Research on the Mechanism of Neuro-modulation using Ultrasound Neuro-modulation Chip

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Background, Motivation and Objective:

As a non-invasive method, ultrasound can pass through the intact skull and activate deep brain neurons, gaining increasing attention. The interaction between ultrasound and nerve cells is complex as ultrasound has multiple physical effects, such as mechanical, cavitation and thermal effects. The fundamental mechanism of ultrasound neuro-modulation has not been elucidated. The aim of the study is to investigate whether the mechanical effects, particularly for acoustic radiation force, is the main reason leading to the activation of neurons.

Statement of Contribution/Methods:

The ultrasound neuromodulation chip is a surface acoustic wave chip, consisting of interdigital transducers (IDTs) and an annular polydimethylsiloxane channel. The device was fabricated using a standard microelectromechanical system technology, ensuring the stability and repeatability. Radio frequency signals at 28.026 MHz were generated by an arbitrary waveform generator, and applied to IDTs. Human neuroblastoma SH-SY5Y cells, similar to neurons can generate discharge activity, are widely used in neuroscience research. Calcium imaging was utilized to study the neural activity while harmonic waves generated by cavitation effects were measured by a Laser Doppler Vibrometry (LDV). Additionally, the temperature elevation during stimulation process was monitored by an infrared thermal imager.

Results/Discussion:

Compared to travelling waves, the acoustic radiation force on cells is much larger, and thus the standing wave is established to simulate the cells. Fig. 1.a shows the response of SH-SY5Y cells to ultrasound stimulation in a standing wave with different input powers of 1.11 w, 1.99 w and 2.30 w. When pulse duration is held constant at 27 ms, the change of fluorescence intensity increases with the increment of input power and acoustic radiation force. The maximum increase in the intensity of GCaMP5.0 fluorescence is 82% (n = 6). From fig. 1.b, during the stimulation process, the temperature elevation is around 0.3 ℃ and no change of fluorescence is detected. Besides, fig. 1.c shows that no higher harmonic signals can be detected by the LDV, indicating no cavitation occurs. Thus, the acoustic radiation force induced by ultrasound may be the dominant reason leading to the neural activity.

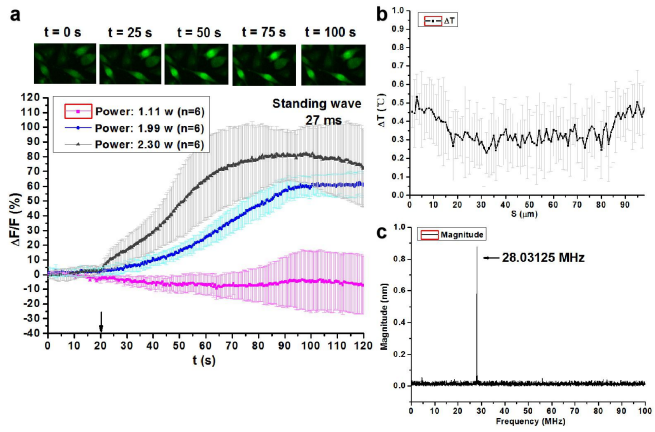

Fig. 1.a. At t = 20 s, the percentage of calcium imaging fluorescence enhancement of SH-SY5Y nerve cells stimulated by standing waves under different input powers (1.11 w, 1.99 w and 2.30 w). False-color images showing the changes in GCaMP5.0 fluorescence in SH-SY5Y nerve cells responding to the ultrasound stimulation. Warmer colours indicate Ca^{2+} elevations in SH-SY5Y nerve cells; b. Temperature rise before and after stimulation. All data were analysed using the Fisher's exact test, with error bars showing the standard error of the proportion; c. Harmonic waves generated by cavitation effects measured by a LDV. The fundamental frequency is 28.03125 MHz.