Single cell and population encoding in input and associative layers of mouse auditory cortex across strains

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Introduction

Sound stimuli are encoded by populations of neurons in the primary auditory cortex (A1). Sound stimuli are encoded by a series of processing filters that propagate to associative layers 2/3. Given the hierarchical structure of A1, the encoding of sound information is further transformed between layers, but the nature of this transformation is unclear. Since stimulus information is represented in populations of neurons, we investigated the spatiotemporal organization of neuronal population activity across layers. Mice on the C57BL/6 background are commonly used to study cortical processing, yet these mice develop high frequency hearing loss with age making them less optimal choice for auditory research. In contrast, mice on the CBA background retain better hearing sensitivity in old age. Therefore, we performed comparative analysis of neuronal populations from both adult (≥ 8weeks) C57BL/6 mice and C57CA57 mice. We used in vivo 2P imaging of pyramidal neurons in cortical layers L2/3 and L4/5 of awake mouse A1 to characterize the populations of neurons that were active both during tonal stimuli and in the absence of any stimuli. We further characterized the spatiotemporal population activity via neuronal ensembles, defined as neurons that are active within or during successive temporal windows at the temporal resolution of our imaging rate.

Experimental Methods

Animal preparation and imaging

- We used anesthetized mice that received CFlux under the Thy1 promoter (Kato et al., 2014, J. Soc. Nerovis 2012) on a C17F7 background which has a generic mutant that predisposes them to early age-related hearing loss. To address this we used for the first generation of a hybrid mouse line that provides a non-mutated copy of the mutated gene (CFlux/CFlux-Btg).
- Additionally, some L2/3 and L4/5 are labelled with GCaMP6s and GCaMP6f, respectively, in the auditory cortex and were imaged with neural plate and cranial cranial window.

Data Analysis

- B-Image experiments were performed on awake mice. Mouse age imaging was performed using a 670 laser. Xeon Core I5 mouse (3.20 GHz, 80 cores).
- Multi-scale frequency channels were used to determine the firing rate of auditory thalamus. A peak firing rate was determined using the peak firing rate.
- B-Image experiments were performed on awake mice. Mouse age imaging was performed using a 670 laser. Xeon Core I5 mouse (3.20 GHz, 80 cores).

Image Processing and Data Analysis

- Individual ROIs were manually selected from the time-averaged image after motion correction.
- The VOI contained 10-15 neurons, and single neuron ROIs were used for further analysis.
- Significant neuronal responses were determined through comparison of baseline to stimuli of different frequencies.
- Spike activity was performed using Neuropack.

Results

Fewer high frequency BFs in C57 mice

C57 mice had a broader distribution of cells with BFs in the mid-frequency region (6-17kHz), but a reduced number of neurons with high frequencies (≥25kHz), compared with primate high frequency hearing loss.

BF and CF are less aligned in C57 mice

A1 contains co-active neuronal ensembles

Neuronal ensembles exhibit critical dynamics

How does a sound stimulus perturb ensemble activity in A1?

Summary & Conclusions

Tuning of ensembles is similar in both strains

- Included ensembles in A1 nuclei with widely varying tuning preference.
- Defined a large range of ensemble sizes and duration.
- Found a large range of ensemble size and duration.
- Tunning of ensembles in A1 nuclei with widely varying tuning preference.

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- Characterized the population activity via neuronal ensembles, defined as neurons that are active within or during successive temporal windows at the temporal resolution of our imaging rate.

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