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AI and deep brain stimulation: what have we learned?

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Deep brain stimulation (DBS) is a well-established approach for treating movement disorders such as Parkinson's disease, dystonia and essential tremor. However, the outcomes are variable, and researchers are now exploring artificial intelligence-based strategies to help improve DBS procedures.

Deep brain stimulation (DBS) has been used to treat patients with movement disorders such as essential tremor, Parkinson's disease (PD) and dystonia for more than 20 years. In recent years, the technique has been applied to various brain circuits in an attempt to treat mental health disorders. Most carefully selected patients with movement disorders benefit to some degree from surgery, although the outcomes are highly variable. Many factors contribute to this variability, some of which are inherent to the patient, such as disease characteristics at baseline. However, other factors — for example, those related to precise electrode position and electrical parameters — are potentially modifiable. [AQ1](#) [AQ2](#) [AQ3](#)

Artificial intelligence (AI) is defined as the application of advanced analysis and logic-based techniques, including machine learning, to interpret events and to support, augment and automate decisions and actions. The possibility of using AI to improve DBS protocols is attracting considerable interest; however, such applications are still at an early stage, and their benefits remain to be fully established.

“The possibility of using AI to improve DBS protocols is attracting considerable interest”

The two most explored areas for the use of AI are to facilitate target localization and to select electrical stimulation parameters — two key factors that determine outcomes. The optimal location of the electrodes within the targets area remains a matter for debate. Programming is time consuming, can take several visits and is dependent on the skills and experience of the programmer. In addition, the development of directional electrodes has increased the number of options, making the process more complex. Automated or partly automated programming, using AI based on imaging, electrophysiology and/or clinical data, is now being explored.

AI and DBS target identification

For DBS therapy to be effective, accurate target volume identification and segmentation is required, both for initial targeting of the electrode and for post-operative programming. Traditional atlas-based registration algorithms use anatomical structures defined on an atlas template to segment individual neuroanatomy on MRI scans. Although these techniques can provide reasonable results for large, readily visible structures, they do not fare well for segmenting smaller, less conspicuous nuclei with high individual variability, such as the subthalamic nucleus (STN) — a common DBS target for PD.

The segmentation of deep brain nuclei is an important potential application for AI in DBS. Supervised deep learning applications using convolutional neural networks have demonstrated good performance and rapid inference when trained and tested on large datasets. Deep learning applications such as QuickNAT[1] and FastSurfer[2] show reasonable accuracy in segmenting larger cortical and subcortical structures but are less accurate for small DBS targets. Perhaps the most promising tool is a computer vision deep learning algorithm, U-Net, which is considered to be the current state-of-the-art segmentation architecture[3]. U-Net has shown superiority to other deep learning algorithms such as Hough-CNN when trained and tested on STN segmentations on quantitative susceptibility mapping MRI sequences in healthy individuals[4].

Another application of AI is in image enhancement or ‘quality transfer’. High-quality MRI datasets, for example, from ultra-high-field MRI, have been used to train deep learning algorithms to identify noise, distortion and artefacts in lower-quality MRI datasets, resulting in images with increased resolution and signal-to-noise and contrast-to-noise ratios[5]. This approach allows direct visualization of DBS targets using conventional, clinically available MRI systems with all the image-quality advantages of higher-field research scanners.

An additional potential application of AI is denoising of diffusion MRI or resting-state functional MRI (fMRI) data[6]. These modalities are widely used for studying brain connectivity and the networks that are targeted in DBS and other neuromodulation techniques.

AI and DBS programming

Several groups have developed algorithms to guide or automate DBS programming. Some approaches are based on modelling of the field of stimulation combined with imaging of the contact position. This is a difficult process owing to the complexity of the neural network surrounding the electrodes. In addition, the mechanisms that underlie the effects of DBS are only partly known and are more complex than axonal activation, which has been used in many models. Depending on the complexity of the model, the need for powerful computer processing could be an obstacle.

