Transcranial FUS-Evoked Functional Imaging in Non-Human Primates

Introduction

Focused Ultrasound Stimulation(FUS) has emerged as a promising noninvasive technique for modulating brain activity and the neurovascular unit. Combining transcranial FUS with functional ultrasound imaging (fUSI) enables simultaneous, noninvasive neuromodulation and real-time monitoring of its effects. In this study, we demonstrate the feasibility of fully transcranial FUS-fUSI in non-human primates (NHPs).

Methods

Transcranial FUS-fUSI was performed in anesthetized male macaques (10-14 yrs 2 Cynomolgus, 1 Rhesus , multiple sessions). A 0.5 MHz FUS transducer (z = 2.5cm focal peak, a.ii) and broadband imaging transducer were coaxially aligned and positioned over the skull to deliver 250 ms amplitude modulated FUS pulse trains followed by high frame rate Doppler imaging (800 Hz) at 1 Hz prf. FUS stimulation duration (5-30 s), pulse duration (50-250 ms) and pressure were varied (0.97-1.81 MPa). Post-stimulation microbubble injection followed by contrast enhanced Power Doppler (CEPD) and Ultrasound Localization Microscopy (ULM) enabled visualization and registration as well as validation of underlying vasculature. Next, cross-correlation with canonical hemodynamic response function followed by a Bonferroni correction was used to extract regions of activation. Correlation maps were overlaid on CEPD images and cerebral blood volume (CBV) traces over time were plotted for different stimulation parameters at vascular regions of interest (ROIs).

Results and Discussion

Hemodynamic changes were increased with pressure in vasculature located at and surrounding the FUS focal region (a.ii–iv). Across ROIs both the number of activated CEPD pixels (1782-4682) (a. ii-iv; d. i,ii) and the percent change in CBV increased with higher acoustic pressures (up to 7.5% - b) and longer stimulus durations (up to 8.2% - c). Peak duration and area under the curve (AUC) also scaled proportionally with FUS pulse duration (c). Notably, distinct regions of negative and positively correlated pixles could be separately mapped to different vascular compartments identified in the ULM maps (a.v). These findings indicate that transcranial fUSI is feasible in primates during transcranial FUS with the latter capable of reliably driving functional hemodynamic changes in the targeted regions, opening new directions for translational ultrasound guidance of neuromodulation and neuroimaging.