fMRI Study of Sound Pressure Level Processing in the Central Auditory System

Jevin W. Zhang[1,2], Condon Lau[1,2], Joe S. Cheng[1,2], Kyle K. Xing[1,2], Iris Y. Zhou[1,2], Matthew M. Cheung[1,2], and Ed X. Wu[1,2]

[1]*Laboratory of Biomedical Imaging and Signal Processing, The University of Hong Kong, Hong Kong SAR, China, People's Republic of,* [2]*Department of Electrical and Electronic Engineering, The University of Hong Kong, Hong Kong SAR, China, People's Republic of*

Introduction - Intensity is an important physical property of the sound wave and is usually reported as sound pressure level (SPL). Non-invasive functional magnetic resonance imaging (fMRI) can improve our understanding of auditory physiology. Preliminary fMRI studies observed increased signal change with SPL along the pathways of the central auditory system[1, 2]. However, these studies employed a narrow SPL range and few sampling points. To examine SPL processing in detail, we measure the hemodynamic responses in the rat inferior colliculus (IC), lateral lemniscus (LL), medial geniculate body (MGB) and auditory cortex (AC) over a broad 72dB SPL range using sparse temporal sampling[3]. The rat is a suitable model for functional imaging studies of the subcortex because it occupies a larger portion of the brain (compared to humans).

Methods - *Rat preparation:* Sprague-Dawley rats (200~250g, N = 7) were used. Rats were anesthetized with 3% isofluorane for induction and maintained at 1%. Key vital signs were monitored by sensors from SA Instruments, Inc. *Rat stimulation:* Monaural broadband noise stimuli were produced by a closed-field electrostatic loudspeaker (TDT EC1) and driven by an amplifier (TDT ED1) and waveform generator (Hewlett-Packard 33120A). Sound was delivered to the left ear canal via a 1m long custom built tube. Rats were stimulated in a block design paradigm of 10s sound off then five blocks of 10s off and 50s on. During on periods, sound was played for 5 seconds (4Hz burst rate and 92% duty cycle) every 10 seconds (Fig. 1). The SPL of the broadband noise during each block was randomly chosen from seven settings (17 to 89dB in 12dB increments). SPL was measured at the end of the tube using an M50 microphone (Earthworks) and varied by adjusting the output voltage of the waveform generator and the gain of the amplifier. The microphone was calibrated by a sound level calibrator (B&K 4230, 94dB, 1kHz). SPLs below 65dB were not directly measured, but were estimated from the output voltage and gain. The paradigm was repeated 14 times per rat resulting in ten blocks at each SPL. *MRI protocol:* Rats were scanned in a 7T Bruker scanner with a surface receiver coil. GE-EPI scans (FOV = 32x32mm^2, data matrix = 64x64, TR = 10.0s, TA = 1.0s, TE = 18ms, nine 1mm slices with 0.2mm gaps) were acquired every 10s (Fig. 1). *Data analysis:* The images were realigned using SPM8 (Wellcome Center, UCL). Blocks corresponding to the same SPL were averaged. Functionally defined ROIs were drawn around the contralateral IC, LL, MGB and AC according to the rat brain atlas[4] (Fig. 2). The activation map for this purpose was computed by applying the t-test on the average images from all seven SPL settings. Time series from all activated voxels ($p < 0.01$, cluster size > 2) within the ROIs were averaged and transformed into BOLD signal change for each SPL and structure. One-way, repeated measures ANOVA with Tukey's test was used to compute p-values for statistical comparisons.

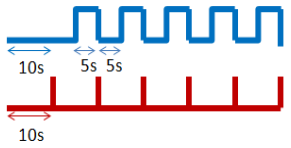

Fig. 1: One block of the stimulation paradigm (top, lows for silence and highs for sound) and fMRI scan acquisition every 10 seconds (bottom).

Results - Amongst the seven animals, IC (7/7), LL (7/7), MGB (5/7), and AC (5/7) are activated and one representative animal is shown in Fig. 2. The IC and LL show increasing signal changes with SPL while AC does not show that trend. Fig. 3 shows the BOLD signal change slopes in IC and LL are significantly different from those in AC and MGB ($p < 0.001$). Tables 1 and 2 confirm the IC and LL signal changes generally increase with SPL. The MGB signal changes at 65 and 89dB are higher than those at 17 and 29dB ($p < 0.01$). In the AC, signal changes show no significant differences between the seven SPLs ($p > 0.05$).

