Functional MRI of spontaneous absence seizures in a genetic rat model

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Purpose:
To identify using functional MRI (fMRI) the regions involved during spontaneous absence epilepsy seizures in a genetic rat model (Genetic Absence Epilepsy Rat from Strasbourg: GAERS) [1].

Methods:
Spontaneous seizures were measured during MR experiments using electroencephalography (EEG). To do so, animals (n=3) were equipped with three carbon electrodes located on the skull near the midline (frontal, parietal and occipital). Two additional carbon electrodes were used to monitor cardiac activity (ECG). Because absence epilepsy is suppressed by anaesthesia, animals were maintained under neuroleptanalgesia.
FMRI was performed at 2.35T. An iron contrast agent (Sinerem®, Guerbet, France) was used to enhance MR signal changes. Functional images were acquired using Echo Planar Imaging (FOV=35mm, 2 shots, matrix size=48*48, 15 contiguous slices 1.5mm thick covering the whole brain, TR=3s, TE=20 ms). Functional imaging lasted at least 1h30, and data were acquired using several sessions to prevent overheating of the gradients. EPI activations were superimposed on a T1-weighted anatomical scan (3D-MDEFT, isotropic 1/3 mm).
Processing of fMRI data was preformed using Statistical Parametric Mapping 5 (www.fil.ion.ucl.ac.uk/spm). Brains were normalised to the atlas of Paxinos and Watson [2] and maps of t-statistics were derived using as a regressor the output of a seizure detection algorithm fed with EEG signals acquired during fMRI.

Results:
Highly significant (p<0.001, FWE corrected) and reproducible seizure-related activations and deactivations were found. Figure 1 shows an example of co-registered fMRI and EEG time series in S1. Activations (Fig 2, left) were found in the ventrobasal thalamus, the primary somatosensory cortex (S1) and the primary motor cortex (M1), which are well-known to be part of the thalamocortical network involved in the generation of absence seizures. The cerebellum and the intermediate reticular nucleus were also found activated. In addition, several areas were found to be deactivated (Fig 2, right) such as the striatum, M2, the visual cortex (V1, V2) and the medial geniculate nucleus.

Conclusions:
FMRI shows strong responses to spike-and-wave discharges during absence epilepsy in the GAERS. Most of the identified structures are known from intracerebral EEG to be involved in the generation or control of spike-and-waves discharges. Therefore this experimental study validates the use of fMRI/EEG in epileptic patients suffering from absence epilepsy.

References:
[1] Danober L, et al. Pathophysiological mechanisms of genetic absence epilepsy in the rat. Prog Neurobiol 1998;55:27-57.
[2] Paxinos G & Watson C. 1997. The rat brain in stereotaxic coordinates, 3 ed. Academic Press, Inc., San Diego.

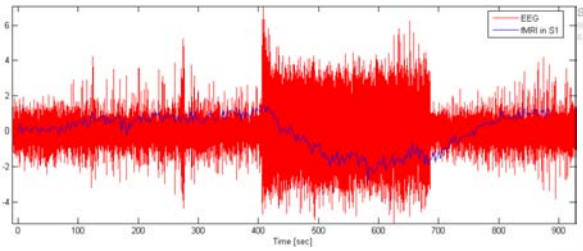

Fig 1: 15 min recording of simultaneous EEG (red) / fMRI (blue). fMRI time series corresponds to the activated cluster in S1 shown in Fig 2.

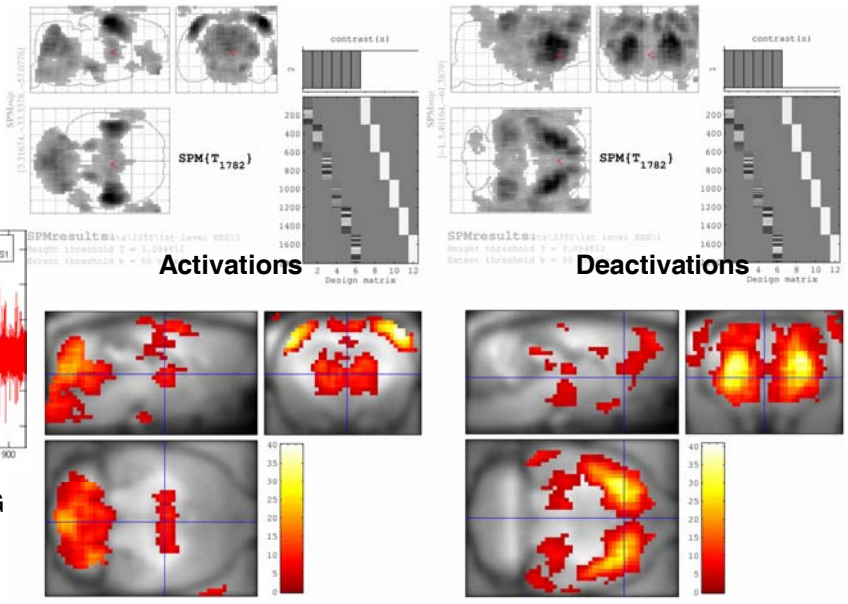

Fig 2: Activations (left) and deactivations (right) obtained for p<0.001, FWE corrected, in a single rat. The design matrix (regressors for fMRI) in the upper right corner contains EEG information recorded in 6 separate sessions of 15 minutes.