Some recent models also include clinical data and aim to automatically determine the stimulation settings for optimal target activation without adverse effects[7]. Models focused solely on the combination of electrode position and clinical data related to outcomes and adverse effects have also been proposed in a group of patients, so as to inform a predictive model of automated programming[8]. Boutet et al.[9] used a more complex approach based on fMRI data obtained from a group of patients with optimized STN DBS parameters to inform a machine learning model that could be used to predict optimal settings in another group of patients.

DBS conventionally involves the delivery of stimulation with **AQ4** constant electrical parameters that are adjusted periodically during hospital visits. Over the past 20 years, however, there has been increasing interest in developing closed-loop or adaptive systems that would adjust the stimulation parameters according to the patient’s condition or activity. Those approaches have mostly involved simple algorithms that instruct the stimulation to be switched on or off or to a different amplitude when the recorded signal reaches a specified threshold. This approach has produced promising results in patients with PD[10]. In the future, machine learning could integrate a broader range of information and deliver more complex parameters of stimulation.

Future prospects

“The practical use of AI applications in ... DBS needs to be validated in long-term, prospective studies”

The practical use of AI applications in the field of DBS needs to be validated in long-term, prospective studies. These techniques are expected to be particularly useful if the target is difficult to identify, if the DBS effect is not immediate, or with electrodes with more complex designs. The focus should be on reducing variability in outcomes and increasing long-term benefits. However, it is important that the expected increase in cost does not make surgery less accessible to patients and that the quality of human interaction with the clinical team remains a priority, owing to the complex multidimensional aspects of those diseases.

Competing interests The authors declare no competing interests.

References

1. Roy, A. G., Conjeti, S., Navab, N., Wachinger, C. & Alzheimer’s Disease Neuroimaging Initiative. QuickNAT: A fully convolutional network for quick and accurate segmentation of neuroanatomy. *Neuroimage* **186**, 713–727 (2019).
2. Henschel, L. et al. FastSurfer - a fast and accurate deep learning based neuroimaging pipeline. *Neuroimage* **219**, 117012 (2020).
3. Ronneberger, O., Fischer, P., Brox, T. (2015). U-Net: Convolutional Networks for Biomedical Image Segmentation. In: Navab, N., Hornegger, J., Wells, W., Frangi, A. (eds) Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015. MICCAI 2015. Lecture Notes in Computer Science(), vol 9351. Springer, Cham. https://doi.org/10.1007/978-3-319-24574-4_28 **AQ5**
4. Milletari, F. et al. Hough-CNN: deep learning for segmentation of deep brain regions in MRI and ultrasound. *Comput. Vis. Image Underst.* **164**, 92–102 (2017).

5. Lin, H. et al. Low-field magnetic resonance image enhancement via stochastic image quality transfer. *Med. Image Anal.* **87**, 102807 (2023).
6. Jurek, J. et al. Supervised denoising of diffusion-weighted magnetic resonance images using a convolutional neural network and transfer learning. *Biocybern. Biomed. Eng.* **43**, 206–232 (2023).
7. Malekmohammadi, M. et al. Automated optimization of deep brain stimulation parameters for modulating neuroimaging-based targets. *J. Neural Eng.* **19**, 046014 (2022).
8. Roediger, J. et al. StimFit — a data-driven algorithm for automated deep brain stimulation programming. *Mov. Disord.* **37**, 574–584 (2022).
9. Boutet, A. et al. Predicting optimal deep brain stimulation parameters for Parkinson’s disease using functional MRI and machine learning. *Nat. Commun.* **12**, 3043 (2021).
10. Little, S. et al. Adaptive deep brain stimulation for Parkinson’s disease demonstrates reduced speech side effects compared to conventional stimulation in the acute setting. *J. Neurol. Neurosurg. Psychiatry* **87**, 1388–1389 (2016).