CASE STUDY

nVoke: Assessing microcircuit function in the medial prefrontal cortex

"nVoke has made it possible for us to measure how optogenetic inhibition alters multineuronal patterns of activity in freely behaving mice. This is leading us to a previously unattainable understanding of the links between the activity of a specific subtype of mPFC neurons, multineuronal patterns of activity, and behavior."

– Vikaas Sohal, Ph.D, UCSF

Overall research goals

Vikaas Sohal studies how alterations in patterns of activity within the prefrontal cortex contribute to behavioral abnormalities associated with neuropsychiatric disorders. His long-term goal is to identify ways to normalize these patterns of activity in order to develop new treatments for these disorders.

Need

We want to identify multineuronal patterns of activity within the medial prefrontal cortex (mPFC) and understand their causal relationship to behavior. Ideally we would be able to resolve multineuronal patterns of activity with high resolution, using in vivo GCaMP imaging, and be able to study how these patterns and behavior change as a function of optogenetic inhibition.

Approach

Hypothesis: Optogenetic inhibition of a specific subpopulation of mPFC neurons will alter multineuronal patterns of activity and anxiety-related behavior

- Using a Cre-driver mouse, halorhodopsin (NpHR3.0 inhibitory opsin; red) was injected into the mPFC to target a specific subpopulation of mPFC neurons. Subsequently, synapsin GCaMP (indicator; green) was injected into the same location of the mPFC.
- Behavioral output: examine open arm exploration in elevated plus maze in mice.

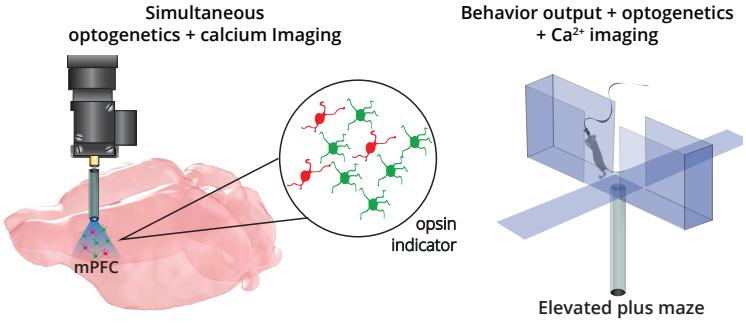

Figure 1. NpHR3.0 (inhibitory; red) opsin in mPFC, GCaMP (indicator; green) in mPFC.

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Findings

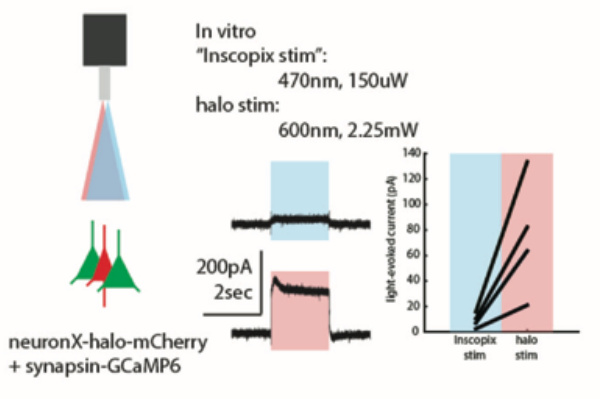

Figure 2. In vitro validation: inhibitory currents elicited by the Red LED are much stronger than those elicited by light for imaging.

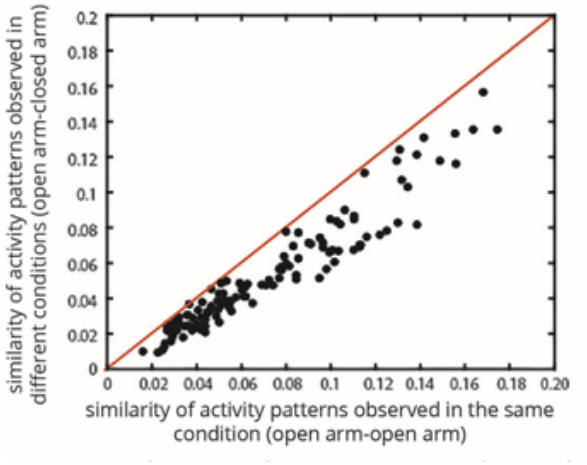

Figure 3. Multineuronal activity patterns observed in the open and closed arms are different.

- mPFC neurons exhibit different multineuronal patterns of activity during exploration of the open vs. closed arms of the elevated plus maze
- Inhibiting a specific subtype of mPFC neurons attenuates differences between the open and closed arm patterns

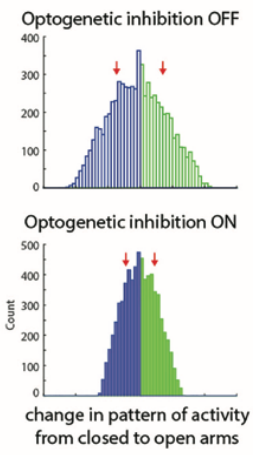

Figure 4. Inhibition of specific mPFC neurons attenuates changes in activity from the closed to open arms.

- This inhibition also appears to increase open arm exploration.
- The change in open arm exploration appears to correlate with the ability of optogenetic inhibition to reduce the differences between patterns of activity in the open and closed arms (in progress)

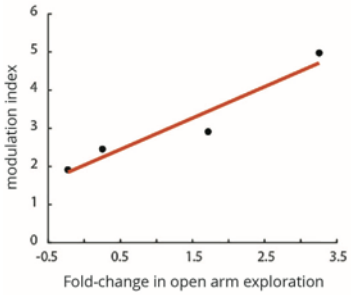

Figure 5. Ongoing: the degree to which inhibition modulates activity seems to correlate with changes in behavior.

Functional implications

As illustrated in the previous figures, this is leading us to a previously unattainable understanding of the links between the activity of a specific subtype of mPFC neurons (which we target with halorhodopsin), multineuronal patterns of activity (visualized using GCaMP imaging), and behavior. nVoke has made it possible for us to measure how optogenetic inhibition alters multineuronal patterns of activity in freely behaving mice.

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