BOLD fMRI Study of the Rat Superior Colliculus Responding to a Moving Visual Stimulus

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Introduction – The superior colliculus (SC), or tectum, is a midbrain structure in vertebrates critical for directing eye movements[1]. It possesses neurons that are highly sensitive to moving stimuli[2]. To date, functional imaging has only been used to study the SC's response to a stimulus moving at one speed[3]. Few fMRI studies have been conducted on the human SC because of technical challenges[4-5]. The rat SC occupies a significantly larger portion of the brain and receives a greater fraction of retinal projections. Thus, the rat is more suitable for studying SC function. In this study, we apply BOLD fMRI on rats to measure the SC's hemodynamic response during five different speeds of moving visual stimulation.

Methods - *Animal preparation*: Sprague-Dawley rats (N = 8) were used in this study. Each animal was inducted at 3% isofluorane and maintained at 1%. Animals were scanned in a 7T Bruker scanner with a surface receiver coil. Respiration rate was monitored with a pressure sensor, heart rate and blood oxygen level with a pulse oximeter, and rectal temperature with a temperature probe. *MRI protocol*: Three 1.0mm thick slices (spaced 0.2mm apart) were positioned to cover the SC (Fig. 1a). Four optical fibers were positioned linearly 7cm in front of the left eye (right eye blocked) along the nasal-temporal direction. 7cm is the minimum focus distance of the rat eye[6]. The fiber cores spanned approximately 6˚ of the visual field and were illuminated by identical LEDs. A block-design BOLD experiment consisted of one randomly chosen LED on for 40s (static) followed by 20s of moving stimulation (Fig. 1b) at one of five speeds (7, 14, 41, 82, or 164˚/s across the visual field. dt = 240, 120, 40, 20, 10ms, respectively). This was repeated for five blocks, one at each speed (Fig. 1c). Speeds were presented in random order. Starting 30s after first LED on, 310 gradient-echo EPI scans (0.5 x 0.5mm^2 voxels, TR = 1.0s, TE = 18ms, α = 56˚) were acquired. The experiment was repeated 15 times per animal with > 2 minutes rest in between. *Data analysis*: The 310 images from each experiment were registered to the mean image of the first experiment using AIR5.2.5[7]. The sequence of images was split into five sets, each covering 5s before to 60s after onset of stimulation, for a total of 75 sets per animal. Images from sets corresponding to the same speed were averaged, resulting in five 65 images long BOLD data sets per animal. Stimulate6 was used to correlate the stimulation paradigm with a data set and identify responsive brain regions. ROIs were drawn around the ipsilateral and contralateral SC (iSC and cSC) according to the rat brain atlas[8]. The iSC ROI was drawn at least one voxel away from the midline. Time series from all voxels within the ROIs were averaged and transformed into BOLD signals (units of % BOLD) by averaging the responses from 5s before to 60s after the start of each stimulus and dividing by the amplitude from 5s before to onset of stimulation. The response amplitude, defined as the average BOLD signal from 5 to 20s after onset of stimulation, and the number of responsive voxels, defined as having correlation coefficient (cc) > than a threshold, were computed from the BOLD signals. Statistically significant differences between speeds were determined using one-way, repeat measures ANOVA with Tukey's HSD test.

Results - Figure 2 shows responsive voxels are concentrated in both hemispheres of the SC, lateral geniculate nucleus (LGN), and visual cortex (VC). Almost the entire SC is responsive from 7 - 82˚/s. The number of responsive voxels is smaller at 164˚/s. Figure 3 shows significant responses in both hemispheres of the SC. The response amplitude differences between hemispheres may be due to the conservative definition of the iSC ROI. The largest amplitudes are at 41 and 82˚/s and the smallest at 164˚/s. The responses during 41 and 82˚/s stimulation appear to take longer to reach steady state. Figure 4 shows response amplitude is significantly higher at 41 and 82˚/s ($p < 0.01$) and lower at 164˚/s ($p < 0.01$). The number of responsive voxels is significantly lower at 164˚/s ($p < 0.05$) and slightly higher at 82˚/s ($p < 0.05$ compared to 7 and 164˚/s). Theses findings are largely independent of cc threshold.

Discussion – This study has observed significant SC responses to stimuli moving at 7 to 164˚/s with reduced response at 164˚/s. The SC, LGN, and VC respond to moving stimulation in this study and also to flicker stimulation in earlier rat studies[9-10]. The significant reduction in BOLD response at 164˚/s appears to agree with electrical recording studies on albino rats, which observed electrical responses up to 90˚/s, although higher speeds may not have been tested[11]. An extensive ipsilateral SC response to motion has also been observed in frogs[12]. The findings of this study represent the first functional imaging measurements of speed dependence in the SC. Future studies will examine the differences in SC hemodynamic response between smooth and apparent motion (this study).

