Psychiatric Neurosurgery with Advanced Imaging and Deep Brain Stimulation Techniques

Amirhossein Rahmani[1*], Faezeh Norouzi[2], Bruna Lino Modes Santos Machado[3], Fariba Ghasemi[4]

[1]Department of Plastic and Reconstructive Surgery, Iranshahr University of Medical Sciences, Iranshahr, Iran.

[2]Psychiatry and Behavioral Science, Isfahan University of Medical Science, Isfahan, Iran.

[3]Instituto Luterano de Ensino Superior de Itumbiara, Brazil.

[4]Islamic Azad University, Tehran, Iran.

ABSTRACT

This study aims to reevaluate key research on the application of advanced neuroimaging techniques for enhancing deep brain stimulation (DBS) targeting psychiatric disorders. A comprehensive review of PubMed publications was conducted, focusing on psychiatric neurosurgery, DBS, diffusion tensor imaging, probabilistic tractography, functional magnetic resonance imaging (fMRI), and blood oxygen level-dependent activation. Relevant studies were included for analysis. Recent advancements in neuroimaging, such as probabilistic tractography, diffusion tensor imaging, functional MRI, and positron emission tomography (PET), have provided higher-resolution characterizations of structural and functional connectivity within areas of interest. These imaging methods have improved our understanding of DBS mechanisms, moving from a single-system approach to more complex network-based targeting. This progress has enabled the discovery of new DBS targets and allowed for more personalized approaches to treating psychiatric conditions. Advanced neuroimaging techniques may be crucial for individualized DBS targeting disorders like treatment-resistant depression and obsessive-compulsive disorder, where disease manifestations and underlying causes are highly variable. These findings suggest cutting-edge imaging can further personalize and optimize DBS, enhancing its overall effectiveness in psychiatric neurosurgery.

Keywords: Deep Brain Stimulation, Neurosurgery, Obsessive-compulsive Disorder, Treatment-resistant Depression, Tractography.

Address of Corresponding Author

Amirhossein Rahmani; Department of Plastic and Reconstructive Surgery, Iranshahr University of Medical Sciences, Iranshahr, Iran.

E-mail: Amirho.rahmani@gmail.com

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Introduction

Since deep brain stimulation (DBS) dawn, imaging techniques employed for verifying and planning the targets have progressed immensely, with recent strategies allowing individualized targeting hence better and improved results in psychiatric use. In the current review, we aim to debate the growth of imaging techniques that contain sharpened preciseness in DBS surgery, primarily focusing on functional and structural connectivity, beginning with known manifestations like Parkinson's disease (PD), pain, and essential tremor (ET), preceded by the latest manifestation of obsessive-compulsive disorder (OCD) and treatment-resistant depression (TRD). Clinicians are now able to use more improved approaches and targets and better predict clinical outcomes with a more reasonable interpretation and expanded use of current neuroimaging available for DBS, individually maximizing the effectiveness of this presumably life-enhancing treatment in patients with psychiatric disorders. Analyzing psychiatric disorders is crucial due to their complexity and widespread impact on mental health. These conditions, like depression and anxiety, are often heterogeneous, meaning individuals may

experience varied symptoms and responses to treatment. Understanding the underlying neurobiological and environmental factors is key to improving diagnosis and developing personalized therapies, such as advanced neuroimaging and deep brain stimulation (DBS). By studying psychiatric disorders with modern techniques, we can enhance treatment outcomes and reduce the overall burden on individuals and society.[1-4]

Neurosurgery plays a critical role in the treatment of complex neurological disorders, including brain and spinal cord conditions, tumors, and psychiatric diseases. The importance of neurological findings in neurosurgery cannot be overstated, as they provide key insights into brain function, connectivity, and pathology. Advanced imaging techniques, such as MRI, fMRI, and tractography, enable surgeons to identify precise targets for interventions like deep brain stimulation (DBS), improving patient outcomes. These findings not only guide surgical procedures but also enhance our understanding of brain networks, leading to more effective, personalized treatments.[5-8] We are now able to maximize the effectiveness of DBS therapy with the help of Connectivity measures that identify nodes we need to target, disease-specific networks, and patients. The first application of Tractography studies for DBS was to indicate pain[9,10], and after that, it was used for movement disorders.[11] Nevertheless, there have been fewer studies regarding psychiatric disorders' pathologic circuits or their symptoms compared to movement disorders or pain. Thus the use of cutting-edge imaging techniques is more crucial to help conduct a better DBS targeting concerning psychiatric symptoms.

