Observing Diffusion-Weighted Imaging with Short Term Neuron Activity after Transcranial Focused-Ultrasound Induced Blood-Brain Barrier Opening in Small Animal

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Target Audience: This property would fit the need for who involve in neurophysiological, neuromodulation, or blood-brain barrier issues.

Purpose: Focused ultrasound (FUS) with the presence of microbubbles has been confirmed to be able to induce blood-brain barrier (BBB) opening.[1] Magnetic resonance imaging currently serves as a useful tool to monitor the BBB integrity and even excessive FUS energy induced erythrocytes extravasations. However, subtle brain function and anatomical change may not yet been fully explored.[2] This study attempts to employ diffusion-weighted imaging (DWI) and the neuron activity monitoring to concurrently observe brain anatomical/ functional modulation after FUS-BBB opening.

Methods: Eleven Sprague-Dawley rats under isofluorane anesthesia were sonicated in left S1FL somatosensory cortex (1 mm posterior and 4 mm lateral to the bregma) by using a 400-kHz focused ultrasound in three groups (peak pressure: Group 1: W/O exposure; Group 2: FUS exposure with mechanical index (MI) = 0.5; Group 3: exposure MI = 0.8; burst length = 10 ms, PRF = 1 Hz, duration = 90s) in the presence of MBs (Sonovue, Bracco; 0.025 mL/kg IV injection). Animals were post-operationally monitored by using a 7.0-T MR imager (ClinScan 70/30 USR, Bruker). ADC maps were computed from DWIs which were obtained from the diffusion weighted RARE in 12-direction: TR/ TE = 2500 ms/21.6 ms, slide thickness = 1 mm; matrix = 128×128; b = 1000 secs/mm^2. Other twenty SD rats were induced to characterize its FUS-induced brain activity suppression/ recovery by observing the time course of somatosensory evoked potential (SSEP). Both groups were observed in 1hr and 2-day post-FUS.

Results: Results showed that process of BBB opening indeed transiently modulate brain perfusion (ADC) and neuronal activity (SSEP) change at the exposure site. Low FUS exposure successfully induced BBB-opening and also induced transient ADC value reduction as well as SSEP suppression. In high FUS exposure, a more profound ADC value reduction was noticed and the recovery duration was prolonged, indicating the water diffused significantly in BBB opening site (Fig. 2). Also, the SSEP magnitude and latency representing neuron activity showed more profound suppression in high FUS exposure level, and the recovery dynamics was observed to be slower than ADC recovery. The lower energy exposure made less dropping of ADC value and the amplitude of SSEP which maintain an unchanged latency in time course recovered in 2 days (Fig. 3, 4).

Discussion: We infer that the BBB-opening decreased the oxygenated blood supply because of the temporal edema [3] in the S1FL area under the both FUS exposure level. Such effects caused the neuron could not work because of the chaos of neurotransmitters in sodium channel.

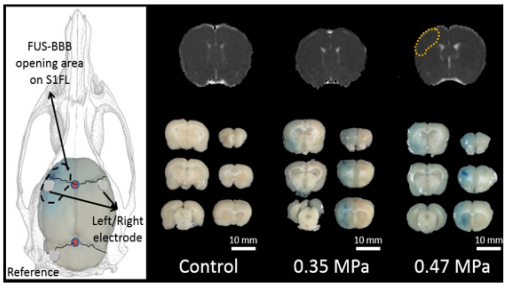

Fig. 1

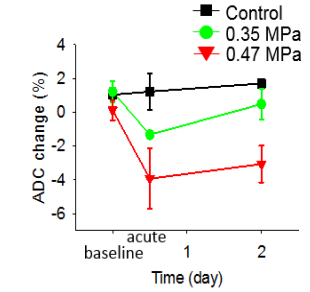

Fig. 2

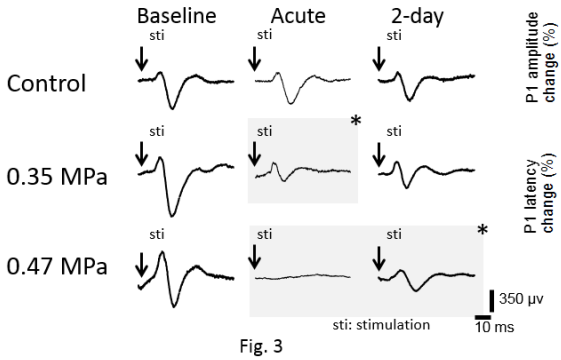

Fig. 3

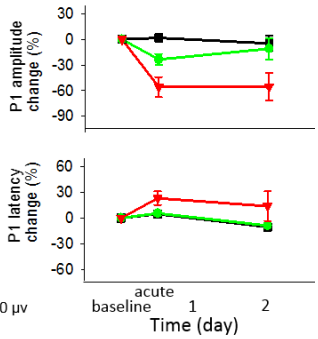

Fig. 4

Conclusion: This study provides observation of brain water diffusion change during FUS-BBB opening process, and first provide evidence showing this CNS intervention may also have potential in modulating local neuron activity. Detail correlations and mechanism between water diffusion/neuron activity modulations with FUS-BBB opening should be further investigated.

Conflict of Interests: The authors declare that there is no conflict of interests.

Reference:

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Figure 1: Left: The position of the electrodes relative the skull marker (Bregma and Lambda) of the animal
Right: Representative Evans Blue dye stained brain sections after FUS-induced BBB disruption and corresponding ADC map.

Figure 2: Comparison of ADC changes between the experiment and control S1FL area under various acoustic pressure FUSs in long term.

Figure 3: Long term changes of SSEPs waveforms of experiment S1FL

Figure 4: Long term changes of positive wave of SSEPs in experiment S1FL