coils that nest within one another like Russian dolls. The coils are kept cool by ultracold liquid nitrogen, circulating through channels between them. Just before an experiment, the researchers drain the coolant to prevent it from vaporizing, fire up the magnet, and then flood the coolant back in.

Even with its improved design, the new 60-tesla magnet may not top the high-field heap for long. Researchers at the Los Alamos branch of the National High Magnetic Field Laboratory already have designs on the drawing board for a 100-tesla pulsed magnet. A prototype of the new machine is expected next year and the full 100-tesla device is scheduled to be built by 2002.

–ROBERT F. SERVICE

NEUROBIOLOGY

A New Route to Treating Schizophrenia?

Last month's shootings of two Capitol Hill police officers were a sad reminder of how far we are from a cure for schizophrenia, the debilitating mental illness that plagues the alleged murderer. But work described in this issue suggests a new approach to schizophrenia drugs that may someday lead to better therapies for the condition, which afflicts 1% of the population of the United States alone.

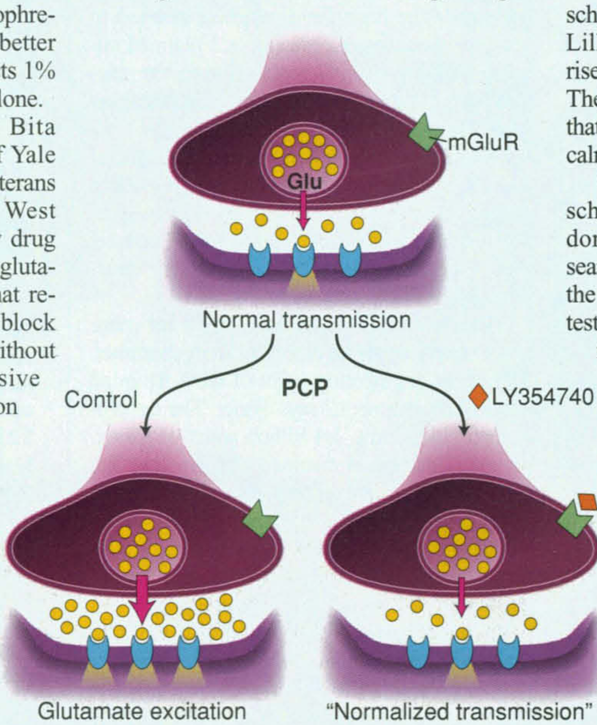
On page 1349, neuroscientists Bita Moghaddam and Barbara Adams of Yale University School of Medicine and Veterans Administration Medical Center in West Haven, Connecticut, report that a new drug that lowers brain levels of the chemical glutamate—one of the neurotransmitters that relay messages between neurons—can block schizophrenia-like symptoms in rats, without apparent side effects. "It's impressive work," says schizophrenia researcher Jon Horvitz of Columbia University in New York City. "This is a promising avenue for a drug that attenuates schizophrenic symptoms."

Such drugs are badly needed. Current schizophrenia medications, known as neuroleptics, work by blocking the action of another neurotransmitter, dopamine, and they are far from ideal. While patients who take them often see reductions in paranoia and hallucinations, the drugs offer little relief from other symptoms, such as poor attention spans, jumbled thoughts, and difficulty interacting with other people. What's more, the neuroleptics often cause troubling side effects, including uncontrollable tremors similar to those in Parkinson's patients. "We are desperate for compounds that might treat psychosis that are not primarily dopaminergic," says schizophrenia specialist David Pickar of the National Institute of Mental Health (NIMH) in Bethesda, Maryland.

The psychoactive drug phencyclidine, or PCP, offered tantalizing hints that a different approach might work. Researchers have known for many years that PCP—"angel dust"—induces schizophrenia-like symptoms in healthy people, an effect that's been attributed to its ability to block the *N*-methyl-D-aspartate (NMDA) receptor, one of a number of receptors in the brain through which glutamate exerts its effects. That finding led scientists to hypothesize that a depression of glutamate transmission in the brain might contribute to schizophrenia. Efforts to treat schizophrenia with drugs that rev up the NMDA receptor didn't pan out, however, largely because the agents can cause serious side effects such as seizures. Meanwhile, scientists and drug developers focused on dopamine, as evidence accumulated that the effectiveness of neuroleptics is proportional to their ability to block dopamine transmission in the brain.

