Auditory fMRI study of frequency-modulation direction selectivity in the rat subcortex

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INTRODUCTION The direction of frequency-modulation (FM) sweep is an important acoustic cue for human language and animal vocal communications. Such direction selectivity for FM sweep is suggested to emerge in the inferior colliculus (IC) and FM direction selectivity topography correlates with the tonotopy of the central nucleus of IC (CIC) [1]. To investigate such complex FM direction processing in developmental and disease models, functional MRI (fMRI) with high spatial resolution and large field of view (FOV) is well-suited. While previous fMRI studies had identified cortical regions involvement in FM direction discrimination [2], studies in subcortex is limited. Also, most auditory fMRI studies used sparse temporal sampling to reduce the adverse effects of scanner noise at the cost of efficiency [3]. However, it has been demonstrated that this approach is not optimal to study the hemodynamic response in rat IC [4]. Therefore, we investigated FM sweep direction selectivity in the rat subcortex using continuous GE-EPI.

METHODS Normal male SD rats (N=5, 300-350g) were used. fMRI procedures were similar to those in our earlier rat auditory fMRI studies [5].

Auditory stimuli: The FM sweep stimulation (using paradigm shown in Fig 1) was delivered to the rat left ear canal via a custom-made tube with the right ear plugged. Sound pressure level (SPL) measured at the tip of the tube was 85dB.

Image acquisitions: Animals were mechanical ventilated with 1.5% isoflurane during experiments. The animals were imaged on a 7T MRI scanner (Bruker PharmaScan) using a surface receiver coil and GE-EPI sequence. The parameters TE/TA/TR = 18/500/1000 ms, $\alpha = 56°$, FOV = 32x32 mm^2, data matrix = 64x64, eight 1.0 mm slices and 0.2mm gap were used. Six sessions of fMRI were acquired for each animal.

Data analysis: The fMRI images were realigned and spatially smoothed using SPM8 in MATLAB. For individual animals, general linear model (GLM) analyses were applied for all six sessions. The resulting activation maps ($p<0.05$) underwent paired t-test for conditions upward>downward and upward<downward. For each condition, the average time-series within voxels of significant difference ($p<0.05$ and cluster>2) in IC were transformed to percentage BOLD signal changes by normalizing to the baseline signal (i.e. mean of first 10 time points).

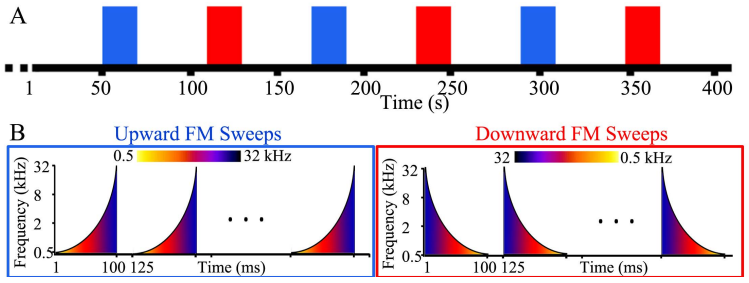

Fig1. Stimulation paradigm consisted of six interleaved blocks of upward and downward FM sweeps with 20s on and 40s off in each block (A). Logarithmic FM sound repeatedly swept from 0.5 to 32kHz (upward) or 32k to 0.5 kHz (downward) in 100ms intervals, with 3ms ramp time and 80% duty cycle (B).

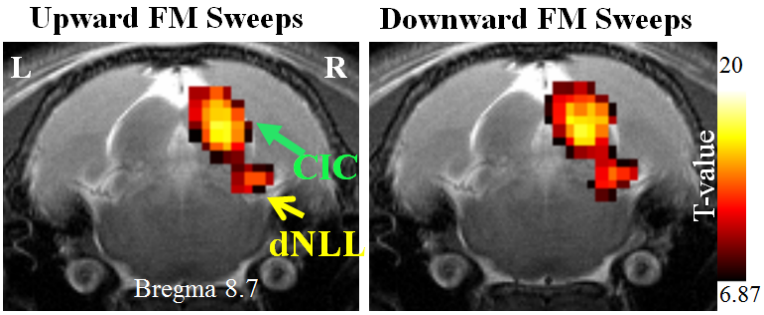

Fig. 2: Activation t-maps for upward and downward sweeps in one representative animal ($p<0.001$). IC and dNLL were activated by both stimulations.

RESULTS Fig. 2 shows activation t-maps ($p<0.001$) for upward and downward sweeps in one representative animal. IC and dorsal nuclei of lateral lemniscus (dNLL) were activated by both stimulations. Higher t-values were observed in IC than those in dNLL, which is consistent with previous report [5]. Paired t-tests were performed to compare the BOLD signal changes in upward and downward sweeps for the 6 pairs of beta-maps. For upward>downward, 4.6 ± 1.67 voxels in the dorsal part of CIC were significantly activated (t-value = 3.1 ± 0.52) (Fig. 3), while no activated voxels were found for upward<downward. Also no voxels in the dNLL were activated in either condition. Fig. 4 shows the time-series averaged within all voxels where significantly greater BOLD signal changes for upward than downward sweeps in all animals was observed. The averaged BOLD signal difference was 0.18%±0.05%.

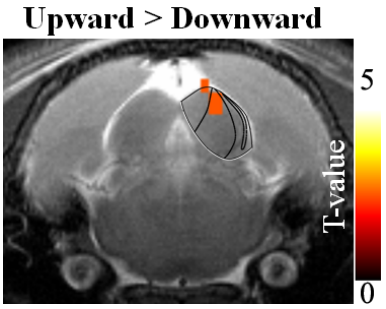

Fig. 3: Paired t-test results for the 6 pairs of beta-maps for the animal shown above ($p<0.05$).

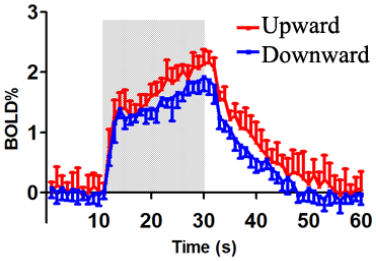

Fig. 4: Averaged time-series (mean ± SEM) within all voxels are significantly activated for upward > downward sweeps in all animals.

DISCUSSION AND CONCLUSION CIC is tonotopically organized with low character frequency (CF) neurons clustered dorsally and high CF neurons clustered ventrally. Neuroelectrophysiology study has shown that neurons sensitive to upward sweeps are distributed more toward the dorsal areas, and conversely those sensitive to downward sweeps are located more in the ventral areas [5]. The BOLD signal changes measured in this study suggested that the dorsal CIC is more selective to upward sweep (Fig.3). Downward selective regions were not identified probably due to a lower population of downward selective neurons (38%) than upward selective ones (61%). dNLL didn't show any directional selectivity [6]. In conclusion, fMRI is feasible to probe the FM sweep direction selectivity in rat subcortical structures. Future studies should examine the effect of FM sweep speed, sweep range and SPL on direction selectivity. Given its non-invasive property, fMRI may also be feasible to study FM sweep processing in animal injury or plasticity models.

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