

Chemical clues to schizophrenia

Researchers announced last week what they termed "the first direct understanding" of the symptoms of schizophrenia. Philip Seeman and Tyrone Lee of the University of Toronto reported that key areas of the brains of schizophrenic patients contain about twice the normal numbers of receptors for a chemical, dopamine, that carries signals between nerve cells. They speculate that schizophrenics are thus oversensitive to their own brain signals and are flooded with unusual thoughts, hallucinations and illusions. A variety of previous observations have implicated the transmitter dopamine in schizophrenia, but this research specifies its nature.

Seeman believes that his results lead to new approaches to curing schizophrenia, which affects more than one percent of the U.S. population. A blood test for schizophrenia may also be a result of the experimentation on dopamine receptors.

The rationale behind the recent discovery, Seeman explains, is to find just where the effective antischizophrenic drugs work. That information should reveal where schizophrenia is generated.

Scientists from four countries cooperated to obtain postmortem brain tissue from 48 people, including 20 schizophrenics, who died of heart attacks, car accidents or suicide. The dopamine receptors were counted by measuring the amount of a radioactively labeled drug, haloperidol, adsorbed to different regions of the brain. Haloperidol is an antischizophrenic drug that binds specifically to dopamine receptors, according to Seeman.

Lee and Seeman found an increased number of receptors in only two brain areas, the limbic region (an area responsible for "emotional thinking") and the caudate nucleus (an area that modulates body motion). Seeman and Lee believe that the difference is directly related to the disease and is not merely a consequence of its treatment. The researchers found the substantially increased number of dopamine receptors in six patients who had never received any drugs.

The suggestion that schizophrenics have too many receptors is consistent with earlier data implicating the dopamine system. Amphetamines, which trigger dopamine release, can produce symptoms of schizophrenia, as can too high a dose of L-dopa, a chemical precursor of dopamine administered for Parkinson's disease. At first, researchers thought the problem was one of too much transmitter chemical, but Oleh Hornykiewicz of the Clarke Institute of Psychiatry in Toronto and the University of Vienna demonstrated that the brain content of dopamine is normal in schizophrenia.

There is, however, another disease caused by abnormal dopamine levels. The brains of people with Parkinson's disease lack many of the dopamine-pro-

ducing cells. Those patients are treated with L-dopa. However, Hornykiewicz, who introduced L-dopa therapy, had kept frozen brain samples of patients from before the treatment was discovered. Frequently, when there is a deficit of transmitter in the nervous system, the receiving cells increase the number of receptors—as if to increase their chance to detect the weak signal. Seeman has analyzed the brains of five patients who had received no drugs and found that the receptor levels were higher than normal, as high as in schizophrenics. This, Seeman says, "closes the jigsaw puzzle."

The results on dopamine receptor number have not yet been confirmed by other investigators. Solomon Snyder and colleagues at Johns Hopkins University, using a different technique, have observed more variability in receptor number among schizophrenic patients and among controls, and no consistent differences between the two groups. Lee told the scientists that he could not yet rule out a tighter binding between the antischizophrenic drug and an altered receptor. Seeman cautions that the results rest on a sometimes uncertain diagnosis of schizophrenia. "This is just a beginning," he says.

A report of more preliminary research, also presented at the meeting of the Society for Neuroscience in Anaheim, Calif., suggested a different chemical

basis of schizophrenia. Frank Ervin of the University of California at Los Angeles and Roberta Palmour of the University of California at Berkeley identified a peptide in the blood of several schizophrenic patients. The peptide is nearly identical to a pituitary hormone found in normal people. The researchers report that the peptide—called leu-endorphin—dropped one hundred fold in concentration after 16 dialysis treatments when the patients were approaching normalcy. They have also observed high levels of leu-endorphin in patients who relapsed after several weeks. When partially purified leu-endorphin was injected into animals, it caused convulsive patterns in brain wave tracings. According to Ervin, this result indicates an effect on the limbic system, one region assumed to be involved in emotional disturbances. Other scientists are skeptical of this peptide being a specific schizophrenia toxin. More experiments will be needed to rule out the possibilities that the chemical is a response to the stress of dialysis or to the suspension of drug treatment. The substance might also represent a reaction to the abnormalities of schizophrenia, rather than its cause.

Whether or not the extra dopamine receptors and leu-endorphin turn out to play key roles in schizophrenia, the research indicates that new techniques of radioactive drug assay and biochemical analysis are valid tools in the search for clues to the basis of mental illness. □

Chasing Chinese chicken cancer

Rural planners in China's Ho-nan Province did not know it in 1967, but their massive relocation of workers to dig an earthen canal laid the groundwork for what may be one of the largest medical experiments in history.

In one fell swoop, party officials inadvertently solved a logistical problem that confronts disease researchers all over the world. Their transfer of 50,000 peasants fortuitously created a test group (and a control group in those left behind) large enough for scrupulous statistical analysis. When they ordered the peasants to leave their chickens behind, they also unwittingly isolated a major clue to the origin of cancer of the esophagus—the leading cause of death in that corner of the world. These two quirks of fate may provide scientists with new leads to the natural causes of cancer, report a group of U.S. researchers just returned from the People's Republic of China.

Robert W. Miller, an epidemiologist with the National Cancer Institute, said his scientific group toured Linh-sien County, the site not only of the Red Flag Irrigation Canal but also of a variant of esophageal cancer unique to that area but not to humans. "Their chickens have a remarkably similar carcinoma in the squamous cells lining their gullets," Miller told SCIENCE NEWS.

Chinese medical scientists have long believed that the chicken and human tumors are analogous, but prior to this decade they could not tell which came first—the chicken or the human cancer. As Miller noted, it is virtually impossible to sort out the myriad carcinogens and other pathogens which dovetail to provoke tumors. "They didn't know if the disease passed from human to bird, from bird to human, or from an outside influence to both populations concomitantly."

But the local "barefoot doctors"—a kind of paramedic peculiar to China who combine simple surgical procedures with a knowledge of medicinal herbs—monitored the chicken flocks the peasants purchased when they resettled. Two and a half years later they found a chicken with gullet cancer. Since then, 12 chickens in the new flocks have shown the disease, while the neighboring, parent flock of 2,400 birds has never had a single case.

Chinese epidemiologists began putting these clues together. The disease had passed from humans to chickens in a previously "no-risk" area for chickens. So it was not the environment—not the previously suspected chemicals in the water, nor a shortage of trace elements such as molybdenum in the soil, nor foodstuffs