High-resolution sparse-sampling fMRI reveals tonotopic organization of human inferior colliculus

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Introduction. The inferior colliculus (IC) is located on the dorsal surface of the mammalian midbrain. IC is a laminated structure, and results in animal models indicate that sound frequency is encoded in the dorsal-ventral direction within the laminated depth of IC[1]. We performed experiments to non-invasively explore these properties in human IC using high-resolution fMRI.

Methods. Functional images were obtained on a 3T scanner using BOLD contrast, an interleaved spiral readout[2], 1.2-mm isometric voxels (17-cm FOV, 8 slices, TE = 40 ms, TR = 1 s, 3 shots), and the product array coil. A double-oblique quasi-coronal prescription covered the IC. We utilized a novel sparse-sampling approach to provide quiet periods for the presentation of auditory stimuli. T1 equilibrium was maintained by consistent application of slice-selective excitations. Every 12 s, the acquisition gradients were energized for 3-s periods, during which all 3 spiral interleaves were obtained. Auditory stimuli were presented immediately before the acquisition period. High-resolution T1-weighted anatomical images were obtained on the same slice prescription to facilitate registration onto a reference anatomy. Subjects (N=3) received auditory stimuli using a pair of MRI compatible earphones.

To measure the encoding of auditory frequency (tonotopy), stimuli consisted of five sound presentations with increasing frequencies, log spaced on 0.25—8 kHz, followed by a silent period. The presentations and silent period were spaced at 12-s intervals, so that the entire stimulus repeated with a 72-s period; this sequence was repeated five times to create 6-min runs. Each 6-s-duration presentation included two sets of three 1-s-duration bandpass-filtered white-noise pulses. The first set of 3 pulses had a slightly different frequency (typically 2%), lower or higher than the second set of 3 pulses. To control attention, subjects continually performed a challenging frequency-discrimination task upon each stimulus presentation pair. In each imaging session, subjects performed this task for 8—12 runs. Data from each run were compensated for motion and slow temporal trends. We then fit a sinusoid to the data to obtain complex amplitudes, which were then transformed to a reference volume (IR-prepared SPGR, 0.7-mm voxels, obtained in a separate session) that had been segmented to identify the superficial boundary of the brainstem. A smooth surface was fit to this boundary (Fig. 1), and a distance map from this surface provided a vector depth coordinate that we utilized to create depth profiles of the response evoked by the stimuli. We also utilized the silent periods to create individual sound vs. silent contrasts. These contrasts could be averaged through the depth of IC to improve signal quality, then displayed upon the brainstem surface (Fig. 1).

Results. Individual image volumes showed minimal distortion and SNR ~15—20, similar to our previous high-resolution imaging results in superior colliculus[3]. Depth-averaged sound-silence contrasts show substantial regions of IC with significant activation (Fig. 1). Phase maps confirm a tonotopic organization within the inferior portions (central nucleus) of IC (Fig. 2), with lower frequencies represented by more superficial (dorsal) IC, with higher frequencies encoded by deeper (more ventral) IC. Depth profiles (from region marked with the dotted line in Fig. 1) of single-condition frequency contrasts confirm this tonotopic organization (Fig. 3). Responses to the low-frequency stimulus show a peak response amplitude that is substantially more superficial than those evoked by a high-frequency stimulus.

Conclusions. We demonstrated a novel combination of MRI methods that provide both high spatial resolution and sparse sampling suitable for studies of human auditory brainstem structures such as inferior colliculus. We used these methods to obtain maps that confirm a laminar tonotopic organization in human IC.

[1]Schreiner, C. E. & Langner, G. Laminar fine structure of frequency organization in auditory midbrain. *Nature* **388**, 383-6 (1997). [2]Glover, G. H. & Lai, S. Self-navigated spiral fMRI: interleaved versus single-shot. *Magn Reson Med* **39**, 361-8 (1998). [1]Katyal, S., Zughni, S., Greene, C. & Ress, D. Topography of covert visual attention in human superior colliculus. *J Neurophysiol* **104**, 3074-83.

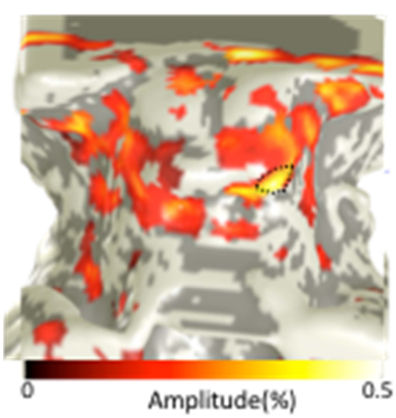

Figure 1: Activation on midbrain surface

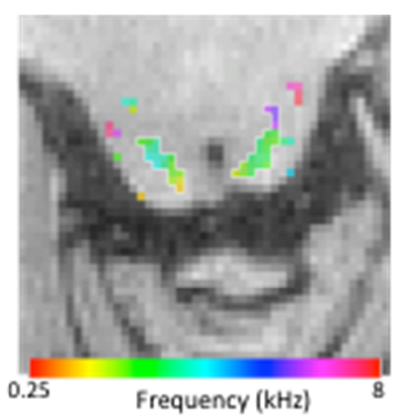

Figure 2: phase map

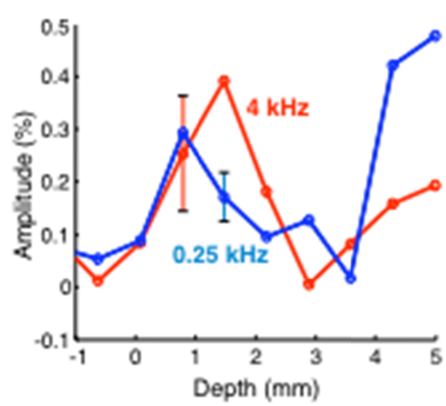

Figure 3: laminar profiles