Behavior

Memory's neural hit in schizophrenia

People who suffer from schizophrenia frequently endure taunts and jibes of imaginary voices and construct bizarre scenarios of being persecuted by outside forces. And as if that weren't enough, these people are easily distracted and forgetful.

A new study links memory deficits in schizophrenia to altered activity in two related brain areas already known to help healthy volunteers remember information.

A team of neuroscientists led by Stephan Heckers of Massachusetts General Hospital in Boston used positron emission tomography (PET) scanning to examine brain activity—reflected by blood flow changes—in 13 men diagnosed with schizophrenia and 8 men with no psychiatric disorders. PET scans were obtained as participants tried to remember previously studied word lists.

In half the trials, participants were instructed to think about possible meanings for words as they studied them, a strategy that typically aids recall. In the other half, the men were told to count the number of right angles formed by the letters in each word, a task that usually makes recall harder.

Healthy men indeed remembered more words after thinking about their meanings. Neural activity on the right side of the hippocampus, a brain structure critical to the awareness of previously learned information, surged during recall, Hecker's group reports in the August NATURE NEUROSCIENCE. Right-angle trials generated increased activity in a patch of tissue at the front of the brain that mediates mental efforts to generate memories.

In contrast, men with schizophrenia remembered more words after counting right angles; they outperformed healthy men on this task but not on word meaning trials. Hippocampal activity in the schizophrenia group started out high and remained unchanged during both memory tests. Several areas at the front of the brain associated with attention and mental effort exhibited activity surges as these men, but not those without schizophrenia, consciously recalled words in both trials.

In schizophrenia, an inability to exert the mental control needed to ignore automatically evoked word meanings may aid recall on right-angle trials, the researchers suggest. —*B.B.*

Tracing the brain's reading network

A new study indicates that reading requires the angular gyrus, a brain structure that maintains connections to areas involved in speech comprehension and the integration of alphabetic letters with their corresponding sounds.

The reading disorder known as dyslexia may often reflect an inability of the angular gyrus to work in concert with these related brain regions, hold neuroscientist Barry Horwitz of the National Institute on Aging in Bethesda, Md., and his coworkers.

Horwitz's team administered positron emission tomography, or PET, scans to 17 dyslexic men, all of whom had long-standing reading difficulties despite having IQs in the normal range, and 14 men who read well. Brain imaging was performed as participants read difficult nonsense words (such as "phalbap," in which "ph" would be pronounced as "f") and real words with unusual pronunciations (such as "choir").

For good readers, these tasks induced simultaneous blood flow surges on the left side of the angular gyrus and in several brain areas that integrate the visual and linguistic information needed for effective reading, the scientists report in the July 21 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. The men with dyslexia exhibited increased activity in all of these areas except one—the left angular gyrus.

The new findings complement evidence that dyslexia may stem from disturbances in various parts of a brain network that begin working together during childhood as a result of continued exposure to written language, according to the researchers (SN: 3/7/98, p. 150). —*B.B.*

Biomedicine

View of HIV infection crystallizes

Simple security cameras have recorded the tricks employed by burglars to break into a building, but it has taken X rays to capture a crystal-clear snapshot of how HIV gains entry into cells. That long-sought picture, described in the June 18 NATURE and June 19 SCIENCE, reveals details of how the AIDS virus avoids the immune system. It also suggests new targets for drugs and hints that certain vaccine approaches will fail.

The image focuses mainly on gp120, a protein studding the outer envelope of HIV. The virus uses that protein to latch onto the immune cells it infects. Because of its flexible structure, gp120 has proven difficult to freeze into crystal form—a necessary step before X rays can be shined at the protein to reveal its shape.

After trimming portions of gp120 considered unimportant for binding to immune system cells, researchers led by virologist Joseph Sodroski of the Dana-Farber Cancer Institute in Boston and X-ray crystallographer Wayne A. Hendrickson of the Howard Hughes Medical Institute at Columbia University in New York finally created a crystal of the protein bound to two other molecules. One of those molecules is CD4, the immune cell surface protein to which HIV initially binds. The other is an antibody known to prevent gp120 from attaching to a protein called CCR5, the second site on the immune cells to which HIV binds.

The image of gp120 derived from this crystal shows in great detail how the HIV protein binds to CD4. It highlights such features as a ball-shaped protuberance on CD4 that fits nicely into a deep cavity on gp120. Such intimate contacts offer an appealing target for drug developers looking to design small molecules that would interfere with HIV's attempts to infect cells.

The picture of gp120 also helps explain how the AIDS virus eludes the body's defenses. The protein is coated with sugar molecules that are difficult for the immune system to recognize. Moreover, the parts of gp120 that bind CCR5 remain shielded by several loops of amino acids until the virus makes contact with CD4. At that point, gp120 apparently undergoes a shape change that peels back those loops and creates a snug fit between itself and CCR5.

"One way to view [the loops] is as an umbrella that shields the critical regions of gp120 from the rain of antibodies thrown at it," say John P. Moore and James Binley of Rockefeller University in New York in a commentary accompanying the NATURE article. They warn that this umbrella may prevent vaccines designed to induce antibodies to gp120, such as the one undergoing testing in the U.S. and Thailand (SN: 7/11/98, p. 31), from stopping HIV infection. —*J.T.*

The intestinal beat goes on

To speed food on its digestive journey, intestines normally contract about a dozen times every minute. Researchers have long believed that a thin layer of specialized cells, the intestinal cells of Cajal, drive this steady rhythm. Now, a Canadian research team has isolated the hard-to-find cells from mice and demonstrated that the cells undergo electrical oscillations at about the same rate as intestinal contractions. "We've shown rhythmic electric activity in cells that we're 100 percent sure are intestinal cells of Cajal," says Jan D. Huizinga of McMaster University in Hamilton, Ontario, an author of the study, which was reported in the JULY NATURE MEDICINE.

Kenton Sanders of the University of Nevada School of Medicine in Reno notes that other researchers, including a Japanese group working on the problem several years ago, have provided similarly compelling proof of pacemaker activity in the intestinal cells. As researchers learn what makes these cells tick, the data may help determine whether the intestinal cells of Cajal play a role in various gastrointestinal illnesses. "It could be that the loss of these cells leads to some intestinal disabilities," says Sanders. —*J.T.*