High-speed depth-targetable control of genetically defined neurons in freely moving mammals: technology development and neuropsychiatry application

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We have developed both microbial opsin-based genetic tools and solid-state optical approaches to allow specific cell types, even deep within the brain, to be controlled with millisecond precision in freely behaving mammals [1-4]. Use of a fiberoptic approach allows depth targeting of hypothalamic cells (here, the hypocretin cells in the lateral hypothalamus), establishing for the first time a causal relationship between frequency-dependent activity of a genetically defined neural circuit and a specific complex mammalian behavior central to clinical conditions like narcolepsy. The fiberoptic approach also is compatible with targeting superficial structures like M2 motor cortex, and together with a custom commutator, optical control of locomotion in freely moving and even rotating mammals is achieved. Finally we demonstrate integration of millisecond-scale optical control with simultaneous millisecond-scale optical imaging, designed to be adaptable to intact-circuit preparations. Together these neuroengineering advances raise the prospect of determining the role of activity in specific cell types in neuropsychiatric disease.

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