Images of Obsession

The peculiar symptoms of obsessive-compulsive disorder appear to be linked to a mismatch in the brain's metabolic activity

By BRUCE BOWER

Every day, a young woman shakes her clothes for a half hour and washes herself for up to six hours, haunted by the thought that germs might infect her with a deadly disease. A man cannot prevent himself from driving back to check every place on the road where he has hit a bump, because thoughts that he has run someone over torment him at every turn. Another man stops cooking for fear he will poison his wife and refuses to use electrical appliances because he worries about causing a fire.

These people illustrate some of the symptoms of obsessive-compulsive disorder, a strange brew of recurrent ideas and impulses that are often experienced as repugnant (obsessions) mixed with ritualistic, seemingly senseless behaviors aimed at preventing harm and warding off anxiety (compulsions). An estimated 2 percent of the adult population in the United States suffers from obsessive-compulsive disorder at some time in their lives, and one-third of them develop the disorder during childhood.

French physician and psychologist Pierre Janet described obsessive-compulsive disorder, using the term "psychasthenia," in a classic 1903 publication. Not long afterward, Sigmund Freud conceived of obsessions and compulsions in his patients as complex psychological defenses used to deal with unconscious sexual and aggressive conflicts.

In contrast with this long history of clinical observation, little is known about what parts of the brain help to produce the disorder's bizarre thoughts and acts. But that is beginning to change.

In the March Archives of General Psychiatry, scientists at the University of California at Los Angeles School of Medicine suggest that there is an imbalance in the energy-conversion rates of two structures in the frontal lobes of obsessive-compulsives. The two brain regions normally work together to help channel and control incoming sensations and perceptions.

While this metabolic mismatch accompanies obsessive-compulsive symptoms, says psychiatrist and project director Lewis R. Baxter Jr., it is not necessarily a cause of the disorder.

The new report is based on positron emission tomography (PET) scans of 14 obsessive-compulsives, 14 individuals with severe depression and 14 controls with no psychiatric diagnoses. PET-scanning devices transform quantitative measures of metabolic activity throughout the brain into color-coded pictures. As in many other PET experiments, a radioactively labeled glucose compound was used to gauge tissue reponses, since glucose is a prime energy source in the brain.

Compared with depressed and control subjects, obsessive-compulsives had significantly increased glucose metabolism in a frontal lobe region on the left hemisphere, known as the left orbital gyrus. The right hemisphere's corresponding orbital gyrus showed no substantial jumps in activity. In addition, the metabolic rate in the left orbital gyrus, relative to that of the entire left hemisphere, was markedly elevated among obsessive-compulsives, and stayed high even among eight subjects whose symptoms eased after treatment with an antidepressant drug.

Since all of the obsessive-compulsive subjects were right-handed, says Baxter, it appears that activity in the dominant-hemisphere orbital gyrus is most affected. A left-hander with the diagnosis was recently given a PET scan by the UCLA researchers, and an increased metabolic rate in the right orbital gyrus was observed.

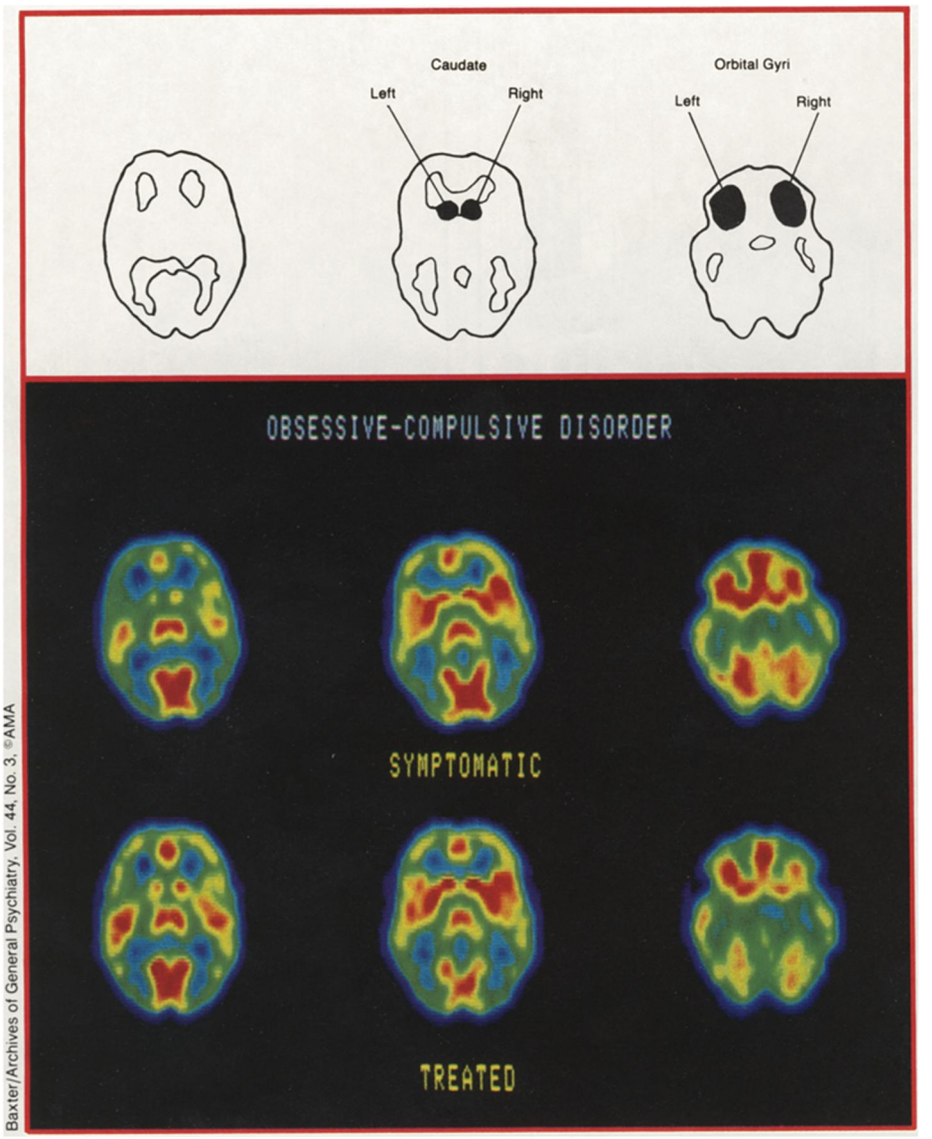
Animal studies, notes Baxter, indicate that the orbital gyri are involved in directing attention toward specific objects. Damage to this area can cause animals to engage in repetitive behaviors.