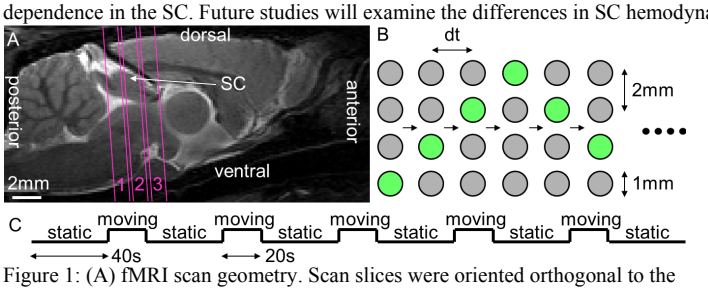

Figure 1: (A) fMRI scan geometry. Scan slices were oriented orthogonal to the sagittal plane. The location of the SC plus the anterior, posterior, dorsal, and ventral sides of the brain are indicated. (B) Illustration of moving stimulus. Green circles indicate illuminated fibers and gray circles unlit fibers. Each row of four indicates the illumination condition during an interval dt. At the next dt, a neighboring fiber is illuminated. (C) Stimulation paradigm. Five blocks of 40s static illumination and 20s moving stimulation as illustrated in (B).

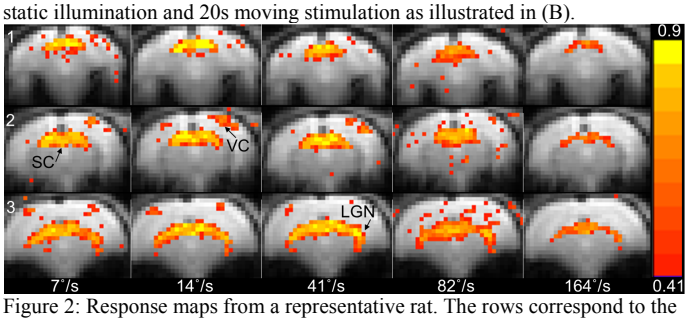

Figure 2: Response maps from a representative rat. The rows correspond to the scan slices and the columns correspond to the stimulation speeds. Only voxels with cc > 0.41 are color coded. The SC, VC, and LGN are labeled.

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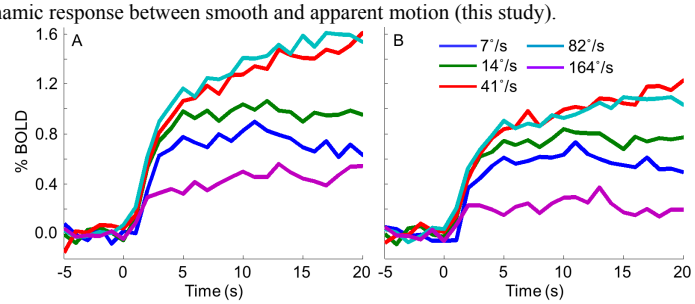
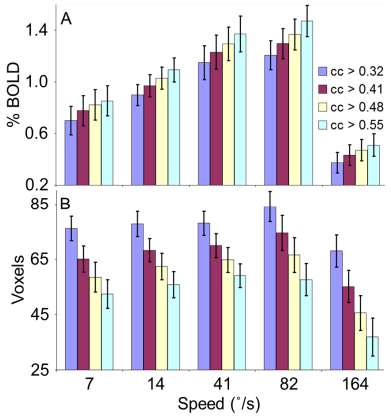


Figure 3: Mean BOLD signal from the cSC (A) and iSC (B) ROIs of all animals for each speed. Only voxels with cc > 0.41 are included. The time axes indicate time from onset of stimulation.



Speed (˚/s)

p	7	14	41	82	164
7	-	0.05	0.01	0.01	0.01
14	0.05	-	0.01	0.01	0.01
41	0.01	0.01	-	NS	0.01
82	0.01	0.01	NS	-	0.01
164	0.01	0.01	0.01	0.01	-

p	7	14	41	82	164
7	-	NS	NS	0.05	0.05
14	NS	-	NS	NS	0.01
41	NS	NS	-	NS	0.01
82	0.05	NS	NS	-	0.01
164	0.05	0.01	0.01	0.01	-

Figure 4: Mean and standard error (across all animals) of response amplitude (A) and number of responsive voxels (B) in the cSC for different speeds. Plots are presented for different cc thresholds. The p-value tables indicate levels of statistical significance (eg. $p < 0.01$) for different comparisons computed for cc < 0.41. $p > 0.05$ indicated by NS.