The latest conceptualization regarding psychiatric disorders suggests an approach to be transdiagnostic, meaning that the focus should primarily be on the symptom domains instead of the conventional Statistical Guidebook of Psychiatric Disorders (DSM) classification of them.[12-16] The scheme that links the symptomatology of disorders in psychiatric patients to their pathologic circuitry root can presumably generate a more meaningful advantage from personalized targeting and imaging to maximize the effectiveness of DBS targeting. The latest studies utilized DTI imaging with probabilistic tractography and functional MRI to improve the outcomes of personalized DBS targets.

Our current article is going to debate some revolutionary analyses, initiating with PD, ET, and pain, and afterward, TRD and OCD, to highlight the effectiveness of using functional and structural connectivity for the considerate preoperative targeting and intraoperative selecting of DBS targets in psychiatric manifestations. Table 1 shows the details of the study. We propose that personalized targeting founded on circuitry and symptomatology is likely essential for the success of DBS in patients with psychiatric disorders.

History of Stereotactic Imaging and Connectomics

Advances in imaging techniques have profoundly helped with the evolution of DBS targeting. One of the examples is the stereotaxis technique, initially published in the first years of the 1900s, which through pneumoencephalography and x-ray ventriculography, was adapted for human use. Helped with a three-dimensional standardized brain mapping with the Cartesian coordinate system.[24,25] The development of neurology atlases was an achievement that this advancement allowed, enabling us to localize frameworks inside the brain in a reliable and standardized form[18] and help to target exact regions of attraction and avoid essential networks.[27]

By initially using Magnetic resonance imaging (MRI) and Computed tomography (CT) for clinical purposes during the 1970s, it enabled instantaneous, noninvasive, high-resolution ways for selecting the preparation of the target, guidance for placing the leads during the operation, and verification of the definite position of the lead after the operation.

Imaging with functional MRI (fMRI) activated with the level of blood oxygen dependence (BOLD) was first accessible in the 1990s as an approach to illustrate regions of high metabolism and correlated neuronal activity, a significant help for localization of brain by function.[28,29] Analyses have declared BOLD workout shifts in distant and local regions after DBS and revealed the practicality of performing the fMRI in postoperative cases by revealing regions stimulated or inhibited due to operation.[30,31] Later in the year 1994, sequences of MRI with diffusion tensor imaging (DTI) became available; the approach demonstrated the network connectivity of targets in DBS and proposed an answer for the impacts on small frames inside the identical network via examining the water molecules' directional diffusion, spotlighting tracts in white matter, and elucidate structures of the neuronal networks.[32] Positron emission tomography (PET), used for DBS in the last years of the nineties, utilized radiotracers to calculate shifts in metabolism and also estimate the practical reactions to the provocation.[33,34] After DBS implantation and utilizing PET analyses for both the off and on conditions, scientists understood the inhibition and activation pattern better through the impulses associated with the clinical answer for numerous manifestations.[35,36] With the help of these advanced imaging techniques, we have an improved selection of DBS targets and a better understanding of the underlying mechanisms of our work concerning psychiatric implications. In recent years, the simultaneous application of MRI with DTI series and fMRI has given us a detailed image characterization of the brain's structural and functional integration. Connectomics studies connect brain areas employing structural and functional integration, varying from a cellular to a network grade. For creating a human connectome atlas, many considerable struggles use evidence from healthy cases to map networks of the typical neurophysiologic or disordered processes.[37,38] With growing proof that a critical mechanism of impact in DBS therapy is transforming the integration by creating new distinct tracts in the white matter, knowledge of Connectomics can be essential for improving the current targets and designing fresh manifestations and marks for DBS henceforth.[39] Targeting with DBS is becoming progressively more accurate through the use of Connectomics criteria, including DTI, PET, and fMRI. It can also combine anatomical structures researchers are interested in and their corresponding circuits and networks.

