Behavioral Report of Optogenetic Stimulation of Somatosensory Cortex Hand Representation in Non-Human Primates

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Optogenetics offers a new level of stimulation precision, harnessing genetic targeting techniques to deliver cell-type specific information into the brain by optical means. The development of optogenetics as both a research tool and clinical application requires proof-of-concept experiments in Non-Human-Primates [1–3] .One potential clinical application of optogenetics is to deliver somatosensory feedback to restore sensation in individuals with spinal cord injuries or neurodegenerative disorders as part of a brain machine interface. In a pilot experiment we sought to show that optogenetic stimulation of the hand representation in somatosensory cortex (S1) of a Non-Human Primate could be reliably detected. Here we report the first use of optogenetics to deliver a perceptible stimulation in somatosensory cortex in Non-human Primates, a starting point for genetics-based causal analysis of the somatosensory system and possible clinical application.

We injected an optogenetic construct consisting of a channel-rhodopsin variant combined with a promoter targeting excitatory cells (AAV5-CaMKII-C1V1-EYFP) into the hand representation of S1 at three cortical locations. We combined electrical recordings and optogenetic stimulation using a custom coaxial optrode [4]. Electrophysiological recordings confirmed the receptive fields of recorded neurons responded to distal digits of the contralateral hand. We first trained the monkey to perform a Yes/No tactile vibration detection task. Once trained on the vibration detection task, we switched to a Yes/No optogenetic stimulation detection task (Figure 1). In the Yes/No optogenetic stimulation detection task, the monkey reported that it detected the optogenetic stimulus by quickly removing its hand from a capacitive touch sensor within 750 ms of the stimulation indicating a “Yes” response. The monkey reported the absence of the stimulus by retaining its hand on the touch sensor for twice as long (1500 ms) indicating a “No” response. 50% of trials were stimulation trials where “Yes” responses were rewarded, and 50% of trials were catch trials where no stimulation occurred and “No” responses were rewarded.

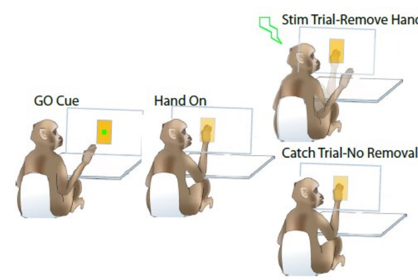

Figure 1 – Yes/No Optogenetic detection Task – a monkey was trained to report when it perceived optogenetic stimulation by rapidly (<750ms) removing its hand (Yes Response). On 50% of trials the stimulation was present (Stim Trial) and the monkey was rewarded for rapidly removing its hand. On the other 50% of trials, no stimulation occurred (Catch Trial) and the monkey was rewarded for retaining its hand on the touch sensor for twice as long (1500ms).

We quantified the detectability of the optogenetic stimulation by comparing the probability of reporting detection during stimulation trials (Hits) with the probability of reporting detection during catch trials (False Alarms). After 7 sessions, the monkey performed the optogenetic detection task with an accuracy of 86.71 ± 5.70% (n = 11). The optogenetic stimulation detection rates were comparable with the vibration detection rates. Further experiments characterized the effects of varying the stimulation duration and intensity on detection rates. Overall we show that optogenetic stimulation of S1 can be reliably detected by Non-Human Primates. Future research will entail more thorough examination of the discriminability of different stimulation parameters and cell-type specificity.

III. References

[1] I. Diester, M. Kaufman, and M. Mogri, “An optogenetic toolbox designed for primates,” *Nature …*, vol. 14, no. 3, pp. 387–397, 2011.

[2] A. Gerits, R. Farivar, B. R. Rosen, L. L. Wald, E. S. Boyden, and W. Vanduffel, “Optogenetically Induced Behavioral and Functional Network Changes in Primates,” *Current Biology*, pp. 1–5, Jul. 2012.

[3] M. Jazayeri, Z. Lindbloom-Brown, and G. D. Horwitz, “Saccadic eye movements evoked by optogenetic activation of primate V1.,” *Nature neuroscience*, vol. 15, no. 10, pp. 1368–70, Oct. 2012.

[4] J. Wang, I. Ozden, M. Diagne, F. Wagner, D. Borton, B. Brush, N. Agha, R. Burwell, D. Sheinberg, I. Diester, K. Deisseroth, and A. Nurmikko, “Approaches to optical neuromodulation from rodents to non-human primates by integrated optoelectronic devices.,” *Conference proceedings : ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference*, vol. 2011, pp. 7525–8, Jan. 2011.

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