Dynamic illumination of spatially restricted o

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Dynamic illumination of spatially restricted or large brain volumes via a single tapered optical fiber

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Introduction

Optogenetic modulation of neuronal activity has become the dominant method of examining the behavioral consequences of activity in specific neuronal populations *in vivo*. This is due to the synergy of advances in two distinct but well-connected fields: the development of ever-improving light-activated modulators of electrical activity1–3 and of technologies to deliver light within the brains of free-moving animals4–8. Nevertheless, attaining the full potential of optical neural control requires new technologies to better control the spatial

Results

Design principles of tapered optical fibers

TFs are multimode fiber optics that have been engineered to taper gradually from their full width (125-225 μm) to ~500 nm. The taper angle is small ($2° < \psi < 8°$) such that the taper

Illumination of large brain volumes with TFs

deliver light *in vivo* across a spatially extended volume of tissue surrounding the thin fiber. Minimal c-fos was induced in animals that expressed ChR2 in iSPNs but were not

To examine the suitability of this technique for restricted light delivery in brain tissue, site-selective light delivery as a function of θ was evaluated in fluorescein-stained acute mouse brain slices. Both 0.22 NA/ψ= 2.2° and 0.39 NA/ψ = 2.9° TFs allowed near-continuous tuning of the illuminated brain region in both cortex and striatum (Fig. 5d-g). Tissue absorption and scattering shorten the propagation of emitted light into the tissue, further constraining the spatial geometry of the illuminated area. This leads to spatially separated

(θ_2): 1.18±0.18, n=4/2/1 sessions/days/mouse;

illumination of large brain structures with minimal invasiveness and light power. Although effective stimulation of neuron cell bodies expressing ChR2 can be obtained with power densities in the range 1-5 mW/mm^2 [24,25] (and sometimes <1 mW/mm^2, depending on the

using its full NA, as necessary to achieve light output from the entire fiber face. As far as we

PBS three times. Slices were then incubated with Sybr Green 1:10.000 (Thermo Fischer Scientific Inc.) for 20 min on an orbital shaker in dark and thoroughly washed with 1X PBS.

Analysis of c-fos induction

Transgenic adult (*Ador2a-Cre; Ai32*) animals (P>60) were anesthetized with isoflurane and placed in a small animal stereotaxic frame (David Kopf instruments). Under aseptic

fluorescence intensity summed from the left and right hemispheres was normalized to one such that the fluorescence per hemisphere is expressed as a fraction of the total for that section. No comparisons were made between sections.

Multielectrode array recordings

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calculated (black) and measured (red) emission lengths (evaluated as the full widt-h half

(*middle*

c, Schematic of experimental preparation as in (a) showing placement of a flat-faced f (FF).
d, As in (b) showing c-fos induction by light delivery from a FF in dorsal (*left,* 0.22 NA) oF ventr (

