ELECTROPHYSIOLOGICAL RESPONSES EVOKED BY LOW-ENERGY FOCUSED ULTRASOUND FROM INDIVIDUAL NEURONS USING A WHOLE-CELL PATCH CLAMP SETUP

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BACKGROUND, MOTIVATION AND OBJECTIVE

Full characterization of the cellular and electrophysiological mechanisms involved in Neurostimulation/modulation by Low-Energy Focused Ultrasound (LEFUS) is necessary for further development of this promising technology. The aim of this work was to integrate a LEFUS-system with a patch-clamp platform for study of LEFUS-modulated and/or -stimulated electrophysiological responses from individual cultured neurons.

STATEMENT OF CONTRIBUTION/METHODS

Mouse primary neurons and human neural progenitor cells were plated onto 35-mm diameter Petri dishes perfused with artificial cerebrospinal fluid. Electrophysiological activity in the neurons was recorded using a whole-cell patch-clamp setup in current-clamp mode. The LEFUS system consisted of a 2.2-MHz planar transducer (PZT4, Ø: 10-mm), coupled with a conical waveguide filled with agarose gel for focusing and transmission of the ultrasound wave to the Petri dish. LEFUS exposures were administrated as trains of twenty pulses (150 cycles / pulse, 20 pulses, pressure = 32.3 kPa – 100 kPa, PRF = 250 Hz - 1 kHz). Neuromodulation studies consisted in measuring changes, induced by LEFUS exposures, in the activation threshold of patched cells to electrical stimulation (current level required to trigger an action potential: AP). Neurostimulation experiments consisted in measuring direct electrophysiological responses to LEFUS exposures in the form of triggered action potentials or electrical discharges from the patched neuron.

RESULTS, DISCUSSION AND CONCLUSIONS

Preliminary data showed that the activation threshold of an ultrasound-treated neural cell could be modulated. The activation threshold required for triggering an AP could be both elevated and lowered following FUS treatment. These results provide an initial indication that the electrophysiological activity of individual neurons can be modulated using LEFUS. Further studies are currently being conducted to support this observation. This project was supported by the French National Research Agency (ANR-16-TERC-0017) the LabEx DevWeCan, and the Focused Ultrasound Foundation (Centers of Excellence).

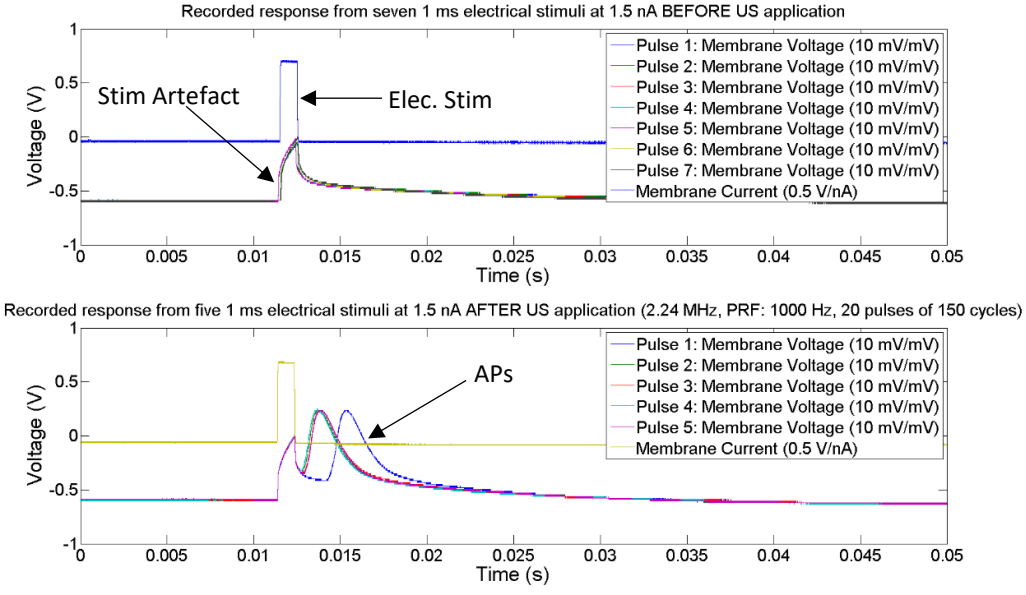

Figure 1 - Lowering of the activation threshold for electrical stimulation following application of LEFUS