

Referenced EEG Offers a New Way to Prescribe the Right Medication

Summarized by Thomas T. Thomas

Prescribing medication to treat a brain disease is often a matter of trial and error, with a patient going through several regimens before finding one that works. A recently patented system called Referenced EEG (electroencephalogram) may help speed up this process. **Mark Schiller, MD**, the speaker at our September 24 meeting, explained how it works. He is assistant clinical professor in psychiatry at the University of California, San Francisco, has a practice in the city associated with San Francisco General Hospital, and does research on Referenced EEG with a firm called CNS Response.

For years, doctors and patients alike have yearned for a simple blood test that will tell them what medications are appropriate to a person's condition. "While Referenced EEG is not as simple as a blood test," Schiller said, "there's no pin prick—therefore it's more comfortable."

In its simplest form, Referenced EEG first reads the electrical signals from firing neurons in the brain, which presents a profile of brain activity. The system identifies abnormalities in the pattern and correlates them with a database of EEGs from other patients having similar abnormalities and the medications to which they have responded in the past. The system uses entirely statistical methods to match the EEG pattern to a particular medication without performing a diagnosis derived from the patient's symptoms.

"The method is based on the work of Stephen Suffin, a pathologist who entered psychiatry and also had a background in computer programming at IBM," Schiller said. "Suffin noted that psychiatry doesn't work like normal medicine, where you can compare physical abnormalities among patients and test your diagnosis with treatment."

Suffin administered EEGs to define what activity in a normal brain looks like by comparing people of different ages and ethnicities on different continents, all of whom had no psychiatric complaint. He discovered that the brain looks the same regardless of gender and ethnicity, but it does look different at different ages. He then took EEGs from a group of approximately



MARK SCHILLER, MD

3,000 patients with brain disease who had been stable for six months to two years on their medications. This built a database of EEG responses to some 10,000 medical trials. “It takes time to build one of the newer medications into the database,” Schiller observed.

In current practice, a psychiatrist makes a diagnosis based on the pattern of symptoms compiled in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM IV) of the American Psychiatric Association. These symptoms are defined by the observations and experiences of other psychiatrists. The hierarchies can be vague and often have a great deal of overlap between diseases. But, from this diagnosis, the psychiatrist will prescribe a medication. This method has a 30 to 35 percent success rate with the most refractory patients.

“Based on the two formal studies we have done with Referenced EEG—and that we can talk about, now that the patent was awarded in September 2003—this new system is showing a success rate of 80 percent,” Schiller said. Referenced EEG has been shown to work well with depression, bipolar disorder, eating disorders, and even substance abuse.

Instead of diagnosing an illness based on symptoms, Referenced EEG works directly with the brain’s physiological abnormalities. In general medicine, it is common for people to present with different symptoms but have an underlying abnormality. For example, a person suffering a heart attack may be nauseated or not, may be short of breath or not, and so on through a list of symptoms. Conversely, a person may have chest pain that is due to a heart attack or an embolism. Like general medicine, Referenced EEG follows the physiology and doesn’t care about the diagnosis of symptoms.

“However,” Schiller warned, “we are not sure yet about primary psychotic disorders like schizophrenia and schizo-affective disorder. We can’t claim an 80% success rate with those illnesses and don’t recommend abandoning diagnosis.” Schiller’s colleagues had a study on psychotic disorders under way in a locked facility in southern California, but then the county lost its contract and the team lost access to the patients. Until another study can be started, the actual usefulness of Referenced EEG with primary psychotic disorders remains in question. “Still,” he said, “we believe the system can be helpful with these illnesses.”

The process, he said, takes about 30 minutes, with the patient awake but quietly resting in a chair. Putting electrodes on the patient’s head takes up most of the time. These electrodes read electrical signals but do not send anything into the brain. The main requirement for a successful reading is that the patient be at five half-lives from any medications and be in a steady state. (A half-life is the time the body takes to eliminate half of the medication.) For most psychiatric medications, this period is three to seven days, although for some it can be as long as forty days.

For more information on Referenced EEG, see the articles on line at drmarkschiller.com. After his remarks, Schiller took questions from the audience.

