bSSFP fMRI Study of Sound Amplitude Modulation in Inferior Colliculus

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Introduction – Amplitude modulation (AM) is an essential feature of most natural acoustic signals and it is important in variety of sound perceptual tasks. By spatial shifts of excitation, brain neuronal maps optimize information processing. The periodotopic map in inferior colliculus (IC) is based on the temporal analysis of periodic envelop or AM information [1, 2]. The balanced steady state free precession (bSSFP) sequence is a fast MRI acquisition sequence free of image distortion, susceptibility-induced signal loss, and sporadic scanner noise. Our previous work demonstrated that sparse temporal sampling is not a prerequisite in auditory fMRI studies of the IC [3, 4]. Here we employed the bSSFP and continuous imaging instead of echo planar imaging (EPI) and sparse temporal sampling to investigate the spatial representation of AM encoding in IC.

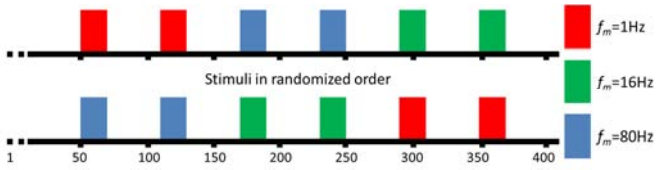

Fig. 1: Acoustic stimulation paradigm for the AM study consisted of three different stimuli. Each stimulus was presented by two continuous blocks in one fMRI session and was in random and interleaved order.

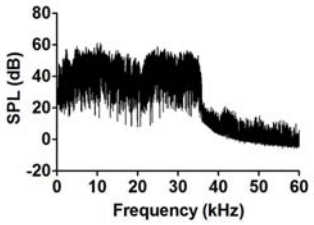

Fig. 2: Power spectrum of the unmodulated broadband noise used in the experiment. It was later modulated by 1, 16 or 80 Hz sinusoidal waveform as the stimulation.

Methods – *Animal preparation:* Sprague-Dawley rats (250 – 300g, N = 5) were examined. Animals were anesthetized with 3% isofluorane for induction and maintained at 1%. *Animal stimulation:* Monaural broadband noise stimuli were produced by a free-field magnetic loudspeaker (TDT MF1) and driven by an amplifier (TDT SA1). Sound was generated by the computer with a high soundcard and was delivered to the left ear canal via a 165 cm long custom built tube. **(i)** Animals were stimulated in a block design paradigm of 40s sound off then six blocks of 20s on and 40s off. In one fMRI session each stimulus was performed by two continuous blocks and randomly interleaved (Fig. 1). The fMRI session was repeated for three to six times each animal. The stimuli were broadband noise (Fig. 2) sinusoidally modulated by 1, 16 or 80 Hz and the modulation depth was 80%. The modulation equation was $A(t)=[1+mSin(2f_mt)]N(t)$, where $A(t)$ was the AM sound, m the AM depth, f_m the modulation frequency and $N(t)$ the broadband noise. **(ii)** For comparison we also performed the tonotopic mapping experiment using sweeping paradigm in one animal [4]. This paradigm contained 22 cycles and for each cycle the sound frequency swept linearly from 1 to 40 kHz or from 40 to 1 kHz in 40s [4]. *MRI protocol:* Animals were scanned in a 7T Bruker scanner with a surface receiver coil. 2D bSSFP scans were acquired with TR = 3.8ms, TE = 1.9ms, FA=30°, phase advance = 180°, FOV = 32x32mm^2, data matrix = 64x64 (zero-filled to 128x128) and NEX=4 (temporal resolution=1s). The 1.2mm thick slice was positioned along the longest axis of IC (Fig. 3). *Data analysis:* Images in the first 10s of each scan session were discarded. The remaining images were realigned and smoothed with a Gaussian kernel of 0.25mm full width at half maximum using SPM8 (Wellcome Center, UCL). **(a)** The two continuous blocks in each session corresponding to the same stimulus were averaged. A general linear model (GLM) analysis was applied for the averaged blocks to calculate three voxel-wise response estimate coefficient (beta-value) maps and t-value maps for each animal. We averaged the three t-value maps and searched the significant activated voxels by setting the $t > 3.15$ (equivalent to $p < 0.001$) and cluster > 2. To highlight the gradual location changing of f_m preference, we subtracted the beta-value map at the low f_m (1 Hz) from that at the high f_m (80 Hz). **(b)** To generate the tonotopic map, we first computed the amplitude and phase at the cycling frequency (0.025 Hz) on the pixel basis, and then we generated the coherence (based on the amplitude information) and tonotopic map (based on the activation delay time estimated from the phase information) [4].

