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Brief Report

A Nose Towards the Future: Reimagining Deep Brain Stimulation with Deep Focus

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ABSTRACT

Neuromodulation is undergoing a paradigm shift, moving beyond the binary of invasive versus non-invasive interventions. This report describes two emerging techniques, DeepFocus and Vagus Nerve Stimulation (VNS) that exemplify this evolution. DeepFocus, utilizes nasal anatomical access to deliver focal electrical stimulation to deep brain regions implicated in mood and reward, such as Brodmann area 25 and the medial orbitofrontal cortex. Paired with the DeepROAST computational platform for precise current modelling, DeepFocus demonstrates strong, targeted electric fields in cadaveric studies without requiring craniotomy. In contrast, VNS, an approved therapy for epilepsy, depression, and stroke rehabilitation, modulates brain function indirectly via afferent vagal pathways and shows durable clinical benefit, particularly when paired with task-specific rehabilitation. While DeepFocus remains in the preclinical stage, it offers unprecedented deep brain targeting with minimal invasiveness. VNS, though requiring implantation, is already integrated into standard care. These techniques are not mutually exclusive but represent complementary strategies in a growing toolkit of personalized neuromodulation that promise to transform treatment for neurological and psychiatric disorders.

Keywords: Deep brain stimulation, Neuromodulation, DeepFocus, Vagus nerve stimulation, Computational modelling.

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INTRODUCTION

Deep Brain Stimulation (DBS) has long been a mainstay in the treatment of neurological and psychiatric disorders such as Parkinson's disease, treatment-resistant depression, and obsessive-compulsive disorder.[1-3] DBS has remained a mainstay in the treatment of neurological and psychiatric disorders because of its unparalleled ability to deliver precise, adjustable, and continuous modulation of specific brain circuits implicated in disease.[4,5] Unlike pharmacological therapies, which often have systemic side effects and variable efficacy, DBS offers a targeted approach that can be fine-tuned in real-time to meet individual patient needs. Its success in treating movement disorders such as Parkinson's disease where it dramatically reduces motor symptoms and medication reliance has solidified its clinical value.[5] Furthermore, its expanding application to conditions like treatment-resistant depression and obsessive-compulsive disorder has demonstrated that direct electrical modulation of dysfunctional neural networks can yield significant, lasting improvements where other interventions fail.[6] Despite its invasiveness, the predictable efficacy, reversibility, and adaptability of DBS have made it a cornerstone therapy for patients with otherwise refractory conditions. DBS is typically performed by a specialized team led by a functional neurosurgeon, often in collaboration with neurologists, neurophysiologists, and imaging specialists.[7] The procedure involves the surgical implantation of thin electrodes (Figure 1) into specific deep brain targets, such as the subthalamic nucleus or globus pallidus for Parkinson's disease. Using advanced neuroimaging techniques like MRI and CT scans, the surgical team creates a 3D map of the patient's brain to guide precise electrode placement. During the procedure, patients are often kept awake under local anaesthesia to allow real-time neurological assessment as microelectrodes record brain activity and test stimulation is applied. Once the electrodes are optimally positioned, they are connected to a pulse generator implanted in the chest, similar to a pacemaker, which delivers continuous electrical impulses to modulate abnormal neural activity. The system can then be externally programmed and adjusted to optimize therapeutic benefit while minimizing side effects. This intricate, multidisciplinary process reflects the complexity and precision required to safely and effectively implement DBS. While clinically effective, invasive DBS carries significant risks, including bleeding, infection, hardware complications, and a long recovery process. In contrast, non-invasive techniques like Transcranial Electrical Stimulation (TES) offer greater safety and

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ease of use but suffer from a critical limitation: they primarily affect superficial cortical areas and lack the ability to precisely target deep-seated brain regions where many psychiatric and neurological disorders originate.[8]

In a recent study, Guo *et al*., propose a paradigm-shifting approach to this longstanding problem.[9] Their technique, named DeepFocus, introduces a minimally invasive method of delivering electrical stimulation to deep brain structures by exploiting the anatomical access provided through the nasal cavity. Specifically, electrodes are placed under the cribriform plate and within the sphenoid sinus locations that lie in close proximity to the deep structures located at the base of the brain (Basal nuclei, Caudate nucleus, Putamen, Globus pallidus, Subthalamic nucleus, Substantia nigra, Hypothalamus, Amygdala, Nucleus accumbens, Ventral tegmental area, Medial orbitofrontal cortex).[10,11] These are combined with standard scalp electrodes to generate customized electrical fields. Crucially, the DeepFocus pairs this novel physical approach with a computational platform called DeepROAST, which simulates and optimizes current injection patterns using detailed anatomical models that account for the complex geometries and varying conductivities of cranial structures. The predicted benefits reported from this novel approach are striking. In both simulations and cadaver studies, DeepFocus produced stronger and more focal electric fields in several key regions of the brain's reward circuitry, such as the medial orbitofrontal cortex and Brodmann area 25. These regions are known to play essential roles in emotion, decision-making, and mood regulation, and have been implicated in disorders ranging from depression to addiction.[12,13] The ability of DeepFocus to generate neural response-strength fields in these deep structures without the need for open-brain surgery marks a significant step forward in neuromodulation technology.