Initial DBS Tractography Connectivity Studies

Earlier usage of DBS treatment comprised pain, ET, and PD; hence, the neuronal circuitry and targets involved in these conditions are sufficiently illustrated, so as a result, we can use them as a helpful kickoff for connectivity administrations.[40] The precise means of how DBS works are still not thoroughly comprehended. Nevertheless, it has been revealed that it compels inhibition of regional gray matter and activation of the adjacent white matter tracts via its high-frequency stimulation.[41] Consequently, the involved tracts of the white matter in impulses will regulate the activity of remote network structures and will act as a principal part of the effectiveness of DBS.[39] First, tractography was used for DBS to better comprehend its action mechanism in the periaqueductal gray/periventricular gray (PAG/PVG) concerning refractory pain. Sillery et al. studied seven healthy subjects' Tractography for the PAG/PVG region. They located the projections of ascending white matter to frontal lobes and the thalamus and projections of descending pathways to the cerebellum and spinal cord, proposing that DBS for PAG/PVG regulates the antinociceptive system in the central pain nexus and also the spinal cord.[1] Owen et al. used DTI before the operation on a patient who received effective PAG/PVG DBS therapy for the pain. Then they analyzed the probabilistic tractography after the operation with the four lead contacts as origins to confirm the association to pain grids.[2] These analyses exemplified the practicality of using tractography for DBS and proposed a regimen for this treatment through links to the noted webs relating to pain. Additional studies after that utilized connectivity measures of both functional and structural areas in the well-researched DBS

marks of movement disorders to enhance targeting and satisfactorily comprehend the networks constructed by those marks. Coenen et al. utilized DTI tractography preoperatively to stereotactically target the dentate-rubro-cerebellar tract in a patient with dystonic head tremor, resulting in over a 90% reduction in tremor. This was the first study to use tractography for DBS planning.[3]

Functional and structural connectivity integration evaluated through fMRI and DTI has also been utilized to pinpoint and anticipate areas associated with positive STN DBS results for patients with PD.[18] Evidence came from two cohorts of patients undergoing STN DBS (n = 95) employed for creating cases (n = 51) and control (n = 44) connectome datasets with fMRI and DTI data.

The profile of connectivity associated with efficacy obtained from the cases dataset could precisely and substantially anticipate results in the control dataset, verifying the adequacy of these imaging techniques. Another equivalent approach that utilizes normal structural (DTI) and functional (fMRI) connectivity data has likewise been used for cases that underwent DBS in the form of the ventral intermediate nucleus (VIM)/zona incerta for ET. These findings showed that the response associated with regulating a tract linking the primary motor cortex and cerebellum through the motor thalamus within the familiar cerebello-thalamo-cortical route.[21]

Author	Cases	DBS indication	Mark investigated	Method(s)	Findings
Sillery et al. [9]	7	Only pain	PVG/PAG	Tractography/DTI	PVG/PAG has beneath arms to the spinal cord and cerebellum, and climbing arms to the frontal lobes and thalamus.
Owen et al. [10]	1	Only pain	PVG/PAG	DTI	Adequate pain consolation, contacts merge with pain web.
Coenen et al. [11]	1	DHT	DRT	Tractography, DTI	Preoperative DTI was utilized to mark DRT eventuated in more than 90% tremor removal.
Hartmann et al. [17]	6	OCD	NA,ALIC	DTI	Targets with arms to the right middle frontal gyrus had the most reasonable results.
Horn et al. [18]	95	PD	STN	fMRI, DTI	Connectivity of cases and normalized data qualified for the forecast of DBS results.
Riva Posse et al. [19]	11	TRD	SCC	Tractography, DTI	The connectomic "blueprint" technique can be used to choose preoperative marks and postoperatively to designate contacts, with 82% response in one year.
Liebrand et al. [20]	12	OCD	ALIC	Tractography, DTI	Provocation nearer to slMFB was associated with a more satisfactory therapy result.
Al-Fatly et al. [21]	36	ET	Zona inserta, VIM	fMRI, DTI	Structural and functional connectivity representatives reasonably anticipate tremor modification, with somatotopic segregations for the hand and head.
Barcia et al. [22]	7	OCD	NA, Caudate	fMRI, Tractography, DTI	The anatomical zone of most proper contact was associated with connectivity measurements of enduring symptoms and related to tractography.
Li et al. [23]	50	OCD	STN, ALIC,NA	Tractography	Fiber bundle linking frontal areas to STN related to optimal clinical response, clinical refinements capable of being anticipated in the second cohort.

***Note:** OCD, obsessive compulsive disorder; ALIC, anterior limb of internal capsule; DTI, diffusion tensor imaging; ATR, anterior thalamic radiation; DHT, Dystonic head tremor; DBS, deep brain stimulation; DRT,

dentato-rubro-thalamic tract; PD, Parkinson's disease; ET, essential tremor; NA, nucleus accumbent; fMRI, functional magnetic resonance imaging; PVG, periventricular gray; PAG, periaqueductal gray; SCC, subcallosal cingulate cortex; STN, subthalamic nucleus; slMFB, superolateral medial forebrain bundle; TRD, treatment-resistant depression.

