Neuroimaging Offers Window on Mood Disorders

BY MIRIAM E. TUCKER
Senior Writer

PITTSBURGH — Neuroimaging may soon become an important clinical tool for the diagnosis and treatment of mood disorders, Dr. Mary L. Phillips said at the Seventh International Conference on Bipolar Disorder.

Emerging data suggest that functional magnetic resonance imaging (fMRI) can identify specific neural biomarkers that may help distinguish patients with bipolar disorder from those with unipolar disorder. These data may also help physicians assess which patients will respond to which psychotropic medications and possibly even predict which healthy individuals at high genetic risk will go on to develop bipolar disorder, said Dr. Phillips, who is with both the University of Pittsburgh, where she is professor of psychiatry and director of the functional neuroimaging program, and the Institute of Psychiatry in London, where she is with the section of neuroscience and emotion.

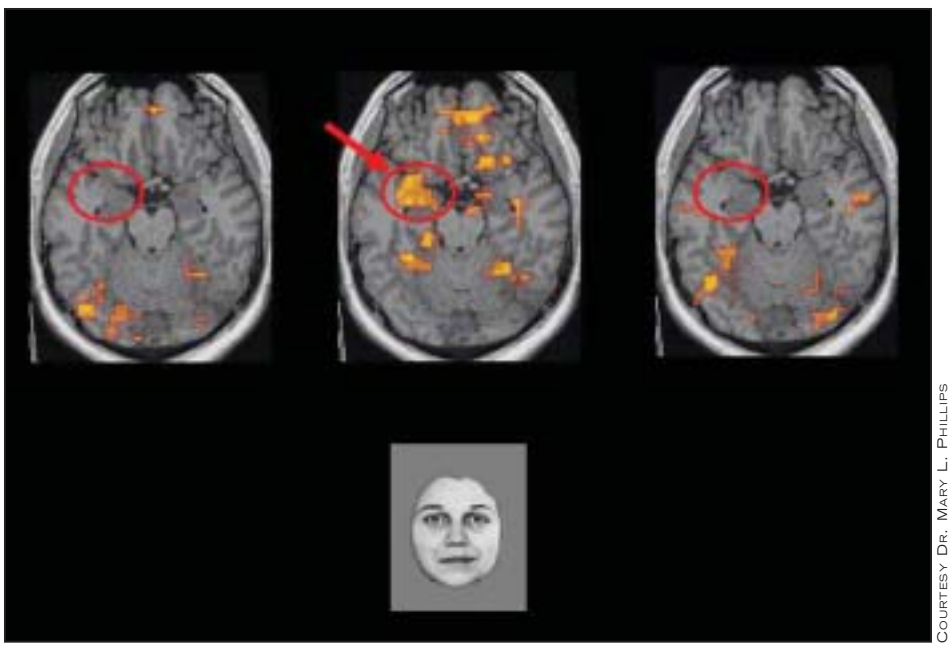
"We've moved beyond blue sky high-level science for its own sake. We're now using neuroimaging to ask and answer real-life clinical problems," she said at a press briefing held during the conference.

Improving the diagnostic capability of those who treat bipolar disorder is a research priority and is likely to be the first bedside use of the technology. Bipolar disorder is frequently misdiagnosed as unipolar depression, often for as long as 8-10 years, before patients receive a correct diagnosis and treatment.

Using fMRI to record neural responses to pictures of people with facial expressions of varying emotions, Dr. Phillips and her London associates found distinct differences between a group of 12 patients with a diagnosis of bipolar I disorder, 9 with major depressive disorder, and 11 healthy control subjects.

The bipolar group demonstrated increases in both subcortical (ventral, striatal, thalamic, and hippocampal) and ventral prefrontal cortical responses, particularly to expressions of mild and intense fear, mild happiness, and mild sadness; activity was diminished in the dorsal prefrontal cortical area to the majority of facial expressions (Biol. Psychiatry 2004;55:578-87).

The results are in line with the fact that one of the specific subcortical areas that show abnormally elevated activity, the ventral striatum, is associated with the processing of expressions of emotion and reward. Interestingly, activity in this area was most elevated by pictures of faces showing expressions of mild happiness rather than to faces showing more extreme emotions. This may be explained by the fact that mild expressions of happiness are more frequently observed in everyday life, and may be seen as especially rewarding in people with bipolar disorder, Dr. Phillips said in an interview.



COURTESY DR. MARY L. PHILLIPS

This fMRI shows the different patterns of brain activtiy in reponse to mild happy faces among healthy controls, bipolar patients, and unipolar depressed patients.

The dorsal prefrontal cortical area, where the bipolar patients demonstrated reduced brain activity, comprises the regions primarily associated with regulation of emotion. Reduced activity in these regions may therefore underlie the emotional lability experienced by people with bipolar disorder, she said.