But the Yale workers took a new look at glutamate, using rats treated with PCP, which develop symptoms, such as frantic running and incessant head-turning, thought to parallel psychotic symptoms in humans. As expected from previous work, the drug raised dopamine concentrations in the rats' brains. But much to the surprise of the researchers, for reasons as yet unknown, PCP also caused a surge in brain glutamate levels. This suggests that abnormally high, rather than low, glutamate activity might underlie the rats' reactions to PCP. Moghaddam then speculated, she recalls, that "if we block glutamate activation, maybe we can block these behavioral effects."

To avoid side effects, Moghaddam and Adams wanted to block glutamate activity only in those parts of the brain where it might be elevated. So, they turned to a drug called LY354740 that is under development at Eli Lilly & Co. in Indianapolis for other psychiatric disorders such as anxiety. LY354740 stimulates a subgroup of the so-called metabotropic glutamate receptors, which sit on the terminals of glutamate-releasing neurons and act as regulators of glutamate levels: As shown in rat experiments by Lilly's Darryle Schoepp and colleagues, LY354740 dampens output of the neurotransmitter when its levels get too high but doesn't interfere with normal levels. By stimulating these receptors, Moghaddam and Adams hoped, they could selectively lower glutamate levels in their PCP-treated rats.



A calming influence. By binding to a metabotropic glutamate receptor (mGluR), LY354740 prevents the PCP-induced surge in glutamate excitation.

K. SUTLIFF, ADAPTED FROM D. SCHOEPP

The plan worked. In seven control rats, PCP caused glutamate levels to rise more than twofold in the prefrontal cortex, one of the brain regions that goes haywire in schizophrenia, but the six animals given the Lilly drug experienced no such glutamate rise, although their dopamine levels surged. The treated rats also escaped the symptoms that PCP induced in the controls. They stayed calm and showed little head-shaking behavior.

What's more, the drug might even act on schizophrenia symptoms that neuroleptics don't relieve. With food rewards, the researchers trained other rats to alternately visit the two arms of a T-shaped maze. This is a test of working memory, a type of short-term memory used to make decisions or draw conclusions that is often severely impaired in schizophrenia. Control rats treated with water and PCP suffered memory lapses, choosing the wrong arm about half the time under certain conditions. But rats pretreated with LY354740 made a wrong choice just 30% to 40% of the time, about the same rate as normal rats. This suggests that the drug reduces this PCP-induced cognitive deficit.

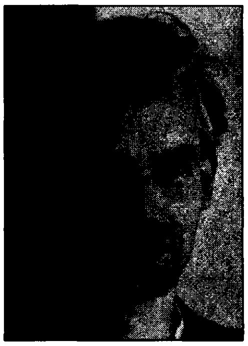
Of course, many a drug that has looked promising in animals has failed in human trials. Researchers worry, for example, that PCP-induced symptoms in rats do not accurately reflect schizophrenia in humans. Lilly will not say whether the company plans to test LY354740 in schizophrenia patients, but it has conducted early clinical trials of the drug for other diseases, including anxiety and nicotine withdrawal. "It's a very exciting approach to a number of psychiatric disorders," says Steven Paul, the head of Eli Lilly's research labs. Pickar of NIMH hopes that schizophrenia will be among them. "If the compound will be tolerated well," he says, "you have something that's got to get into humans." –INGRID WICKELGREN

MATHEMATICS

Top Honors Go to Math With a Physics Flavor

BERLIN—Mathematicians officially anointed four new superstars when the 1998 Fields Medals were presented here last week at the opening ceremonies of the International Congress of Mathematicians. There is no Nobel Prize in mathematics, and the Fields Medal, awarded every 4 years by the International Mathematical Union (IMU), has become the discipline's highest honor. Unlike Nobels, Fields Medals are traditionally awarded only to mathematicians no older than 40 and are intended as much to encourage future work as to recognize past achievement.