Results – Fig. 4A&C show the beta-value maps corresponding to three different modulation frequency (f_m) from one representative animal and averaged maps from five animals. Beta-value represents the activation strength from the GLM estimation. The most activated voxels shift from dorso-medial to vento-lateral IC with increasing f_m. This spatial shift can be clearly seen in the subtraction map (Fig. 4B&D). The positive subtraction beta-value means that voxel responded to high f_m more and the negative value means that it responded more to low f_m. Fig 5A shows the coherence map which represents the activation strength in the tonotopic mapping experiment using sweeping paradigm. Fig. 5B shows the tonotopic (i.e., spatially specific frequency encoding) map. The yellow arrows in Fig. 4B&D and 5B show the general spatial encoding gradient for the AM frequency and tonotopy gradient. The orthogonal representation of the two different gredients can be observed in the same animal.

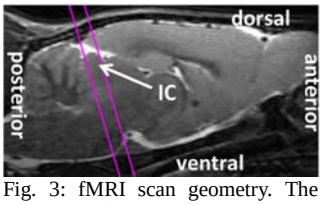

Fig. 3: fMRI scan geometry. The location of IC and the anterior, posterior, dorsal and ventral sides of the brain are indicated.

Discussion – In this study we demonstrated the detection of spatial encoding of amplitude modulation (AM) sound frequency using continuous bSSFP fMRI. Furthermore, the AM frequency encoding gradient was observed to be orthogonal to the sound spectrum frequency encoding or tonotopy gradient. Our in vivo findings here paralleled by the electrophysical recording studies by others. Recordings in the central nucleus of IC show a simple gradient orthogonal to the main tonotopic gradient [5]. Rees and Moller also showed that in anaesthetized rat IC the most effective modulation frequency was below 100 Hz [6]. Their data also showed that the neuron firing rate increased monotonically with increasing modulation depth and some saturated or decreased after the depth reached 80%. Our findings can help us understand more about the auditory processing and hearing disorders.

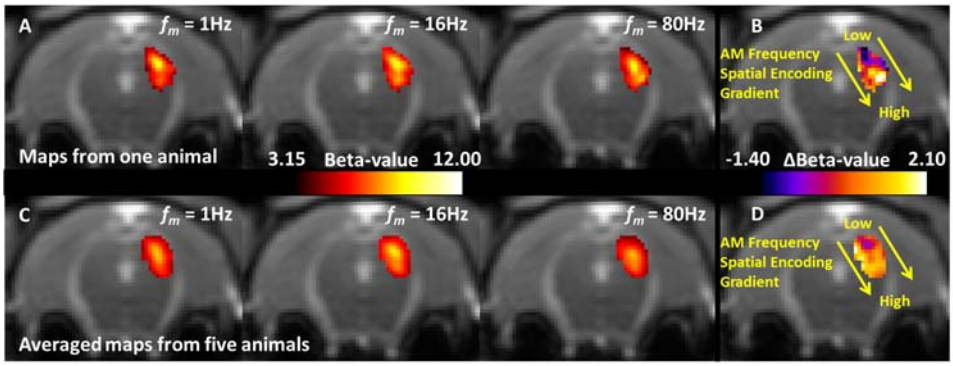

Fig. 4: (A&C) The beta-value maps overlaid on the smoothed bSSFP images from a representative animal and the averaged maps from five animals. The three columns correspond to the three f_m stimuli. The color bar on the center left indicates the beta-value. (B&D) The subtraction map by subtracting the beta-value map at the low f_m (1Hz) from that at the high f_m (80Hz) from one animal and averaged maps from five animals. The color bar on the center right indicates the beta-value. The yellow arrows indicate the AM frequency spatial encoding gradient.

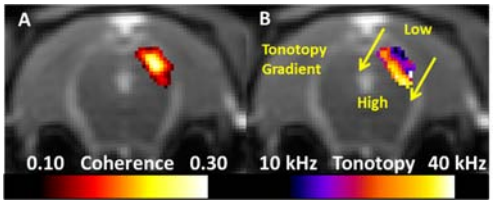

Fig. 5:(A) The coherence map of the same animal as in Fig. 4A&B. The color bar on the bottom left indicates the coherence value. (B) The tonotopic map. The color bar on the bottom right indicates the responsive frequency. The yellow arrows indicate the tonotopy gradient from low frequency to high frequency.

References – [1] Joris, P.X., Physiol Rev, 2004; [2] Frisina, R.D., Hear Res, 2001; [3] Zhang, J.W., Neuroimage, 2012; [4] Cheung, M.M., Neuroimage, 2012; [5] Langner, G., Hear Res, 2002; [6] Rees, A., Hear Res,1983.