Schizophrenia and brain imbalance

The possibility that biochemical problems, perhaps including a brain abnormality, are related to schizophrenia has been generally accepted for years. And for about the last decade, scattered bits of evidence have hinted that the left brain hemisphere might be a major site of any such dysfunction in schizophrenics. For example, a large body of clinical and experimental evidence indicates that schizophrenia is connected with a left brain-associated thought disorder characterized by illogical and irrational patterns, along with poor conceptualization and abstraction abilities. Other studies have uncovered apparent disturbances in lateral balance, primarily a higher incidence of left-sidedness among schizophrenics.

Now, in two separate studies of 72 schizophrenics and 48 control group members, University of Pennsylvania psychologist Raquel E. Gur reports that "schizophrenia is associated with ... both left hemisphere dysfunction and overactivation." The findings could have implications for medication, as well as psychotherapy, she says.

The first experiment involved the performance of two tasks designed to measure verbal and spatial information processing in the two hemispheres. Twenty-four schizophrenics were matched against 24 controls (12 males and 12 females in each group). In contrast to the controls, the schizophrenics showed a right hemisphere superiority on both verbal and spatial tasks, "indicating a left hemisphere dysfunction in the initial processing of verbal information," says Gur.

In the second test, lateral eye movements were recorded as measures of hemisphere activation following the presentation of various types of information and were measured in 48 schizophrenics and 24 controls. "The schizophrenics had significantly more rightward eye movements," Gur says, "indicating left hemisphere overactivation."

The two results combined, she suggests, provide a "new framework" for examining the cognitive aspects of schizophrenia. It appears that "schizophrenics overactivate the very hemisphere that is dysfunctional," Gur reports in the April JOURNAL OF ABNORMAL PSYCHOLOGY. "This combination of events may explain why schizophrenics are so often described as using faulty logic." Conversely, she says it may also be possible that it is the left brain overactivation that triggers dysfunction, rather than vice versa.

The role of drug treatment in left hemisphere dysfunction remains unclear, says the psychologist. Two unpublished reports on the phenothiazines, a major medication for schizophrenia, do not implicate the drugs as a potential cause of the hemisphere abnormality. In fact, one of the reports indicates that "if anything, phenothiazines tend to attenuate laterality effects in schizophrenia." Still, Gur cautions that no research has been published in this area and that it is conceivable that "dysfunction [could] result from medication." All the schizophrenic patients in her study were on phenothiazines, she says. Her "next step" is to compare schizophrenic groups on medication with those off drugs.

Regarding psychotherapy, Gur says her results dictate a "more reasonable approach" than some therapists may have attempted in the past. "Therapy should try to correct the illogical thinking—since the left hemisphere is responsible for logic," she said in an interview. Rather than "focusing on the internal approach" that tries to "uncover" the causes of the patient's conflict, Gur says therapy should try to make sure the patient stands on his own two feet. The therapist-patient interaction should deal with things like "spending money, dressing, eating — things most of us take for granted," she says. "Then, once the patient gets out of the withdrawal stage, you might be able to get at some insight."

Gur cautions that it is too early to say whether left brain dysfunction and overactivation are a cause or effect of schizophrenia. "We can't make any claims like that," she says. "We need longitudinal, predictive studies. All we can say now is that schizophrenia is *associated* with left brain dysfunction." □

Ocean eddies from space

Huge ocean eddies, important in studies ranging from phytoplankton productivity to pollution-tracking to meteorology, are numerous in this remarkable photo taken by Landsat from 915 kilometers up. At least eight individual eddies can be seen, some up to 30 km across, says Richard S. Williams Jr. of the U.S. Geological Survey in Reston, Va. Three well-developed double eddies show distinct stream currents as much as 70 km long.

The case of the missing memorandum

The facts are in on the allegation that Charles A. Thomas Jr. did recombinant DNA experiments at Harvard Medical School without appropriately notifying the National Institutes of Health. Last December for the first time, the institute directed an investigator to stop recombinant DNA research (SN: 12/31/77, p. 420). While responding to an Environmental Defense Fund request for information, administrators discovered Thomas had not filed the required Memorandum of Understanding and Agreement (MUA), which outlines how proposed research meets the safety guidelines.