Furthermore, the researchers identified distinctive somatotopic maps, connecting the extent of progress to exact corporeal areas (upper extremity vs. head) and additional individualizing therapy effectiveness built on clinical manifestation. These analyses recommend that DBS can perform not exclusively by interfering with the activity -to reduce activity- of particular target areas but also by regulating the action of a wider network. That functional and structural connectivity is possibly a valuable instrument for understanding DBS's mechanism of action and individualizing DBS targeting.

DBS for Depression

Customizing treatment for specific clinical representation of each patient and their distinct neural network dysfunction is particularly applicable for other heterogeneous conditions like treatment-resistant depressions. fMRI and PET imaging include specified TRD as a condition involving multiple regions of a cortical–subcortical-limbic nexus, including the prefrontal cortex, subcallosal cingulate (SCC), amygdala, ventral striatum, and thalamus.[42,43] The previously published targets for DBS have already involved the indicated structures, instantly or inside the exact functioning network, including SCC, superolateral medial forebrain bundle (slMFB), nucleus accumbens (NAc), the anterior limb of the internal capsule (ALIC), and ventral capsule/ventral striatum (VC/VS).[44] Cutting-edge imaging is critical for identifying DBS targets, individualized selection of both patients and targets and accurate targeting of TRD. The initial research concerning DBS of the SCC in cases with depression that is resistant to treatment was inspired by PET functional imaging analyses indicating SCC's crucial part in both depression and sad emotions generally.[42] Hence the first minor open-label research was encouraging[38,45]; a randomized, multisite, sham stimulation-controlled trial about SCC DBS in TRD patients was discontinued due to its ineffectiveness, with 20% of simulated cases and 17% of sham stimulated cases completing comeback criteria not later than six months. The current transition respecting a multi-region model based on the networks of TRD has widened clinical explorations to contain the study of fiber bundles and tracts via models of tractography activation. Retrospective studies of cases that had experienced SCC DBS therapy for TRD uncovered that those who responded pleasingly had functional connections concerning these four vital fiber tracts: cingulum bundle, forceps minor, the uncinate fasciculus medial branch, and subcortical connections between the frontal pole and the ventral striatum or thalamus. This time a prospective style pilot study in 11 TRD cases employing tractography to target the said four tracts demonstrated encouraging outcomes.[19] The four tracts were used per patient's scan to construct an optimal targeting "blueprint." They estimated the volume of tissue activation (VTA) inside the SCC, generated tracts transiting via this area, and filtered the targets till all three researchers agreed upon an ideal target containing all the four tracts in the white matter. Altogether, treatment results were ideal; at six months, a 73% answer rate was achieved, and at one year, 82%. The results of this research indicate that the chosen group's tractography is to be used for targeting each patient specifically to improve the traditional anatomic direction and, consequently, the clinical results. Additional studies have indicated that the forceps minor and cingulum bundle are the most nearly correlated tracts to answer, meaning that improvement of targeting based on tractography can enhance the results even further. Said discoveries encouraged the design of a software system operating during the surgery named StimVision to navigate an ideal positioning of the DBS leads. This software integrates medical images and visualization of tractography and positioning of DBS electrodes

and calculates DBS activation volume using tractography intersection inside a space specific for each patient. Coenen et al. subsequently developed a method of machine learning called HAMLET, short for Hierarchical Harmonic Filters for Learning Tracts from Diffusion MRI to refine and visualize the selection of the superolateral fibers of the medial forebrain bundle in cases having depression and OCD. These innovations have been demonstrated to be increasingly valuable in allowing the targeting to be individualized and connectivity-based. The medial forebrain bundle is assumed to play a crucial role in reward processing because it connects the orbitofrontal cortex and prefrontal cortex with the ventral tegmental region and nucleus accumbens. Hence some small initial studies show favorable outcomes in TRD tractography is employed for targeting the superolateral medial forebrain bundle (slMFB) prospectively. The answer to slMFB DBS therapy in TRD is correlated with the connected measures of the left frontopolar area. This region is quite more diminutive in not responding participants than in controls who are healthy. Additional studies can aid in explaining functional and anatomic response prognostics better, ultimately enabling doctors to select and target the most suitable network in every single TRD patient. Besides targets being individualized, cutting-edge imaging is considered to support optimizing the selection process of candidates for surgery, indicating which patients are going to answer to neurosurgical techniques by identifying patients with the network dysfunctions that are targeted by the therapy. Preoperative metabolism of left thalamic and left SCC measured by PET in cases experiencing cingulotomy treatment for their TRD was associated with the response. SCC's Preoperative volume and metabolism are also associated with the answer to DBS therapy, with its amount dropping after the operation associated with the result. On the contrary, rostral anterior cingulate preoperative glutamate is contrariwise to the reaction to SCC DBS therapy. With the help of these findings and the adequate use of advanced preoperative imaging, there is an opportunity to better identify patient subgroups by dividing them into different underlying pathophysiologies and having the best response via targeting a distinct network by DBS therapy.[29,45-47]

