Functional MRI of Visual Development in Rat Superior Colliculus

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INTRODUCTION

Functional MRI (fMRI) techniques provide the capability for visualizing dynamics of neural activities with spatiotemporal specificity and resolution that has not previously been available with other non-invasive methods. Recent fMRI studies have demonstrated its values for probing postnatal circuit refinement and plasticity (1,2). To date, there are many aspects of brain development that still need to be explored, such as neurosensory and neuromotor development, development of cognition with learning processes, memory and language acquisition, as well as brain repair and plasticity after perinatal injury (2,3). In this study, the development of the rat visual pathway was studied using blood oxygenation level–dependent (BOLD) contrast from the time of eyelid opening (P14) to adulthood (P60). By studying BOLD-fMRI measurements in the rat superior colliculus, we determined that the regional BOLD response in these animals undergoes a systematic increase in amplitude especially over the third postnatal week.

MATERIALS AND METHODS

Visual Stimulation Paradigms: Sprague Dawley rats (n=7) were prepared and scanned at postnatal days (P) 14, 21, 28 and 60. Fiber optic cables with 2 green light-emitting diodes (LEDs) were placed bilaterally at about 1 cm away from each eye of the rats. The LEDs were flashed at a frequency of 1 Hz and a pulse width of 50 ms for each eye. A standard block-design visual stimulation protocol of 40 s of rest followed by stimulation for 20 s repeated for 3 blocks was used. The rats were allowed to rest for few minutes between stimulation sets, and 3-6 sets of data were recorded from each rat for each eye.

MRI Protocols: All MRI measurements were acquired utilizing a 7 T Bruker scanner. Under inhaled isoflurane anaesthesia (3% induction and 1% maintenance), animals were kept warm under circulating water at 37°C and were imaged using a receive-only surface coil. Single-shot SE-EPI sequence was acquired with FOV = 3.2 x 2.4 cm^2 and matrix resolution = 64 x 48 (zero-filled to 64 x 64), slice thickness = 1.5 mm, number of slices = 6 and TR/TE = 2000/21ms.

Data Analysis: All the fMRI data analyses were performed using the STIMULATE software package (Stimulate, Center for Magnetic Resonance Research, University of Minnesota). Correlation threshold was set at 0.1. Time profiles of BOLD signals were collected from each side of the rat superior colliculus. Percentage changes of BOLD signals were calculated and averaged among animals from the same age groups.

RESULTS

In Figure 1, the averaged BOLD time courses showed a trend of increasing amplitude of the activated BOLD signals as the rat grew; The responsiveness improved markedly with age starting the third postnatal week (P21). The averaged stimulus-induced percentage signal change was 0.28±0.17% for P14, 0.39±0.27% for P21, 0.81±0.25% for P28, and 1.30±0.32% for P60 upon left eye stimulation; and 0.33±0.11% for P14, 0.42±0.04% for P21, 0.86±0.43% for P28, and 1.29 ± 0.21% for P60 upon right eye stimulation. For both left and right eye stimulations, Student's t-test comparisons for all age-group pairs showed significant differences ($p < 0.05$) except for P14 vs P21 ($p>0.15$) (Fig 2).

DISCUSSIONS AND CONCLUSION

Our results constitute the first fMRI report in evaluating the visual development of rat superior colliculus from the time of eyelid opening (P14) to adulthood (P60). Similar to a previous study on the development of hemodynamic responses in rat somatosensory cortex (1), age increase was associated with the increase in BOLD signal amplitude in rat superior colliculus. The marked rise in responsiveness starting the third postnatal week was also consistent with a previous study on functional postnatal development of the rat primary visual cortex evaluated using visual evoked potentials (4). Our experimental approach can be potentially useful in establishing the links between where and when maturational changes occur in the brain, and how these changes are related to the visual sensory development.

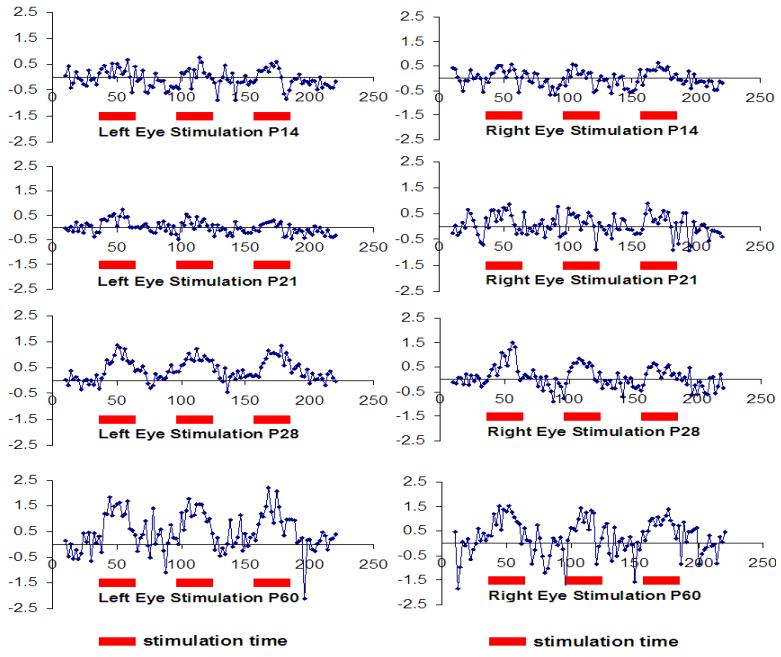

Fig 1: Population-averaged BOLD responses to visual stimulation. Mean time courses were computed from activated voxels in superior colliculus (SC), and averaged across all animals in each age group. Increasing age is seen to associate with an increase in BOLD signal amplitude in the stimulation period (red lines).

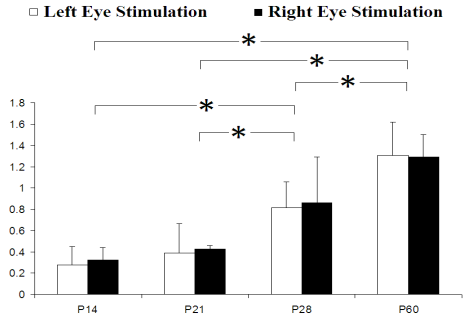

Fig 2: Age-dependent trends in BOLD fMRI responses to visual stimulation in young rats (from postnatal day 14 to 60), including the paired t-test (* $p< 0.05$) between different time points.

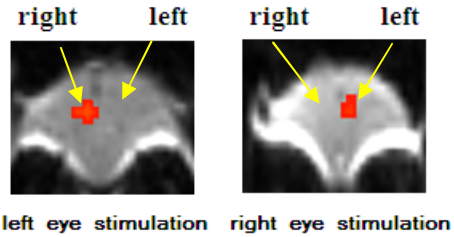

Fig 3: The overlay of activation map onto the EPI images upon left and right eye stimulation. Note the activations in the superior colliculus contralateral to the stimulated eye.

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