Borcherds



Gowers

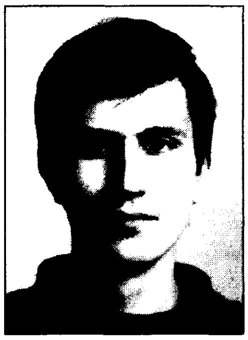
The four new medalists are Richard E. Borcherds of the University of Cambridge and the University of California, Berkeley; William Timothy Gowers of Cambridge; Maxim Kontsevich of Institut des Hautes Etudes Scientifiques, Bures-sur-Yvette, France, and Rutgers University; and Curtis T. McMullen of Harvard University. In addition, Peter Shor of AT&T Laboratories in Florham Park, New Jersey, received the IMU's Nevanlinna Prize—meant to be the equivalent of the Fields Medal in theoretical computer science—and Andrew Wiles of Princeton University was given a special one-time award for his proof of Fermat's Last Theorem.

Much of the work honored by the medals shows the influence of physics. "I think that's not an accident," says Borcherds. "At the moment, theoretical physicists are churning out enormous numbers of amazing new ideas. My guess is that this is going to continue well into the next century." McMullen remarks that when he was in graduate school, gauge theories from particle physics were all the rage. "I used to think, 'I don't do that kind of trendy mathematics,'" he says. But now he finds himself working on mathematics connected to the notion of renormalization, a kind of scaling technique used in physics to study phase transitions such as the change from ice to water.

The links to physics are strongest in Kontsevich's work. He first gained international attention for his doctoral thesis, in which he proved a conjecture of Edward Witten, a mathematical physicist at the Institute for Advanced Study in Princeton. The conjecture made the surprising prediction that one could use certain calculations in algebraic geometry to produce a solution to an equation from a completely different area, the Korteweg–de Vries equation from the study of nonlinear waves. Kontsevich has also done important work in topology. For example, he produced a vast generalization of the notion of linking numbers for knots—numbers that give a measure of how intricately two knots are entangled—which originated in the 1800s with the mathematician Carl Friedrich Gauss.

Although McMullen has worked in a variety of mathematical areas, from topology to the theory of computing, much of his work has focused on dynamical systems—systems that evolve over time. McMullen has studied systems in which a simple process is iterated many times to produce complicated dynamics. These processes depend in very subtle ways on certain parameters, which McMullen has analyzed through renormalization. He has also used ideas from dynamical systems to produce important results in other areas, such as topology.

Borcherds's route toward physics started in finite group theory. An example of a finite group is the collection of integers from 1 to 12 under the operation of "clock arithmetic," so that, for instance, 8 + 5 = 1. The concept sounds simple, but it gives rise to an enormous variety of mathematical flora and fauna. Mathematicians have worked for decades on classifying all the finite groups. One of the strangest they have uncovered is the "monster group," which has some 10^{53} elements and a little-understood structure. Conjectures about the monster came to be known as "monstrous moonshine" because they were considered so improbable, but Borcherds solved one of the most famous of these conjectures by inventing a fruitful new concept, called a vertex algebra. Vertex algebra has since proven important in physics as well, especially in a field theory that is an underpinning of theoretical particle physics, including string theory.



Kontsevich

McMullen

In contrast to the work of the other medalists, Gowers's work has little if any connection to physics. It focuses on objects that form part of the standard tool kit for many areas of mathematics: infinite-dimensional Banach spaces. Named after the Polish mathematician Stefan Banach, who worked in the 1930s, these spaces are akin to the familiar Cartesian plane, which is the natural home of two-dimensional vectors, except that they exist in infinite dimensions. Gowers solved a number of famous problems, originally stated by Banach, that had gone unsolved for decades.

Shor's work has received far more attention outside mathematics than has that of the Fields Medalists. After doing important research in combinatorics and graph theory, Shor startled the world in 1994 by proving that a quantum computer—based on the ability of atoms or particles to exist in several quantum states at once—could solve a real problem: factoring numbers at a speed vastly greater than that of conventional computer algorithms. Besides sparking great interest among scientists and mathematicians, the work also has raised concerns about the security of cryptographic codes based on the difficulty of factoring large numbers. Since then, Shor's results in quantum error–correcting codes and fault tolerance have raised hopes that quantum computers might one day become a reality (see *Science*, 7 August, p. 792).

But the longest and loudest applause

Two more winners. Peter Shor *(left)*, a quantum computing expert, and Andrew Wiles, prover of Fermat's Last Theorem, received special awards.

PHOTOS: INTERNATIONAL CONGRESS OF MATHEMATICIANS