In contrast, the group with unipolar depression showed diminished neural responses to all emotional expressions except mild sadness. Severity of depression correlated positively with hippocampal response to mild sadness in both patient groups, while the healthy controls demonstrated increased subcortical responses to intense happiness and mild fear, and increased dorsal prefrontal cortical responses to intense expressions of sadness.

Dr. Phillips is now replicating these findings in Pittsburgh, with larger groups of bipolar patients. Results in the Pittsburgh patients have shown that the same patterns occur in subjects with active and with remitted disease, suggesting that the test would be specific to the disease state, regardless of current symptoms. Those data are currently being prepared for submission to a journal.

"I see in the not-too-far-distant future that we might be able to perform a brain imaging scan the same way that people get chest x-rays. It's not going to be the only tool we have, but it will be part of a battery of tests, along with blood tests and paper-and-pencil cognitive tests," Dr. Phillips predicted.

However, she cautioned that because the use of fMRI in psychiatry is still relatively new, there are not as yet enough normative data with which to compare people with various psychiatric abnormalities. Those data are now being gathered. "So perhaps not tomorrow, but within the next 10 years, I would like to see at least a basic paradigm, such as face task," she said at the press briefing.

"If we can do anything to identify and accurately diagnose people with bipolar disorder earlier, that has to be a good thing," Dr. Phillips said at the conference, which was sponsored by the University of Pittsburgh. ■

Consider Comorbidities When Selecting Treatments for Insomnia

WASHINGTON — Insomnia is a disorder of hyperarousal rather than one of sleep deprivation, Thomas Roth, Ph.D., said at the annual meeting of the American Academy of Clinical Psychiatrists.

Because 90% of people with insomnia have other comorbid conditions, insomnia was seen as a symptom rather than an independent disorder until 2005. That's when the National Institute of Mental Health declared that insomnia met the criteria for a disorder, which include impairment in function and quality of life that is associated with specific symptoms and rooted in physiology.

When treating a patient who complains of chronic sleep problems, be sure to ask these key questions, Dr. Roth said in an interview:

► What is the nature of the nighttime sleep problems (difficulty falling asleep, difficulty staying asleep)?

► What is the nature of daytime consequences (daytime sleepiness, impaired function)?

► What is the frequency and duration of symptoms?

► Does the patient have any comorbid medical or psychiatric conditions?

Prevalence data are limited, but about 30% of the general population has some type of disturbed sleep, said Dr. Roth, director of research and chief of sleep medicine at the Henry Ford Hospital in Detroit.

Many patients with insomnia report that the daytime impairment and distress resulting from insomnia are more frustrating for them than their difficulty sleeping at night. Psychiatrists may be able to address these complaints.

Chronic pain is a common comorbidity in insomnia patients. "The less you sleep, the more sensitive you are to pain," Dr. Roth said. Sleep loss increases the body's inflammatory response and heightens pain sensitivity, and several studies have shown that increasing total sleep time can decrease pain sensitivity.

Treatment of insomnia remains a challenge, but recognition of the role of hyperarousal and the frequency of comorbidities allows for new therapeutic targets, including some sedating antidepressants.

Depending on the nature and severity of the sleep impairment, many patients can benefit from sleep aids immediately, Dr. Roth said.

—Heidi Splete

Single Dose of Doxepin Eases Transient Adult Insomnia

MINNEAPOLIS — A single 6-mg dose of doxepin significantly cut the time needed for adults with transient insomnia to fall soundly asleep, based on data presented at the annual meeting of the Associated Professional Sleep Societies.

The single dose of doxepin also significantly improved the overall duration and quality of the participants' sleep. "These data suggest that doxepin 6 mg may improve all aspects of sleep impairment in adults with transient insomnia," reported Dr. Howard Schwartz medical director of Miami Research Associates, a research facility and sleep lab.

The 283 subjects who received one 6-mg dose of doxepin reached persistent sleep an average of 13 minutes earlier than the 282 subjects who received a placebo. The reduced time to sleep was the primary end point of the study, which was sponsored by Somaxon Pharmaceuticals, a manufacturer of doxepin.

The 565 participants were otherwise healthy adults who underwent a prestudy phase advance (a technique conducted in a sleep lab to induce transient insomnia). The subjects then received either the drug or a placebo, and their sleep was evaluated using single-night polysomnography data and a patient questionnaire that they completed the next morning.

The polysomnography data also showed that, compared with the placebo group, the doxepin group had a significantly longer total sleep time (51 minutes), woke up significantly later (39 minutes), and reported significantly improved sleep efficiency, compared with the placebo group. In addition, sleep efficiency improved by an average of 10% in the doxepin group, compared with the placebo group, during each of 8 hours and during each third of the night's measurements.

—Heidi Splete