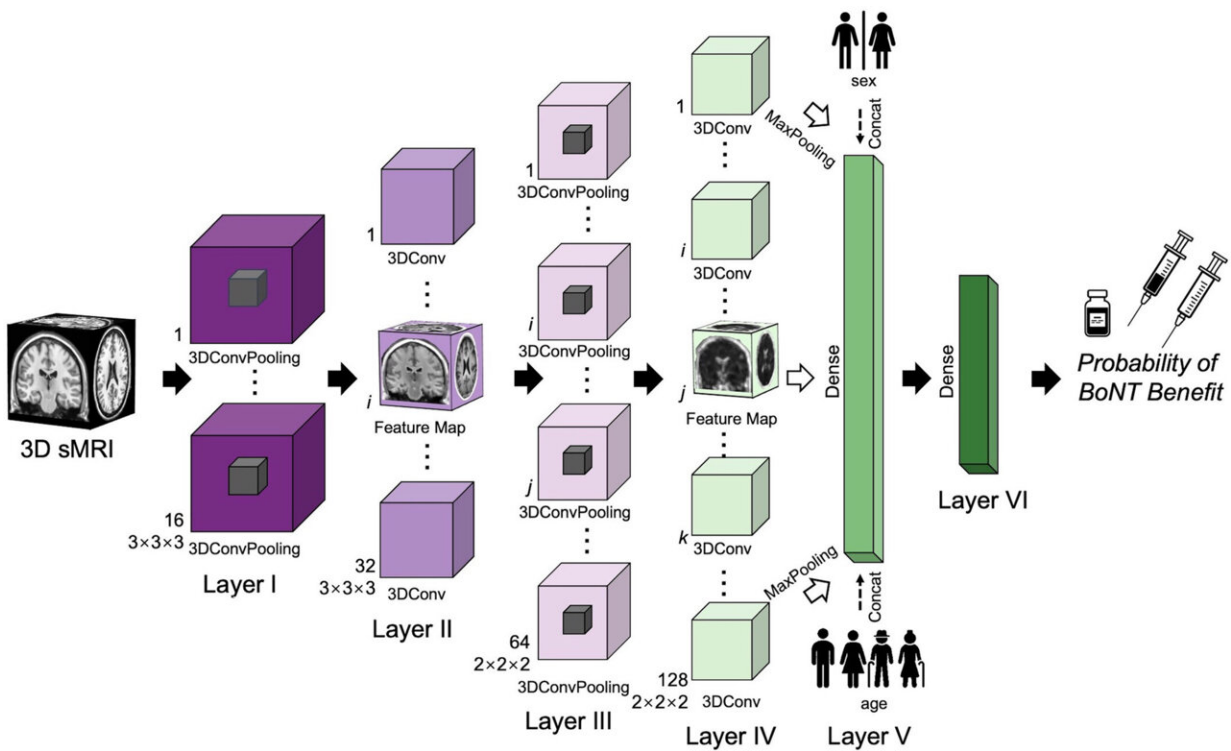


AI tool predicts which patients with dystonia respond to Botox treatment with 96% accuracy

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The architecture of 3D convolution neural network of the DystoniaBoTXNet model. Raw brain structural magnetic resonance imaging (sMRI) is used as input into DystoniaBoTXNet, which consists of 4 convolutional layers (3DConv) for feature extraction and representation learning (layers I–IV) and 2 fully connected dense layers (Dense) for classification (layers V–VI). A maximum pooling operation (3DConvPooling) is used to decrease the dimensions in layers I and III. The number and size of filters are set at 16 and $3 \times 3 \times 3$ for layer I, 32 and $3 \times 3 \times 3$ for layer II, 64 and $2 \times 2 \times 2$ for layer III, and 128 and $2 \times 2 \times 2$ for layer

IV, respectively. The biological variables (sex and age) are concatenated with the image feature map flattened by the adaptive 3D global maximum pooling (MaxPooling) operation. The output of the DystoniaBoTXNet model is the individual probability of botulinum toxin (BoTX) benefit. Credit: *Annals of Neurology* (2022). DOI: 10.1002/ana.26558

Dystonias are potentially disabling neurological conditions that can greatly affect quality of life. Effective treatments are sparse, with botulinum toxin (Botox) injections into the affected muscles considered the first-line therapy. However, the injections do not work for every patient with dystonia, and there has been no established way for clinicians to determine who would benefit and who would not prior to treatment initiation.

In a new study published November 28 in *Annals of Neurology*, an [artificial intelligence](#) platform called DystoniaBoTXNet used brain MRIs to automatically identify which patients would respond to [botulinum toxin](#) treatment with 96.3% accuracy.

Such a platform can inform clinicians' treatment decisions, according to senior study author Kristina Simonyan, MD, Ph.D., Dr. med, director of Laryngology Research at Mass Eye and Ear, a member of Mass General Brigham, and professor of Otolaryngology–Head and Neck Surgery at Harvard Medical School.