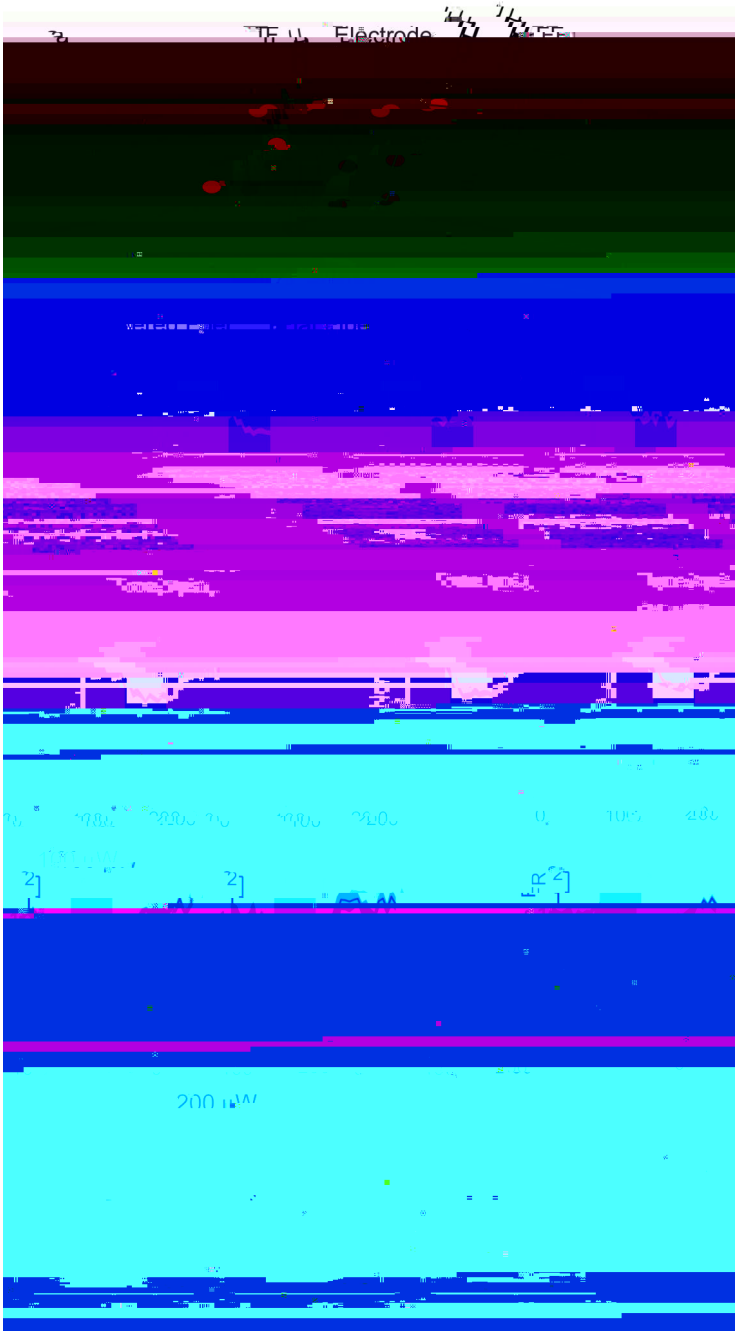

Figure 4. Optogenetic manipulation of motor cortex with TFsc

a, Schematic of the experimental preparation. A 16 channel multi-electrode array is placed

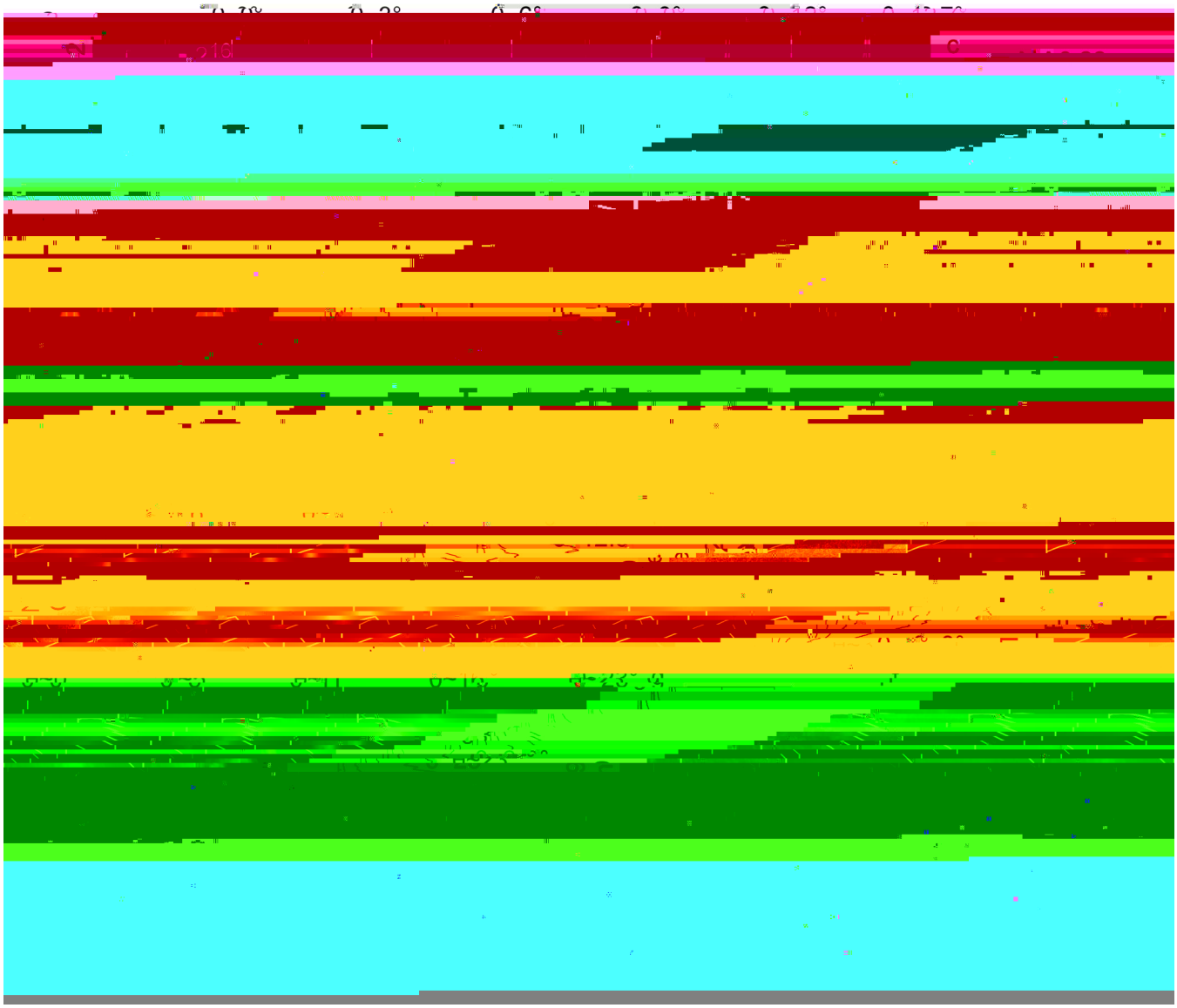

Figure 5. Site selective light delivery with TFs

f, Site selective light delivery with a 0.39NA/ ψ=2.9° TF implanted into the striatum of a fluorescently stained mousery ain slice.
g, Normalized fluorescence intensity profiles, measured beside the taper, from the fluorescence images in (f).

