Functional MRI detects chronically enhanced somatosensory activation maps following multiple seizures in rats.

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Introduction.

We have documented in rats that following seizures there are disturbed alterations in areas of the neocortex that regulate forelimb movement (1). Furthermore, using electrophysiological techniques neocortical movement representations or "motor maps" become larger in rats with seizures (2,3) homologous to the changes in motor maps reported in humans with epilepsy. The objective of the present study was to determine whether repeated seizures also change neocortical somatosensory maps and whether such changes were persistent. Thus, we used functional magnetic resonance imaging (fMRI) in rats following 20 repeatedly elicited seizures to see whether after seizure-induced alterations in the somatosensory maps to forepaw stimulation could be detected using this technique.

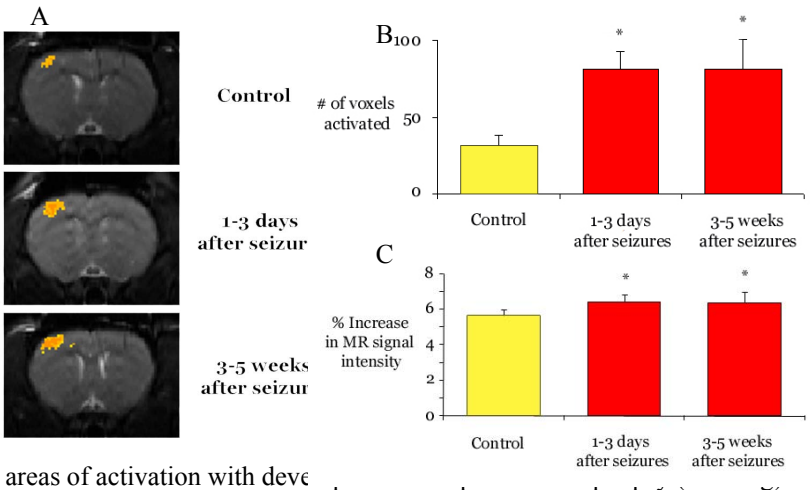
Methods

Seizures were elicited in rats twice a day, five days a week for a total of 20 times by delivering electrical stimulation through carbon fiber electrodes (4) implanted in both the callosum and sensorimotor neocortex of adult Long-Evans rats. Stimulation consisted of a 1 second train of 60Hz biphasic rectangular wave pulses of 1 msec in duration and separated by 1msec at an intensity of 100uA greater than after discharge threshold levels. Functional MR imaging studies were performed in control rats or in rats 1-3 days or 3-5 weeks after the last seizure. On the day of fMRI, animals were anesthetized with alpha-chloralose, intubated and ventilated and mean arterial blood pressure and temperature were monitored continuously. MRI scans were acquired using a 24mm X 18 mm elliptical surface coil positioned over the head and a 9.4T MR system equipped with a Bruker Biospin Avance II console. T2 weighted anatomical images were acquired using a multislice fast spin echo sequence (TR = 3000 ms, TE = 60 ms, field of view = 3 X 3 cm^2). Functional images were collected in five transverse slices (thickness = 1.5 mm) within the forebrain containing the sensorimotor cortex. The functional MR experiment consisted of a total of 64 images acquired during no stimulation or during forepaw stimulation on conditions (3mA, 3Hz,3ms) during the acquisition of images 13-26 and 39-48. Voxels of activation in response to forepaw stimulation were those voxels with signal intensity changes correlating at $p<0.00001$ to the on-off stimulation time course.

Results

During forepaw stimulation activation within the sensorimotor cortex was detected as voxels with intensity changes correlating significantly to the on-off stimulation paradigm. (Figure). At 1-3 days following seizures there was an expansion of the activation within the sensory-motor cortex resulting in an enhanced activation that persisted at 3-5 weeks after seizures (Figure). The intensity increases during stimulation were also greater following seizures compared to those in control animals. Bilateral activation was observed in about half of the rats 1-3 days following the last seizure.

Figure.
*Representative functional MRI images during electrical stimulation of the right forepaw (A). Voxels of activation (orange) are detected in the sensory motor cortex. Rats imaged 1-3 days after 20 seizures and 3-5 weeks after 20 seizures show significantly greater activation in the sensorimotor cortex in response to forepaw stimulation compared to control (B). The intensity changes observed during forepaw stimulation also were greater either 1-3 day or 3-5 weeks following seizures compared to controls (*P<0.05, different from control).*



Discussion and Conclusions

This is the first fMRI study to show increased areas of activation with deve[illegible]s confirms data obtained with more invasive electrophysiological recording and cortical stimulation methods to map motor area changes (2,3).These data indicate that there is considerable neuroplasticity and development of new pathways during the progression of epilepsy.Whether comparable plasticity of cortical maps is present in humans should be tested using fMRI in future studies, considering that such seizure-induced changes may be involved in producing interictal behavioural disturbances.

References

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