Monaural and binaural contributions to interaural-level-difference sensitivity in human auditory cortex

CrossMark

G. Christopher Stecker [a,*], Susan A. McLaughlin [b], Nathan C. Higgins [a]

[a] Department of Hearing and Speech Sciences, Vanderbilt University School of Medicine, Nashville, TN, USA
[b] Institute for Learning and Brain Sciences, University of Washington, Seattle, WA, USA

ARTICLE INFO

ABSTRACT

Whole-brain functional magnetic resonance imaging was used to measure blood-oxygenation-level-dependent (BOLD) responses in human auditory cortex (AC) to sounds with intensity varying independently in the left and right ears. Echoplanar images were acquired at 3 Tesla with sparse image acquisition once per 12-second block of sound stimulation. Combinations of binaural intensity and stimulus presentation rate were varied between blocks, and selected to allow measurement of response-intensity functions in three configurations: monaural 55–85 dB SPL, binaural 55–85 dB SPL with intensity equal in both ears, and binaural with average binaural level of 70 dB SPL and interaural level differences (ILD) ranging ±30 dB (i.e., favoring the left or right ear). Comparison of response functions equated for contralateral intensity revealed that BOLD-response magnitudes (1) generally increased with contralateral intensity, consistent with positive drive of the BOLD response by the contralateral ear, (2) were larger for contralateral monaural stimulation than for binaural stimulation, consistent with negative effects (e.g., inhibition) of ipsilateral input, which were strongest in the left hemisphere, and (3) also increased with ipsilateral intensity when contralateral input was weak, consistent with additional, positive, effects of ipsilateral stimulation. Hemispheric asymmetries in the spatial extent and overall magnitude of BOLD responses were generally consistent with previous studies demonstrating greater bilaterality of responses in the right hemisphere and stricter contralaterality in the left hemisphere. Finally, comparison of responses to fast (40/s) and slow (5/s) stimulus presentation rates revealed significant rate-dependent adaptation of the BOLD response that varied across ILD values.

Introduction

The abilities of humans and other animals to accurately localize, segregate, and understand sound sources in space depends critically on binaural hearing. Auditory brainstem mechanisms compare inputs arriving from the two ears in order to assess differences in the arrival time and intensity of sound at the ears, termed interaural time differences (ITD) and interaural level differences (ILD), respectively. Binaural processing throughout the auditory pathway involve both excitatory-excitatory interactions (e.g., temporal coincidence detection for ITD processing) and excitatory-inhibitory interactions that give rise to ILD sensitivity.

In mammals, the initial sites of binaural interaction are located within the brainstem superior olivary complex, but sensitivity to ITD and ILD is found throughout the auditory pathway. In the auditory cortex (AC), a majority of neurons exhibit binaural sensitivity (Kitzes, 2008), consistent with the observation that accurate sound localization in both humans

and other mammals is profoundly disrupted by AC lesions (e.g., Jenkins and Masterton, 1982; Heffner, 1997; Zatorre and Penhune, 2001; Malhotra et al., 2004). The majority of binaurally sensitive neurons in AC respond best to contralateral stimulation, i.e. sounds presented to the contralateral ear, from within the contralateral hemifield, or with values of ITD or ILD favoring the contralateral ear. That contralateral bias is detectable at a neuronal population level (e.g., Nakamoto et al., 2004; Harrington et al., 2008) and also in human evoked potentials (Ungan et al., 2001; Palomäki et al., 2005; Salminen et al., 2009; Briley et al., 2013) and blood-oxygenation-level-dependent (BOLD) responses measured with functional magnetic resonance imaging (fMRI; Woldorff et al., 1999; Jäncke et al., 2002; Langers et al., 2007; Schönwiesner et al., 2007; Gutschalk and Steinmann, 2015). The current study aimed to parametrically quantify ILD sensitivity in the human AC in order to describe the shape of BOLD response-ILD functions in each hemisphere and better understand the nature of contralateral bias in human AC.

