

Title:

Stimulation of intact brain circuits in awake behaving rodents with transcranial pulsed ultrasound

Authors:

*Y. TUFAIL, W. TYLER;

ASU, TEMPE, AZ

Abstract:

Many brain stimulation technologies have demonstrated to be effective and safe. Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are the most widely used brain stimulation interventions for humans but have certain physical limitations and are still being assessed for efficacy in disease and cognitive models. Using transcranial pulsed ultrasound as a neurostimulation technique has now been well demonstrated both *in vitro* and *in vivo*. As an alternative method, ultrasound provides an advantageous technique over TMS and tDCS as it has better spatial resolutions and greater access to deeper brain circuits. Based on our prior observations, here we show the design and initial implementation for a wearable ultrasonic neurostimulation device. Stimulation of the anesthetized mouse motor cortex revealed direct transcranial stimulation as evidence by cortical electrophysiology and electromyography. Stimulation of motor cortex in the awake behaving animal revealed direct involuntary motor control. These findings are the first to show that ultrasound can be used to noninvasively stimulate the awake behaving animal.

Title:

Precise neural stimulation of the retina using focal ultrasound

Authors:

*M. D. MENZ¹, O. ORALKAN², E. GULEYUPOGLU², P. KHURI-YAKUB², S. BACCUS¹;

¹Neurobio., ²Stanford Univ., STANFORD, CA

Abstract:

Focused ultrasound is a promising technology for stimulation of the brain that is non-invasive, and capable of passing through the skull. The mechanisms of action of ultrasonic neural stimulation may be mechanical or thermal, but the effects are not completely understood. We have used the isolated retina to characterize the effects of ultrasound on an intact neural circuit. A key advantage of the retina is that it can also be stimulated by its natural stimulus, light. In the isolated salamander retina, we recorded the spiking responses of ganglion cells to ultrasound and light using an array of 60 electrodes.

Ultrasound stimuli at a frequency of 40 MHz were delivered from a piezoelectric transducer in saline at a working distance of 4 mm. Pulse trains lasting 3-30 microseconds continued for one second, and were presented at a frequency of 0.5 Hz. The focal spot was 50 microns in diameter and spanned the retina in depth. For comparison of ultrasound responses to light responses, we also presented a flashing light at 0.5 Hz.

Strong ultrasound stimuli evoked precise responses that looked qualitatively similar to strong visual responses. Ultrasound responses were stable for 300 s, contained ON and OFF transients of different types, and showed sustained activity. Temporal jitter at stimulus offset was comparable between light and

ultrasound stimuli, and was often less than 10ms. However, the fastest ultrasonic latencies were shorter than the fastest visual latencies. Further, the relative strength of OFF vs. ON response for the ultrasound stimulus was often very different from those of the flash, as were the response kinetics. This indicates that ultrasound stimuli activated some cells downstream of photoreceptors. The effects decayed to half maximal over 300 μm , considerably larger than the ultrasound stimulus focal spot. This lateral spread is within the spatial scale of lateral connections, including those from horizontal and amacrine cells.

Ultrasound is thus likely stimulating interneurons within the circuit.

These results indicate that ultrasound stimulation is an effective and temporally precise method to activate the retina downstream of photoreceptors. Because the retina is the most accessible part of the central nervous system in vivo, ultrasonic stimulation may have diagnostic potential to probe remaining retinal function in cases of photoreceptor degeneration, and therapeutic potential for use in an electronic retinal prosthesis. In addition, ultrasound may have potential for basic understanding of dynamic activity in the interneuron population of the retina.