

Transcranial focused ultrasound meets brain–computer interfaces: Emerging applications and future directions

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Brain-computer interfaces (BCIs) establish direct brain-external device communication to restore motor, sensory, and cognitive functions. Traditional invasive BCIs using microelectrode arrays offer high resolution but are limited by surgical risks, foreign body responses, and biocompatibility issues.¹

Transcranial focused ultrasound (tFUS) has emerged as a non-invasive alternative that penetrates the skull and precisely targets deep brain structures. Primarily via mechanical effects such as acoustic radiation force, membrane deformation, and mechanosensitive ion channel activation, with thermal effects negligible at neuromodulation intensities. Unlike electrical stimulation, tFUS reaches subcortical regions without implantation, reducing procedural risks. Recent studies demonstrate reversible, safe modulation of cortical and subcortical areas, supporting tFUS as a novel BCI interface.²

Advances in acoustic modeling, transducer design, and decoding algorithms have improved tFUS targeting and BCI robustness. However, challenges remain in skull aberration correction, real-time artifact-free bidirectional communication, and ethical considerations. This review examines tFUS principles, BCI applications, signal integration, and translational challenges.

BASIC PRINCIPLES OF FOCUSED ULTRASOUND AND NEURAL MODULATION MECHANISMS

Physical properties and neural interactions

tFUS employs low-frequency ultrasound focused into millimeter-scale focal volumes through the intact skull. At BCI neuromodulation intensities ($I_{\text{sppa}} < 10 \text{ W/cm}^2$), neuromodulation arises predominantly from mechanical mechanisms: oscillatory pressure waves induce membrane deformation, activating mechanosensitive ion channels and modulating excitability through ion flux changes. Temperature elevations remain below 0.1°C at these intensities; thermal effects are relevant only at ablative intensities.

Targeting precision and deep brain modulation

tFUS can achieve millimeter-scale focal zones under optimized conditions, offering higher spatial specificity than conventional non-invasive electrical or magnetic stimulation. Skull-induced aberrations are mitigated by CT-based correction, though in-vivo validation remains limited.

Unlike optogenetics requiring genetic manipulation, tFUS offers non-genetic, transcranial stimulation without ionizing radiation, enabling selective engagement of discrete nuclei.³

Temporal dynamics and reversibility

tFUS produces rapid onset and reversible effects post-stimulation. Pulsed tFUS typically excites, while continuous/higher-intensity pulses inhibit, though inter-individual variability is notable.

TYPES OF TRANSCRANIAL FOCUSED ULTRASOUND APPLICATIONS IN BRAIN-COMPUTER INTERFACES

tFUS-based motor intention decoding

tFUS modulates motor area excitability, influencing intention decoding. In non-human primates (NHP), tFUS has been shown to modulate motor-related neural activity and support decoding of motor intentions when combined with neural signal recording devices.³

When combined with EEG or other neural signal recording devices, tFUS can enhance BCI classification. For example, tFUS targeting V5 has been shown to reduce visual motion BCI error rates.⁴ tFUS alters EEG signatures, such as ERP amplitudes and mu/beta oscillatory power changes, as well as

fNIRS hemodynamic responses. These complementary signals can serve as decoding features extracted via time-frequency analysis, supporting a causal relationship between stimulation and improved decoding. Closed-loop integration creates adaptive BCIs, and the transcranial approach offers safer alternatives to cortical implants.

tFUS-mediated sensory feedback BCIs

Proof of concept human studies suggest that tFUS may enable artificial somatosensory feedback by targeting the primary somatosensory cortex, evoking tactile sensations non-invasively to potentially enhance neuroprosthetic embodiment and control precision. Human studies demonstrate that tFUS elicits localized tactile percepts with anatomical specificity up to a single finger, and evokes sonication-specific EEG potentials.

Combining tFUS feedback with EMG creates bidirectional closed-loop systems, improving immersion through synchronized percepts. The transcranial approach avoids infection risks of invasive prostheses. Challenges remain in parameter standardization and perceptual reproducibility.⁵

Deep brain region modulation for BCIs

Traditional non-invasive BCIs have limited access to deep brain structures. In rodents, hippocampal tFUS enhances spatial memory in Morris water maze. NHP amygdala tFUS modulates fear conditioning. Early-phase human studies have demonstrated feasibility in deep targets including the thalamus and caudate, and reported clinical improvement in a minimally conscious state patient after thalamic stimulation. tFUS offers reversible deep circuit modulation, though skull attenuation, targeting accuracy, and thermal safety remain key challenges for clinical translation.^{1,5}

SIGNAL DECODING AND SYSTEM INTEGRATION OF tFUS-BCIs

Multimodal signal fusion strategies

Because tFUS itself does not generate decodable electrical signals, tFUS-BCIs must integrate with neural recording modalities such as EEG, fNIRS, or fMRI. These modalities offer complementary readouts: EEG captures neural oscillations with high temporal resolution, while fNIRS and fMRI provide hemodynamic detail with better spatial coverage.

However, multimodal integration faces several challenges. At the system level, precise temporal synchronization, spatial co-registration, and low-latency embedded decoding are required for real-time operation. At the signal level, concurrent tFUS-EEG also introduces unique artifacts from coupling-medium vibration and driver-circuit electromagnetic interference, which differ from conventional ocular and muscular artifacts. While independent component analysis can separate standard artifacts, it may not fully eliminate tFUS-specific interferences, requiring dedicated mitigation strategies (Figure 1).