Vagus nerve stimulation, in contrast, operates through a different mechanism. Traditionally delivered via an implanted device in the chest, VNS targets a peripheral nerve in the neck that, through its afferent pathways, exerts widespread influence across brain circuits.[14,15] Initially approved decades ago for refractory epilepsy and treatment-resistant depression, its reach has now extended. US FDA-approved applications now include chronic migraine and stroke rehabilitation, with a compelling new stroke study showing sustained upper limb recovery one-year post-treatment.[16,17] Here, patients undergoing intensive motor rehabilitation paired with VNS demonstrated durable gains in strength, coordination, and quality of life and these were maintained long-term following a crossover to active VNS. Both VNS and DeepFocus are redefining what it means to be minimally invasive in neuromodulation. DeepFocus trades scalp diffusivity for surgical safety, bypassing implants and opening a fresh anatomical perspective. VNS, while requiring implantation, engages the brain indirectly yet profoundly, offering therapeutic benefits across epilepsy, depression, headache, and motor rehabilitation. Even non-invasive VNS alternatives are gaining momentum, though efficacy remains under critical scrutiny.[18,19] Clinical application-wise, VNS today is already integrated into patient care. For stroke survivors, paired motor rehabilitation and VNS has become an approved treatment with evidence of lasting functional gains. VNS devices are also US FDA-approved for epilepsy and depression and widely used for chronic migraine, with growing interest in inflammatory diseases and for cognitive enhancement.

When compared to currently available tools, DeepFocus occupies a unique and highly promising niche. Invasive DBS systems, such as those developed by Medtronic and Boston Scientific, offer high precision and therapeutic power but require craniotomy and carry all the risks associated with brain surgery.[20,21] On the other end of the spectrum, non-invasive approaches like TES and Transcranial Magnetic Stimulation (TMS) are widely used and carry minimal risk but are fundamentally limited in how deep they can safely and effectively stimulate.[22-24] TES struggles with the diffusion of electrical current through the skull, resulting in weak and poorly targeted stimulation. TMS penetrates slightly deeper, but with less spatial specificity and limited access to subcortical regions. More experimental methods, such as focused ultrasound and temporal interference stimulation, are still in early stages of development and clinical testing, and face hurdles related to safety, scalability, and reproducibility.[25,26] By offering a method that is minimally invasive yet capable of robust and focal stimulation of deep brain areas, DeepFocus represents a compelling middle ground. It maintains the safety and ease of use associated with external devices while significantly expanding the reach and specificity of brain targets.[9] Importantly, this approach opens new doors for the treatment of conditions rooted in the reward and affective circuits of the brain. Disorders such as depression, anxiety, addiction, and chronic pain all linked to dysfunction in deep limbic and prefrontal areas could potentially benefit from a method that modulates these regions more directly and effectively, without the need for implants or surgical intervention.

In its current form, DeepFocus is still in the preclinical stage, and further studies in live human subjects will be essential to establish its safety, tolerability, and therapeutic efficacy. However, the foundational work presented by Guo *et al*.,[9] demonstrates not only technical feasibility but also an elegant fusion of anatomical insight and computational optimization. Their method reflects a broader trend in neuroscience and bioengineering: moving beyond traditional dichotomies of "invasive" versus "non-invasive" toward a new class of precision tools that are both functionally potent and minimally disruptive. The future of brain stimulation may well be defined by approaches like DeepFocus grounded in anatomical realism, powered by simulation, and aimed squarely at previously unreachable therapeutic targets. In this vision, the nose is no longer just an entryway for scent, but a novel corridor to the inner workings of the mind. Guo and colleagues[9] have not merely proposed a new technique; they have extended the boundaries of neuromodulation and introduced a compelling concept that could reshape the field in the years to come.

While DeepFocus offers a promising route for minimally invasive access to deep brain regions, the anatomical approach of placing electrodes under the cribriform plate and within the sphenoid sinus presents several potential clinical challenges. The cribriform plate is a thin, perforated bony structure that separates the nasal cavity from the brain's anterior cranial fossa,[27] and breaching this area raises concerns about cerebrospinal fluid leakage, risk of meningitis, and direct injury to the olfactory bulb, potentially leading to anosmia or altered smell perception. Similarly, accessing the sphenoid sinus[28] a deep, air-filled cavity near critical neurovascular structures such as the optic nerve, internal carotid arteries, and pituitary gland poses risks of inadvertent trauma, infection (sinusitis spreading intracranially), and inflammation. Ensuring sterile technique, precise navigation, and safe fixation of electrodes in these anatomically sensitive zones will be paramount. Moreover, the long-term tolerability of nasal and sinus-based implants, their interaction with mucosal tissue, and the risk of device displacement due to normal physiological processes such as nasal airflow or sinus drainage will require rigorous evaluation. Addressing these potential complications through careful design and clinical trials will be essential before DeepFocus can transition from preclinical promise to routine clinical practice.

