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MRI-guided Focused Ultrasound Neuromodulation, Review Article

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A B S T R A C T

MRI-guided Low Intensity Focused Ultrasound is superior to other minimally invasive neuromodulation procedures in terms of spatial resolution and activating deeper brain areas. Parkinson's, Alzheimer's, essential tremor, brain cancer, epilepsy, nerve block, medicine administration, and stroke benefit from MRI-guided LFUS. This minimally invasive neurostimulation approach is also safe . Future clinical trials should focus on Focused Ultrasound for neurologic diseases.

MRI-guided Low Intensity Focused Ultrasound is a new modality for performing incision-less neurosurgical procedures such as thermoablation. According to emerging evidence, low-intensity can also be used for neuromodulation with several advantages, including high spatial precision and targeting deep brain regions. We review the existing data on the biological mechanisms of MRI-guided Focused Ultrasound, neuronal activity emerging indications for neuromodulation, and the strengths and limitations of this approach.

Keywords:Low intensity; High intensity; Focused; Ultrasound; MRI-guided; Neurology

1. Background

Ultrasound is widely used in medical diagnostic and therapeutic procedures. Images of internal organs are provided by the device that generates and records ultrasound waves. A focused ultrasound beam is used in urology to disintegrate kidney stones. Ultrasound is used in ophthalmology for cataract surgery via phacoemulsification. Ultrasound is also used in physical therapy and medical rehabilitation.

The mechanical power of ultrasound is a distinguishing feature that can be altered in various ways. The ultrasonic pulse's intensity, frequency, duration, and shape can all be changed. In ultrasound therapy, three mechanisms (thermal, stress, and cavitation) must be considered. Each of these non-linear physical processes is important in sonication treatment, which uses ultrasonic pulses to destroy targeted tissue.

The main advantage of the method, which does not require anesthesia and provides incisionless treatment through the intact skull, is its non-invasiveness. The procedure is distinguished by high precision imaging, excellent tissue differentiation (intraoperative MR guidance allows for 1 mm accuracy in targeted location), and safety (real-time thermal and procedural monitoring). The procedure is painless and can be performed without the need for hospitalization. It has an immediate therapeutic effect and allows for a quick return to normal activities. The procedure has a low risk of complications (no risk of infection, blood loss, shift of brain structures or allergic reactions). It contains no ionizing radiation and can thus be repeated as needed. The method's efficacy has been clinically proven (1).

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Novel diagnostic applications of ultrasonography include the diagnosis of carpal tunnel syndrome during pregnancy with good acuity(2), Optic nerve ultrasound for early diagnosis of optic neuritis in multiple sclerosis(3), using Optic nerve sheath diameter as a predictive parameter of ischemic stroke outcome (4), measuring the geometrics of brain structure with clinical importance(5, 6), and Doppler ultrasonography as an alternative diagnostic tool.(7) Sometimes, MRI could be different order of manual neuro-inflammation disease, like ankylosing spondylitis and pain (8).

MRI-guided Low Intensity Focused Ultrasound is a new modality for performing incision-less neurosurgical procedures such as thermoablation. According to emerging evidence, low-intensity can also be used for neuromodulation with several advantages, including high spatial precision and targeting deep brain regions. We review the existing data on the biological mechanisms of MRI-guided Focused Ultrasound, neuronal activity emerging indications for neuromodulation, and the strengths and limitations of this approach.. Neurostimulation and Neuromodulation are less invasive. tDCS(9), rTMS(10), and wave-based neuromodulation are examples. Neuromodulation is a new neuroplasticity approach with potential for neurodegenerative and neuroinflammatory illnesses [11].Neuromodulation's processes include electromagnetic field, gene expression change, microglial inhibition, neuroregeneration, and plasticity induction [12].

FDA approves Low-Intensity Focused Ultrasound's safety profile (FDA). It's a minimally invasive approach for neurologic diseases (11, 12).This unique treatment method has modest neurological side effects . Mild to moderate adverse effects by Low Intensity Focused Ultrasound included neck pain and sleepiness (most common), problems with attention, muscle twitches, anxiety, scalp tingling, and transient headache without any life-threatening severe adverse effects (13).Most studies imply LIFU ultrasound is safe (14).Transcortical Low-Intensity Focused Ultrasound side effects vary by brain region (15).Low-Intensity Focused Ultrasound may stimulate deep brain nuclei, cortical, and peripheral neurons by mechanically pressurizing cellular membrane ion channels (16).LIFUS can improve diabetic neuropathy (17).

LIFUS can inhibit, stimulate, or ablate tissue depending on stimulation conditions. Focused Ultrasound has a higher spatial resolution and can stimulate deeper brain structures than non-invasive electric or magnetic(18, 19) brain stimulation. MRI-guided Low Intensity Focused Ultrasound is a neuroprotective minimally-invasive therapeutic approach with implications for a wide range of neurological disorders (e.g., essential tremor, neuropathies, Parkinson associated and essential tremors, brain tumors, etc.)(20, 21)

2.Focused Ultrasound (LIFU) in Parkinson's disease

Subthalamotomy and thalamotomy by High-Intensity Focused Ultrasound enhance motor symptoms and lessen tremors in Parkinson's patients. Low-Intensity Focused Ultrasound may cause ipsilateral weakness, ataxia, speech difficulties, and orofacial/finger paresthesia (22, 23).Unilateral thalamotomy by High-Intensity Focused Ultrasound enhanced quality of life and capacity to do daily activities in tremor-dominant Parkinson's disease patients without cognitive-behavioral or mood side effects (24).

