Views Into the Living Brain

The visible man and the visible woman, a concept once limited to educational toys, is now an immediate goal of biomedical research. The internal structure of an individual can be observed from outside the body by the technique of X-ray transmission tomography (CT scans, SN: 3/13/76, p. 171). Now an approach using radioactive chemicals is baring the body's biochemical workings, creating possibilities for mapping brain activity, analyzing disease and following drug actions.

So exciting is the possibility of analyzing biochemistry in specific locations, noninvasively in living persons, that the National Institutes of Health has earmarked about $10 million for work on the method. In the past two years interest has exploded, says Michel M. Ter-Pogossian of Washington University in St. Louis. But, because the procedure requires the expense of a cyclotron and the cooperation of an extensive team of different specialists, only about six medical centers in the United States and a few in Europe are working on the technique.

The strategy is to label biologically important molecules with a radioactive atom that emits high-energy electromagnetic radiation. The labeled molecule is administered to a person, and external detectors record the location of the label over time. The technique, called Positron Emission Tomography (PETT), differs in two ways from routine uses of radioactive chemicals in medical diagnosis. The radioactive atoms used — carbon-11, nitrogen-13, oxygen-15 and fluorine-18 — all decay with emission of positrons. Annihilation radiation of positrons is particularly well suited for external detection, and the short lifetimes of the radioactive atoms (half-lives of 2 to 110 minutes) provide only a minimal dose of radiation to a subject. The other innovation is the use of detectors that sweep their focus across specific points on a plane through the body. A computer then reconstructs the "slices" on a screen, showing the distribution of a biochemical tracer in the same way that CT scans show the absorption of X-rays.

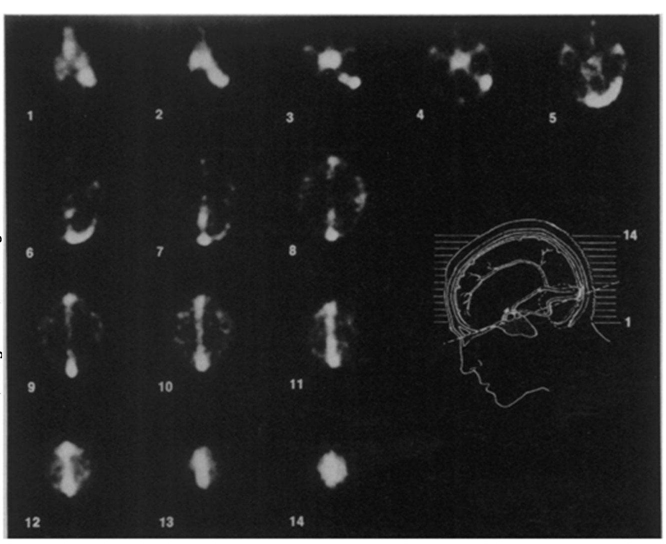
The short lifetime of the radioactive labels dictates precisely orchestrated teamwork among the physicists, chemists, mathematicians, biologists and physicians involved in each project. The radioactive atom must be generated in a cyclotron and immediately used to label the chemical to be followed. In the past, there was skepticism about whether important molecules could be synthesized so rapidly, but imaginative chemists have now labeled more than 100 biological compounds including drugs, proteins, amino acids, fatty acids, alcohols and sugars. As an example of ingenious chemistry, Ter-Pogossian described synthesis using carbon-11 (half-life of 20 minutes). The standard procedure for incorporating a long-lived radioactive carbon into glucose had been to expose a green plant to radioactive carbon dioxide for several days. But working with carbon-11, chemists discovered they could obtain a radioactively labeled glucose in less than an hour if they starved Swiss chard leaves in the dark, then exposed them to labeled carbon dioxide and intense light for just 20 minutes.

The brain and the heart have been the focus of the first PETT research. Animal researchers have been able to identify specific areas participating in a brain activity, such as vision, by slicing sections of an animal's brain (SN: 11/11/78, p. 324). Similar information, although at a lower resolution, is now available from living human brains. At the meeting in St. Louis of the Society for Neuroscience, Martin Reivich of the University of Pennsylvania and collaborators at Brookhaven National Laboratory described recent experiments. Visual stimulation of the left half of the visual field caused the glucose analog, ^{18}F-fluorodeoxyglucose, to concentrate in the area known to process visual information on the right side of the brain. Rapid stroking of the right hands of other subjects gave a dramatic increase in glucose analog uptake in the brain's sensory and motor areas that correspond to the hand. During a listening task in which the subject heard a story through just one ear, the researchers were surprised to observe the greatest activity on the right side of the brain, regardless of which ear was used. Reivich proposes that they were observing an area of higher processing. They now plan to do experiments investigating brain activity in response to pure tones, rather than stories.

Medical investigations using PETT should allow physicians greater insight into diseases, even those that cannot be mimicked adequately in animal models. D. Comar of the Hospital of Orsay in France has used the technique to pinpoint where the damage is in the brain of a stroke victim and to follow changes during recovery. The researchers in St. Louis have similarly examined the sites and extent of heart damage in patients in the cardiac care unit. "PETT allows you to look at the infarct directly. You can follow therapy and recovery," Ter-Pogossian says.

In other medical research, David Kuhl of the University of California at Los Angeles has been examining epileptics. Between their seizures he finds decreased metabolism by the cells, as well as decreased blood flow, at specific brain sites. However, during seizures the metabolic activity in those areas increases to double the activity of the other side of the brain. In a preliminary experiment, Reivich and colleagues have seen depressed metabolism in one brain area of a schizophrenic.

Following the fate of drugs is also an important application of the PETT technique. A drug may be metabolized differently throughout the body, yet previously it could only be traced in the blood. Now researchers can directly measure the specific activity of a drug within an organ. For example, Comar is looking at labeled chlorpromazine in brains of schizophrenic patients. The potential of the procedure for both basic and medical research, Reivich says, is only limited by ingenuity. □



Ter-Pogossian, Washington Univ.

Fourteen computer-reconstructed slices through a living human brain show the course of a blood vessel. A whiff of carbon-11-labeled air introduces the positron-emitting tracer into the blood and external detectors reveal its distribution.

Magnetic moments for hyperons and quarks

Magnetism has taught physicists a lot. That is especially true in the study of the structure of atomic and subatomic systems. In an article in the Nov. 13 PHYSICAL REVIEW LETTERS a group of physicists from the University of Michigan, Rutgers — The State University and the University of Wisconsin (L. Schachinger and 14 others) list some of the major advances made with the aid of magnetism in the last 70 years or so. They do this as a preface to the report of their own achievement, a very precise measurement of the magnetic moment of the particle called the lambda hyperon, and to set the atmosphere for a discussion of the things that can be deduced from that