

Ultrasound stimulation of Lateral Habenula induces the modulation effect in mouse model of depression

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Background, Motivation and Objective

Activation of the lateral habenula (LHb) leads to increases in depressive-like behaviors, whereas inhibition of LHb ameliorates depressive symptoms (Nat. Med. 22. 254-261; Nature 554.317-322; Nat. Neurosci. 17. 1146-1152). Non-invasive low-intensity pulsed ultrasound has been employed to directly modulate the neurons and has a potential application toward different neurological disorder treatments. However, its effectiveness over anti-depressive effects has not been fully elucidated. In this study, we aimed to determine whether ultrasound stimulation of the LHb is capable of inhibiting neuronal excitability in a mouse model of depression.

Statement of Contribution/Methods

A mouse model of depression was created by the aversive stimulus for 28 days continuously. Coronal slices containing the LHb were obtained under ice-cold artificial cerebrospinal fluid (ACSF). The ultrasound neuromodulation chip, based on the surface acoustic waves, ($f = 27.35$ MHz, PRF = 1 kHz, DC = 50%, $I_{SPPA} = 465$ mW/cm², 120s sonication duration) was used to stimulate slices (Fig. 1a). The energy of ultrasound localized to the substrate surface and facilitated stimulation of region-specific slice using a relatively small input power. Spontaneous firing and neuronal excitability of LHb neurons were recorded by patch-clamp.

Results/Discussion

Fig. 1b shows that the frequency of action potentials of LHb neurons was significantly decreased during ultrasound stimulation ($n = 8$, $p < 0.001$). Moreover, it was observed that the firing rate of LHb neurons was rapidly inhibited during the process of ultrasound stimulation ($n = 6$, $p < 0.001$). The results suggest that noninvasive ultrasound stimulation could serve as a new strategy for modulation of neuronal excitability in LHb neurons and prove the potential of ultrasonic neuromodulation on treatment for depression.

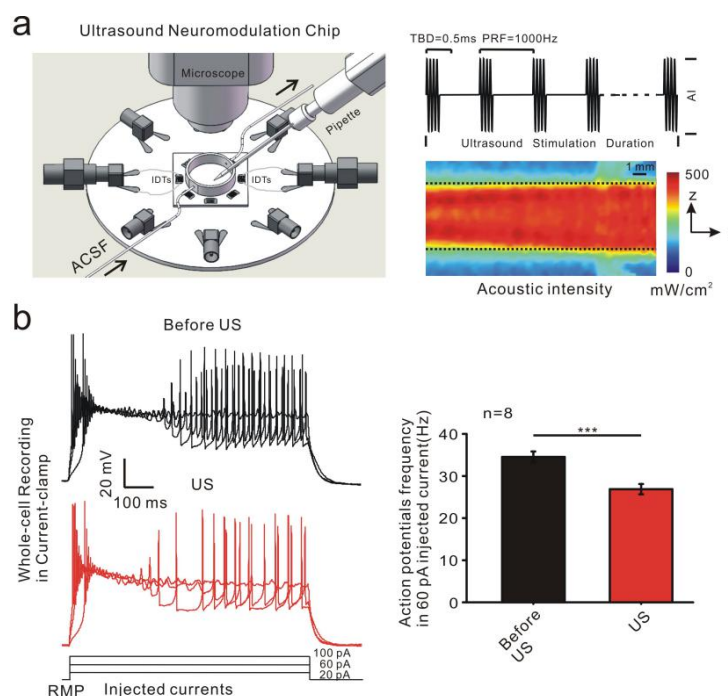


Figure 1. a. Experimental setup and ultrasonic parameters for slices stimulation. b. Ultrasound stimulation decreases the frequency of action potentials of LHb neurons ($n=8$, $P<0.001$).