CASE STUDY

nVoke: Study of inter-regional functional connectivity between BLA and NAc

"With the nVoke platform, we are for the first time able to reveal how influencing communication between the BLA – NAc functionally drives network activity and behavioral expression in vivo."

– Alice Stamatakis, Ph.D, Scientist at Inscopix

Need

A wealth of data shows that the connection between the basolateral amygdala (BLA) and the nucleus accumbens (NAc) plays a critical role in reward circuitry underlying emotion and motivated behaviors[1-7]. How neural networks transmit information between the basolateral amygdala (BLA) to the nucleus accumbens (NAc) to mediate reward, remains unclear. Our ability to gain insight into how these two brain regions communicate selectively during reward behaviors has only recently become accessible with the latest technological advances that allow us to probe and map functional connections underlying behavior.

Approach

Does stimulation of amygdalar connections within the forebrain alter calcium dynamics in neurons encoding reward behaviors?

- In *Figure 1*, Chrimson (excitatory; red) opsin was injected in BLA, GCaMP (indicator; green) was injected in NAc.
- A lens probe is implanted into NAc to stimulate BLA terminals + image NAc neurons.
- nVoke is a 455 nm LED (EX-LED) for GCaMP excitation plus a 590 nm LED (OG-LED) for selective activation of red-shifted opsins.
- Mice had access to an open place preference chamber for 30 minutes. When the animals crossed into the stimulation-paired side of the chamber, it received 1s of 20Hz OG-LED every 5s. If the mouse crossed into the no stimulation-paired side, no OG-LED stimulation was evoked.
- Imaging via the EX-LED occurred during the entire 30 minutes.

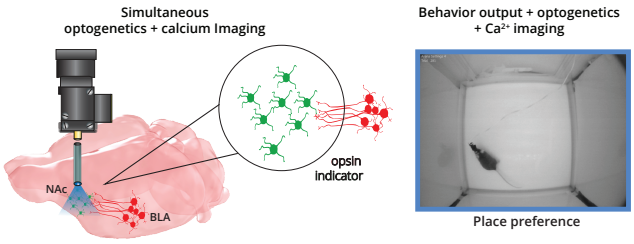

Figure 1. Chrimson (excitatory; red) opsin in BLA, GCaMP (indicator; green) in NAc.

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Findings

Gaining new insights into the neural circuitry of reward using nVoke

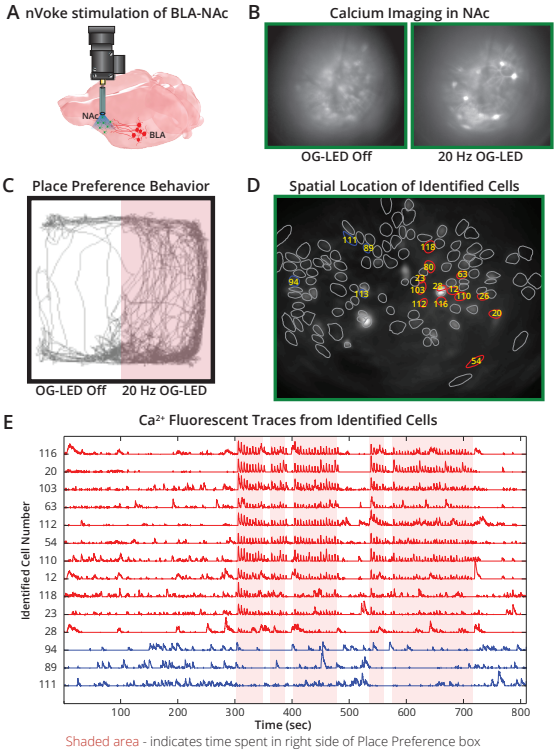

Figure 2. **A.** Schematic showing nVoke stimulation of terminal projections from the BLA to NAc with simultaneous imaging of local NAc neurons.
B. Activation of BLA terminals increases calcium responses in NAc neurons.
C. Activation of BLA terminals is rewarding with subjects exposed to a Place Preference paradigm.
D. Spatial activity data was extracted from the fluorescent signals, identified (gray, red, and blue cell outlines), numbered in yellow and analyzed by nVoke analysis software.
E. Individual cell activity traces (116, 20, 103) show changes in Ca^{2+} fluorescence signalling over time. Red cell traces indicate that these neurons are more active when the OG-LED stimulus is turned "ON" Blue cell traces indicate that these neurons are more active when the OG-LED stimulus is turned "OFF".

Functional implications

Here we demonstrate the feasibility of simultaneous optogenetic manipulation and calcium imaging in freely behaving mice. With the nVoke platform, we are for the first time able to reveal how influencing communication between the BLA - NAc functionally drives network activity and behavioral expression *in vivo*.

The Inscopix value

nVoke is a revolutionary product that combines optogenetic manipulation and wide-scale calcium imaging in a single, integrated system for gaining new insights into the neural circuitry of behavior. With nVoke, neuroscientists are now able to mechanistically define and observe the neurocircuitry involved in brain function and behavior, perform cutting-edge optogenetic manipulation with *in vivo* calcium imaging during awake and actively behaving animals, and reveal how specific neural circuits, and large-scale cellular activity are causally related to phenotypic expression *in vivo*.

References

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