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Brain Imaging Aids Study of Severe Depression

By MARGIE PATLAK

A colorful brain imaging tool is helping researchers home in on the underlying brain chemistry defects that trigger certain types of severe depression.

"We now know where to look in the brain for the error that produces depression," says neuroscientist Michael Phelps of the UCLA School of Medicine.

The latest findings confirm the belief of many scientists that some types of severe depression are not a controllable personality trait, but rather a brain disorder. "I hope that our findings will destigmatize psychiatric illness," says psychiatrist Wayne Drevets of Washington University School of Medicine. "If you've got one of these severe types of depressions that we've studied, you can't just pull yourself up by your bootstraps and shape up without proper drug treatment."

Similar technology may soon help psychiatrists distinguish patients with a depression stemming from a brain abnormality from people with a different form of depression that is more responsive to psychotherapy. "A person can get depressed after losing their spouse or their job and recover after getting talk therapy," Drevets says. "But that's a very different kind of depression than the severe biochemical kind that tends to be inherited and isn't amenable to talk therapy."

Phelps' research team in Los Angeles, and Drevets and neurologist Marcus Raichle at Washington University in St. Louis used positron emission tomography (PET) scans to uncover the portions of the brain that are abnormal in depressed individuals. PET scans dynamically reveal those parts of the brain that are active by showing, in a color-coded map, how much of a radioactively labeled sugar or oxygen is taken up by the various brain regions from the bloodstream.

When the St. Louis group compared the PET scans of severely depressed patients to those of normal volunteers who were asked to think a sad thought, they discovered some striking differences. One area of the brain was equally active in both the depressed and normal subjects (presumably the part responsible for the sad thought). But another brain area, part of a region called the caudate nucleus, was markedly underactive in the depressed patients.

This area, which is thought to play a role in regulating emotion, continued to be underactive in the patients even after the depressive episode had passed, additional PET scans revealed.

According to Raichle, the preliminary findings suggest that although depressed and normal people use some of the same parts of their brains when feeling sad, depressed patients may be more susceptible to having frequent sad feelings because of an underlying brain defect—perhaps a malfunctioning caudate nucleus. The results were presented at a recent National Academy of Sciences symposium on brain research.

Some of Raichle's findings are confirmed by those of Phelps, who consistently found the head of the caudate nucleus underactive in patients with depression as compared to normal individuals. The PET findings also complement studies on people who have experienced a stroke or another disorder that damages the head of their caudate nucleus. These people develop many symptoms of depression, according to Drevets.

But when some of the patients Phelps studied recovered from their depression, their caudate nucleus activity approached normal levels. These findings, which are contrary to those of Raichle, suggest that lowered caudate nucleus activity may be one of depression's symptoms and not necessarily the underlying cause of the disorder, says Phelps' colleague, UCLA psychiatrist Lewis Baxter.

Because more than three-quarters of a brain chemical called dopamine is found in the caudate nucleus and two other connecting brain structures, Phelps speculates that faulty regulation of this neurotransmitter lies at the heart of depression.

Evidence for this theory comes from the fact that many drugs that foster profound changes in mood, such as cocaine, amphetamines and some types of antidepressants, work by altering the amount of dopamine in the brain.

Phelps has recently harnessed PET to highlight areas in the brain that are heavy dopamine producers. He hopes to apply this type of imaging to assess if altered dopamine synthesis in the caudate nucleus is tied to depression.

"The biochemical imaging we can do with PET," says Phelps, "allows us to get closer and closer to the origin of depression."

Patlack is a free-lance writer.