

Functional MRI of Substantia Nigra upon Visual Flash Illumination

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INTRODUCTION: In the mammalian midbrain, increasing evidence suggested a direct projection from the superior colliculus (SC) to the substantia nigra (SN) (1-3), which is potentially responsible for detecting salient visual events (3-4). However, the functional characteristics of this connection are still largely unknown. This study explores the capability of blood oxygenation level-dependent (BOLD) fMRI to detect simultaneous activations in SC and SN upon visual flash illumination, in order to understand the basic visual properties and hemodynamic responses in this functional connection.

MATERIALS AND METHODS: Animal Preparation: Two fiber optic cables, each with a green light-emitting diode (LED) at one end, were placed bilaterally at about 5 mm in front of each eye of 17 adult Sprague-Dawley rats (260-300 g). The LEDs were flashed unilaterally (n=12) or bilaterally (n=8) at a frequency of 1 Hz and a pulse width of 5 ms in separate experimental sessions. Stimuli were synchronized with the scanner under computerized control using LabVIEW v8.0, with a standard block-design visual stimulation protocol of 40 s of rest followed by stimulation for 20 s repeated for 3 blocks. The rats were allowed to rest for few minutes between stimulation sets, and 2-4 sets of data were recorded for each rat.

MRI Protocol: All MRI measurements were acquired utilizing a 7 T Bruker scanner. Under inhaled isoflurane anaesthesia (3% induction and 0.8-1% maintenance), animals were kept warm under circulating water at 37°C and were imaged using a receive-only quadrature surface coil. T2WI was acquired using the 2D RARE pulse sequence. Single-shot SE-EPI sequence was acquired with TR/TE = 2000/21ms, FOV = 3.2 x 3.2 cm² and matrix resolution = 64 x 64, slice thickness = 0.8 mm, and number of slices = 10. Respiration rate, heart rate, SpO₂, end-tidal CO₂ level, and end-tidal isoflurane level were monitored throughout the experiments.

Data Analysis: All the fMRI data analyses were performed using the STIMULATE software package after co-registration, slice-timing correction, spatial smoothing and temporal filtering. Correlation threshold was set at 0.2 with a cluster size of 3 pixels. Time profiles of BOLD signals were collected from both sides of the SC and SN for binocular stimulation, and from the contralateral side of SC and SN only for monocular stimulation. Percentage changes of BOLD signals were calculated and averaged among animals from the same groups. Data were presented as mean ± standard error of mean. Two-tailed paired t-tests were performed between SC and SN of the same group of animals. Results were considered significant when p<0.05.

RESULTS: As shown in Figure 1, upon monocular stimulation, activations were observed predominantly in the contralateral SC and SN, and occasionally in the visual cortex of both hemispheres; whereas upon binocular stimulation, activations were found in the SC and SN in both hemispheres. The time profiles of BOLD responses in Figure 2 showed a hemodynamic delay in the order of seconds for both SC and SN after initial stimulation before reaching the peak height. In addition, significantly lower BOLD percent changes were observed in the SN of both groups than SC before reaching the peak height after stimulation (p<0.05). No significant difference was observed in the peak amplitude between SC and SN of both groups (p>0.05).

DISCUSSION AND CONCLUSION: Upon unilateral visual flash illumination, the superficial layers of the contralateral rat superior colliculus have been shown to be strongly activated in BOLD-fMRI (5-7) in consistency with the current results. The activation of contralateral SN upon monocular visual stimulation in this study might be supported by a previous anterograde tract tracing study in rat revealing a significant projection from the SC to the ipsilateral SN containing dopaminergic neurons (3). It has also been suggested that the SC is a primary if not exclusive source of short-latency, short-duration visual afferents to dopaminergic neurons in SN for visual activations (4). The significantly lower BOLD percent changes in SN than SC before reaching similar peak heights in both groups appeared to associate with the longer initial onset and peak latencies in visual evoked potentials recorded from SN than superficial SC in response to whole-field flashes, as would be predicted if the colliculus acts as a relay for visual information destined for ventral midbrain (3). The current results of having the same visual event initiating afferent inputs to both SC and SN could have important implications for interpreting the responses to biologically salient sensory events in relation to novelty, intensity or reward within the SC-SN connection (1,4). Future fMRI studies are also envisioned that measure the interactions between SC and SN in normal development, disease, plasticity and therapy in longitudinal studies, an example being the developmental plasticity of SC-SN functional connections upon neonatal hypoxic-ischemic injury to SN (8).