When considering Parkinson's medicines, consider quality of life and mental side effects (25). MRI-guided LFUS is non-inferior to DBS in treating parkinsonian tremors (26).No major side effects were recorded one year after Low-Intensity Focused Ultrasound for Parkinson's disease. Simultaneously, tremors and disabilities improved (27). MRI-guided Low-Intensity Focused Ultrasound improves focused hand dystonia (28). Focused Ultrasound thalamotomy reduced MS tremors (29, 30). The effectiveness of image-guided needle tenotomy was superior, compared to alternative treatments for chronic tendinopathy (31).

3.Focused Ultrasound (LIFU) in essential tremor

High-Intensity Focused Ultrasound thalamotomy improved essential tremors .The adverse events included sensory and gait abnormalities (32, 33).Bilateral thalamotomy can improve essential tremors as well as unilateral HIFU (34).Low-Intensity Focused Ultrasound improves essential tremors and patients' quality of life (35, 36).Low Intensity Focused Ultrasound relieves tremors in non-essential tremor patients (37).

MRI-guided Low Intensity Focused Ultrasound modifies blood-brain barrier permeability (38), which may enhance medicine delivery to the hippocampus area in Alzheimer's disease (39, 40). MRI , combined with artificial intelligence, could diagnose and manage Alzheimer's disease with better quality (41). Concentrating ultrasonography may reduce B-amyloid plaques in the hippocampus (42).Low Intensity Focused Ultrasound affects brain glucose metabolism to enhance Alzheimer's cognition (43).Low Intensity Focused Ultrasound targeting the hippocampus or substantia nigra improves neurodegenerative dementia in 62.5% of patients independent of therapy . Fine and gross motor skills also improved in degenerative situations (44).

4.High-Intensity Low Intensity Focused Ultrasound (HIFU) for medication delivery

MRI-guided Low-Intensity Focused Ultrasound improved Trastuzumab administration to Her2-positive brain-metastatic breast cancer cells (45).Non-Low Intensity Focused Ultrasound and microbubble medication delivery have been beneficial (46).In an investigation, low-Intensity Focused Ultrasound enhanced gene vector transport to the brain, indicating future implications for clinical trials of CNS gene therapy (47). Low-Intensity Focused Ultrasound improves medicine delivery to Parkinson's patients (48). Low-Intensity Focused Ultrasound increases immunotherapeutic agent trafficking to the brain to treat brain cancers (49). Low-intensity focused Ultrasound is also effective for cancer/chemotherapy-related neuropathy (50).

5.Low intensity Low Intensity Focused Ultrasound (LIFU) for Ischemic Stroke

Stroke ranks sixth in mortality and disability in the U.S.A million people a year have ischemic CNS episodes (51). Low-Intensity Focused Ultrasound may stimulate brain cells . Low-Intensity Focused Ultrasound induces neuronal function in ischemic stroke experimental models, decreases recurrence, and induces neuronal repair, neuro-angiogenesis, and neuroplasticity when provided rapidly (less than an hour) after ischemic stroke .In rat stroke models, LPFU promotes brain-derived neurotrophic factors and inhibits recurrence (52).Deep cerebellar Low-Intensity Focused Ultrasound restored interhemispheric balance after ischemic stroke (53).Low-intensity focused Ultrasound reduced the apparent diffusion coefficient in rat stroke models (ADC). Its effectiveness relies on how quickly an ischemia episode is treated. More improvement happens with earlier therapy. ADC assesses cerebral water diffusion in diffusion-weighted imaging (DWI).It determines ischemic lesion extension and tissue damage (54, 55).Low-Intensity Focused Ultrasound decreased brain edema, reduced neuroimmune response in the infarct core and penumbra, and enhanced Purkinje cell survival in rat models of middle cerebral artery stroke (56).It also shows the neuroprotective impact of LFUS .

MRI-guided LIFU on the brain improves stroke recovery. MRI-guided LIFU can be used both acutely and in several sessions following AIS to reduce stroke load by increasing perfusion to the major ischemic region and penumbra (57). Low-Intensity Focused Ultrasound enhanced rTPA thrombolysis in rat carotid artery thrombosis.In carotid thrombosis, low-intensity focused Ultrasound enhanced rTPA reperfusion (58).

6.Other neurologic disorders

Low-intensity Focused ultrasound ablates brain seizure foci. It might cure epilepsy . Drug-resistant epilepsy patients can safely receive focused Ultrasound (59). Focused Ultrasound can relieve chronic pain by targeting the pain circuit, thalamus, anterior cingulate cortex, and ventral striatum/internal capsule (60).Focused Ultrasound may assist alleviate peripheral sensory problems (61). To investigate glenoid labral lesions, direct magnetic resonance arthrography (MRA) of the shoulder is considered the "preoperative" diagnostic modality of choice (41).

Deep brain stimulation and lesioning procedures like stereotactic radiosurgery targeting mainly the somatosensory thalamic pain circuits yielded mixed results.

The ability to impact the affective domain of chronic pain received increased attention and a renaissance of deep brain stimulation for chronic pain treating the affective sphere of pain. Incisionless techniques like magnetic resonance-guided focused Ultrasound exhibited promising results and offered additional therapeutic options. Other non-invasive (transcranial magnetic stimulation) and less-invasive cranial (motor cortex stimulation) and spinal neuromodulation (spinal cord stimulation) should be considered before cranial neuromodulation (62).

7.Conclusion

Focused Ultrasound on neuronal structures can stimulate or inhibit neurons, depending on the procedure parameters. This has implications for many neurologic disorders, including Parkinson's disease, Alzheimer's disease, essential tremor, brain malignancy, epilepsy, nerve block, medication delivery, and stroke. Focused Ultrasound has few and mild side effects, with no major side effects.

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