Effect of Propofol on Thalamocortical Connection: a high-field MR study of Functional Connectivity on Rats

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Introduction

The mechanism of anesthesia, a state of profound neurological suppression, is still poorly understood. One of the unresolved issues concerns the alteration of neural network under anesthesia. Functional connectivity MR imaging (fcMRI) allows non-invasively investigating the activity of neuro-network in vivo. The objective of the present study is to utilize fcMRI to investigate the effect of propofol,,a widely used intravenous anesthetic, on cerebral functional connectivity of rats .

Method

All procedures were conducted in accordance with international guidelines on the ethical use of animals. Thirty Sprague-Dawley rats were randomly divided into two groups, i.e., group I (n=15) which was given 80 mg/kg of propofol by intraperitoneal (ip), and group II (n=15) which was given 160 mg/kg of propofol ip. Five minutes after the loss of righting reflex, functional and anatomical images of each rat were acquired using a single shot gradient echo EPI sequence (TR/TE = 2000/27.5 ms; slice thickness = 1 mm, matrix = 96 × 96, flip angle = 85°, FOV = 50 × 50 mm) and a gradient echo pulse sequence (TR/TE=2500/240 ms; slice thickness = 0.5 mm; matrix = 224 × 224; flip angle = 90°, FOV = 50 × 50 mm) respectively with a 3T MR system (Achieva, Philips, Nederland) using a 4 channel phase array rat head coil. MR data was processed using Statistical Parametric Mapping (SPM2) (http://www.fil.ion.ucl.ac.uk/spm/software/) and ,Marsbar including region of interest (ROI) identification, low-pass filtering and correlation maps (functional connectivity maps) calculation. A seed, consisting of a 9(3×3) voxels was then placed in the left thalamus which is considered to be an important region involved in general anesthesia. ROIs corresponding to selected structures were delineated using the 3D digital reconstruction of the Paxinos and Watson rat brain atlas coregistered and normalized to the rat brain template[1,2]. The time series of ROI voxels were averaged and low-pass filtered with a 0.15Hz cutoff frequency to retain frequencies known to contribute to functional connectivity, as demonstrated in previous study to create a single low-frequency reference time series[3]. Based on simple regression method, this low-frequency reference time series was then cross-correlated voxel-by-voxel with the whole brain to form the correlation maps (functional connectivity maps).

Result

The connectivity maps of propofol anesthesia at low dosage in group I exhibited functional connectivity between thalamus and ipsilateral primary somatosensory cortex (S1) as well as contralateral secondary somatosensory cortex (S2)($p<0.005$, uncorrected). Whereas no significant functional connectivity between thalamus and other cerebral areas was observed in group II ($p<0.005$, uncorrected)(see figure 1).

Conclusion and Discussion

The absence of functional connectivity in the thalamocortical network observed in high propofol concentration group was consistent with the hypothesis that anesthesia attenuated brain function in a dose-dependent and highly specific fashion[4]. Our findings also support another hypothesis that propofol induced general anesthesia involves the disruption of functional interactions within thalamocortical neural networks[5]. The global disconnection and regionally suppressive effects of anesthesia should indeed be considered as two distinct, equally important phenomenon in comprehensive study of central anesthetic action.

Further study by combining regional cerebral blood flow (rCBF) with functional connectivity will provide further insight into the mechanism of anesthesia.

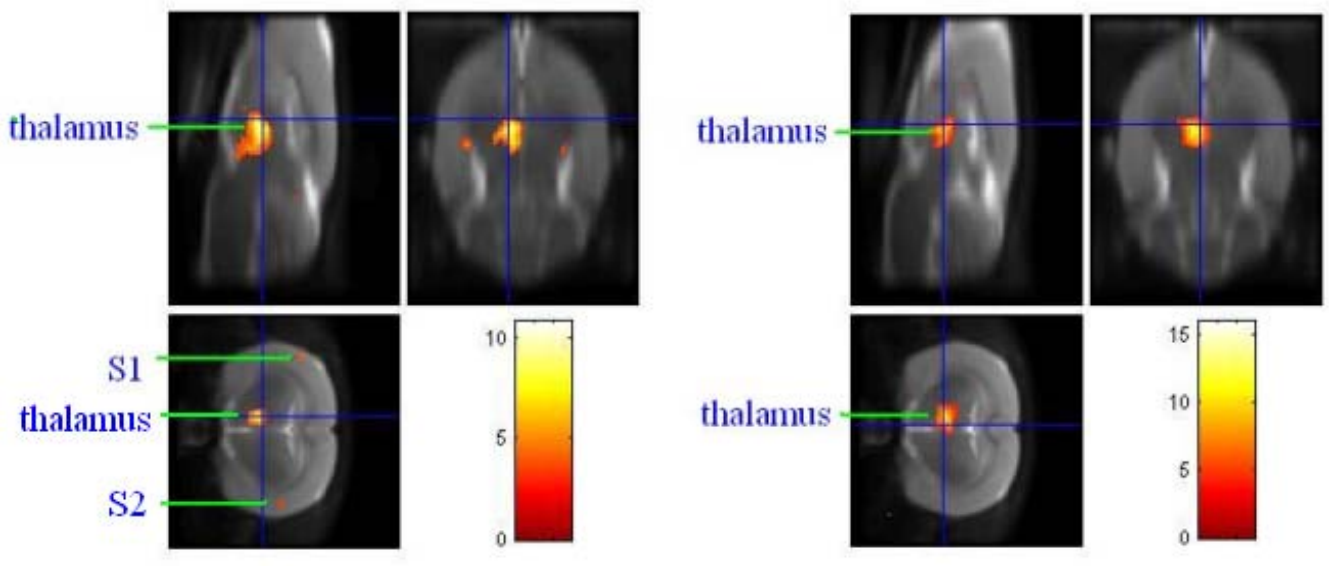

Figure 1:Sectional images of low dosage propofol anesthesia group (left panel) showed functional connectivity amongst thalamus and ipsilateral primary somatosensory cortex(S1), contralateral secondary somatosensory cortex (S2) ($p< 0.005$,uncorrected), whereas, in high dosage propofol anesthsia group (right panel),the functional connectivity of thalamus was virtually absent ($p<0.005$, uncorrected).

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