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Functional magnetic resonance imaging of sound pressure level encoding in the rat central auditory system

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ABSTRACT

Intensity is an important physical property of a sound wave and is customarily reported as sound pressure level (SPL). Invasive techniques such as electrical recordings, which typically examine one brain region at a time, have been used to study neuronal encoding of SPL throughout the central auditory system. Non-invasive functional magnetic resonance imaging (fMRI) with large field of view can simultaneously examine multiple auditory structures. We applied fMRI to measure the hemodynamic responses in the rat brain during sound stimulation at seven SPLs over a 72 dB range. This study used a sparse temporal sampling paradigm to reduce the adverse effects of scanner noise. Hemodynamic responses were measured from the central nucleus of the inferior colliculus (CIC), external cortex of the inferior colliculus (ECIC), lateral lemniscus (LL), medial geniculate body (MGB), and auditory cortex (AC). BOLD signal changes generally increase significantly ($p<0.001$) with SPL and the dependence is monotonic in CIC, ECIC, and LL. The ECIC has higher BOLD signal change than CIC and LL at high SPLs. The difference between BOLD signal changes at high and low SPLs is less in the MGB and AC. This suggests that the SPL dependences of the LL and IC are different from those in the MGB and AC and the SPL dependence of the CIC is different from that of the ECIC. These observations are likely related to earlier observations that neurons with firing rates that increase monotonically with SPL are dominant in the CIC, ECIC, and LL while non-monotonic neurons are dominant in the MGB and AC. Further, the IC's SPL dependence measured in this study is very similar to that measured in our earlier study using the continuous imaging method. Therefore, sparse temporal sampling may not be a prerequisite in auditory fMRI studies of the IC.

Introduction

Hearing is a complex ability that converts information from the sound pressure wave into perceptions. Vibrations of the sound wave cause displacements of the basilar membrane and the organ of Corti moves with the basilar membrane. The electrical signals are transduced from mechanical vibrations by the organ of Corti and transferred to the cochlear nucleus (CN) (Dallos and Corey, 1991). The CN sends the signals to the ipsilateral and contralateral superior olivary complexes (SOCs). Signals are then primarily transferred to the contralateral lateral lemniscus (LL), inferior colliculus (IC), medial geniculate body (MGB) and primary auditory cortex (AC) (Longstaff, 2005). The IC is composed of a central nucleus (CIC) adjacent to the external cortical nucleus (ECIC) (Winer and Schreiner, 2005). These structures are responsible for processing the physical information of the sound. One important piece of information is intensity, which is customarily reported as sound pressure level (SPL) (Pierce, 1989). Intensity is important for mediating arousal, emotions, and motivations (Bradley and Lang, 2000) and it is frequently studied in auditory neuroscience. For adult humans, intensity is one of the key stimulus features used to estimate target distance (Barbour, 2011).

Auditory neuroscience has primarily used psychophysical and invasive techniques to study SPL encoding in the brain. Psychophysical techniques have been used extensively to study how SPL and other sound properties, such as the critical bandwidth (Zwicker et al., 1957) and duration (Florentine et al., 1996), affect the perception of loudness (Fletcher and Munson, 1933; Moore et al., 1997; Zwicker and Scharf, 1965). Invasive electrical recording studies have reported SPL dependence in neuronal firing rates throughout the brain (Barone et al., 1996; Kelly et al., 1998; Palombi and Caspary, 1996b; Polley et al.,

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2007; Semple and Kitzes, 1993; Tan et al., 2007; Wu et al., 2006; Zhang et al., 2004, 2006). Minimally invasive optical imaging has also been used to examine the auditory cortex (Higgins et al., 2010; Kalatsky et al., 2005; Storace et al., 2010). In contrast to traditional invasive techniques, non-invasive functional magnetic resonance imaging (fMRI) has large field of view and can simultaneously examine multiple auditory structures (Cheung et al., 2012a; Jancke et al., 1998; Sigalovsky and Melcher, 2006). Blood oxygenation level-dependent (BOLD) contrast measures the hemodynamic response and is the most widely used contrast in fMRI (Ogawa et al., 1990). Measuring changes in the hemodynamic response with SPL provides a means to examine SPL encoding in the auditory system.

The majority of fMRI studies are performed using the conventional continuous imaging method, where image acquisition is equally spaced during the repetition time (TR) (Brechmann et al., 2002; Cheung et al., 2012a,2012b; Jancke et al., 1998; Mohr et al., 1999; Sigalovsky and Melcher, 2006; Talavage and Hall, 2012). Continuous imaging is potentially problematic for fMRI investigations of auditory physiology because the acoustic scanner noise is present during auditory stimulus presentation (Moelker and Pattynama, 2003). A sparse temporal sampling paradigm can reduce the adverse effects of scanner noise (Hall et al., 1999). In sparse imaging, a single image volume is acquired shortly after the end of stimulus and baseline conditions. Functional imaging is still possible because the hemodynamic delay causes the fMRI signal change to occur several seconds after the stimulus. Importantly, the sound stimulus is not corrupted by the scanner noise as long as TR is considerably longer than the duration of the hemodynamic response (Hall et al., 1999). Most human auditory fMRI studies, using continuous or sparse imaging, have only examined the cortex, although some studies have examined subcortical structures (Abrams et al., 2011; Griffiths et al., 2001; Guimaraes et al., 1998; Kovacs et al., 2006; Krumbholz et al., 2005; Melcher et al., 2000; Röhl and Uppenkamp, 2012; Röhl et al., 2011; Schönwiesner et al., 2007; Sigalovsky and Melcher, 2006; Thompson et al., 2006). Subcortical structures, such as the IC, have been studied less partly because of their small size, motion related to cardiac pulsations, severe susceptibility artifacts (Di Salle et al., 2003), and deep position near the brainstem. The rat is a suitable model for functional imaging studies of the subcortex because its subcortex occupies a larger portion of the brain and is located closer to the skull compared to in humans (Glendenning and Masterton, 1998). The rat's hearing is also much more sensitive than that of a human at high frequencies. Humans can hear a 10 dB SPL sound with frequency from 250 Hz to 8.1 kHz while a rat can hear the sound from 5 to 45 kHz (Heffner and Heffner, 2007).

