Brain morphing technology simplifies the surgical treatment for movement disorders

By David F. Salisbury
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A system that morphs brain images can significantly simplify a neurosurgical technique called deep brain stimulation (DBS) that is gaining popularity in the treatment of movement disorders, including tremor, rigidity, stiffness and slowed movement, caused by a variety of neurological conditions ranging from dystonia to multiple sclerosis, from Parkinson's to obsessive-compulsive disease.

Since it was approved in 1998, DBS has proven to be highly effective when standard drug therapies either do not work or have lost their efficacy. However, the fact that it is an extremely long, difficult and expensive operation, which involves implanting electrodes deep in the brain, has limited its availability. Since the procedure's approval in 1998, the number of DBS operations performed has grown gradually to about 3,000 annually, although more than 100,000 people a year stand to benefit. In order to reduce the length, difficulty and risk of the procedure, a team of electrical engineers and neuroscientists at Vanderbilt University has developed a pilot guidance system that automates the most difficult part of the operation: identifying the proper location to insert the electrodes. To work, the electrodes must pass through small nuclei deep in the brain that are about the size of a pea and are not visible in brain scans or to the naked eye. The researchers – writing in a special issue of the journal *IEEE Transactions on Medical Imaging* published Nov. 1 – report that the new system can do a better job of identifying the proper location to insert the electrodes than an experienced neurosurgeon.

"The biggest problem with the procedure is that the surgeons cannot see the structure where they have to put the electrode and, as a result, they must spend a considerable amount of time searching for it," says Benoit Dawant, professor of electrical engineering, computer engineering and radiological sciences at Vanderbilt University, who is developing the guidance system in collaboration with Peter Konrad, associate professor of neurological surgery and biomedical engineering.

The only way that the target region can be identified is by its electrical characteristics. So the surgeons must first insert a recording electrode and monitor the electrical activity of the neurons that it touches. Sometimes they have to remove and reinsert the electrode two or more times. Sometimes they have to insert three or four electrodes at the same time in order to find the illusive spot.

"I tell patients that it is something like playing a big game of battleship," says Konrad, who helped pioneer the procedure. "Like the game, you don't know where the target is until you've made a hit."

Each time the surgeons are forced to reinsert the electrode, it increases the risk of damage to the brain and the length of the operation. When surgeons decide that they have hit the right spot, they implant a stimulating electrode and test it to determine if it reduces the patient's symptoms. Because muscle disorders typically occur only while a person is awake, the patient must remain conscious through the entire procedure.

The operation can take as long as 8 – 12 hours to properly place one electrode. (Most patients require two, one in each hemisphere.) "This is extremely rough on patients, who have to be awake through the surgery and have to be locked to the bed," says Konrad. "Anybody who performs this surgery quickly appreciates the need to trim the procedure down to a shorter process."

The computer-aided guidance system compensates for variations in the three-dimensional brain structure of each patient, something very difficult for surgeons to do on their own. It reduces operating times by increasing the odds that the surgeons begin searching very close to the target.

To develop the system, Dawant's team, which includes doctoral students Pierre-Francois D'Haese, Srivatsan Pallavaram and master's student Ebru Cetinkaya, began with the brain scans of 21 post-operative DBS patients. Next, the researchers developed a sophisticated, multi-dimensional method for morphing one brain scan into another and used this to combine all 21 brain scans to form a reference brain atlas.

"When we do this, we end up with an atlas with the electrode positions that form a tight cluster," says Dawant. "That tells us that we have done a very good job of conforming one brain to another."

Once they developed the atlas, the researchers began testing how well it predicts the invisible target's location in new patients. They did this by morphing the reference brain, with its cluster of electrode positions, onto a scan of the patient's brain. They then selected a point in the center of the cluster as their predicted target location.

In six implantations (two apiece in three patients), Dawant's team provided predictions to Konrad and his colleague Chris Kao, research assistant professor of neurological surgery, when they were planning the operation. In four cases, the surgeons used the system's prediction and found the target area in the first pass. In another six implants, the team did not provide their predictions in advance. In five cases, the surgeons had to make a second insertion to locate the target area and in three cases the final implant location was closer to the target identified by the guidance system than it was to the initial location selected by the surgeons.

"Now, with the use of the atlas, what we are basically doing is plugging the patient's MRI brain scan into the computer and about three to four hours later it spits back a morphed or warped target that we can use to plan the following week's surgery," says Konrad. This innovation, along with other improvements such as the use of rapid prototyping to create customized insertion platforms, has substantially reduced the length of the operation: "Now we are down to putting in both electrodes in under five hours: We have reduced a two-day procedure down to five hours!"

Not only does the guidance system save the patient from the risk of a prolonged procedure or undergoing two procedures, it also should cut hospital costs significantly, Konrad adds.

Despite its invasive nature, Konrad argues that deep brain stimulation has some important fundamental advantages when compared to drug-based therapies for many patients. "Generally, the people who come to us for DBS are people who have had some success treating their condition with drugs, but they have come to the point where they are having so many side-effects that they cancel out the success," he says. "These are focal diseases that only seriously impact a small portion of the nervous system. When you take a pill you can't make it just go to the affected area: It goes everywhere, so you get a ying-and-yang effect: You get the positive effect of the drug in the intended target and you get all of the negative effects in all of the other places."

By contrast, stimulation therapy is directed at just the portion of the nervous system that is damaged, patients do not appear to develop a tolerance to it, so it remains effective for years. And it provides steady and consistent relief so DBS patients do not experience the "on-off" phenomenon experienced by many of the Parkinson's patients taking drugs, says Konrad.

The technique may also be effective in treating other types of conditions as well. For example, recent research suggests that DBS may be effective in treating a broader range of “psychiatric” disorders, such as clinical depression.

“All the work that Dr. Dawant is doing here is creating the infrastructure that will allow us to chart out and map the targets of opportunity for many other diseases that otherwise may not be so easily identified on MRI scans,” says Konrad.

The researchers plan a number of improvements to the guidance system. They have begun to collect data on the effectiveness of the operations and will use that to refine their predictions. They have also set up a system that will collect electrophysiological data from the patient’s brains that is collected during the procedure so they can add it to the brain atlas as well. And finally they intend to begin creating individual atlases for different conditions – Parkinson’s, essential tremor, dystonia, etc. – in case the precise location of the neurological damage may differ.

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A patient’s success story

Mark was born in Michigan in 1979 with hyperkinestic dystonia. He suffered from violent, uncontrolled motions throughout his body. As a young child he made some progress. He learned to talk, walk, manipulate objects with his hands and learned to ride a bicycle. But then, when he was about six, his condition began to get worse. Heavier and heavier dosages of sedatives were needed to repress his controllable movements. By the time Mark was 12, this condition had reached the point where he was taking so much medication that he was barely conscious and his quality of life was almost non-existent.

Then, In 2001. when Mark was 12 years old, Dr. Konrad implanted a pair of stimulating electrodes in his brain. A month after the operation, the surgeon programmed the electrodes to optimize the suppression effect of the tiny electric signals that they produce. Home video clips document the dramatic improvement that Mark made as a result of the operation. The video is narrated by Dr. Konrad.

Today, Mark’s dystonia is under control and he is living a relatively normal life. In fact, he recently joined a Boy Scout troop and enjoys hiking and camping out. The only restriction the doctors have put on him is a prohibition against playing violent sports like football.