The ‘NeuroResonator’ – A Transcranial Ultrasound (‘TUS’) Device Modulating Consciousness and Cognition

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Several stimulation techniques have been developed to non-invasively modulate brain function, alter mood and consciousness, and treat mental and cognitive disorders. These include transcranial magnetic stimulation (TMS), transcranial direct current and alternating current stimulation (tDCS, tACS), and transcranial ultrasound (TUS). Ultrasound (US) consists of mechanical vibrations, typically 0.5 to 8 megahertz, and has been used in medicine for nearly a century. At high intensities US can heat and damage tissue but at low, sub-thermal intensities and durations (FDA guideline <750 mW/cm²) TUS is safe and painless. Motivated by EEG and fMRI evidence of asymmetrical frontal activity being related to mood and mood disorders, we conducted trials of TUS targeting inferolateral frontal cortex. Using a medical imaging GE ultrasound device, our group published the first human (double blind) TUS study for mood in 2013. In subsequent studies using a commercial device (Thync, Inc.), we’ve shown that TUS for 15 or 30 seconds at 150 mW/cm² to right fronto-temporal cortex results in 30 to 40 minutes of mood enhancement (as measured by Visual Analogue Mood Scales, VAMS, and Global Affect scores). EEG recordings showed increased gamma activity near the TUS site, and no change in EEG activity over the contralateral hemisphere. Additionally, for some participants, TUS at the vertex, which targeted the anterior cingulate cortex, resulted in anecdotal ‘out-of-body experience’ and uncontrolled laughter. These studies suggest the promise of TUS for successfully treating depression and other psychiatric disorders. Moreover, recent studies showed that TUS improves Alzheimer’s symptoms and pathology in animal models, suggesting the merit of human trials. The mechanism by which TUS might alter conscious mood, or enhance cognition is unknown, as are mechanisms for TMS, TDCS and TACS. It may be noted that microtubules, composed of tubulin, the brain’s most prevalent protein, and major components of the neuronal cytoskeleton (which destabilize in Alzheimer’s) have electro-mechanical resonances in megahertz. Functional vibrations of microtubules may be important for consciousness and cognition, and a therapeutic target for TUS. With a new device, the ‘NeuroResonator’ (Berkeley Ultrasound) we plan clinical studies of TUS effects on depression, Alzheimer’s, traumatic brain injury, post-traumatic stress disorders and emergence from anesthesia.

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The treatment of mental and cognitive disorders can be approached through non-invasive brain stimulation techniques including transcranial magnetic stimulation (TMS), transcranial direct current stimulation (TDCS), transcranial alternating current stimulation (TACS) and transcranial ultrasound (TUS).
Ultrasound (US) consists of mechanical vibrations, e.g. in megahertz (MHz), used in medical imaging and therapy for nearly a century. Unlike other modalities, TUS can be focused, and penetrates through (rather than around) the brain. At low doses (FDA: < 750 mW/cm$^2$) and brief durations, TUS is safe and painless. Recent studies show TUS improves Alzheimer’s memory dysfunction in animals, and enhances mood and cognition in humans.

Using a General Electric ultrasound imaging device, our group (Hameroff et al, 2013) published the first human (double blind) TUS study on mental states. With subsequent studies using a commercial device (U+, Thync), we (Sanguinetti et al., 2015) have shown that 15 to 30 seconds of low intensity (< 150 mW/cm$^2$) TUS at 0.5 MHz or 2 MHz results in 30 to 40 minutes of mood enhancement (Visual Analogue Mood Scales ‘VAMS’, and Global Affect scores). In vitro, ultrasound promotes neuronal growth and stabilizes microtubule disassembly, possibly by MHz resonance in microtubules. TUS is safe and painless when transmitted at non-thermal intensities, and may be beneficial for mental states and cognitive function in brain injury, Alzheimer’s, post-traumatic stress disorders, depression, coma, pediatric developmental delay and meditation. We plan such studies with the ‘NeuroResonator’, a new TUS device from Berkeley Ultrasound.

The NeuroResonator is specifically designed to modulate human mental and cognitive states and disorders at non-thermal ultrasound intensities. It has two output transducers whose ultrasound parameters can be regulated through a convenient user interface. Placement on various locations on the scalp with an external headset strap allows TUS at one or two locations at various settings (frequency, pulse modulation, duration). Generally we use 0.5 MHz to right fronto-temporal scalp for mood enhancement, but in preliminary, as-yet-unpublished results, other sites have been shown safe at sub-thermal exposures. The NeuroResonator can also drive transcranial alternating current stimulation (tACS), another promising approach for neuromodulation.

The parameter spaces for TUS and tACS, especially in relation to particular clinical situations are vast. With the NeuroResonator we are seeking collaborative researchers to safely explore these parameters for various clinical situations. The device is based on Open Source software that allows lightly trained users to modify the existing device for specific needs.

While mechanisms for effects of TMS, tDCS and tACS are unknown, TUS is thought to act via mechanical action on neurons, and specifically on cytoskeletal structures and dynamics inside brain neurons, e.g. MHz resonances in microtubules. We believe TUS offers unique opportunities to repair neurons, regulate synapses, improve cognition and optimize mood and mental states.

As animal studies have shown TUS improves Alzheimer’s symptoms and pathology, we envision TUS treatment in humans of Alzheimer’s disease (in which microtubules are disrupted), traumatic brain injury, pediatric developmental delay, coma, PTSD, mood disorders and in meditation.

We invite TSC 2015 conference participants to try the NeuroResonator, e.g. for mood enhancement, at our conference demo booth.

References


- Indian physicists find signatures of hidden information-processing network G.S. Mudur