Minimally-invasive optogenetics in the non-human primate

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Targeted modulation of neural activity in the central nervous system can alleviate symptoms of neurological disease in humans. However, current therapies, such as electrical stimulation, are highly invasive and of limited long-term efficacy due to their inability to target specific cell-types. Optogenetics is a powerful new technique that allows for temporally-precise, cell-type specific control of neural activity[1-2], with the potential to significantly improve clinical outcomes. Optogenetics has already been successfully applied in the rodent to probe the neural mechanisms underlying behavior and disease[3-4], but its application in the non-human primate (NHP), a critical step toward clinical application in humans, has been slow to develop[5-10].

One key challenge has been the delivery of viruses and light to the brain, which, in primates, must pass through a thick and opaque dura mater that overlies the cortex. Here, we report optogenetic modulation of neuronal responses in the alert and behaving macaque monkey after replacement of the native dura with a transparent artificial dura[11-12]. This approach enables the use of fine glass micropipettes to inject virus with minimal tissue damage, as well as transdural illumination which obviates the damage that would otherwise occur as a result of lowering optical fibers into the brain. It also permits visualization of the underlying cortical micro-vasculature and the fluorescence generated by opsin-expressing neural tissue, which has proven to be helpful in targeting electrodes and illumination to the appropriate cortical locations.

This approach promises to greatly assist in the dissection of cortical circuits underlying perception and behavior in the NHP, and should greatly advance ongoing efforts to translate this exciting new technology into a viable therapy for human neurological disease.

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