Predicting Drug Response from Brain Waves

A device helps to pair patients with the right antidepressant.
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Brain waves measured using a simple device just one week into treatment can indicate whether a depressed patient should continue taking a medication or be switched to another. The study, which was conducted at nine sites across the U.S., could signi cantly reduce the time it takes to effectively treat major depression.

Mind reading: The system above was used to predict whether patients should be kept on one antidepressant or switched to another. The strap around the subject's head contains electrodes that pick up brain waves. The strap hooks up to a hockey-puck-size device that digitizes and filters the EEG signal before sending it on to a laptop for processing.

"Selecting the right antidepressant medication is a bit of a shot in the dark," says Andrew Leuchter, professor of psychiatry at UCLA and lead author of the study. "The first medicine we choose only gets the patient well about a third of the time."

Antidepressants must be taken for approximately eight weeks before it's clear whether or not the medicine will have an effect. Patients frequently have to try two to three medications before finding an

effective one, meaning the search for the right medication can take many months. “This leads to prolonged disability, prolonged suffering, and the chance that the patient may never get well,” says Leuchter. “Some patients say, ‘I don’t need this,’ and drop out of treatment.” The testing process studied by Leuchter and his colleagues, which takes only 15 minutes, could help those suffering from depression find relief faster.

For the study, the researchers used a customized version of a quantitative electroencephalography (QEEG) system to study the brainwave patterns of 375 people suffering from major depression. The device, developed by Aspect Medical Systems of Norwood, MA, consists of a few electrodes mounted on a strap that is worn across the patient’s head. (Aspect Medical provided funding for the study and employs Leuchter as a consultant. Leuchter is also a minor shareholder in the firm.) The strap hooks up to a hockey-puck-size device that digitizes and filters the EEG signal, as well as performing some basic processing. That device plugs into a laptop computer, which does the bulk of the signal analysis.

Unlike a standard QEEG system, which requires bulky equipment and is often housed in its own lab, the Aspect Medical system is small and portable. Leuchter says the system doesn’t require a lot of specialized training like traditional QEEG systems, either; it took only a few hours to train staff to use the device. “The process is so simple, even a doctor can do it,” he says. While the device is still far from commercialization, the ultimate intent is to offer it to physicians.

Scientists measured brain activity before the patient was on any medication and then again one week after starting the popular antidepressant escitalopram, which targets a chemical messenger called serotonin. The patients were then randomly assigned to one of three groups: one group continued on escitalopram alone; one group was switched to another common antidepressant, bupropion, which acts on the chemical messengers norepinephrine and dopamine; and the third group took both medications.

To predict which patients would respond to escitalopram, the researchers looked for particular changes in brainwave patterns between the first and second QEEG. Using an algorithm that considers various QEEG characteristics, called the antidepressant treatment response (ATR) index, the researchers found that they could accurately predict whether the patient would respond to the escitalopram 74 percent of the time. Leuchter says that's much better than any other method currently available.

Earlier research had shown that the ATR index was relatively accurate at predicting a patient's response to escitalopram. But this study went further, by determining that the biomarker could also be used to determine whether a patient would benefit by switching to another drug. "This is the first study that I am aware of that can predict differential response to two different medications," Leuchter says. The research was published this month in the journal *Psychiatry Research*.

Dr. Dan Iosifescu, a coauthor of the study and director of translational neuroscience in the psychiatry department at Massachusetts General Hospital, explains that telling a patient they won't respond to a drug isn't "terribly useful" unless you can also tell them that they are more likely to benefit from another medication. After the success of this study, Iosifescu says it will be valuable to see whether the same results are found with other antidepressants.

The methodology used in the study could also be applied to drugs for other diseases, such as schizophrenia and Alzheimer's disease, suggests Dr. Monte Buchsbaum, a professor of psychiatry and radiology at the University of California, San Diego, and editor-in-chief of *Psychiatry Research*.

Dr. Marcus Ising, a molecular psychology researcher at the Max Planck Institute of Psychiatry, says the study is helpful, but he believes it would be more valuable to try to find biomarkers that would evaluate the pathology of depression, as opposed to the effect of a drug.

Leuchter says that previous studies showed that the signal detected by the frontal electrodes comes from the anterior cingulate, a part of the brain that is “heavily involved in mood regulation,” so it makes sense that the signal would indicate antidepressant responsiveness.