Cerebral Response to Electrical Stimulation at the Different Anesthetic Intervals: an fMRI study

X-Y. Fu[1,2], T. Yu[1], P. Xie[1,2], Y. Tu[1,2], S. lui[2], H. Cheng[3], T-J. Zhang[2], X-Q. Huang[2], and Q-Y. Gong[2,4]

[1]Department of Anesthesiology, Zunyi Medical Collge, Zunyi, Guizhou, China, People's Republic of, [2]Huaxi MR Research Center(HMRRC), Huaxi Hospital,Sichuan University, Chengdu, Sichuan, China, People's Republic of, [3]School of Science and Technology, University of Electronic Science and Technology, Chengdu, Sichuan, China, People's Republic of, [4]Division of Medical Imaging, University of Liverpool, London, United Kingdom

Introduction

Functional MR imaging (fMRI) has been widely used to study pain processing in vivo in small animals[1]. Activations of the lateral thalamus, contralateral primary somatosensory cortex (SI), contralateral primary somatosensory cortex (SII) and insula were thought to be related to the sensory-discriminative neuro-network during pain processing. However, it is still unclear how anesthesia affects such cerebral function during pain processing. Thus, present study aims to investigate brain responses to electrical stimulation in rats at different anesthetic intervals using highfield fMRI.

Methods

Experiments were conducted in accordance with the guidelines for care and use of laboratory animals. Six Sprague-Dawley male rats which weigh 300-350g, and approximately 90 days old were lightly anesthetized with intraperitoneal injection of chloral hydrate 300 mg/kg. All images were acquired using a 3.0T MR imaging system (ACHIEVA, Philips, Netherlands) with a four channel phase array rat head coil. Slice 2 was positioned at Bregma +4.2 mm according to Paxinos and Watson' rat brain atlas (1998) using the posterior tip of the corpus striatum as the anterior–posterior reference and the anterior tip of the hippocampus as the horizontal anatomical reference images. Functional and anatomical images of all rats were acquired using a single shot gradient echo EPI sequence(TR/TE: 2000/27 ms, flip angle: 90°, matrix: 96×96, FOV: 50×41 mm, slice thickness: 1.0 mm, total 110 volumes, 20 axial slices) and a gradient echo pulse sequence (TR/TE = 2500/240 ms; slice thickness = 1mm, matrix = 96×96, flip angle=85°,FOV=50×50mm) respectively. After being anesthetized, all rats were immediately scanned using above sequences and repeatedly four times with an interval of 10 min. Total scan time for each experiment was 3 min 55s. While under anesthesia, the rats were then scanned repeatedly for four times with an interval of 10 min. For electrical stimulation, the current pulse of 2 mA were used with 500μs pulse length at a frequency of 3Hz. The tail of the rats was stimulated using off-on-off-on paradigm with 30 scans-rest and 10 scans-stimulation. Functional data analysis was performed using spm2 (http://www.fil.ion.ucl.ac.uk/spm/software/).The activation threshold was set at P<0.001. Only groups that showed at least four activated pixels were considered significant. Functional images were normalized to a standardized rat brain template provided by Adam J. Schwarz [2].

Results

Activation in the cortex during stimulation of tail was reported in previous rat study[3]. Our results show that incidence and amplitude of activation in the brain vary across the sequential anesthetic intervals (Table 1, Figure 1).

Table 1 Functional imaging of brain network to electrical stimulation in rats at the different anesthetic intervals

Anesthetic interval	Regions of brain activation
10 min	Midbrain, Thalamus, Caudate putamen(Cpu)
20 min	Medulla oblougata, Temporal association cortex(TeA), Midbrain
30 min	Cerebellum, TeA, Midbrain, Thalamus, SI, SII, Cingulate cortex
40 min	Cerebellum, Midbrain, Thalamus, SI, SII, Cingulate cortex, Frontal cortex

Discussion

Following the above sequential anesthetic intervals, we observed that there were increased incidence and amplitude of activation in rat brain. A previous study has shown that the areas of activations depend on the animal's level of awareness[4]. The fuctional MRI can therefore provide further evidence for brain processing of nociceptive stimulation at the various anesthetic intervals. It is likely that increasing incidence and amplitude of activation indicates decreased anesthetic depth. Further study on a larger cohort is necessary to clarify the relationship between activation map of brain and anesthetic depth.

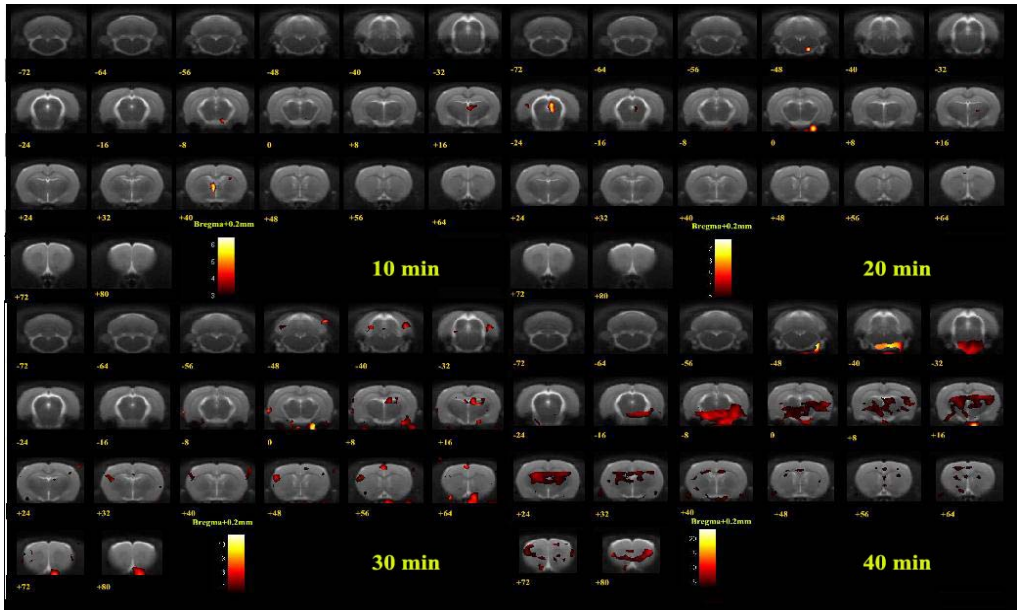

Figure 1 Activation maps of rat tail electrical stimulation at 10, 20, 30 and 40 min after being anesthetized. There were increased incidence and amplitude activation in the brain across the sequential anesthetic intervals.

Reference

1.Lowe A S,et al.Neuroimge,2007.35(2):p719-28.

2. Schwarz A J,et al. Neuroimge,2006.32(2):p528-50.

3.Spenger C,et al.Experimental neurology,2000.166(2)p246-53.

4.Keilholz SD,et al.Magetic resonance in medicine,2004.52(1):p89-99.