Signal processing and decoding algorithms

Support Vector Machine (SVM) and Convolutional Neural Network (CNN) classifiers are commonly used to identify EEG features. Preliminary NHP studies suggest that post-tFUS event-related potential (ERP) amplitude changes may serve as decoding features for motor-related brain-computer interface classification.³ Preprocessing typically includes artifact removal, time-frequency feature extraction, and dimensionality reduction.

Real-time decoding requires $<100 \text{ ms}$ latency. As a future direction, deep learning optimization via pruning, quantization, and knowledge distillation has been proposed for embedded deployment, though no published tFUS-BCI

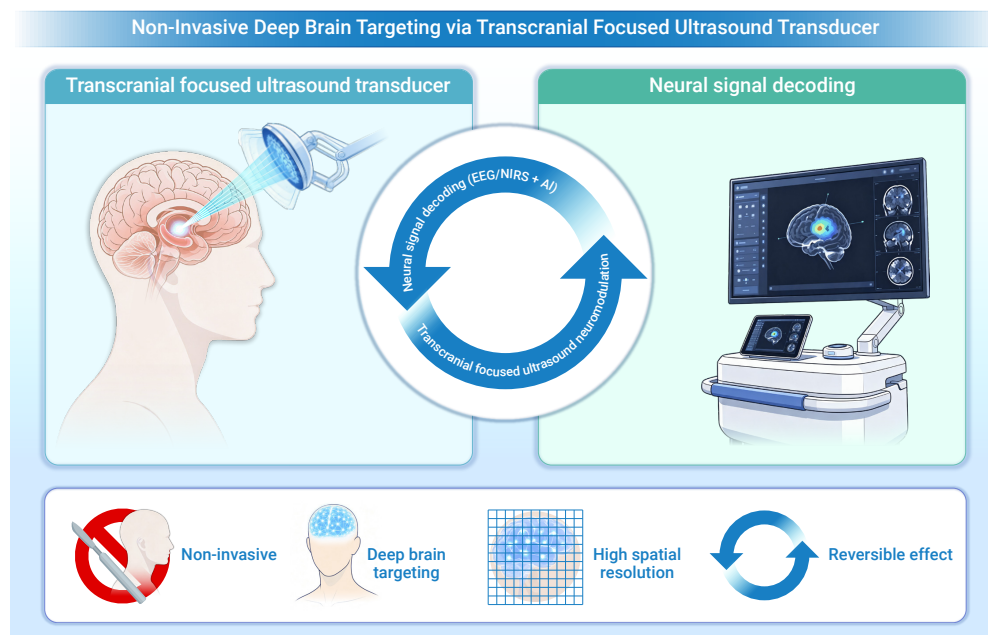


Figure 1. Schematic illustration of the transcranial focused ultrasound mediated brain computer interface system

stimulation duration, and pulse repetition frequency—vary widely across research groups, limiting reproducibility and cross-study comparison.

CONCLUSION

Focused ultrasound represents a transformative BCI modality offering transcranial, deep-targeted, reversible neural interfacing. Its properties confer advantages in motor decoding and sensory feedback, enabling high-precision circuit modulation without blood-brain barrier breach. While challenges in standardization, safety, miniaturization, and clinical validation remain, tFUS-based BCIs represent a promising path toward safer, more adaptable neurotechnology.

study has yet implemented these techniques.

Closed-loop control and adaptive strategies

Closed-loop tFUS-BCIs dynamically adjust parameters based on real-time neural monitoring, maintaining therapeutic windows and preventing over-stimulation.

Reinforcement learning and adaptive filtering enable continuous self-calibration. Rigorous safety validation is required for sensitive region modulation.

ADVANTAGES AND CHALLENGES OF tFUS IN BCIs

Core advantages: Noninvasiveness and high spatial precision

tFUS combines noninvasive transcranial delivery with millimeter-scale spatial precision and deep targeting. Compared with tDCS and TMS, it can reach subcortical structures without craniotomy; compared with invasive DBS, it avoids surgical risks while retaining relatively focal modulation. Dynamic beam control further enables multi-target stimulation, and the non-surgical approach supports repeated or chronic interventions essential for neurorehabilitation.⁵

Major challenges: Safety, standardization, and variability

Clinical translation faces substantial challenges in safety and parameter standardization. Anatomical variability in skull morphology causes differential attenuation, necessitating personalized calibration. Current regulatory intensity limits were established for diagnostic ultrasound and are not directly applicable to therapeutic neuromodulation; dedicated safety limits for low-intensity tFUS neuromodulation remain a regulatory gap. Thresholds for excitatory versus inhibitory paradigms, as well as safe exposure levels for vulnerable populations such as infants and patients with craniocerebral injury, are not yet established. Key parameters—including acoustic pressure, duty cycle,

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AUTHOR CONTRIBUTIONS

F.H. and Y.L. conceptualized the review, performed the literature search, and drafted the manuscript. G.C. critically revised the manuscript for important intellectual content and supervised data extraction. R.H. and J.Z. supervised the project, acquired funding, and critically revised the manuscript. All authors contributed to the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.

DATA AND CODE AVAILABILITY

Not applicable.