Challenges of identifying cognitive abilities in severely brain-injured patients

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Only by employing complex machine-learning techniques to decipher repeated advanced brain scans were researchers at NewYork-Presbyterian/Weill Cornell able to provide evidence that a patient with a severe brain injury could, in her way, communicate accurately.

Their study, published in the Feb. 13 issue of the *Archives of Neurology*, demonstrates how difficult it is to determine whether a patient can communicate using only measured brain activity, even if it is possible for them to generate reliable patterns of brain activation in response to instructed commands. Patients in a minimally conscious state or who have locked-in syndrome (normal cognitive function with severe motor impairment) and can follow commands in the absence of a motor response may not generate clearly interpretable communications using the same patterns of brain activity, the researchers say.

While less sophisticated methods have been shown successful, the authors say their new approach provides important new insights into brain function and level of consciousness. It also identifies mechanisms of variation in brain activity supporting cognitive function after injury.

"In these studies we have reanalyzed earlier published data that demonstrated an effort to communicate using brain activations alone that apparently failed but was nonetheless a clear effort to generate a response," says Dr. Nicholas D. Schiff, professor of neurology and neuroscience and professor of public health at Weill Cornel Medical College, and a neurologist at NewYork-Presbyterian Hospital/Weill

Cornell Medical Center. "Importantly, the reanalysis with new, more sensitive methods provides evidence that the problem with communication may reflect a mismatch of our expectations in designing the assessment, rather than a failure on the subject's part in an attempt to accurately communicate with us."

"Our study shows that multivariate, machine-learning methods can be useful in determining whether patients are attempting to communicate, specifically when applied to data that already show evidence of a signal in univariate, more standard methods of analysis," says the study's lead author, Jonathan Bardin, a fourth-year neuroscience graduate student at Weill Cornell Medical College.

"It is our clinical and ethical imperative to learn as much as possible about their ability to communicate," he says. "A simple bedside exam is not good enough."

"We need a set of methods that are both powerful and simple, and we are not there yet, as this study shows," adds Dr. Schiff. "We are using quite complex tasks to perhaps detect just the few of many patients who are conscious."

Patients Differ in Abilities

This study is a continuation of NewYork-Presbyterian/Weill Cornell research into how fMRI can establish a line of communication with brain-injured patients in order to understand if they can benefit from rehabilitation, and to gauge their level of pain and other clinical parameters that would improve care and quality of life.

It specifically follows up on a study published in the journal Brain last February that demonstrated use of fMRI to detect consciousness in six patients (either locked-in or minimally conscious) resulted in a wide, and

largely unpredictable, variation in the ability of patients to respond to a simple command (such as "imagine swimming -- now stop") and then using the same command to answer simple yes/no or multiple-choice questions. This variation was apparent when compared with their ability to interact at the bedside using gestures or voice.

Some patients unable to communicate by gestures or voice were unable to do the mental tests, while others unable to communicate by gestures or voice were intermittently able to answer the researchers' questions using mental imagery. And, intriguingly, some patients with the ability to communicate through gestures or voice were unable to do the mental tasks.

The researchers say these findings suggest that no exam yet exists at this time that can accurately assess the higher-level functioning that may be, and certainly seems to be, occurring in a number of severely brain-injured patients.

"There are people whose personal autonomy is abridged because they don't have a good motor channel to express themselves despite, in some cases, having a clear mind and opinions and desires about themselves and the world," Dr. Schiff says about those results.

"Not all minimally conscious patients are the same, and not all patients with locked-in syndrome are the same," he says.

Sensitive and Flexible Methods Are Needed

This main new result of this study is a reinterpretation of findings from a 25-year-old patient who was the only one of six who showed an ability to use the fMRI signal for communication in the earlier research. But her results were confusing because it seemed that she was consistently responding to the answer that was directly after the correct answer,

Bardin says.

"It's often seen in patients like this -- she had a stroke that damaged her brain -- that there can be a cognitive delay in some area of the brain. FMRI is a readout of blood flow instead of actual neural activity, so these delays could be caused by an interruption of blood flow due to damage or could just mean they are working on the problem more slowly, and the answer looks wrong because it is given in the next response period."

To understand this, Bardin employed a newer technique, which he says has sprung out of machine-learning research, to instruct a computer to evaluate multiple fMRI scans from the patient after she answered the two questions a number of times.

This so-called multivariate approach used the same data gathered for the first study, which, in the typical "univariate" analysis, specifically looks at functioning in the brain's Supplementary Motor Area (SMA), which is active when "normal" subjects imagine doing something.

In contrast, the multivariate analysis examines whether there is a pattern of activity in any part of the brain that is consistent from one scan to the next.

"When there is significant damage to the brain, it can rewire itself so that functions associated with SMA could be processed somewhere else," Bardin says.

Using this complex approach, the researchers found that, indeed, the patient had consistently attempted to communicate answers to both questions -- but at a delayed speed.

The researchers say that one approach to analyze fMRI scans is not

better than the other for all patients and that univariate methods should always be carried out first. Multivariate approaches can be especially sensitive to noise, leading to false positives if used on their own. If the standard approach reveals a signal, the multivariate approach could be used to gain further insights and possibly identify response in patients where the univariate results are ambiguous.

"We did all these things to simply show that we think this patient was trying to communicate," Bardin says. "You have to be very careful in your data analysis before saying anything strongly about what a patient can or cannot do."

"Rigid experimental paradigms like those used in the field can very well miss important information about these patients," Dr. Schiff says. "This is all extremely complex and messy, but we should expect that. Given the injuries some of our patients suffer, their cognitive abilities are very difficult to detect behaviorally or through simplistic tests or scans."

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