Several studies have reported contralateral biases in AC BOLD responses to monaural stimulation of the left and right ears (Jäncke et al., 2002; Langers et al., 2007; Woods et al., 2009). Those data are consistent with AC sensitivity to ILD (monaural stimulation being a special case of very large ILD), but do not systematically characterize

* Corresponding author.
E-mail addresses: g.christopher.stecker@vanderbilt.edu (G.C. Stecker), smcl@uw.edu (S.A. McLaughlin), nathan.higgins@vanderbilt.edu (N.C. Higgins).

ILD sensitivity *per se*. In particular, the specific contributions of binaural and monaural pathways to ILD sensitivity in AC BOLD responses have not been clearly delineated. In contrast to studies of ITD, in which contralateral preference (Krumbholz et al., 2005b; 2007; von Kriegstein et al., 2008; Johnson and Hautus, 2010) [though see Woldorff et al. (1999) and Ungan et al. (2001)] may be taken to indicate purely binaural sensitivity, apparent ILD tuning is likely to include some influence of monaural intensity cues, given the anatomical predominance of the crossed monaural pathway (see Stecker and Gallun, 2012). Moreover, to the extent that binaural interactions *do* play a role in ILD tuning of AC BOLD responses, it is not entirely clear whether such interactions predominantly facilitate or suppress the BOLD response. Of these possibilities, suppression is strongly implicated by studies reporting incomplete binaural summation (Jäncke et al., 2002; Krumbholz et al., 2005a; Woods et al., 2009). Even so, the specific nature of binaural interaction remains poorly understood in that attenuation of the binaural BOLD response might reflect some combination of ipsilaterally driven neural inhibition in the ascending pathway and/or occlusion of ipsilateral responses by a stronger contralateral response (Kimura, 2011). Although it is not possible to tease apart the various contributions of neuronal excitation and inhibition that contribute to the AC BOLD response, a major goal of this study was to better describe the positive and negative influences of contralateral and ipsilateral input and infer, where possible, the types of binaural interactions that shape activity in human AC.

In this study, we measured response-ILD functions in the human AC using BOLD fMRI. Since the goal was to study ILD sensitivity parametrically, we presented sounds that varied in intensity at the two ears. In some conditions, sounds were presented monaurally to the left or right ear (i.e. monotically). In other conditions, sounds were presented with equal intensity at the two ears (diotically) across a range of average binaural level (ABL). In yet other conditions, sounds were presented with differing intensity at the two ears (dichotically). In that case, ABL was fixed and ILD varied across a range of values favoring the left or right ear. All of these conditions were intermixed within scanning runs, allowing for direct comparison of AC BOLD responses across binaurally distinct stimuli equated for differences in monaural intensity.

Methods

Data were collected in the Diagnostic Imaging Sciences Center at the University of Washington, Seattle. All procedures, including recruitment, consenting, and testing of human subjects followed the guidelines of the University of Washington Human Subjects Division and were reviewed and approved by the cognizant Institutional Review Board.

Subjects

Ten adults (four male) between 18-50 years of age participated in the study. All self-reported as right handed, with normal hearing and no history of neurological disorder. One participant was the second author, and another was a graduate student not directly involved in the project. Other participants were naive to the focus of the study and were paid for their participation. Standard procedures for informed consent were followed, and written consent obtained from all participants.

Stimuli and task

As illustrated in Fig. 1, stimuli comprised trains of Gabor clicks (Gaussian-windowed tone bursts) in which each click consisted of a 4 kHz cosine multiplied by a Gaussian temporal envelope with $\sigma = 221\mu s$. The resulting spectral bandwidth was also Gaussian, with $\sigma = 750$ Hz (half-maximal bandwidth ≈ 1.8 kHz). The peak-to-peak interclick interval (ICI) was either 3 ms for standard stimuli, or 2 ms for rare detection targets. Such stimuli carry psychophysically salient ITD and ILD cues, and have been used extensively to study listeners' sensitivity to those cues in numerous behavioral experiments (e.g., Stecker

and Brown, 2010; Stecker et al., 2013). Depending on the stimulus condition, click trains consisted of either 32 clicks (train duration = 95 ms) or 4 clicks (train duration = 11 ms). Click trains were synthesized at 48.828 kHz (Tucker-Davis Technologies RP2.1, Alachua FL) and presented via piezoelectric insert earphones (Sensimetrics, Malden MA) enclosed within circumaural ear defenders. Combined, the ear defenders and foam inserts provide roughly 40 dB attenuation of outside noise.

