Project 1
Proposal Title: Cross-sensory modulation in the mouse visual thalamus
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Abstract:

**a. Rationale**

Different sensory modalities often interact with each other as sensory information flows from peripheral sensory organs to higher-order brain areas. However, such cross-modal interactions are poorly understood, especially in lower-order sensory areas. Among these areas, the visual thalamus is strongly driven by stimuli from the retina, the peripheral organ driving vision, but it also receives weaker inputs from various non-visual brain nuclei. Using single-cell trans-synaptic tracing on principal cells in the visual thalamus (Rompani et al., Neuron 2017), we found that two nuclei of the lateral lemniscus, DLL and VLL, project to the visual thalamus (unpublished data). These nuclei receive direct input from the cochlear nucleus and are implicated in the acoustic startle reflex, suggesting that visual responses in the visual thalamus might be modulated by auditory inputs. **Here, we will test the hypothesis that these auditory inputs control the responses that the visual thalamus transmits from the retina to the visual cortex by prioritizing some visual features over others, depending on the mouse’s behavioral needs or the valence of the auditory stimulus.**

**b. Aims**

This project has two aims:

1) Determine how acoustic startle delivered via the lateral lemniscus alters visual responses in the visual thalamus.

2) Determine how conditioned auditory input alters visual responses in the visual thalamus.

Both aims will be pursued by recording and manipulating visual and auditory responses in the visual thalamus of awake, head-fixed mice using endoscopic calcium imaging and optogenetics. For the first aim, the Rompani lab has transgenic cre lines that specifically label the DLL (r2-cre line) and the VLL (b1r4-cre line), and the Fellin lab is developing thin endoscopic probes to image large fields-of-view in the sensory thalamus with reduced invasiveness. Using these tools, we will determine if DLL and VLL transmit startle-induced responses to the visual thalamus, which visual responses are modulated by these inputs, and whether optogenetic stimulation of DLL and VLL similarly modulate visual responses in the visual thalamus. Out of all visual responses, we predict that the looming response, a dedicated retinal response to a predator swooping from above, will be accentuated by a loud, startling noise, since in nature those two stimuli are frequently paired.

In the second aim, we will image neurons in the visual thalamus and determine how visual responses are changed by conditioned auditory stimuli. Auditory stimuli will be conditioned as follows: a tone paired with appetitive stimuli (e.g. chocolate), a tone paired with aversive stimuli (food shock), and an unpaired tone. After training, large populations of thalamic cells will be recorded using thin endoscopic probes while the mouse is presented with visual stimuli alone or visual stimuli paired with different tones. For the auditory stimuli eliciting a modification of neural activity in the visual thalamus, we will determine the source of this input by imaging axonal terminals of known auditory inputs into the visual thalamus and by selectively manipulating their activity with optogenetics.

**c. Objectives**

Cross-modal modulation likely underlies the circuit’s rapid decision of which sensory stimuli to prioritize. Our objective is to determine how auditory experience shapes visual perception at the level of the visual thalamus. This is important and novel because cross-sensory modulation has been reported in higher-order brain areas, but it is much less understood in early-stage sensory processing areas as the visual thalamus. **Finding the extend of cross-sensory modulation in the visual thalamus will not only inform our models of vision, but reveal general principles of how sensory systems interact to produce an integrated and contextual representation of the external world.**

**d. Integration of expertise of partners**

The Rompani lab has expertise in calcium imaging, virus tracing, and molecular biology, as well as experience working on the visual thalamus. A major challenge when imaging the thalamus is that it is difficult to monitor large fractions of it without removing substantial portions of the overlying brain tissue, which may severe many modulatory afferent input fibers. The Fellin lab is developing a new generation of thin (diameter: 350-500 µm), aberration-corrected endoscopic probes with large field of view (up to 360 x 360 µm²) using two-photon lithography (Antonini et al. bioRxiv 2018). Using these novel probes and the combined expertise of the two labs, we will be able to synergistically study cross-sensory modulation in the visual thalamus with unprecedented spatial extension and minimal invasiveness.