Functional magnetic resonance imaging of the central auditory system following long-term and passive acoustic exposure at moderate sound pressure level

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Target audience – Functional magnetic resonance imaging (fMRI) researchers, auditory physiologists, audiologists, and occupational/environmental health authorities.

Purpose – High sound pressure level (SPL) exposures affect the central auditory system, which processes acoustic information. Such exposures can cause hearing loss, increasing the minimum detectible intensity threshold. Until recently, long-term and passive (not paired with stimulation or behavioral training) acoustic exposures at moderate SPLs that preserve thresholds were not thought to affect adult auditory system function. Functional changes have recently been observed in the auditory cortex (AC) of humans, rats, and cats following such exposures (*1*-*3*). However, more work is needed to understand important changes in subcortical function. Compared to traditional neuroscience techniques and other functional imaging techniques, fMRI is well suited to this need. We hypothesize fMRI signals from the inferior colliculus (IC) and medial geniculate body (MGB) will be different between control and exposure animals.

Methods – In this study, animal subjects were exposed to acoustic noise for two months. fMRI was performed one day after cessation of exposure. fMRI procedures were similar to those in our earlier rat auditory fMRI studies (*4*-*6*). *Animals*: Female Sprague-Dawley rats (N = 8) were employed. Animals were three months old at the beginning of acoustic exposure. *Acoustic exposure*: This study employed an established rat acoustic exposure model that does not shift auditory brainstem response thresholds (*3*). A similar model was previously developed and studied with cats (*2*). The exposure was a 5Hz pulse train. Pulses were repeated 24hrs/day for two months. Each pulse had duration 50ms, was 65dB total SPL, and was low-pass filtered at 30kHz (see Fig. 3). *Acoustic stimulation*: Stimulation during fMRI was delivered to the right ear. The stimulus was a bandlimited noise (see Fig. 3) pulsed at 10Hz and 85dB total SPL. The stimulus was set such that most of the acoustic energy fell within the frequency range of the exposure. *Image acquisition*: Animals were anesthetized with 3% isoflurane for induction and maintained at 1% throughout imaging. fMRI experiments were performed on a 7T MRI scanner (PharmaScan, Bruker Biospin). The GE-EPI sequence for fMRI had TE = 18ms, TR = 1000ms, $\alpha = 56°$, slice dimensions = 40.3x40.3x0.63mm^3 divided into 64x64 voxels, interslice gap = 0.13mm, 10 slices, and 280 repetitions. The scans were repeated ten times per animal. *Data analysis*: The GE-EPI images from each scan were realigned and registered to a template (SPM8, Wellcome Trust Centre). The ten scans were averaged for each animal. Standard period cross correlation was applied to identify activated brain regions. ROIs were defined around activated voxels in the lateral lemniscus (LL), IC, MGB, and AC. The ROI spans the same brain region in controls and exposures.

Results and Discussion – Figures 1 and 2 show activated voxels (CC > 0.16) in the superior olivary complex (SOC), LL, IC, MGB, and AC. The posterior IC of exposures has higher CC voxels. There are more activated voxels in the posterior AC of controls. Table 1 shows the IC and MGB have higher fMRI signal amplitude in exposure animals. The AC has higher amplitude in control animals. The AC data is in agreement with earlier electrophysiology studies (*2*, *3*). Note that study (*3*) was performed on the same rat exposure model. Fewer spikes were recorded from the AC neurons of exposure animals stimulated with a 10Hz pulsed tone at characteristic frequency (CF) (*3*). Both multi-unit activity and local field potential were lower in exposure animals if the stimulus frequency was within the frequency range of the exposure (*2*). Both of these electrophysiology observations reduce fMRI signals. The AC data establishes the accuracy of fMRI for studying functional changes following passive exposure. The IC data may be due to corticofugal modulation of the IC response (*7*). Yan et al. observed that electrical stimulation of an AC neuron shifted the CFs of IC neurons toward the CF of the AC neuron. A similar shift was observed for pure tone exposure at the CF of the AC neuron, although the exposure lasted for only 30 minutes (vs. 2 months in this study). The 2 months exposure may have permanently shifted the CFs of IC neurons toward the exposure frequencies, increasing the fMRI signal. The MGB data may also be due to corticofugal modulation (*8*). Tang et al. similarly observed that electrical stimulation of AC neurons shifted the CF of ventral MGB (largest MGB subdivision in rats) neurons toward the CF of the AC neuron. This shift also increases the MGB signal.

Conclusion – The fMRI results show for the first time subcortical functional changes following passive exposure of adults. This study opens the door for many branches of research. fMRI with different stimuli and paired with pharmacological/surgical manipulations can elucidate the mechanisms behind these changes. For example, pure tone stimuli or swept source imaging (*5*) can study tonotopic changes. Cooling the AC can help confirm that the subcortical changes are due to corticofugal modulation. fMRI can also guide electrode placement and immunohistochemistry analysis in further studies of the subcortex. Our results and earlier results (*1*-*3*) suggest passive acoustic exposures at moderate SPL is a health concern. Animal fMRI will guide subject recruitment in occupational and environmental health studies, which is challenging. fMRI will also guide the development of treatments for hearing disorders targeting specific brain structures. fMRI may become a technique for testing future treatments.

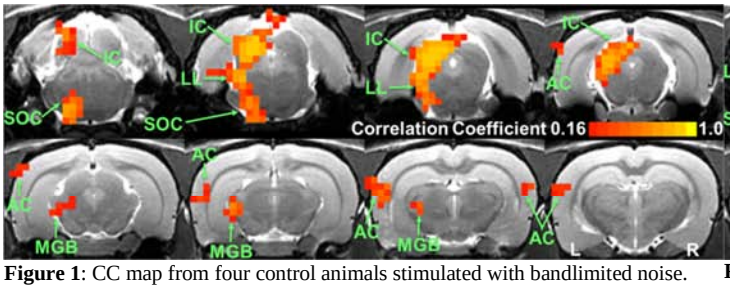

Figure 1: CC map from four control animals stimulated with bandlimited noise.

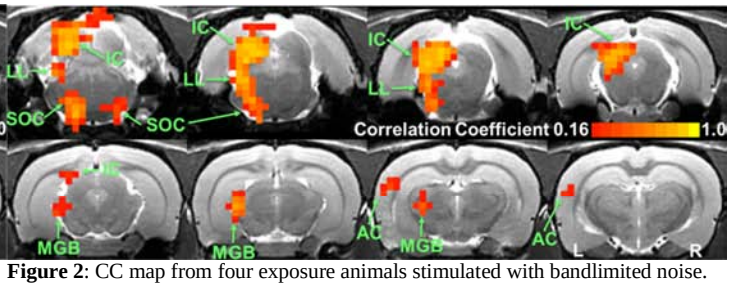

Figure 2: CC map from four exposure animals stimulated with bandlimited noise.

	Control	Exposure
LL	0.45±0.18	0.38±0.18
IC	0.51±0.15	0.69±0.19
MGB	0.04±0.03	0.15±0.10
AC	0.19±0.13	0.06±0.05

Table 1: Mean ± standard deviation of fMRI signal amplitudes measured from four control and four exposure animals.

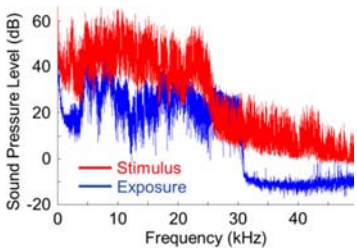

Figure 3: Power spectra of the stimulus and exposure.

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