Image of a melancholy brain

Persons suffering depression show a consistent pattern of decreased metabolic levels in the brain, report scientists from the University of California at Los Angeles. Using positron emission tomography (PET) to measure glucose use throughout the brain (SN: 1/31/81, p. 76), Michael E. Phelps and colleagues find lower than normal metabolic rates in subjects with mild depressive disease. These patients were in the early stages of disease and were not taking drugs.

The metabolic rate is most markedly reduced in areas of the brain involved in fear, anger and other strong emotions and in logic and reasoning, the investigators find. When a subject feels better and exhibits normal behavior, either spontaneously or in response to the drug ritalin, the brain pattern changes, indicating metabolism has increased to a normal level.

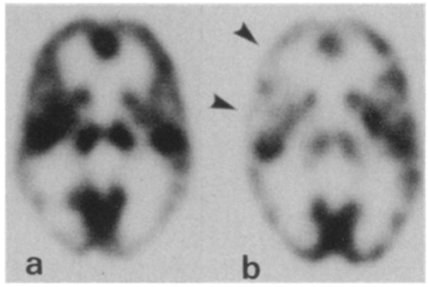
"We can see the biochemical basis of the way you feel for the first time," Phelps said in an interview in Minneapolis at the annual meeting of the Society for Neuroscience. "The metabolism observed corresponds to mood changes and behavioral changes." He anticipates new opportunities for objectively evaluating natural behavior and also drug effects.

Previous biochemical studies on depression, looking at components of blood, urine and cerebrospinal fluid, have failed to turn up consistent, agreed-upon characteristics, Phelps says. With PET scans, Phelps, John Mazziotta, Bob Gerner and Lou Baxter have examined nine persons with unipolar depression and three with bipolar (manic-depressive) disease in a total of 27 studies.

"This is a small number but the findings are so consistent," Phelps says. "Even though they are preliminary, it's amazing." He points out that the differences in brain metabolism are observed at the time of the test, when subjects are not actively expressing their feelings but are just resting quietly.

The subjects with bipolar depressive disease show a different pattern of brain metabolism when they are in a manic state. As with the depressed subjects, the overall level of metabolism is lower than in age-matched normal subjects. But metabolism is much higher than normal in certain regions, including areas that have especially low activity during depression. Another area of the brain shows especially low activity only during mania.

The metabolic images of the brain allow investigators to answer such questions as whether depression is localized to the right or left hemisphere of the brain. Phelps says the studies so far show a greater metabolism decrease in the left side of the brain, in areas thought to process language and analytical functions.



Phelps

The same person, when behaving normally and when depressed, shows different patterns of brain metabolism. During depression (right image), metabolism is decreased (shown by lighter shading), especially in the left hemisphere, frontal area (arrows).

Most strongly affected is the area where the regions exhibiting emotional and logical functions, the anterior cingulate and the frontal cortex, meet. Thus the abnormality could be in what neurobiologists call higher order information processing, perhaps in mood control. A new PET system now being built at UCLA is expected to improve resolution by a factor of 2 or 3 and may be able to pin down these changes to yet smaller regions of the brain.

—J.A. Miller

Cancer genes and chromosome changes

Human cancer may sometimes result from relocation of a gene with malignant potential. Recent work, performed independently in at least four laboratories, indicates that some mouse and human cancers, including Burkitt's lymphoma, are associated with movement of a gene called *myc* from one chromosome to another (SN: 11/13/82, p. 319). Now work at the Memorial Sloan-Kettering Cancer Center in New York implicates a second gene in a similar process.

William Hayward, Benjamin G. Neel, Suresh C. Jhanwar and R.S.K. Chaganti have located the gene called *mos* on the same arm of human chromosome 8 as *myc,* but some distance away. They find *mos* as a spot where breaks are observed in patients with the blood cancer acute non-lymphocytic leukemia. The *mos* gene was first identified in a virus that causes tumors in mice, and it later was discovered in animal cells.

Why should relatively quiescent genes, behaving normally in their original location, suddenly become active, and cancer-causing, after they are moved? The scientists speculate that a cell may become malignant when one of these potentially cancer-causing genes is reinserted into a highly active part of the DNA. Work of several groups has shown that in the case of Burkitt's lymphoma, the human *myc* gene is moved from chromosome 8 to one of three other chromosomes, to specific sites involved in antibody production. In some mouse malignancies, a translocation moves the mouse *myc* gene to the corresponding site in the region of antibody production on a mouse chromosome. The cells with this rearrangement come to predominate in a tumor. "The rearrangement is either the cause of the cells' transformation or it confers on already transformed cells some additional growth advantage," says Ilan Kirsch who worked with Philip Leder at Harvard University. Further intensive research is asking questions about the development and maintenance of the cancerous state and about the general mechanism of translocation.

Other laboratories reporting work on chromosome translocations and cancer genes are those of Michael Cole of St. Louis University and Kenneth B. Marcu of State University of New York at Stony Brook with Carlo Croce of the Wistar Institute in Philadelphia.

—J.A. Miller

Lasker awards

Research that has "significantly increased our understanding of the mechanisms of cancer at the molecular level" was recognized in the 1982 basic research award of the Albert and Mary Lasker Foundation. Hidesaburo Hanafusa of Rockefeller University was cited for work showing in the late 1970s how Rous sarcoma virus, a virus that causes cancer in chickens, captures a gene from a normal cell and uses it to cause malignancy (SN: 5/26/79, p. 344). J. Michael Bishop and Harold E. Varmus of the University of California at San Francisco were honored for work demonstrating that the cancer-causing genes of viruses are virtually identical to normal genes of animals, including man (SN: 3/7/81, p. 149). The award was also shared by Raymond L. Erikson of Harvard University for identifying the protein produced by the cancer-causing gene of a virus (SN: 5/26/79, p. 344). Finally, Robert C. Gallo of the National Institutes of Health was included among the winners for "his tenacious and thorough investigations leading to the discovery of the human T-cell leukemia virus...." Together these findings are the basis of today's active research on the link between viruses and cancer (SN: 11/13/82, p. 316).

The Lasker award for clinical research this year goes to two National Institutes of Health scientists for their work on incurable hereditary diseases. Roscoe O. Brady and Elizabeth F. Neufeld were chosen for their contributions to the diagnosis, potential treatment and screening of lipid storage diseases and mucopolysaccharide storage diseases, both devastating childhood disorders (SN: 7/22/78, p. 59). The Lasker awards are considered the highest U.S. honor for medical research, and many winners subsequently receive a Nobel Prize (SN: 12/2/72, p. 365). □