

Supplementary figure captions

Figure S1: **(A)** Experimental setup. **(B)** Beam steering pattern used during volumetric sonication. The order of the nine “subsonications” is indicated. **(C)** Pulsing scheme used during volumetric sonication. Three 50 s sonifications were delivered with a 25 s pause between sonifications. During each sonication, 10 ms bursts were delivered to the nine locations in sequence, typically every 200 ms.

Figure S2: Histology after volumetric sonication in the hippocampus/LGN in monkey 4. This target was sonicated ~2h before the animal was sacrificed and in seven prior sessions over several months. **(A)** Contrast-enhanced T1-weighted MRI showing BBB disruption. The region with contrast enhancement is indicated (red dotted line). Inset: Low-magnification microphotograph showing histology in the hippocampus/LGN. The approximate location of this section is indicated in the MR image by the white rectangle. **(B)** Low- and **(C)** high-magnification views of the LGN showing normal cell layers and undamaged nerve fibers, respectively. **(D)** Low and **(E)** high-magnification views showing normal-appearing granular cell layer of hippocampus. **(F)**: Small capillaries in the LGN found with a few extravasated red blood cells, presumably from the last sonication session. Only a very small number of such extravasations were found. (**B, F:** H&E; **C:** H&E-LFB **D, E:** Nissl; scale bars: **A:** 1 cm, **B, D:** 1 mm, **C,E-F:** 200 μ m)

Figure S3: MRI and histological effects of sonication delivered at an exposure level that produced tissue damage in addition to BBB disruption. **(A)** T2*-weighted imaging after volumetric sonication (nine locations in a 3×3 grid) in the thalamus at 249 kPa. At three of the nine sonicated locations, severe hypointense spots were observed in T2*-weighted imaging, and they were persistent for the next six months **(B)** Microphotograph of an H&E stained section showing parenchymal damage (box) evident six months after sonication. Macrophage accumulation and scattered brownish granules (hemosiderin deposits, arrows) are also evident. **(C-D)** High-magnification view of hemosiderin deposits from another part of this sonicated region. Prussian blue staining (**D**) was used to verify that the light brown clusters evident in H&E were hemosiderin (**B-C:** H&E; **D:** Prussian blue; scale bars: **B:** 100 μ m; **C-D:** 20 μ m)