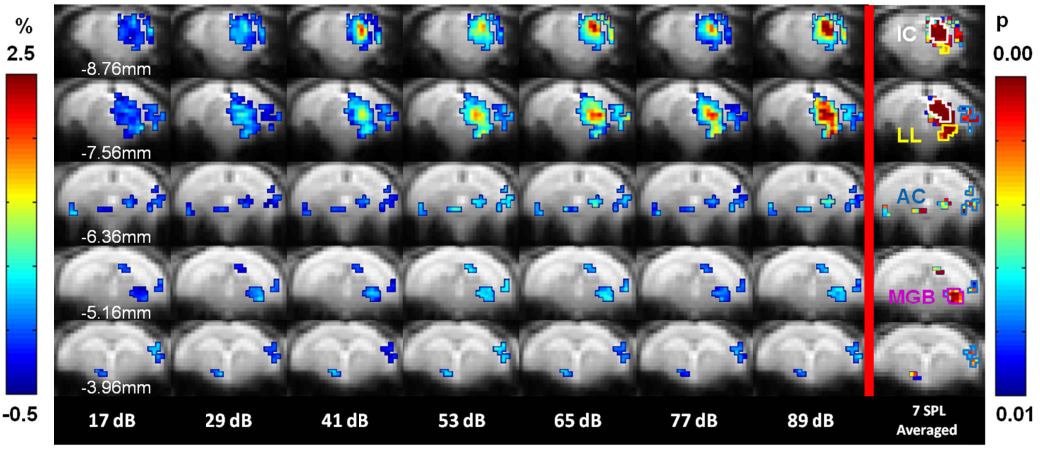

Fig. 2: The seven left columns show the BOLD signal change map from one representative animal under different SPL settings. The color bar to the left shows the signal change scale. The rightmost column shows the activation map from seven SPL averaged data. Functionally defined ROIs for IC (white), LL (yellow), MGB (purple) and AC (blue) are shown. The color bar to the right shows the corresponding p-value. Each coronal slice's distance from Bregma is shown.

IC	17	29	41	53	65	77	89
17	-	ns	**	***	***	***	***
29	ns	-	ns	ns	***	***	***
41	**	ns	-	ns	*	*	***
53	***	ns	ns	-	ns	ns	***
65	***	***	*	ns	-	ns	ns
77	***	***	*	ns	ns	-	ns
89	***	***	***	***	ns	ns	-

LL	17	29	41	53	65	77	89
17	-	ns	ns	ns	**	***	***
29	ns	-	ns	ns	ns	**	***
41	ns	ns	-	ns	ns	*	**
53	ns	ns	ns	-	ns	ns	**
65	**	ns	ns	ns	-	ns	ns
77	***	**	*	ns	ns	-	ns
89	***	***	**	**	ns	ns	-

Tables 1&2: Comparisons of BOLD signal changes at the seven SPLs in IC (top) and LL (bottom). $p > 0.05$, $p < 0.05$, $p < 0.01$, and $p < 0.001$ indicated by ns, *, **, and ***, respectively.

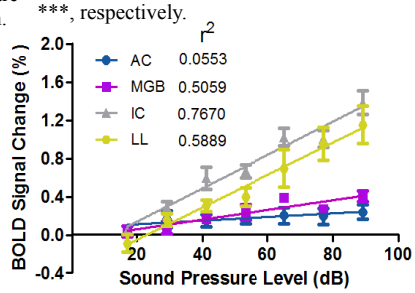

Fig. 3: BOLD signal changes (mean±SEM) vs. SPL and the linear regression lines.

Discussion - BOLD signal change increases significantly with SPL in IC and LL, but not in MGB and AC. BOLD signals are correlated with neuronal spiking activity[5]. Therefore, our results agree with electrophysiology studies that show the majority of LL and IC neuron have monotonic rate intensity functions[6, 7] while many AC and MGB neurons have non-monotonic functions[8-10]. Non-monotonic AC and MGB neurons are likely responsible for reducing the BOLD signal change at high SPLs. This study reports the first fMRI observation of differences in SPL dependences between auditory structures. Human fMRI studies did not observe this because they employed a narrow SPL range with few sampling points, the subcortex is small, or there are interspecies differences.

References - [1] Sigalovsky, Hear Res, 06; [2] Brechmann, Neurophysiology, 02; [3] Hall, Hum Brain Mapp, 99; [4] Paxinos, The rat brain in stereotaxic coord, 98; [5] Mukamel, Science, 05; [6] Kelly, Hear Res, 98; [7] Palombi; Hear Res, 96; [8] Tan, Neuroscience, 07; [9] Zhang, Neuron, 06; [10] Bartlett, J Neurophysiol, 11.