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Transcranial multifocal acoustic holograms

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Background: Focused ultrasound have shown great efficacy in the treatment of many neurological disorders. Through thermal ablation of thalamic and subthalamic areas, treatments have been developed for essential tremor, Parkinson's disease or chronic pain, while at moderate intensity they are used for neuromodulation or blood-brain barrier opening to deliver drugs in a safe and localized manner.However,focusing therapeutic ultrasound into the central nervous system has been limited by two major drawbacks: the aberrant and attenuating effects of the skull and the large mismatch between the volume of the brain structure to be treated and the volume of the ultrasonic beam focus, which forces multiple sonications to cover the desired area. In addition, current technology does not allow the simultaneous sonification of two or more spatially separated volumes.In this work, we present a method based on 3D-printed acoustic holograms to generate multifocal ultrasound beams which match the target structures.

Materials and Methods: Holograms were designed to cover bilateral targets in one single sonication, while minimizing the acoustic field outside. Three experiments were performed, each one corresponding to a different bilateral target: left-and-right hippocampi, putamen, and caudate nuclei, as sketched in Fig. 1(a). The volume of each bilateral target was segmented from MRI images. Then, time-reversal simulations were performed from the selected targets inside the skull towards the location of the ultrasound transducer using CT images of an ex-vivo human skull and pseudo-spectral time-domain methods. The holographic information at 500 kHz was recorded at source location and a phase-only lens based on Fabry-Perot resonators was designed using phase-conjugation methods. The holographic lenses were manufactured with resin photopolymer (FLGPCL04, Formlabs) using stereolithography with a resolution of 50 μm (Form2, Formlabs). The lenses were adapted to a custom 500-kHz piezoelectric focused transducer with an aperture of 100 mm and a focal length of 140 mm. The acoustic field was measured inside an ex-vivo human skull using a needle hydrophone with an active diameter of 500 μm (HNR-500, Onda) and a 3D stepper motor (L-511 PI GmbH) to move the hydrophone using a step of 0.1 mm. A 3D printed support with columns matching the surface of the skull was manufactured to guarantee the relative location between the lens and the skull, as show in Fig. 1(b).

Results: First, left-and-right hippocampi is selected as therapeutic targets, Fig. 2(a). First, left-and-right hippocampi is selected as therapeutic targets, Fig. 2(a). The acoustic field measured experimentally agrees with theory and simulations both in water and considering the skull. The segmented volume of the target is 22.84 mm3. The total sonicated volume, defined as the volume were the pressure is higher than half the peak pressure, is 5.05 mm3, corresponding to 22 % of the selected target volume. Similar results are observed when targeting at putamen, Fig. 2(b), with a volume of 14.48 mm3, and where transcranial focusing using holograms covers a volume of 3.4 mm3 (25 % of the target volume). For the caudate nuclei, Fig. 2(c), with a volume of 16.35 mm3, the sonicated volume is 3.85 mm3 (24 % of the target volume). The emitter-lens system is located always located at center of the parietal-occipital area, demonstrating the steering capabilities of transcranial holograms.

Conclusions: Using acoustic holograms coupled to ultrasonic transducers the shape of the acoustic field can be adapted to complex therapeutic targets in a simple and robust manner. Acoustic holograms compensate the aberrations of the wavefront produced by the skull while, simultaneously, allow bilateral sonications whose acoustic field fits to deep-brain structures such hippocampi, putamen or caudate nuclei. In this work, numerical and experimental results show that more than 20 % of the volume of bilateral targets inside the brain can be covered with a single configuration. Furthermore, the steering capabilities of the acoustic holograms have been demonstrated by focusing at three different structures using one single transducer-skull position.

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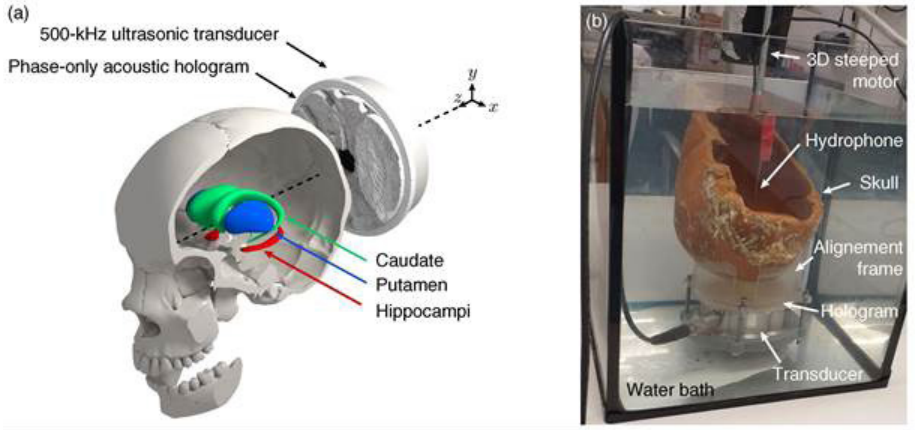


Figure 1. (a) Diagram of the CNS organs to be treated within of the skull and the location of the transducer with the lens to focus the putamen. (b) Experimental setup for the acoustic field measurement.

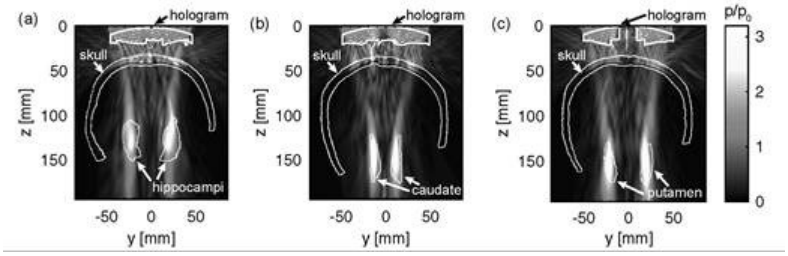


Figure 2. (a) Acoustic field focused at both hippocampi simultaneously. (b) Acoustic field focused at both caudate nuclei. (c) Acoustic field focused at both putamen nuclei.