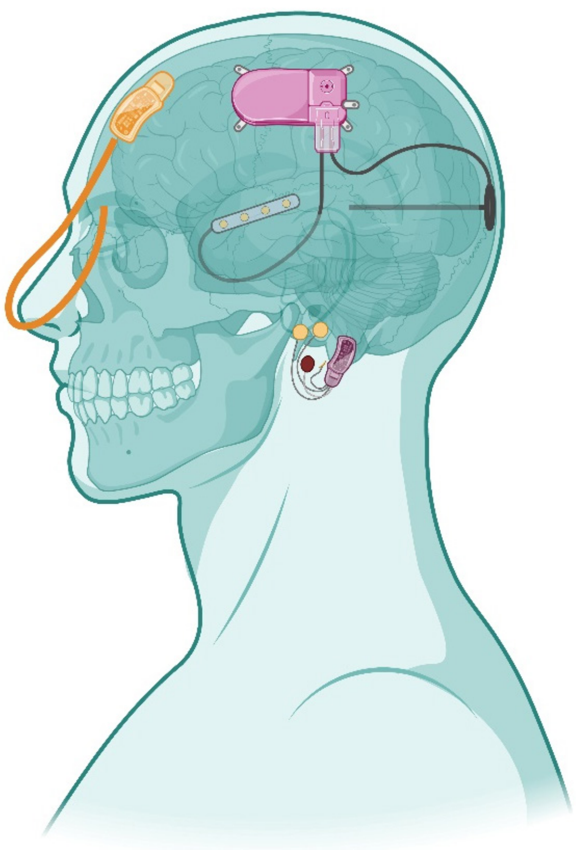

Figure 1: Deep brain stimulation. The image shows electrodes which are surgically implanted in various regions of the brain for targeted stimulations.

While both DeepFocus and VNS represent significant advances in neuromodulation, each approach carries distinct limitations and areas requiring further clinical refinement.[9,18] DeepFocus, though promising in its ability to deliver highly specific stimulation to deep limbic and reward circuits, remains at the preclinical stage. Its anatomical targeting offers a potential advantage for disorders rooted in localized neural dysfunction such as obsessive-compulsive disorder, addiction, or mood regulation yet its reliance on nasal access introduces unique challenges highlighted above. Meanwhile, VNS already approved for several clinical indications requires surgical implantation, with associated risks and post-operative recovery, and while non-invasive alternatives exist, they continue to face questions around efficacy and standardization. Fundamentally, the mechanisms of these techniques differ: VNS induces broad network-level modulation via afferent vagal pathways and neurotransmitter systems, whereas DeepFocus aims for direct, focal electric field displacement.[9,18] These differences imply varying therapeutic profiles, safety considerations, and clinical endpoints. Moving forward, human trials for DeepFocus and improved delivery methods for both technologies will be critical to optimizing their safety, efficacy, and usability in diverse clinical settings.

Despite these distinctions, DeepFocus and VNS represent complementary pillars in a new neuromodulation landscape. VNS already demonstrates real-world clinical impact across a spectrum of disorders. DeepFocus, in contrast, extends a bold experimental projection: that precision targeting of deep brain circuits may one day be achievable without traditional implants or open surgery. As both technologies advance, clinicians and patients will have a richer palette of options from indirect network modulation to direct focal intervention. Together, these methodologies may redefine neuromodulation's narrative from a narrow choice between invasive and superficial, to a more nuanced geometry of access, targeting, and therapeutic insight. In the years ahead, combining approaches or choosing them based on disorder-specific circuitry could mark the evolution of personalized, precision neurotherapy.

CONCLUSION

The landscape of neuromodulation is rapidly evolving, with innovative techniques challenging traditional boundaries between invasive and non-invasive brain stimulation. DeepFocus and VNS represent two distinct yet complementary advancements that broaden the therapeutic horizon for neurological and psychiatric disorders. DeepFocus introduces a novel, anatomically informed approach that enables focal stimulation of deep brain regions via minimally invasive nasal access, offering the potential for precise intervention in circuits traditionally accessible only through open-brain surgery. In contrast, VNS leverages peripheral nerve pathways to exert widespread neuromodulatory effects, with established clinical efficacy in conditions like epilepsy, depression, and stroke recovery. While VNS is already integrated into clinical practice, DeepFocus remains in the preclinical phase, requiring further validation in human trials to assess its safety, tolerability, and efficacy. Nonetheless, both modalities underscore a shift toward safer, more personalized, and circuit-specific neuromodulation strategies. As these technologies continue to mature, their integration or selective application based on disorder-specific circuitry may usher in a new era of precision neurotherapy, where interventions are tailored not only to the disease but to the neural pathways most directly involved in its pathology.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

VNS: Vagus nerve stimulation; **DBS:** Deep brain stimulation; **TES:** transcranial electrical stimulation; **TMS:** Transcranial magnetic stimulation.

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