Functional Asymmetry in Human Primary Auditory Cortex: Identified from Longitudinal fMRI Study

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Introduction: Functional dominance in the left hemisphere for language processing is commonly seen in right-handed individuals [1]. This dominance may be associated with functional asymmetry of fundamental auditory processing at the level of primary auditory areas. Although leftward asymmetry in the cortical volume of the human primary auditory cortex (PAC) has been shown [1], the anatomical-functional relationship in the PAC for linguistic and tonal sound processing, in the context of binaural hearing, has not been conclusively defined. We report functional asymmetry found in the human PAC elicited by auditory word-pair tasks, based on repeated functional MRI (fMRI) measurements. Eight right-handed volunteers underwent nine auditory fMRI sessions, approximately eight weeks apart, for the duration of more than a year. A control fMRI session was also conducted using a simple tonal stimulation. The volume of activation detected within each region-of-interest and its laterality indices were measured across the subjects and sessions.

Method: The study was conducted in accordance with the ethical guidelines set forth by the local Institutional Review Board. Eight healthy volunteers (one female; mean age 35.1±11.6; range: 21-51 years) with no neurological/psychiatric abnormalities participated in the study. All subjects were right-handed, and spoke English as their first language. All experiments were performed using a 1.5 Tesla clinical MR scanner (GE Medical Systems). Each subject was scanned nine times, approximately eight weeks apart (range 21–140 days; mean inter-session period= 56.9 ± 24.6 days) for more than a one-year period (mean 454.9±47.2 days) [2].

The task paradigm was an auditory task delivered binaurally via a MR-compatible headset (Avotec, Jesen Beach, FL). Eighty 2-syllable nouns were selected from the Toronto Noun Pool (Friendly, 1982) and randomly matched to make 40 pairs of nouns. The pairs of nouns, each 2 s in duration, were presented binaurally. We also conducted an fMRI scan using simple-tonal stimulation (frequency centered at 925 Hz, 500ms long; presented at 1 Hz) to examine the presence of any differential activation in the absence of any language content in the sound. In order to quantify the anatomically specific functional activities, the PAC was manually segmented based on high-resolution T1-weighted anatomical images using an in-house segmentation tool. Spatial normalization processes typically deform/warp individual brain anatomy, which may subsequently affect the reproducibility of anatomical space itself. Therefore, the multi-session data sets were processed without spatial normalization. We analyzed the degree of reproducibility of activation from the PAC by measuring the volume of activation detected by fMRI. In the subsequent data analysis, we evaluated the hemispheric asymmetries within two pairs of ROIs by computing functional laterality indices (LI_f) based on the volume of activation [3]. Volume of activation was measured at a statistical threshold of $p<10^{-6}$ applied to all longitudinal functional data. Based on the equation below, LI_f values ranged from –1 (only activation in the left) to 1 (only activation in the right).

$$LI_f = \frac{Vol_{act}^R - Vol_{act}^L}{Vol_{act}^R + Vol_{act}^L}$$ *,whereby Vol_{act} indicate the volume of activation .*

Results: The LI_f, sorted in descending order along with its mean value (in gray bar) are shown in Fig 1 along with the LI_f derived from a simple non-language beep task (in black bar). Although certain variations existed across several sessions, the leftward asymmetry in functional activation was evident. There was no presence of any session-specific trend in LI_f's over time (as examined by linear regression, $p>0.1$ for all subjects).

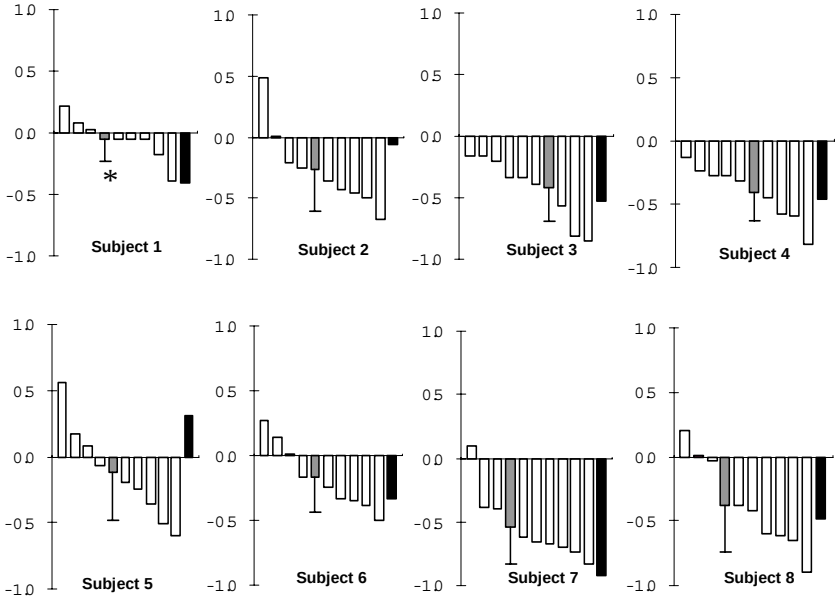

Figure 1. The detailed laterality indices (LI_f) for primary auditory cortex (PAC) measured from 9 different sessions sorted in descending order of LI_f 's. The mean value is plotted in gray with standard deviation. Block bar indicates the LI_f measured from simple auditory stimulation using computer-generated beep. *Data from only 8 sessions were available.

Although it is notable that there were few incidental sessions that showed slight rightward dominance, the averaged LI_f across the sessions indicated leftward dominance in PAC function. The LI_f measured from the simple tonal stimulation demonstrated that leftward functional dominance existed for non-linguistic tonal sound (except for the subject 5) as well. Anatomical laterality was not correlated with functional lateralization.

Discussion: Although variations existed in activation volume between sessions and subjects, we found leftward functional asymmetry in the PAC during both linguistic and non-linguistic sound stimulation. Our findings clearly demonstrate that there is left hemisphere dominance for processing auditory stimuli for right-handed subjects. The strong lateralization in primary auditory processing implies the possibility of a "bottom-up" evolution of human language function and hemispheric dominance rooted in the fundamental differences in auditory function at the level of PAC. This is apposed to the theory that linguistic skills and associated neural processing resulted in cortical dominance [3]. We also found that individual anatomical asymmetry is not correlated with functional asymmetry.

Reference: [1] Anderson et al. *Neuropsychiatry Neuropsychol Behav Neurol.* 1999,12(4):247-54. Yoo et al. *Int J Neurosci*. in press, 2005; [3] Devlin et al. *J Neurosci.* 2003, 23(37):11516-22.