Last week the investigation culminated in two reports, each detailing letters, meetings and conversations among Thomas, the Harvard Medical School Committee on Recombinant DNA Activities and the NIH. An NIH report, submitted by James W. Schriver of the Division of Management Survey and Review found: "Dr. Thomas was in technical violation of the HMS and NIH guidelines dealing with recombinant DNA research."

A second report, by an *ad hoc* Harvard Medical School faculty committee, also records that the required memorandum was not submitted to NIH at the appropriate time. The Harvard report says the failure was the "unintended result of many factors" and ascribes the "web of misunderstanding" to the "unprecedented nature of an untried and complicated supervisory process."

Among the tangles of the web is the fact that Thomas did not specifically state in his grant application or its 1976 renewal request that he planned to do experiments using recombinant DNA (although he did include papers describing his recombinant DNA work and he reported it to another section of NIH in response to an inquiry). When in 1977 the Harvard recombinant DNA committee approved a memorandum for low risk (P2) recombinant DNA research in Thomas's laboratory, the MUA was sent not to NIH, but only to a private foundation funding Thomas's postdoctoral fellow. Members of the Harvard recombinant DNA committee report they were unaware that low risk recombinant DNA work continued in Thomas's laboratory while they considered the submitted MUA.

The NIH Executive Recombinant DNA Committee will now analyze the two reports and make recommendations to the director of NIH. Both reports say that

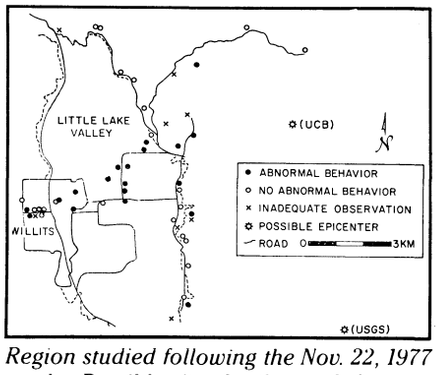
recent changes in NIH procedure would now prevent funding of recombinant DNA research without an approved memorandum, should such a situation arise again. Thomas has recently moved from Harvard to Scripps Clinic and Research Foundation in La Jolla, Calif. □

Anxious animals as quake precursors

Can animals sense an impending earthquake before humans or even seismic equipment detect physical clues? A team of scientists at the University of California at Davis thinks so on the basis of data collected last year following the November 22 earthquake near Willits, Calif. The researchers reported their findings at the American Geophysical Union meeting in Miami Beach last week.

Thousands of references to animal prescience of coming quakes — in legends and, more recently, in scientific literature — piqued sufficient curiosity in this country that a conference was held in September 1976 to explore whether and how scientists might investigate the alleged phenomenon. Animal behaviorist Dale F. Lott took part in the conference but came away very skeptical. When the United States Geological Survey said it would consider funding such research, however, Lott and several of his UC-Davis colleagues were among the first to apply. Their current research team consists of Lott together with another animal behaviorist, Ben L. Hart, geologist Kenneth L. Verosub and anthropologist Mary Howell.

One week after their contract took effect, a magnitude 5.0 earthquake rumbled through the Little Lake Valley area, about 200 kilometers north-northwest of San Francisco. They were ready; within three days they were interviewing some of the area's 3,000 residents about whether they had noticed any unusual behavior in pets or farm animals. About 17 of the 50 households interviewed during the next six weeks reported unusual behavior in some, but not all, of their animals. "The behavior reported was unusual because there was no immediate explanation for it, but it was not bizarre," Lott reported. "It had often been observed other times under circumstances that one would expect to make animals anxious or nervous."



Univ. of Calif.-Davis

Region studied following the Nov. 22, 1977 quake. Possible sites for the quake's epicenter — one proposed by UC-Berkeley, one by the U.S. Geological Survey — vary due to placement of seismic monitors.

