AUDITORY AND VISUAL CORTICES DIFFERENTIALLY MODULATE AUDITORY RESPONSES IN THE MIDBRAIN

Patrick P. Gao[1,2], Jevin W. Zhang[1,2], Shu-Juan Fan[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, HKSAR, China,* [2]*Department of Electrical and Electronic Engineering, The University of Hong Kong, Hong Kong, HKSAR, China,* [3]*Center for Neural Science, New York University, New York, NY, United States*

TARGET AUDIENCE: Researchers who are interested in fMRI and auditory neuroscience.

INTRODUCTION: Sensory pathways contain extensive descending projections [1], yet their functional impact on brainstem activities remains poorly understood. In the central auditory system, the auditory cortex (AC) sends widespread projections to the auditory midbrain nuclei, called the inferior colliculus (IC), in both hemispheres [2, 3]. The IC is a pivotal station for all ascending auditory signals. However, it is unclear how cortical inputs modulate IC auditory processing. Moreover, while anatomical evidence [4, 5] suggests projections from non-auditory cortices, e.g. the visual cortex (VC), directly to the IC, their influence on auditory processing within the IC has not been investigated. In this study, we used BOLD fMRI to measure the sound-evoked responses throughout the IC. To examine the differential functional roles of cortical projections from auditory and visual modalities, fMRI was performed after bilateral ablation of either the AC or VC. Moreover, to examine AC influences on bilateral IC, fMRI was performed after unilateral AC ablation.

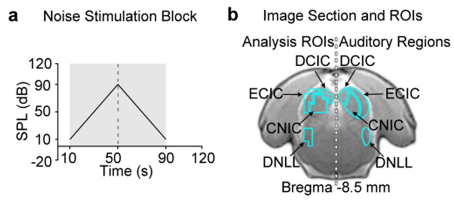

Fig. 1 (**a**) Block paradigm for presenting broadband noise stimulation. The noise sound pressure level (SPL) was linearly modulated during sound-on period. (**b**) 1mm coronal brain section imaged in this study and the definition of analysis ROIs (left) based on atlas (right).

METHODS: Adult male SD rats (~250g) underwent AC or VC ablation surgery and were scanned 2~3 weeks later. Isoflurane (1.2%) was used for anesthesia. For auditory fMRI, broadband noise was presented to the animals in a block paradigm (Fig. 1a), and coronal slice covering the center of IC (Fig. 1b) was imaged continuously using bSSFP that provided relatively smooth scanner noise and 1 s temporal resolution [6]. Activated voxels were identified by the correlation coefficient (CC) between the noise SPL envelope (Fig. 1a) and voxel time series (CC>0.111 for p<0.001, uncorrected). The central nucleus (CNIC), dorsal cortex (DCIC), external cortex (ECIC) of IC and dorsal nucleus of the lateral lemniscus (DNLL, a subcollicular auditory nucleus that projects to the IC, Fig. 1b) were analyzed for the gain of response as measured by the area under the BOLD profiles.

