

## Supporting Information for

### Airy-beam holographic sonogenetics for advancing neuromodulation precision and flexibility

Zhongtao Hu<sup>1#</sup>, Yaoheng Yang<sup>1#</sup>, Leqi Yang<sup>1</sup>, Yan Gong<sup>1</sup>, Chinwendu Chukwu<sup>1</sup>, Dezhuang Ye<sup>1</sup>, Yimei Yue<sup>1</sup>, Jinyun Yuan<sup>1</sup>, Alexxai V. Kravitz<sup>2</sup> and Hong Chen<sup>1,3,4\*</sup>

1. Department of Biomedical Engineering, Washington University in St. Louis, Saint Louis, MO 63130, USA

2. Department of Psychiatry, Washington University School of Medicine, Saint Louis, MO, 63110, USA

3. Department of Neurosurgery, Washington University School of Medicine, Saint Louis, MO 63110 USA

4. Mallinckrodt Institute of Radiology, Washington University School of Medicine, Saint Louis, MO 63110, USA

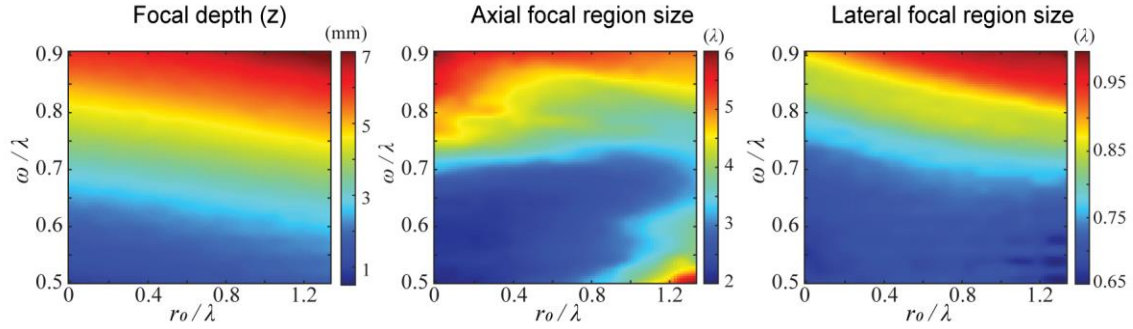
# These authors contributed equally.

\*Corresponding author: Hong Chen

Email: hongchen@wustl.edu

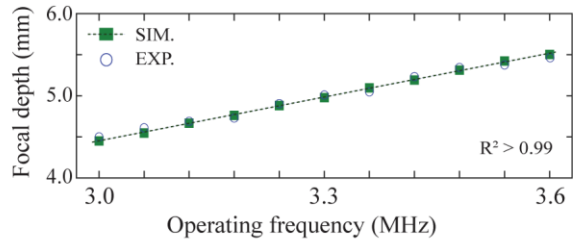
**This PDF file includes:**

Figures S1 to S5



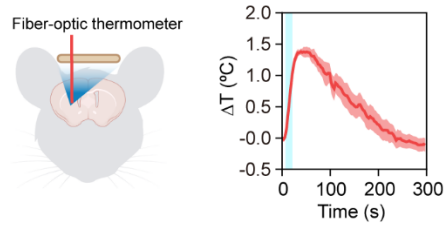
33

34 **Fig. S1.** Airy-beam metasurface's focusing properties are tunable by adjusting design parameters.  
 35 The focal characteristics of the Airy-beam metasurface—specifically, focal depth, axial focal region  
 36 size, and lateral focal region size—are influenced by the parameters  $\omega$  and  $r_0$ , normalized to the  
 37 wavelength  $\lambda$ . Simulations demonstrate that by varying  $\omega/\lambda$  and  $r_0/\lambda$ , the metasurface's focusing  
 38 properties can be precisely adjusted. At an operational frequency of 3.0 MHz, with  $r_0/\lambda$  ranging  
 39 from 0 to 1.3 and  $\omega/\lambda$  from 0.5 to 0.9, we can modulate the focal depth between 0.5 mm and 7.0  
 40 mm. The axial and lateral focal region sizes can be tuned between  $2.0\lambda$  to  $6.0\lambda$  and  $0.65\lambda$  to  $0.98\lambda$ ,  
 41 respectively.