"Typically, a patient with dystonia would undergo a series of dose- and location-finding injections to determine whether botulinum toxin relieves their symptoms. Injections are painful and costly," said Dr. Simonyan.

"Yet, some may find no benefits from this treatment despite multiple

injection attempts, while some might benefit from injections but give up after only one dose or forgo the treatment altogether. With this [artificial intelligence algorithm](#), we can empower clinicians and patients in their therapeutic decision-making by providing them with an objective tool to replace the trial-and-error approach to botulinum toxin efficacy."

Pervasive treatment challenges for patients with dystonia

People with dystonias experience involuntary contractions or tensing of muscles which can lead to uncontrolled movements that significantly impact physical and emotional quality of life.

Isolated focal dystonias affect one part of the body, with common examples including: laryngeal dystonia affecting the vocal cords when speaking, blepharospasm causing involuntary eyelid twitching, cervical dystonia causing the neck muscles to contract and the head to twist painfully and writer's cramp dystonia affecting the fingers during writing. About 35 of every 100,000 people have isolated or primary dystonia—a prevalence that is likely underestimated due to challenges diagnosing the disorder.

Botulinum toxin injections are considered the first-line treatment for focal dystonias. The injection paralyzes the affected muscle, aiming to prevent the involuntary contractions. The effects are usually temporary, and an [injection](#) often needs to be repeated every three-four months for life.

Only about 60% of patients with dystonias undergo these injections, and not every patient responds to treatment. This can be due to underlying biological reasons, complexity of symptoms or the experience and expertise of the injecting physician. This may lead to an overtreatment

of patients who would not respond to botulinum toxin in the first place, and an undertreatment of patients who may respond but never seek out the treatment or might stop the treatment early.

This high variability led Dr. Simonyan and her team to turn to artificial intelligence for finding a solution to objectively assess the benefits of botulinum toxin injections prior to treatment initiation.

Predicting treatment effectiveness with MRIs

In the new study published in *Annals of Neurology*, the research team trained a deep-learning algorithm to analyze the brain MRIs of 284 patients with four types of dystonia who responded and did not respond to botulinum toxin injections. Efficacy of the injections was determined by medical records and physician and patient feedback.

DystoniaBoTXNet revealed there were eight regions of the brain as a neural biomarker of effectiveness of injections. Using this newly discovered biomarker, DystoniaBoTXNet achieved an overall accuracy of 96.3% in predicting botulinum toxin efficacy in focal dystonia, with 100% sensitivity and 86.1% specificity. The platform achieved these results in 19.2 seconds per case.

"Our study shows that DystoniaBoTXNet can be a very robust and easy-to-use AI platform for physicians to use for refined clinical decisions. An AI-generated individual predictive outcome of [botulinum toxin injections](#) prior to treatment administration may help more precise patient selection, fine-tuning of the treatment regimen, or further referrals, thus increasing utilization of botulinum toxin for patients with dystonia," Dr. Simonyan offered as an example.

"On the other hand, the platform may predict that the patient has very low probability of benefiting from injections, which would be

informative for the physician to consider other therapeutic options instead of botulinum toxin overtreatment."

Artificial intelligence tackles problems with dystonia diagnosis and treatment

The DystoniaBoTXNet tool is the second [artificial intelligence platform](#) invented by Dr. Simonyan and her team to aid clinical decision-making. This study builds on previous research led by this team that reported on the success of a separate platform called DystoniaNet capable of diagnosing dystonia from patient MRIs with 98.8% accuracy in 0.36 seconds. Dystonias are notoriously mis- and under-diagnosed, with some studies showing it can take patients up to 10 years to receive a proper diagnosis.

Interestingly, five of the eight regions identified as a neural biomarker of botulinum toxin efficacy by DystoniaBoTXNet in the new paper were previously found to constitute the diagnostic biomarker of DystoniaNet. For years, clinicians have had no objective biomarker for identifying these conditions, therefore the overlapping regions may provide added evidence to their roles in [dystonia](#) that scientists can better explore.

With further study of both platforms, the hope is that one day a patient can enter a clinician's office after experiencing symptoms and undergo an MRI and receive a diagnosis through DystoniaNet; then, DystoniaBoTXNet can help determine whether botulinum toxin treatment would work for them.

To achieve this goal, the researchers are embarking on multiple clinical trials within Mass General Brigham to determine the usefulness of these tools in the clinic. Another future direction of the work is to study whether additional treatments, like deep brain stimulation, might be

predicted by an AI-based tool.

More information: Dongren Yao et al, DystoniaBoTXNet: Novel Neural Network Biomarker of Botulinum Toxin Efficacy in Isolated Dystonia, *Annals of Neurology* (2022). [DOI: 10.1002/ana.26558](https://doi.org/10.1002/ana.26558)

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