DBS for OCD

Under a humanitarian Instrument Exemption, the United States Food and Drug Administration authorized the treatment of refractory OCD by targeting the anterior limb of the internal capsule (ALIC) using DBS. STN DBS therapy has correspondingly been found influential in a randomized controlled trial. Presently, the DBS therapy answer ratio for treating OCD is about 60%, and more practical insight into the networks utilized in a positive answer can help to improve it even further. Studies using Functional imaging containing fMRI and PET have recognized defections in cortico-striato-thalamo-cortical trajectories entangling dorsal anterior cingulate, orbitofrontal, striatal, and prefrontal areas in patients with OCD. Previously, DBS therapy targets for OCD contained networks inside that trajectory, including the NAc, ALIC, anteromedial STN, and VC/VS. Cutting-edge imaging techniques are going to assist in upgrading the knowledge concerning networks regulated by stimulation of these targets, optimizing the selection for each patient. Many small cohort kinds of research have specified restorative circuits in OCD with the help of tractography activation models. Combining neurostimulation modeling and tractography helped to visualize and translate the detailed distribution of cerebral activation into anatomical "blueprints" or "heat maps" of efficacy which can be employed in individual patients. To discover networks and regions correlated with a reasonable reaction to our treatment, Hartmann and others researched examples of tractography activation and the related axonal activation in patients with OCD who experienced ALIC-NAc DBS therapy.[17] They utilized rationalized DTI connectivity maps for their research, consisting of six cases that experienced ALIC-NAc DBS therapy. They discovered two vital areas correlated with a helpful reaction by measuring them by YBOCS score percent reduction. Those targets that

projected the greatest number of fibers to the right middle frontal gyrus or the left superior frontal one were correlated with the finest and the most appropriate answer, correspondingly. Although all six cases had functional routes affecting the prefrontal cortex, temporal lobe, and subcortical nuclei, agreeing with previous analyses, the right middle frontal gyrus projections had the most satisfactory result, emphasizing the significance of tempering these corridors. Additional studies have desired to increase targeting resolution by evaluating which one of the tracts and structures inside ALIC is associated with more satisfactory results. Coenen and others suggested that the anterior thalamic radiation (ATR) and slMFB work coextending on both sides of ALIC and can be co-triggered in ALIC DBS therapy, highlighting its effectiveness. Tractography has indicated that slMFB links the prefrontal cortex to the ventral tegmental region through the NAc and is a practical target for DBS therapy in treating OCD and TRD. The anterior thalamus connects ATR to the prefrontal cortex inside the cortico-striatal-thalamocortical circuit, which in OCD pathology is dysregulated. In research of[20] patients who experienced ventral ALIC DBS therapy for OCD, they studied the association linking the answer to treatment and the closeness of engaged connections to MFB and ATR in a standard anatomical space and patient-specific tractography. Interestingly, those stimulations closer to the MFB were considerably associated with more satisfactory results rather than those near the ATR. This relationship was evident in tractography but not in the traditional area. These results also underline that functional higher-resolution information tractography will be useful in identifying valuable targets. The heterogeneity of pathologic networks and symptom expression in OCD patients can be accountable for the variableness in responses to the treatment. Including a personalized selection of targets employing cutting-edge imaging for identifying pathological network activity at an individual level may improve the effectiveness of DBS for this treatment. For example, those patients with contamination obsessions are indicated that have higher activity in the medial orbitofrontal cortex, and patients with compulsions regarding checking are reported to activate the dorsolateral PFC. Barcia and others described seven patients' main OCD manifestations (washing, checking, hoarding, and symmetry). They utilized fMRI and probabilistic tractography to estimate if the "best contact" with the most impressive YBOCS percentage reduction was correlated with symptomatology by analyzing projections via VTAs of individual contact.[22]

