Brain anatomy yields schizophrenia clues

Subtle but significant changes in brain anatomy are common features of people with schizophrenia, researchers report in the March 22 New England Journal of Medicine. They base their conclusion on brain scans of 15 sets of identical twins, each pair consisting of one twin with schizophrenia and one without.

The findings provide the best evidence yet that nongenetic abnormalities exert an important influence on the development of schizophrenia, says Daniel R. Weinberger of the National Institute of Mental Health (NIMH) in Bethesda, Md., who conducted the study with Richard L. Suddath and three other NIMH colleagues. One possibility is that brain cells for some reason do not migrate to their appropriate destinations during the fetal development of people who later develop schizophrenia, Weinberger says.

In 12 of the 15 twin pairs, the researchers could identify the one with schizophrenia just by looking at magnetic resonance imaging (MRI) scans of the brain. Magnetic resonance imaging is a technique for taking pictures of various structures in a living brain. Visual clues to schizophrenia consisted of clearly enlarged ventricles — three fluid-filled spaces deep within the brain.

Mathematical analysis of the data showed that, compared with their healthy twins, 14 of the 15 schizophrenics had at least one enlarged ventricle and also displayed size reductions in the temporal lobes, the hippocampus and the volume of the left temporal lobe's gray matter. The widely dispersed brain abnormalities occur in areas considered crucial to regulating emotion and motivation.

A control group of seven healthy identical-twin pairs showed no size differences in the same brain structures.

Brain abnormalities were not more severe among the schizophrenics with a long history either of the disorder or of antipsychotic drug treatment, the scientists note. Thus, the changes appear linked directly to schizophrenia, they say.

Previous studies using MRI and computerized tomography have charted an enlargement of brain ventricles among a substantial portion of people with schizophrenia, but researchers disagree over the extent of the brain's shrinkage as well as the cause of the anatomical abnormalities.

Weinberger suggests that early in brain development, a misdirection of cells — possibly caused by a viral infection, autoimmune disorder or birth injury — causes structural abnormalities that remain largely "silent" until the central nervous system undergoes maturational changes in late adolescence, when symptoms of schizophrenia typically emerge.

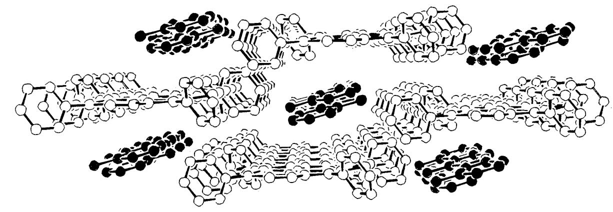
Although his findings and an earlier study of twins by other researchers provide "nearly definitive evidence" of structural brain abnormalities associated with schizophrenia, the significance of the observation remains unclear, writes M.-Marsel Mesulam of Beth Israel Hospital in Boston in an editorial accompanying the research report. Not all schizophrenic patients have large ventricles, Mesulam says, and large ventricles can also appear in people with manic depression or Alzheimer's disease.

Moreover, another research team studying schizophrenic brains has reported detecting clear ventricular enlargement only on the MRI scans of male patients — a finding at odds with the NIMH study, which revealed abnormalities in most of the eight male and seven female twins with schizophrenia. Nancy C. Andreasen of the University of Iowa in Iowa City and her co-workers, who describe the contrasting results in the January Archives of General Psychiatry, maintain that schizophrenia is actually several different disorders and that studies using different proportions of each type may yield different findings.

They add that evidence of metabolic and chemical changes in the brain may reveal more about schizophrenia's perplexing nature than anatomical changes picked up by MRI. *— B. Bower*

Finding chemical tools in a crystal forest

Crystals made of the same kinds of chemicals that enable blood proteins to carry oxygen and chlorophyll molecules to capture solar energy appear suited for such nonbiological roles as pollution control and catalyzing chemical reactions in the lab, and even as exotic research materials that turn liquids into solids without lowering the liquid's temperature.



Strouse et al.

White structures represent the host lattice of a TPP "sponge." Black structures represent guest molecules residing in the sponge's channels.

At the core of these crystals lie flat molecular structures known as tetraarylporphyrins (TPPs), each of which consists of a square-shaped porphyrin molecule with a benzene molecule attached to each of its sides. Chemists at the University of California, Los Angeles, have discovered that TPP molecules self-assemble into channel-ridden crystals.

By modifying the benzene components, Charles E. Strouse and his coworkers say they can control the shape, size and orientation of the channels within the crystals. Such control might enable them to "program" the crystal lattice to "preferentially incorporate guest molecules of a *predetermined* size, shape, handedness and charge," the chemists suggest in the Feb. 28 Journal of the American Chemical Society.

To get a feel for what the chemists have in mind, press the bottoms of your palms and the ends of your fingers together. By further pushing against your fingertips, you can alter the size and shape of the cage defined by your hands, and thus whether you can trap a tennis ball or short stack of crackers.

"That's kind of what these things can do," Strouse says. When TPP molecules crystallize in solutions that also contain dissolved molecules such as toluene (a solvent used in paint), the dissolved molecules get trapped within the regularly spaced channels of the TPP crystals, which the chemists also call "TPP sponges." The sponges resemble zeolites, an already important class of channel-containing crystals, but their flexibility enables them to accommodate a wider variety of guests, Strouse says.

By examining the crystal structures of about 70 TPP molecules that differ in the metal atom that sits at the center of their porphyrin components or in the way their benzene components have been chemically modified, the chemists discovered common structural features that others had not observed, Strouse says.

"They saw the forest despite the trees," comments longtime porphyrin researcher W. Robert Scheidt of the University of Notre Dame (Ind.). Others who study porphyrin crystals focus primarily on just a few structures, and so have not been well positioned to perceive structural similarities across the extended family of TPP crystals, Scheidt says.

Strouse imagines using TPP sponges to sop up organic contaminants from liquids or gases. He also envisions filling the channels with monomers and then using the natural light-harvesting powers of porphyrin to catalyze the linking of monomers into polymers. A more esoteric use involves trapping molecules of a hard-to-crystallize liquid inside the sponges' regularly arranged channels, thus forcing the liquid into a more solid-like form amenable to structural analyses such as X-ray crystallography. "We haven't demonstrated in gruesome detail how effectively one can do that in general," Strouse stresses. *— I. Amato*