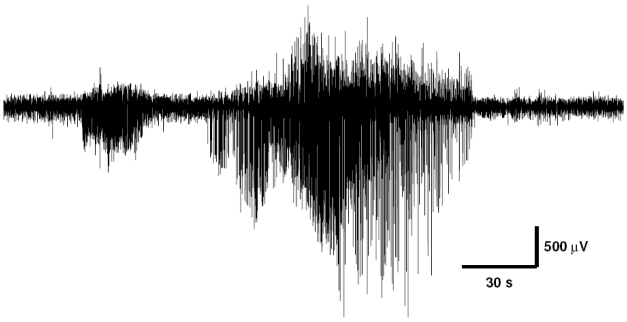

Fig 2. The local FP electrode demonstrated recurrent seizures in the hippocampus lasting from 30 sec to 2 min 25 minutes after kainic acid injection. Gradient artefacts have been removed from the data for clarity.

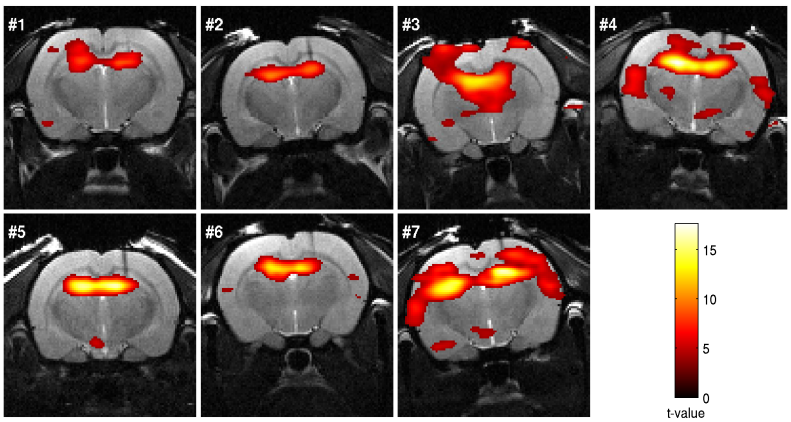

Fig 3. The BOLD activation maps during KA induced seizures.

Discussion

We demonstrated the feasibility of RASER for simultaneous field potential and fMRI measurements under conditions where spin-echo EPI produces severely distorted images due to magnetic inhomogeneity caused by a deep electrode. A challenge for fMRI studies in animal models of epilepsy is the choice of anesthetic agent. Many anesthetic agents suppress evoked responses (2) and can modify cerebral hemodynamics. In the present study we studied epileptic brain activity using for the first time medetomidine anesthesia which, according to our FP data, has only negligible effect on brain activity during seizures and can be used also in follow-up studies (3). It should be noted that as FP data measured directly from hippocampus were used to create a model for the statistical analysis, it is expected that fMRI activation maps show activation areas predominantly in the hippocampus and areas showing synchronous brain activity. Our data proves the feasibility of the present approach and provides a starting point for more complex data analysis. Limitations of RASER include being a single slice method and having a slightly reduced BOLD effect due to pure T2 contrast. However, the presented combination of deep electrode field potential measurements, and fMRI in recovery anesthesia that is not suppressing KA induced seizures provide a unique tool for studying abnormal brain activity in rat epilepsy models.

References: [1] Chamberlain et al., (2007) Magnetic Resonance in Medicine 58:794–799. [2] Rojas et al., (2006) The American Journal of Physiology - Regulatory, Integrative and Comparative Physiology 291:189-196. [3] Weber et al., (2008) The Journal of Neuroscience 28(5):1022–1029.