Two stimulus parameters were manipulated: sound level and presentation rate. Levels ranged from 55 to 85 dB SPL and "silent" (-10 dB SPL[1]), and were assigned independently in each ear to measure BOLD responses in selected binaural sound configurations indicated in Fig. 2. Configurations included an "ABL series" of diotic stimuli whose intensity was the same in both ears and varied from 55 to 85 dB SPL in 5 dB increments. These are indicated by the positive diagonal in Fig. 2; green text gives the values of average binaural level (ABL) in each case. Also included was an "ILD series" of dichotic stimuli with ILD ranging ± 30 dB in 10 dB increments (by convention, negative values correspond to greater intensity in the left ear), a range that roughly encompasses the maximum values of ILD experienced at 4000 Hz by human listeners. These were presented at a constant ABL of 70 dB SPL. Stimuli included in the ILD series are indicated on the negative diagonal of Fig. 2, with red text indicating the ILD in each case. Also included, for comparison to the effects of changing intensity to each ear independently, were monotic stimuli applied to each ear at 55, 70, or 85 dB SPL (dark gray cells in Fig. 2), with the opposing ear held "silent" (-10 dB SPL). Finally, a "silent" configuration was included in which intensity at both ears was set to -10 dB SPL (black cell in Fig. 2).

Temporally sparse image acquisition (see Imaging, below; Hall et al., 1999) was employed to further reduce the effects of scanner noise. Image acquisition occurred at the end of each 12-s block of stimuli. Because BOLD responses are known to adapt or habituate following repeated presentation of similar or predictable stimuli (Harms and Melcher, 2002), one potential concern is that habituation of the response over the block duration could mask any stimulus dependence of BOLD responses that emerges early in the block but decays over time. Two approaches were taken to deal with such effects: First, the timing of auditory stimuli was randomized to reduce stimulus predictability. Second, stimuli were presented at one of two rates: a fast rate of 40 click trains per second and a slower rate of 5 click trains per second. Similar rates were shown by Harms and Melcher (2002) to produce very significant and very minor habituation effects, respectively. Comparing the magnitude of response across the two presentation rates allows an estimate of how much response habituation occurred, and whether such effects may have altered the apparent tuning to ILD.

Stimuli were presented in blocks of 12-s duration, with a single combination of binaural intensities and stimulation rate selected per block. During the block, 160 clicks were presented each second; these were arranged into 5 trains of 32 clicks each ("slow" condition) or 40 trains of 4 clicks each ("fast" condition). The total acoustic energy at either presentation rate was thus equal over each one-second epoch of the block. Click-train onset times were randomized within each second, with the constraint that inter-train gaps could not be shorter than 0 ms (i.e., trains could not overlap in time) or longer than 200 ms in the slow condition or 30 ms in the fast condition. Transition to the next block was triggered by EPI image acquisition each 12 seconds, at which time a new stimulus configuration was presented. Combinations of rate and intensity were presented in random order, with "silent" blocks occurring every 4th block. Three 11-minute runs were completed, each comprising 52 blocks, resulting in a total of 114 presentations of sound blocks (6 per rate/intensity combination) and 42 presentations of the silent condition over the course of the entire

---

[1] The apparatus was configured and triggered identically during sound and silent presentations; for "silent" stimulation, the sound level was simply reduced to -10 dB SPL, a value well below detection threshold in the scanning environment.