nVoke: Study of inter-regional functional connectivity between VTA and mPFC

"The nVoke system gave us an unprecedented ability to simultaneously activate DA terminals while recording activity in anatomically-defined neurons in a freely-moving animal."

– Kay Tye, Ph.D, MIT

Overall research goals

Kay Tye's research employs a multidisciplinary arsenal of innovative techniques in an effort to understand emotional valence, or how "good" or "bad" environmental cues guide behaviors essential for survival. Projects in the Tye Lab are aimed at identifying and dissecting neural circuits that underlie appetitive and aversive motivational processes in both health and neuropsychiatric disease states.

Need

A convergence of data suggests that mesocortical dopamine (DA) signaling may differentially influence subpopulations of neurons within the medial prefrontal cortex (mPFC). Given the dynamic and diverse impact DA has on neurons in the mPFC[6] and that the mesocortical dopamine pathway is sensitive to stressful and aversive experiences[5,1,4], we hypothesized that DA-mediated effects on mPFC neuronal activity may depend on anatomically-defined subpopulations. However, simultaneously recording and stimulating defined populations of neurons in vivo has been a long-standing challenge in the field. With nVoke, we have an unprecedented opportunity to drive the activity of DA terminals in the mPFC, while simultaneously recording its impact on anatomically-defined neuronal populations in a freely-behaving subject.

Approach

How does mesocortical DA influence neuronal activity in mPFC subpopulations underlying aversive and reward-related behaviors?

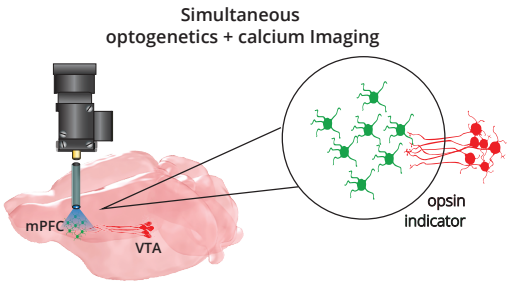

Figure 1. ChrimsonR (excitatory; red) opsin in VTA, GCaMP6m (indicator; green) in mPFC.

Findings

We selectively transduced DA neurons in the ventral tegmental area (VTA) with the red-shifted excitatory opsin ChrimsonR[3] to manipulate VTA DA terminals in the mPFC while simultaneously recording anatomically-defined GCaMP6m-expressing neurons[2].

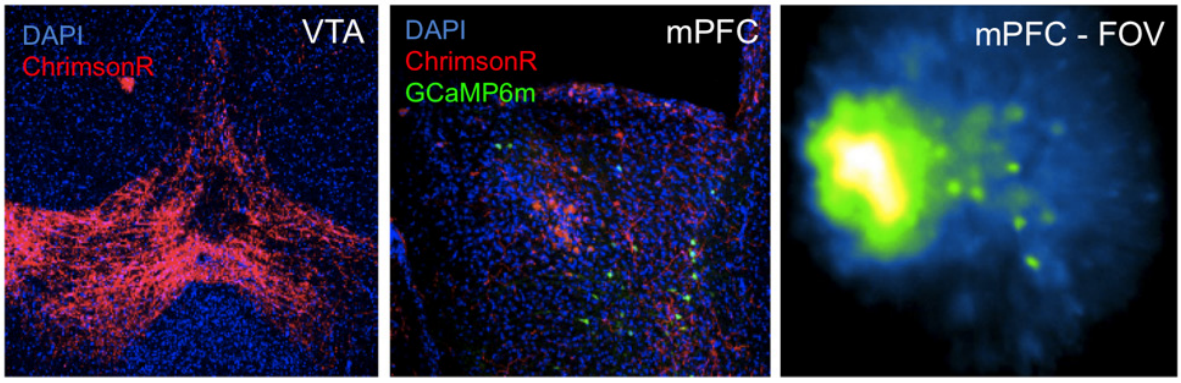

Figure 2. Left panel highlights anatomical specificity of ChrimsonR in VTA neurons. Middle panel shows ChrimsonR in terminal projections within mPFC and GCaMP6m in anatomically-selective mPFC neurons. Right panel shows example of mPFC neuronal calcium responses in the field of view (FOV).

The Inscopix value

Using the nVoke system, we were able to discover precisely how DA influences the neuronal activity of a projection-defined mPFC subpopulation in an awake freely moving mouse!

Given that the recordings and manipulations were done *in vivo*, we were able to discover an effect that was not observed *ex vivo*, where endogenous connectivity is no longer intact.

Reference

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2462 Embarcadero Way
Palo Alto, CA 94303
888.874.6458
info@inscopix.com

www.inscopix.com