CORTICAL MODULATION OF BINAURAL INTERACTION ON THE MIDBRAIN

SHU-JUAN FAN[1,2], JEVIN W. ZHANG[1,2], PATRICK P. GAO[1,2], DAN H. SANES[3], AND ED X. WU[1,2]

[1]*LABORATORY OF BIOMEDICAL IMAGING AND SIGNAL PROCESSING, THE UNIVERSITY OF HONG KONG, HONG KONG, HONG KONG SAR, CHINA,*

[2]*DEPARTMENT OF ELECTRICAL AND ELECTRONIC ENGINEERING, THE UNIVERSITY OF HONG KONG, HONG KONG, HONG KONG SAR, CHINA,*

[3]*CENTER FOR NEURAL SCIENCE, NEW YORK UNIVERSITY, NEW YORK, NY, UNITED STATES*

INTRODUCTION: Binaural interaction, in forms of binaural suppression, summation or mixed effects, is important for recognizing sound cues including spatial information [1]. The net effect of binaural interaction is suppression for neurons encoding both low and high frequencies [2]. While binaural interaction established at lower brain stem levels in the ascending auditory pathway has been well studied, the knowledge of cortical modulation of binaural interaction is very limited. Patients with temporal lobe lesions [3] and primates following unilateral auditory ablation [4] showed behavioral deficits in interpreting the sound cues contralateral to the lesion side. Therefore, auditory cortex (AC) may potentially modulate binaural interaction. In this preliminary fMRI study, such modulation effect was probed in inferior colliculus (IC), the obligatory relay center for all ascending auditory pathways in midbrain in experimental rodents with unilateral primary AC ablation.

METHODS: **Animal Preparation:** Five male Sprague-Dawley rats (~280g, n=5) were subjected to unilateral primary AC ablation (**Fig. 3a**) and examined after about one month. During experiment, animals were anesthetized with isoflurane. **Acoustic Stimulation:** Low and high frequency sound (**Fig. 1a**) were produced by a magnetic speaker (MF1, TDT) and delivered with a block design (20s on and 40s off) in an interleaved manner during each fMRI trial (**Fig. 1c**) into the right ear, left ear or both ears of animals. **MRI Protocols:** fMRI experiments were performed on a 7T Bruker scanner using single-shot GE-EPI (FOV=32×32 mm^2, matrix=64×64, TE/TR=20/1000 ms, 8 slices, thickness/gap=1.0/0.2 mm). **Data Analysis:** The GE-EPI images from each animal were first realigned, then co-registered and averaged among all animals using SPM8 for each specific stimulation condition. A general linear model (GLM) was applied. Significantly activated voxels were determined using threshold of t>3.11 (equivalent to p<0.001) and cluster>2. Two ROIs in dorsolateral and central-medial IC subdivisions were defined by referencing to the Paxinos & Watson's rat brain atlas (**Fig. 3b**). BOLD profiles were averaged within each ROI and across all animals. The averaged BOLD temporal profiles were compared between conditions of uniaural or binaural stimulation with either low or high frequency sounds.

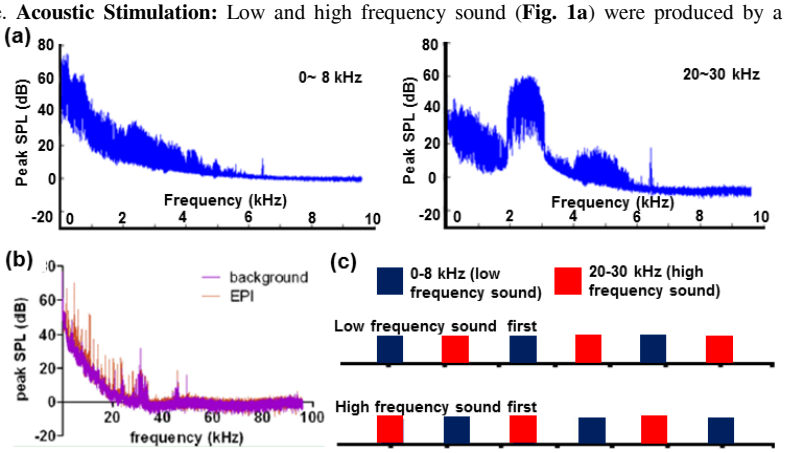

Fig.1 (**a**) Spectrum of low (0-8 kHz) and high (20-30 kHz) frequency sounds. (**b**) Spectrum of scanner background and EPI noise. (**c**) Interleved low and high frequency sounds were presented in each fMRI trial with either low frequency first or high frequency first paradigms. Each paradigm was repeated for 2 to 3 trials for stimulation of left ear only, right ear only or both ears.