For example, a "normally very calm" Arabian horse was found kicking the sides of its box stall about four hours before the quake. The owner tried to quiet it and finally released it into a paddock "where it continued to move about nervously," Lott said. "Horses in neighboring stalls were calm the whole time." Pets often sought the company of their owners while pacing nervously. "A Doberman pinscher, which normally ran about outdoors or slept during the morning, remained in her owner's presence almost continually, vocalizing and acting nervous," Lott reported. "The woman wondered aloud to her husband if she should give the dog a Valium," he said.

"In nearly every case the behavior of the subjects and the internal consistency of their reports convinced us that they were faithfully reporting their recollection," Lott said. "Most of the positive reports came in response to a general question about observed changes prior to the earthquake" and preceded the specific question about animal behavior in the interview, he said. Furthermore, "almost all owners who gave negative reports on all their animals had heard that animals behave abnormally prior to earthquakes and thought that in general it was true," he said. One even seemed disappointed that his goose hadn't shown signs; he had been watching her.

One of the most "convincing" aspects of the data is the nonrandom distribution of positive and negative reports, Lott says. Positive findings were confined primarily to a small region, strengthening the possibility that unusual behavior "was indeed an earthquake precursor and that the physical stimulus which caused that behavior had a limited, definable range," Lott says.

Interviews were designed to establish rapport with individuals and to "convince the interviewee that the interviewer does not have a preferred answer." Most of all, there was an attempt to "get an objective description of the animal's actions." Since animals cannot talk, the scientists must try and read their behavior for clues about what, if anything, the animals are sensing. For this reason, one animal behaviorist participated in each inteview.

The value in looking for animal precursors is not to gain a few hours lead time in evacuating potential earthquake zones but to learn where to look for warning clues, Lott says. If the animals are really sensing something, there must be ways to measure it; he says that's the ultimate objective. The UC-Davis team plans to conduct similar studies at as many as four additional earthquake sites, Lott says. □

Tumors not typed to a T

The immune system resembles a Russian novel: So many characters and subplots keep appearing that it's hard to keep them all straight. For example, take the protagonists known as the T-cells, lymphocytes so named because they are programmed in the thymus gland. Among other things, these cells are in charge of zapping tumors, rejecting organ transplants and giving bacteria the boot. In recent years, it has become apparent that there is not just one type of T-cell, but rather a menage à trois: helper Ts, killer Ts, and suppressor Ts.

Killer T-cells are credited with detecting and destroying tumors. But, obviously, sometimes a tumor slips by the surveillance of the killer T-cells. Karl E. Hellström and Ingegard Hellström of the Fred Hutchinson Cancer Research Center in Seattle, Wash., are coming closer to understanding one of the ways it escapes detection. They reported at the recent annual meeting of the Federation of American Society for Experimental Biology in Atlantic City that antigens (substances foreign to the body that can elicit an immune response) shed by the growing tumors apparently activate supressor T-cells to, well, suppress killer T-cells.

Injecting mice with various combinations of tumor, a form of tumor antigen, killer T-cells and suppressor T-cells, they discovered that tumor growth was enhanced if the tumor antigen was injected along with the tumor. They traced this protective effect of the antigen to a population of suppressor T-cells in the spleen. If these cells are knocked out by irradiation, the tumor antigen can no longer protect the tumor.

Now in the great war waged by the immune system against foreign invaders, the suppressor T-cell is no fifth column. If the killer T-cells were left unrestrained, they might start knocking off innocent body bystanders. The suppressor T-cells are thought to keep in check the incidence of autoimmune disease by hindering the killer T-cells.

Many body components are potentially antigenic and could be attacked by the immune system. Suppressor T-cells are thought to recognize these natural body components and their circulating potential antigens because they are present from birth. Researchers speculate that the circulating levels of the tumor antigen trick the suppressor T-cells into believing that the tumor is part of the body and their suppressive actions become misdirected.

The Hellströms are trying to discover just what the suppressor T-cells do to thwart the killer T-cells. They suspect that the cells may secrete a suppressing substance and are now searching for it. Then perhaps they can suppress it. □