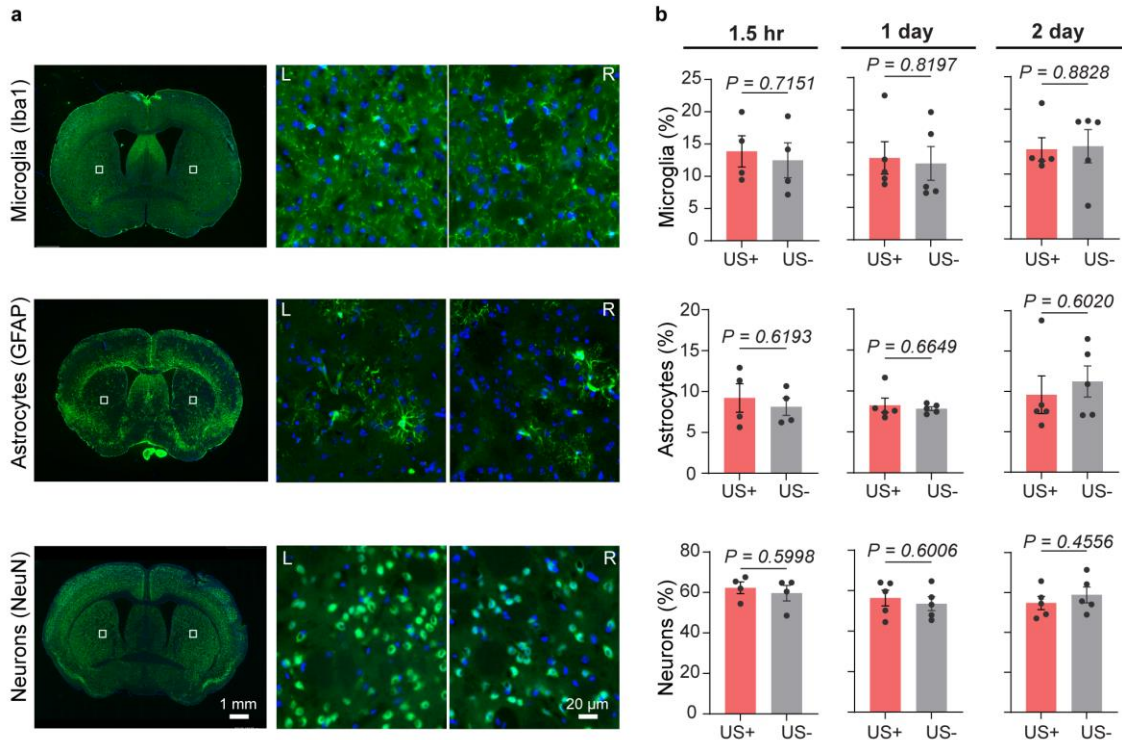
42

43 **Fig. S2.** Calibration of the wearable ultrasound device using hydrophone measurements.  
44 Calibration graph depicting the correlation between focal depth and operating frequency for the  
45 Airy-beam metasurface (referenced in Fig. 1d, e). The plotted data, featuring simulation outcomes  
46 (solid squares) and empirical hydrophone measurements (open circles), corroborate that the  
47 device's focal depth is adjustable via changing the operating frequency of the ultrasound.  
48



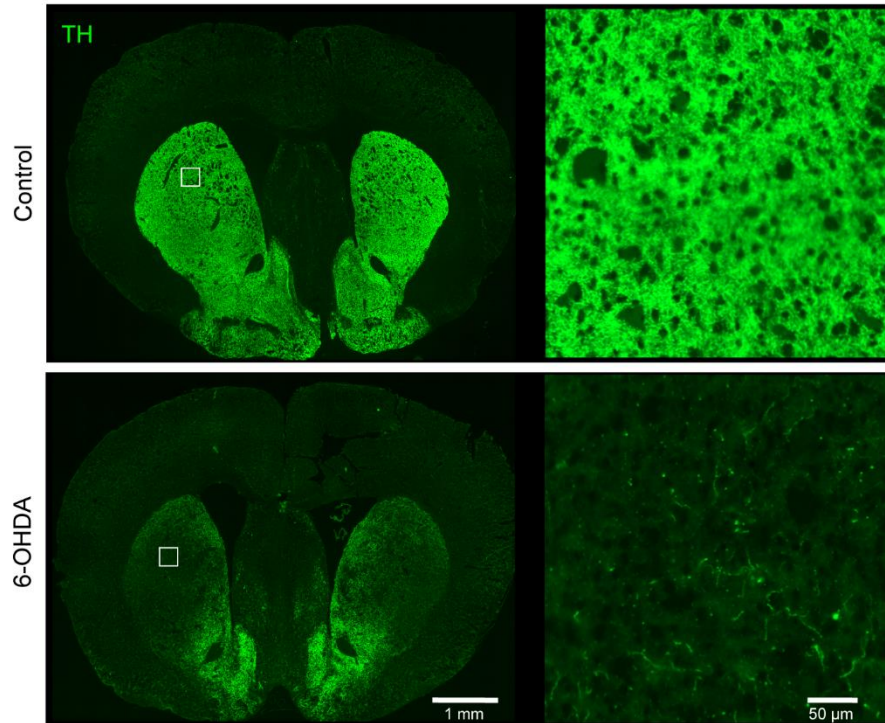
49

50 **Fig S3.** Airy-beam holographic ultrasound induced a mild temperature rise at the target. Left:  
51 illustration of the experimental setup for measuring the temperature at the ultrasound target region  
52 using a fiber-optic thermometer. Right: Temperature increase at the target with the shaded vertical  
53 blue-color bars indicating the ultrasound ON time. Solid red lines and shadows indicate the mean  
54 and s.e.m.



55

56 **Fig. S4.** Evaluation of AhSonogenetics safety. a, Representative fluorescence microscopy images  
 57 displaying immunohistochemical staining of microglia, astrocytes, and neurons post-  
 58 AhSonogenetic stimulation, using Iba1, GFAP, and NeuN as specific markers, respectively in the  
 59 mice sacrificed 1.5 hours after ultrasound sonication. Iba1, GFAP, and NeuN are represented as  
 60 green color while the blue color indicates DAPI. b, Comparative quantification of neuron, astrocyte,  
 61 and microglia populations in the ultrasound-targeted left striatum (US+) versus the unstimulated  
 62 contralateral right striatum (US-) of mice sacrificed at different time points after ultrasound  
 63 sonication including 1.5 hours, 1 day and 2 days. The standard error of the mean is represented  
 64 by error bars, with each point symbolizing an individual mouse (n = 4 mice for 1.5 hr group, n = 5  
 65 for 1 day and 2 days groups). Statistical significance was determined using an unpaired two-tailed  
 66 t-test to calculate  $P$  values.



67

68 **Fig. S5.** Confirmation of striatal dopamine depletion in Parkinson's disease mouse model.  
69 Immunofluorescence staining for tyrosine hydroxylase (TH) showcases the striatal TH levels:  
70 contrast is evident between the dopamine-depleted bilateral striatum of the Parkinsonian mice  
71 (bottom panel) and the intact striatum of healthy control mice (top panel).  
72