Two other frontal-lobe structures, the caudate nuclei, located on opposing hemispheres, also displayed significant jumps in metabolic rate relative to overall hemisphere activity, but only among obsessive-compulsives who improved after drug treatment. Before treatment, the ratio of caudate activity to hemisphere activity was within the normal range for obsessive-compulsive subjects, and it did not increase among those whose symptoms did not improve.

What does all this mean about brain activity in obsessive-compulsive disorder? Baxter and his colleagues propose that dominant-hemisphere activity in the orbital gyrus may increase beyond the capacity of the caudate nuclei to integrate the information relayed its way. (Animal evidence suggests that the caudate and the orbital gyri work jointly in the expression of new behaviors.) They further submit that successful treatment or the periodic easing of symptoms without treatment—not unusual among obsessive-compulsives—is accompanied by abnormally high activity in the caudate region that reestablishes its processing ability.

The invasive thoughts and ritual behaviors of obsessive-compulsive disorder are undoubtedly linked to other brain areas as well, adds Baxter. PET scanners now available that have twice the resolution of the devices used in the UCLA study may be able to pinpoint critical regions.

Nevertheless, says Baxter, "metabolic rates in the forward portion of the frontal cortex distinguish obsessive-compulsive patients rather well from patients with serious forms of depression." This is important because symptoms of severe depression, as well as anxiety, often occur among obsessive-compulsives and create uncertainties in diagnosing the disorder. Obsessive-compulsive disorder also occcurs at a high rate among victims of the brain disorder known as Tourette's syndrome, which results in tics and the



Baxter/Archives of General Psychiatry, Vol. 44, No. 3, ©AMA

Top figures show location of caudate nuclei and orbital gyri in PET scans below. Cerebral glucose metabolism is greatest in red and orange areas. In these scans, it increases markedly in the left-hemisphere orbital gyrus and caudate nuclei of an obsessive-compulsive whose symptoms improved with drug treatment.

involuntary shouting of obscenities.

"The new PET evidence is exciting and I'd love to see it replicated," says psychiatrist Thomas R. Insel of the National Institute of Mental Health. PET scanners are large, intimidating devices, he cautions, and it is hard to tell if the scanning procedure alters the mental state of obsessive-compulsives substantially more than that of healthy controls or depressed patients.

Insel and his co-workers recently completed a study of cortical blood flow – another indicator of brain activity – in 12 persons whose obsessive-compulsive symptoms revolved around a fear of dirt or germs. (The cortex is the outer layer of the brain responsible for "higher" mental functions such as language and problem-solving.) Not surprisingly, cortical blood flow increased slightly when the subjects thought about the objects of their fears. But when they were actually exposed to dirt or to something they habitually associated with germs, cortical blood flow plummeted, even as heart rate and electrical responses in the skin took off.

"This absolutely contradicted our predictions," says Insel. "When people are exposed to the things they're most afraid of, subcortical brain areas may be most activated." This suggestion is consistent with the metabolism increases observed by the UCLA researchers in the subcortical orbitral gyri and caudate nuclei of obsessive-compulsives.

Those two areas contain large quantities of serotonin, a chemical messenger between brain cells that Insel and his colleagues believe plays a major role in obsessive-compulsive disorder. An antidepressant drug called clomipramine – not yet available as a prescription drug in the United States – blocks the action of serotonin and often provides dramatic relief to adult and adolescent obsessive-compulsives (SN: 4/20/85, p.245).

Baxter and his colleagues treated obsessive-compulsives with another serotonin-squelching antidepressant, trazodone hydrochloride. Although clomipramine has been more thoroughly studied, the UCLA investigators say it can also lead to sedation, impotence and tremors. "There is a clear need for new medications to treat obsessive-compulsive disorder," says Baxter.

The NIMH researchers have also found that a patient's obsessive thoughts will rapidly worsen after taking a drug that stimulates a specific class of serotonin receptors. "For some reason, these receptors are supersensitive in many obsessive-compulsives and may create a vulnerability to the disorder," says Insel. The reasons for the supersensitivity, which might include a genetic defect in coding for the receptors' functions or a lack of serotonin in the brain, are not known.

For that matter, the range of environmental and physiological origins of obsessive-compulsive disorder remain poorly understood and debatable. "Brain research may eventually help to understand the psychodynamic processes important for generating obsessions and compulsions," says Insel, "but we're not at that point yet." □