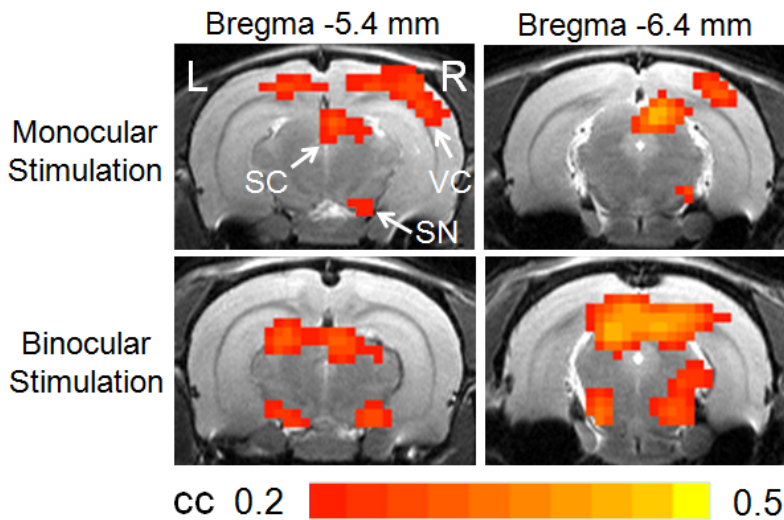


Fig. 1: Typical cross-correlation maps overlaid onto T2WIs at the level of SC and SN at about Bregma -5.4 mm (left column) and -6.4 mm (right column) upon monocular (left eye; top row) and binocular (bottom row) stimulation. (SC: superior colliculus; SN: substantia nigra; VC: visual cortex)

REFERENCES: 1. Coizet V, et al. *J Comp Neurol* 2007;500(6):1034-1049; 2. May PJ, et al. *Eur J Neurosci* 2009;29(3):575-587. 3. Comoli E, et al. *Nat Neurosci* 2003;6(9):974-980. 4. Dommert E, et al. *Science* 2005;307(5714):1476-1479. 5. Pawela CP, et al. *Neuroimage* 2008;41(2):525-534. 6. Van Camp N, et al. *J Neurophysiol* 2006;95(5):3164-3170. 7. Chan KC, et al. *Neuroimage* 2009. 8. Oo TF, et al. *Neuroscience* 1995;69(3):893-901.

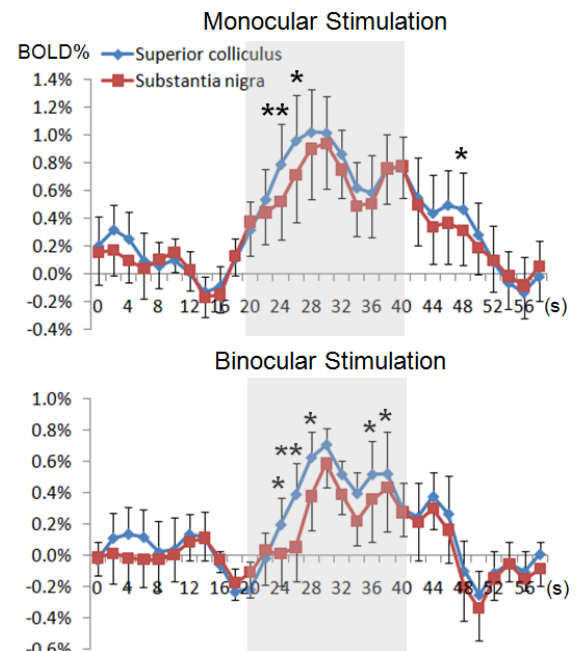


Fig. 2: Average dynamic profiles of BOLD percent changes to monocular (top) and binocular (bottom) visual stimulations in the SC and SN of normal adult rats. The gray period indicates the stimulus on period. (Two-tailed paired t-tests between SC and SN: *p<0.05, **p<0.01)