Noninvasive, ultrasonic cerebrospinal fluid clearance to treat brain injuries

Researchers in the Airan Lab have developed a noninvasive method using low intensity transcranial ultrasound to drive cerebrospinal fluid (CSF) glymphatic and lymphatic flow to clear brain injury waste products from CSF and brain interstitium. Unlike other approaches, this method is nonpharmacologic; free of exogenous agents such as nanoparticles or microbubbles; requires no sensory stimulation nor a specific neural activity pattern; and can be applied when the patient is awake, asleep, or semi-conscious. In mouse models, the ultrasonic CSF clearance (UCC) treatment reduced neuroinflammatory and neuro cytotoxic profiles, improved behavioral outcomes, and increased acute brain injury survival. Effective, noninvasive and versatile, the UCC treatment could be a pivotal tool in treating hemorrhagic, ischemic or traumatic brain injury; migraines; neurodegeneration; intracranial hypertension, normal pressure hydrocephalus; and other chronic brain diseases.

Stage of Development: Proof of Concept

Under funding from Corundum Neurosciences and the Focused Ultrasound Foundation, the Airan Lab is actively designing a prototype device to facilitate UCC treatment protocol in a human trial.

Applications

- Transcranial focused ultrasound treatments for:
 - Hemorrhagic, ischemic, traumatic, and tumor-induced brain injuries
 - Edema, intracranial hypertension, hydrocephalus, and intracranial pressure elevation
 - Autoimmune or infectious encephalitis
 - Migraines, headaches, and concussion

 Epilepsy, sleep and circadian rhythm disorders, and other chronic brain diseases

Advantages

- Noninvasive and nonintrusive can be applied in the awake, asleep, or obtunded patient
- Nonpharmacologic, free of pharmacologic side effects, and free of exogenous agents (e.g. nanoparticles, microbubbles, etc.)
- Effective reduces neuroinflammatory and neuro cytotoxic profiles, improves behavioral outcomes, decreases morbidity and, increases survival for acute brain injury
- Broadly applicable to treat various brain diseases

Publications

• Azadian, M. M., Macedo, N., Yu, B. J., Fame, R. M., & Airan, R. (2024). <u>Ultrasonic</u> <u>cerebrospinal fluid clearance improves outcomes in hemorrhagic brain injury</u> <u>models</u>. *bioRxiv*, 2024-06.

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