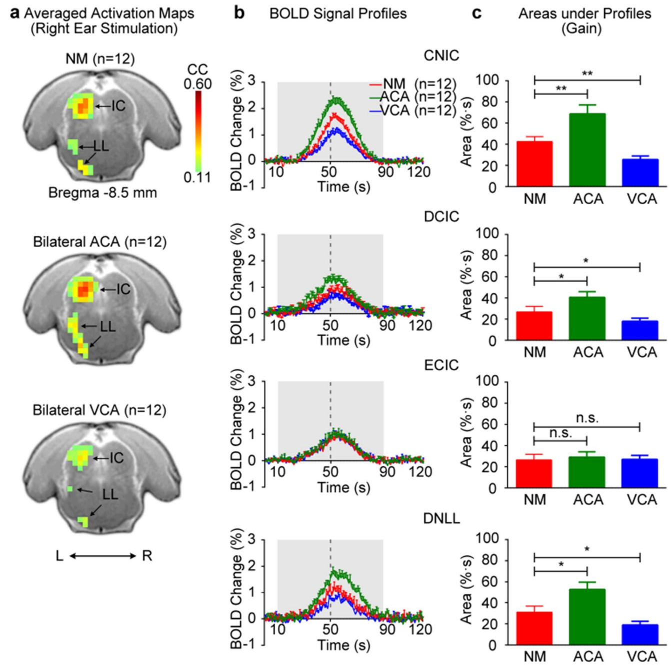

Fig. 2 Auditory and visual cortices differentially modulate gain of IC response. **(a)** Activation maps in normal (NM), bilateral AC ablated (ACA) and VC ablated (VCA) rats under right ear stimulation. (**b**) BOLD signal profiles in different IC subdivisions and LL from the three groups. **(c)** Comparison of the gain (means ± SEM) of response across groups, as measured by the integrated magnitude of BOLD signal changes across the stimulation period (two-sample t-test, *p<0.05, **p<0.01 and n.s. not significant).

RESULTS: Stimulating the normal (NM), bilateral AC ablated (ACA) and VC ablated (VCA) rats in right ear induced BOLD responses in left IC and LL (Fig. 2a). The BOLD signals increased and then decreased in an approximately linear fashion, following the noise SPL change (Fig. 2b). AC ablation increased the gain of response in CNIC, DCIC and DNLL, but not in ECIC (Fig. 2c). In contrast, VC ablation decreased the gain in CNIC, DCIC and DNLL. Note that the BOLD signal profiles, after normalization by their respective gains, were nearly identical across the three groups, and no significant difference was observed for the rising or falling slopes (not shown). This indicates that AC or VC ablation altered the gain of IC auditory responses, but not their kinetics. BOLD responses were also obtained in both sides of right AC ablated rats when stimulated binaurally (Fig. 3a). Compared to normal rats, the response gain increases mainly occurred in the right CNIC, DCIC and DNLL (Fig. 3b).

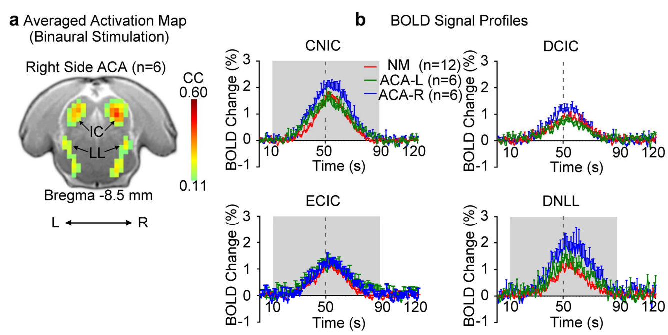

Fig. 3 Auditory cortex influences the gain mainly in ipsilateral IC. **(a)** Activation map in right AC ablated rats under binaural stimulation. **(b)** BOLD signal profiles from both sides of right AC ablated rats and normal rats (same as Fig. 2b).

DISCUSSION/CONCLUSION: Our large-view fMRI results show that projections from AC to the IC exert a net suppressive influence on the gain of IC subnuclei, particularly within the ipsilateral side where extensive ipsilateral corticocollicular projections are present [2, 3]. More importantly, our results reveal that VC provides strong modulatory drive cross-modally to the IC auditory processing. In contrast to AC, it normally increases the responsiveness of IC neurons to auditory stimuli. This effect is likely mediated by the direct projections from VC to IC, as recently revealed in Allen's Brain Atlas [5]. Our results also suggest that both AC and VC influence multiple auditory brainstem nuclei, e.g., the LL. In conclusion, this study reveals the large-scale descending functional influences, from both auditory and visual cortices, on sound processing in different IC subdivisions. These findings provide insights for future studies (e.g. electrophysiology) on the coordinated activity of the auditory neuraxis, and its dysfunction in hearing disorders.

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