Anesthesia level modulate brain activity and connections in Monkey

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Introductions

Resting state-fMRI (rs-fMRI) allows studying aesthesis status through functional connectivity (FC) and amplitude low-frequency fluctuation (ALFF), as well as the mechanisms of different neurological diseases. Non-human primates are valuable for modeling human disorders and for developing therapeutic strategies. More and more transgenic non-human primate models of human diseases have been established and some studies have claimed the FC patterns biomarker in anesthetic monkeys[1]. Recently, different anesthetic regimes have affected the FC patterns in rat and mice[2, 3]. However, little work has been reported in the anesthetic depth affect the monkey brain neuron activity and the FC patterns between different brain regions. In this work several monkeys scanner with different anesthetic depths underlying rs-fMRI to explore the variation of the monkey brain FC patterns and brain region neuron fluctuation.

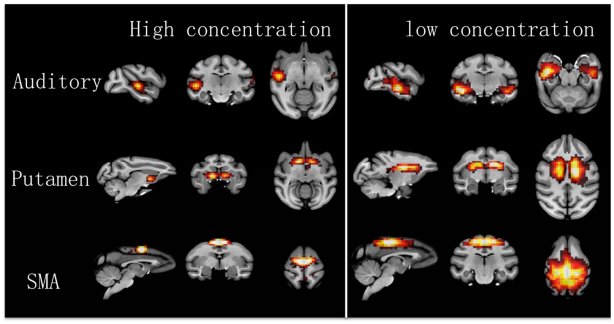

Fig. 1 Compare some ICA component maps, e.g. auditory, putamen and SMA areas, at different anesthesia depths.

Methods

Anesthesia protocols and fMRI were reviewed and approved by IRB of the Institute of Biophysics. Twenty adult healthy macaque monkeys were scanned on 3.0T scanner (Trio TIM, Siemens Magnetom, Germany). A customer made 4-channel transceiver surface coil was used to acquire the functional and anatomical images. Each monkey was initially anesthetized by injecting 4ml propofol stoste. During rs-fMRI, different propofol (1:4 mixture with normal saline) concentrations were dripped from 100ml/h, with 10ml/h decreased, until the monkey have large head motion monitored through EPI images. fMRI data were acquired using a EPI sequence (TR/TE = 2000/29ms, FOV=152mm, FA = 90^0, 1.8 mm iso). Sagittal, high-resolution, T1-weighted MPRAGE structural images were also acquired (TR/TE = 2200/3.93ms, FA = 7^0, 0.5mm isotropic, NEX = 2). Two monkeys were recorded the pulse and blood oxygen saturation with mr-compatible pulse oximetry (SAII, http://www.i4sa.com). The fMRI pre-processing steps using SPM8 (http://www.fil.ion.ucl.ac.uk/spm) included: 1. reorienting to AC-PC plane; 2. slice-timing to compensation slice-dependent time shifts; 3, rigid-body correction to register the fMRI data to anatomic; 4. segmenting the anatomic according to the inia19 template (http://nitrc.org/projects/inia19); 5. normalize fMRI and anatomic images according the segmented results; 6. spatial smoothing the fMRI data with 4mm FWHM gaussian kernels; 7. detrending and band-pass filtering (0.01Hz-0.08Hz) to used before correlation analyze. Group ICA analysis was implemented by FSL melodic module (http://www.fmrib.ox.ac.uk/fsl).

Tab. 1 Compare the components under different anesthesia depths.

Regions	High	Low
Motor	N	S
Somatosensory	L	S
SMA	M	M
Caudate	N	S
Putamen	S	S
Pulvinar	N	S
Visual v1&v2	B	S
Visual v3&v4	B	S
Para-hippocampus	S	S
Auditory	L	S

B: Bilateral; M: Midline; S: Simultaneous both side; N: None.

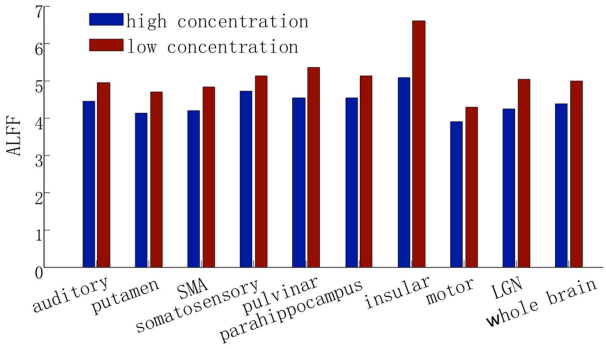

Fig. 2 The ALFF value of different regions at different anesthesia depths.

Results

Although the level of unconsciousness was not consistent across different anesthesia depths, the breathing rate and pulse oximetry during the rs-fMRI scan were almost constant (120±10 per min and 98.5±1.5%, individually), which was different from the mice or rat studies, the breathing rate and pulse oximetry were variable with different anesthetic regimes[3]. Fig.1 shows some ICA components (threshold at Z=3) in high and low concentration of dripped propofol. The auditory, putamen, and SMA area shows larger component cluster at lower concentration than higher concentration. More and more surround neurons were synchronized with core region neurons. Tab. 1 shows the symmetry of cerebral hemisphere in some typical regions, like SMA, motor, visual etc. The fluctuations are more independent at higher propofol concentration, however, become more synchronize at lower propofol even at the same in different cerebral hemisphere. Fig. 2 shows the amplitude of low frequency fluctuation of some typical regions and whole tissue brain. All of the regions presented higher ALFF at lower anesthetic depth, including the auditory cortex and some subcortex, which processing the sound produced the MRI scanner.

Conclusion & Discussion

Different drip concentrations will affect the monkey anesthesia depth. Higher concentration suppresses more neurons activity and also decreases the connections between different cerebral hemispheres and surround regions. Although we didn't find the default mode network even at lower propofol concentration, it maybe the propofol suppress more cortex activity than other anesthesia regimes. However, it opened a new method to explore how the intrinsic network created, and whether the connectome dependent on the neuron activity.

References [1]Mantini, D. *et. al.* J Neurosci, 2011. [2]Grandjean, J. *et. al.* NeuroImage, 2014. [3]Jonckers, E. *et. al.* Magn Reson Med, 2013.

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