the TF implanted in the animal. A camera above the arena monitored the location and depth of the mouse.

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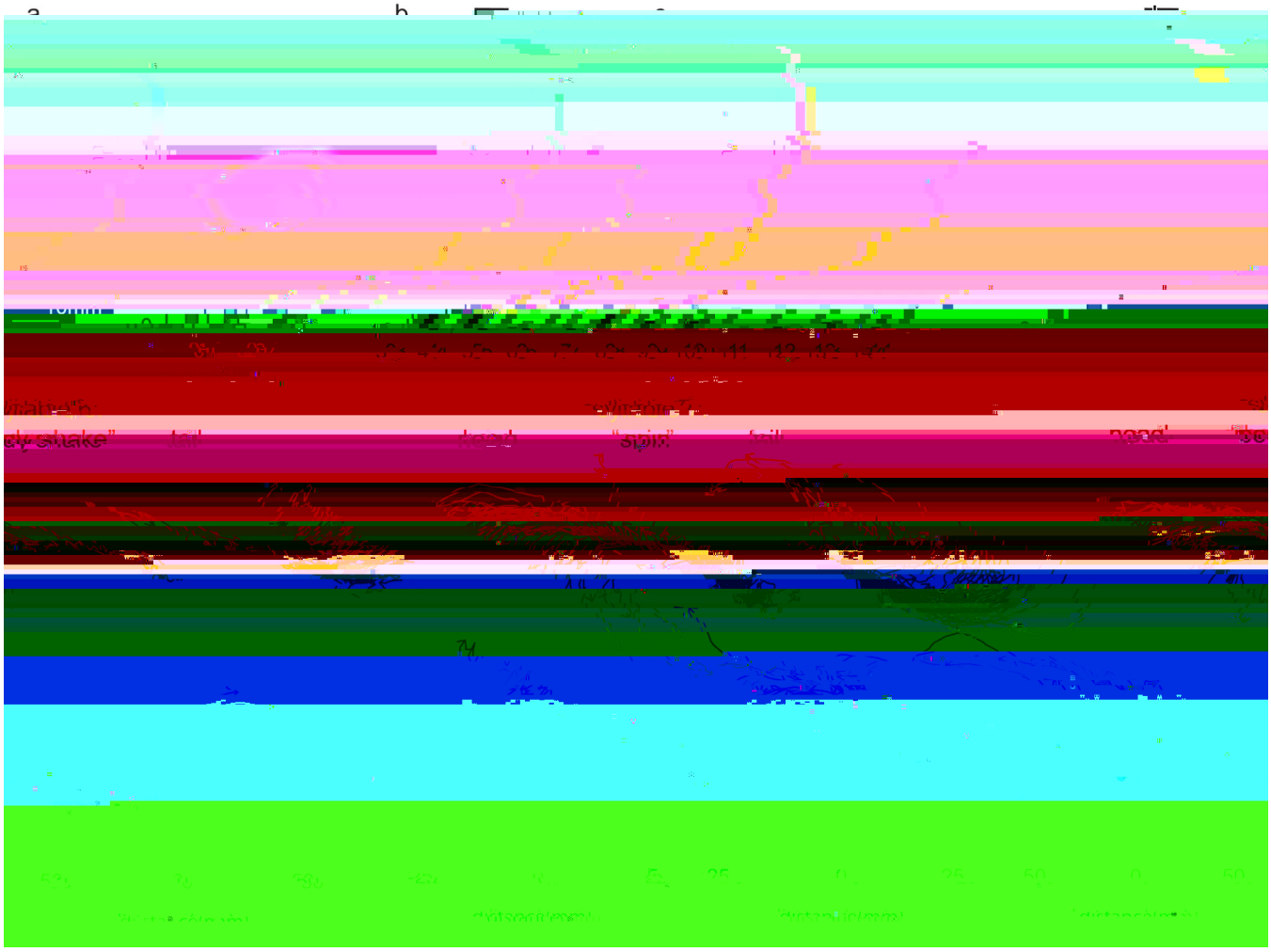

Figure 7. Mapping sub-second structure of behavior during optogenetic manipulation of ventral or dorsal striatum

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