Can you describe the abnormalities that Referenced EEG sees?

In an EEG, neurons firing in the brain set up waves or bands, which have been identified as alpha, beta, delta, and theta. In addition, the instrument can identify signals coming from the front of the brain, the back, and other parts. In all, the machine identifies thousands of variables and reduces them to just 74. Different readings in certain combinations of these variables define the abnormality.

Does the Referenced EEG give clues to which antidepressant to use?

The system can distinguish between subclasses of medications—for example, between SSRIs and MAO Inhibitors. Sometimes it can distinguish between the medications themselves. However, with 74 variables to evaluate, any one of which may be two to four standard deviations from the norm, this can be difficult.

Does a brain on medication look like a “normal” brain?

That seems to be the case, but we do not have enough experience yet to say so definitively. Generally, once patients are stable on a medication, they tend not to come back for a second EEG.

Does your technique evaluate the subconscious?

An EEG will change depending on whether you are awake, asleep, meditating, or even have your eyes closed. But that may not be what you mean. We set up the baseline for a normal brain with people who were awake and without psychiatric complaints.

Have you tried correlations with brain scans and other methodologies?

We are starting to do this, adding on to a study at Stanford University and working with their patient database. EEGs, however, are simpler than brain scans and don't involve the injection of dyes.

For years, people tried to relate EEGs to diagnoses and use them to validate a diagnosis. But research showed you couldn't do that, primarily because diagnoses are observations of symptoms and not direct observations of an abnormality.

Would the EEG of a person who was situationally depressed look different from someone who was clinically depressed?

Depression is difficult—sometimes endogenous and sometimes situational. We think everyone has abnormality patterns that are genetic in origin, but not everyone expresses their genetics. For example, twins can have expression differences. So something situational may trigger a depression that is based on a genetic abnormality.

How do you judge success in your 80 percent success rate?

We use the clinical global improvement scale, which is the simpler of the two methods available. This scale goes from “worsening” to “no improvement” to “mild improvement,” “significant improvement,” and “marked improvement.” We use the last two categories to define success with a medication. All of the trials in our database used this scale, which was applied from one psychiatrist’s observations and from patients’ self-reports.

How did you determine which medications to use in building your database?

We started with the physiology and followed the traditional diagnosis to select a medication. Then we moved directly to the physiology and left the diagnosis behind.

Where have you had your greatest successes?

Referenced EEG is just about equally successful with everything except the primary psychotic disorders. Bipolar, depression, attention deficit, eating disorders, and substance abuse all show up as physiological patterns. We hope to add the psychotic disorders when we can do a study similar to the one aborted in southern California.

Why aren’t you getting bigger grants for this?

We believe it’s because EEG in the past went down the wrong path of diagnosis, and venture capitalists tend to be conservative in backing similar research. Also, as researchers we have our own practices and limited time to pursue the studies.

Will insurance companies pay for this technique?

We had a pilot program with Cigna in Atlanta, but the results did not lead to full acceptance. We need to develop more successes and find a person in a company who will get enthusiastic about Referenced EEG.

Does the technique have success with aphasia, mutism, or autism?

We don’t have a lot of experience with pervasive developmental disorders and learning disorders. But then, medication hasn’t been effective in curing these disorders, either. However, you can treat hyperactivity and related disorders.

If you aren’t interested in the diagnosis, then do you interview the patient before the EEG?

Yes, usually for screening purposes. We can’t read the EEG if the person has a history of epilepsy or major head injury. Also, significant medical illnesses can interfere with the EEG. We require that the patient be clean of substance abuse—two days without alcohol and three days without cocaine or amphetamines. And, as noted above, the person should be stable at five half-lives of any current medication he or she is taking. However, we do allow smoking and caffeine use, because they are already in the database of patients.

What if the person can't safely be taken off medications? Can you read the EEG and then subtract out the effects of the medication?

Theoretically, that may be possible—to manipulate the readings by hand. Perhaps Dr. Suffin would be willing to try it, but I couldn't.

Do you work with other psychiatrists on Referenced EEG?

We can work with others, but usually they ask us to treat the patient for a while, take the EEG, and get the person stable. Then we will send the psychiatrist an automated report.