In this study, we apply fMRI with sparse temporal sampling to measure the hemodynamic responses in the rat CIC, ECIC, LL, MGB, and AC during auditory stimulation at seven SPLs over a 72 dB range. fMRI is well suited to measuring, analyzing, and comparing the SPL effect on different structures at the same time. This study represents the first application of sparse temporal sampling in rat auditory fMRI.

Methods

Animal preparation

All aspects of this study were approved by the local animal ethics committee. Animals were prepared for fMRI sessions as described in our earlier studies (Chan et al., 2011; Cheung et al., 2012a,2012b; Lau et al., 2011a,2011b; Zhou et al., 2011). Normal male Sprague–Dawley rats (200–250 g, N = 7) were used in this study. Rats were anesthetized with 3% isofluorane for induction and maintained at 1% throughout the course of scanning. The rat was placed in the prone position on a body holder with a head motion restricting nose cone and tooth bar. A receive-only quadrature surface coil (Bruker BioSpin, Germany) was placed over the dorsal side of the head. Warm water was circulated within the holder while the rectal temperature, respiration rate, heart rate, and oxygen saturation were monitored by sensors from SA Instruments.

Animal stimulation

Monaural broadband noise stimuli were produced by a closed-field electrostatic loudspeaker (EC1, Tucker-Davis Technologies, USA) and driven by an amplifier (ED1, Tucker-Davis Technologies, USA) and waveform generator (33120A, Hewlett-Packard, USA) (Cheung et al., 2012a,2012b). Broadband noise was used instead of pure tones to obtain larger amplitude hemodynamic responses. A previous study showed that most neurons in the rat IC responded much more vigorously to noise than to pure tone sounds at the neuron's characteristic frequency (Palombi and Caspary, 1996b). Sound was delivered to the left ear canal via a 165 cm long and 1.8 cm inner diameter (tapered to 2 mm over the last 20 cm) custom built rigid tube. The narrow end of the tube was connected to a 6.5 cm long and 2 mm inner diameter flexible tube that entered the left ear canal. The right ear was occluded with cotton wool and vaseline. Rats were stimulated using 10 s sound off then five paradigms of 10 s off and 50 s on. During the on periods, the sound was played for 5 s every 10 s with 4 Hz burst rate and 92% duty cycle (230 ms on and 20 ms off) (Fig. 1). All of the sound stimuli and fMRI scans were synchronized by triggers sent from a custom designed LabVIEW data control system (National Instruments, USA). The SPL of the broadband noise during each paradigm was randomly chosen from seven settings (17, 29, 41, 53, 65, 77, and 89 dB). Similarly high SPLs were used to map frequency organization in human fMRI studies (Formisano et al., 2003). However, the central auditory pathway representing a given frequency in humans is considerably larger than that in rats. Seventeen dB was the lowest SPL where hemodynamic responses were consistently observed in the IC and it was likely close to the SPL of background acoustic noise with the scanner inactive. SPL was measured at the end of the tube using an M50 microphone (Earthworks, USA) and a recorder (FR2, Fostex, Japan). The total SPL was obtained by summation of the mean square sound pressures of all frequencies, $SPL_{total} = 10\log(\sum_{k=1}^{n} 10^{SPL(k)/10})$, where SPL(k) was the SPL at each frequency (Pierce, 1989). Hereafter SPL refers to total SPL except in the caption of Fig. 2. The separation between the end of the tube and the microphone was 0.5 mm. This measurement provided an estimate of the SPL reaching the eardrum, although it did not account for possible auditory distortions between the tip and the eardrum. The recording system was calibrated by a sound level calibrator (94 dB at 1 kHz, Brüel & Kjaer 4230, Denmark). SPL was varied by adjusting the output voltage of the waveform generator and the gain of the amplifier. SPLs below 65 dB were not directly measured, but were estimated from the change of the output voltage (doubling amplitude increased 6 dB) and the amplifier gain. The fMRI session was repeated 14 times per rat resulting in ten presentations of each SPL. Rats were allowed to rest for about 2 min between sessions.

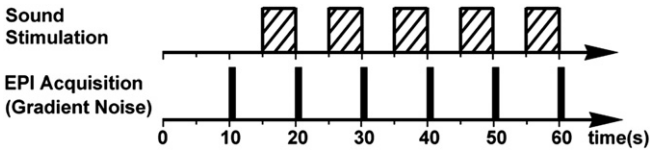

Fig. 1. A schematic representation of the sparse temporal sampling paradigm. Top: The shadows indicate the 5 s long broadband noise stimulation. Bottom: The vertical lines indicate acquisition of a single image volume. The single-shot echo planar imaging repetition time was 10 s and the acquisition time was 1 s. This paradigm was repeated five times in one fMRI session. Each time the total sound pressure level (SPL) of the stimulus was randomly selected from seven settings (17, 29, 41, 53, 65, 77, and 89 dB). The fMRI session was repeated 14 times for each animal and each SPL setting was presented ten times.