RESULTS: BOLD response was predominantly observed in the contralateral inferior colliculus (IC) when sound was presented uniaurally (**Fig. 2**). As compared with uniaural stimulation, BOLD responses in both left and right IC (contralateral and ipsilateral to cortical lesion, respectively) were significantly lower with binaural low or high frequency sound stimulation (paired-t tests, p < 0.05) (**Fig. 3c**). After normalized by baseline uniaural stimulation responses, BOLD response evoked by unilateral stimulation decreased more in right IC than in left IC, and to low frequency sound stimulation than high frequency.

DISCUSSIONS AND CONCLUSION: The observed decrease of BOLD response to binaural stimulation, compared with that to uniaural stimulation, was consistent with previously reported binaural suppressive interactions in IC neurons [1,2]. Such decrease was more obvious in the right IC than in the left IC. This observation indicates that although binaural interaction was mainly mediated by ascending inputs from auditory brain stem [2], it can also be modulated by the descending inputs from AC. When a binaural stimulation was presented, the midbrain response might be dominated by the left IC which mainly received descending inputs from the ipsilateral/left intact AC. Exploring this issue may advance our understandings of auditory neglect observed clinically. Further experiments will be pursued in normal animals and other auditory disorders to shine light on the understanding of cortical modulation of binaural midbrain sound processing.

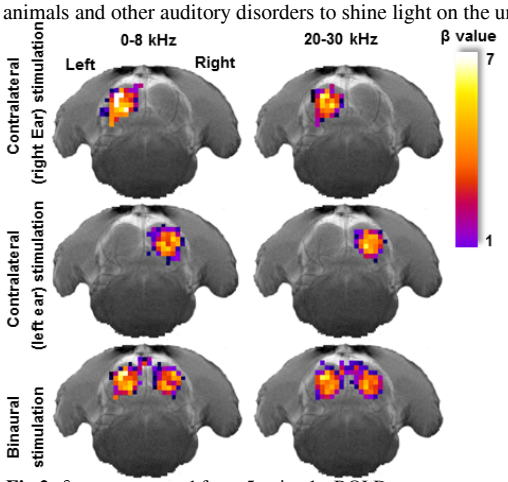

Fig.2 β maps averaged from 5 animals. BOLD response was predominantly observed in the contralateral inferior colliculus (IC) by uniaural stimulation. Both IC showed a reduction in BOLD response when either low or high frequency sound was presented binaurally.

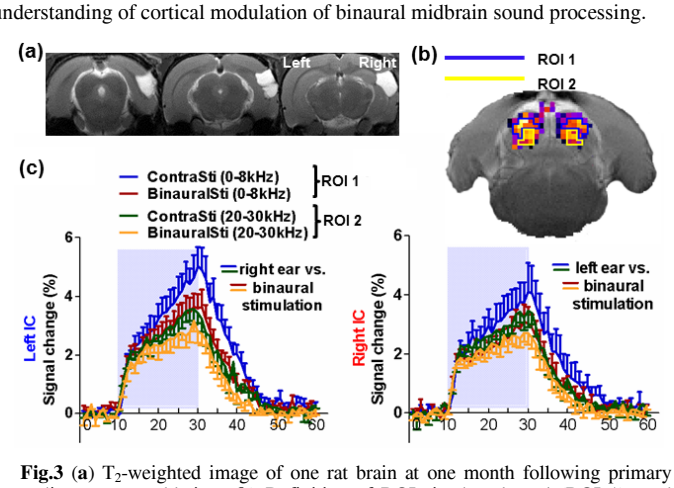

Fig.3 (**a**) T_2-weighted image of one rat brain at one month following primary auditory cortex ablation. (**b**) Definition of ROIs in dorsolateral (ROI 1) and central-medial (ROI 2) IC for quantification of BOLD responses to low and high frequency sound stimulation, respectively. (**c**) Comparisons of uniaural and binaural stimulation induced IC responses in left IC(contralateral to the lesion side) and right IC(ipsilateral to the lesion side).

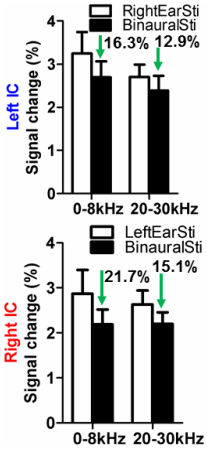

Fig.4 Reduction of normalized BOLD signal changes in left IC and right IC with binaural stimulation.

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