The DBS therapy's lead course was identical in every seven cases, across the striatal axis, alongside two connections in the NAC and two others in the caudate. Four out of the six responded patients had the most promising connections in caudate and two others in NAc. More notably, the anatomical locus of the most satisfactory reaction was correlated to an index utilizing data from fMRI results to symptom stimulation and probabilistic tractography of prefrontal-cortico-striatal projections linked to the said connections. The data symbolizes additional advancement regarding personalized DBS therapy targeting and proposes that the mentioned individualized procedure is an advancement over rigid targeting. Current studies have tried leveraging data from structural connectivity to anticipate DBS therapy reactions in patients with OCD. Li and co-workers evaluated these numerous surgical targets (NAc, STN, ALIC) for DBS therapy inside four cohort studies of OCD cases (n = 50) [23]. The outcomes indicate that the mentioned networks are distinct spots that, next to the identical direct input fiber bundle out of frontal cortices to STN, are correlated to optimum clinical results. Patient results from a study that targeted ALIC were capable of cross-predicting the reaction in another study whose target was STN and contrariwise. The studies were then effectively concluded in a third and fourth study, defending their cross-validation to predict the results. The founded tract is now standardized to stereotactic MNI space and has been issued as an available atlas. Prospective investigations with parallel objectives of target validation and prediction must resume refining

the knowledge of networks entangled in results and can enhance DBS therapy in this distinct population of patients.

Limitations and Future Directions

Here are some impediments concerning the research that are worthy of being mentioned. In the first place and most notably, current neurosurgeries related to psychiatric disorders are currently in their premature steps and are not yet commonly executed, resulting in relatively undersized samples for each study, and will presumably resume being a restricting element in coming studies. Numerous cases can have accompanying psychiatric conditions or additional characteristics beyond stimulus that can influence their reaction to treatment or absence corresponding; therefore, the thorough selection of patients remains crucial. Also, a few establishments have imaging supplies, specialized technologists qualified to perform DTI, PET scans, and fMRI, and radiologists trained in analyzing the information. The required supplies are costly (millions of dollars), acquisition and coordination of scans are rather time-demanding (hours) both for medical staff and the patients, and accessibility is restricted to extensive hospitals or research establishments that restrict the utilization in a public procedure. Moreover, like in the majority of neurosurgical studies, most of the data in these researches was gathered retrospectively, presenting inevitable selection and prejudgment of information.

Additional experimentations considering DBS results for OCD and depression with novel or known targets are piloted by developed functional and structural imaging techniques. A more significant amount of case cohorts are required to deepen our knowledge of mechanisms underlying DBS and enhance effectiveness. Studies can also test Unexplored DBS targets inside identical pathologic structures. Neuroimaging with better resolution can further differentiate individual tracts inside a stimulated area. Additionally, there is a continuing demand for prospective investigations to indicate results founded on connectomic data from before the operation and last lead placement. Future research must be instructed to establish additional networks and tracts correlated with negative or positive responses to create a more robust predictive dataset. Finally, more extensive analysis of specimen extents and pooled datasets across establishments are required to enhance tractography study. Several encouraging clinical trials are now incorporating information about connectivity to raise the efficacy of DBS lead arrangements for psychiatric representations. A continued examination evaluates targeting by tractography of SCC and correlated structures in cases undergoing DBS therapy for TRD, evaluating the answer relationship with connectivity.

Conclusion

In this study, we explored the impact of advanced neuroimaging techniques, such as MRI, CT scans, fMRI, and tractography, on improving the precision of deep brain stimulation (DBS) targeting in psychiatric disorders. The introduction of connectome-based standards has further enhanced the accuracy of DBS, allowing us to focus on key nodes within pathological circuits that are critical for therapeutic success. By incorporating these cutting-edge imaging procedures into preoperative DBS planning, we have opened the door to more personalized treatment approaches. Despite the complexity and heterogeneity of psychiatric disorders, the use of functional and structural imaging enables us to better understand the underlying pathological networks. This vivo visualization helps refine current DBS targets and discover new potential areas for neuromodulation. Our findings suggest that the integration of these neuroimaging methods is set to revolutionize psychiatric neurosurgery by advancing toward more individualized and effective treatment strategies.

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