Noninvasive ultrasound deep brain stimulation of subthalamic nucleus (STN) improves motor function in a subacute MPTP mouse model of Parkinson's disease

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Background, Motivation and Objective

Deep brain stimulation (DBS) of subthalamic nucleus (STN) has been approved by the Food and Drug Administration for the treatment of Parkinson's disease (PD). However, DBS requires an invasive surgical procedure. Ultrasound is a mechanical wave, which can pass through an intact human skull noninvasively and evoke neural activity. In this study, we investigate whether ultrasound stimulation of STN could improve motor performance in a mouse model of Parkinson's disease.

Statement of Contribution/Methods

The experimental apparatus and sonication target was shown in Fig. 1A. C57BL/6J mice (9 weeks old, male) were randomly divided into control-sham, MPTP-sham and MPTP-STN-US groups (n = 9 per group). Mice received MPTP injection (30 mg/kg body weigh; Sigma-Aldrich) for 5 days consecutively or an equivalent volume of saline. For MPTP-STN-US group, seven days of ultrasound (f = 3.5 MHz, I_{spta} = 180 mW/cm^2, PRF = 1 kHz, DC = 50%, 1s sonication duration, 5 s intervals, 30 min/day) was given. After 7 days ultrasound stimulation, the pole test was performed to assess the treatment effect of STN-US on motor performance. In addition, c-Fos immunohistochemistry was conducted to confirm the neural activity induced by ultrasound stimulation.

Results/Discussion

C-Fos staining confirmed that there was a relatively high level of c-Fos expression after STN-US stimulation in Fig. 1B and C. The MPTP-sham mice showed significant increased time for climbing down a vertical rod in the pole test compared with the control-sham mice (control-sham: 5.79 ± 0.85 s, MPTP-sham: 11.27 ± 1.88 s, p = 0.016). The MPTP-STN-US mice decreased the time for climbing down compared with MPTP-sham mice (MPTP-STN-US: 6.55 ± 0.82 s, p = 0.040), as shown in Fig. 1D. Our results demonstrated that ultrasound deep brain stimulation may serve as a powerful tool for noninvasive treatment of Parkinson's disease.

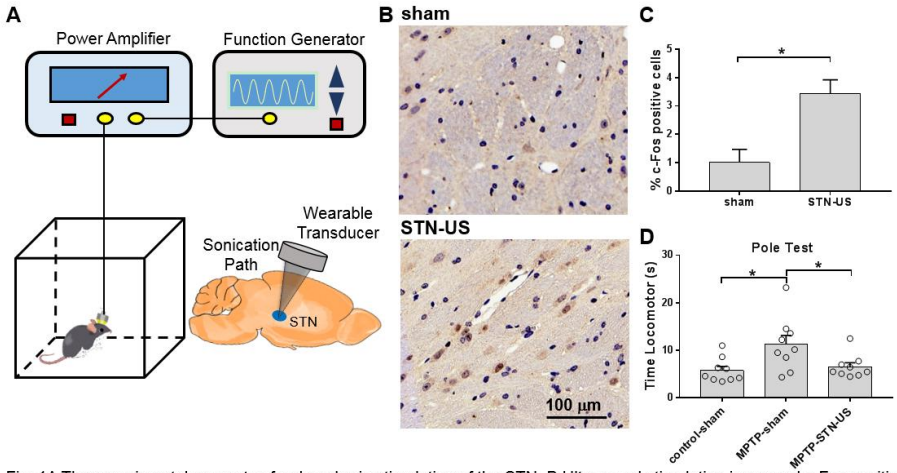

Fig. 1A The experimental apparatus for deep brain stimulation of the STN. B Ultrasound stimulation increased c-Fos positive neurons in STN. C The percent of c-Fos positive neurons in the STN. D Ultrasound stimulation improved motor function in the pole test in MPTP mice (one–way ANOVA: *p < 0.05, mean ± SEM, n = 9 per group).