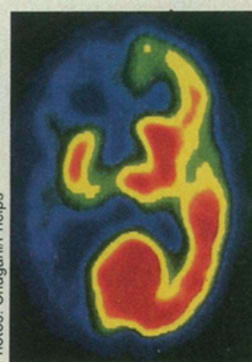
Epileptic PET Probes

Brain imaging is coming of age in the evaluation of infants and children with uncontrolled seizures

By BRUCE BOWER



Ryan regains muscle coordination after surgery with the help of a physical therapist. PET scan of his brain before surgery shows normal activity only in the right hemisphere and in a small, inner portion of the left hemisphere.

Photos: Chugani/Phelps

Ryan Peterson is living proof that half a brain can be better than a whole brain.

Ryan was only 8 hours old when his body began to convulse from his first brain seizure. Over the next few months doctors gave him a variety of anticonvulsant drugs, but his tiny brain continued to churn out seizures at the rate of 15 to 20 per day. If Ryan's internal electrical storm continued, he, like other infants with uncontrollable epilepsy, would probably die of seizure-related complications by age 10.

Faced with this prospect, Ryan's parents brought him to the University of California at Los Angeles School of Medicine, where a team of physicians directed by neurologist Harry T. Chugani searched for the source of the seizures. With the crucial help of positron emission tomography (PET) images of Ryan's brain, they mapped abnormal activity underlying the seizures throughout nearly all of his left hemisphere.

At age 15 months, neurosurgeons removed the extensive mass of seizure-causing tissue.

Now approaching his fourth birthday, Ryan is beginning to talk and take his first steps. His development is slower than that of children born with healthy brains, but his seizures are under control. Chugani expects his intellectual abilities to unfold with few or no hitches. There may be, however, some weakness on the right side of his body, which normally is regulated by the left hemisphere.

"Ryan's mother says it's almost as if he were born at the time of the surgery," notes Chugani.

This and similar cases have shed light on the remarkable recovery powers of the young brain, while at the same time pioneering an important new avenue for PET imaging as a tool for examining infants with uncontrollable epilepsy. Much of this newfound ability can be traced to recent advances in resolution of PET images.

In an upcoming issue of NEUROLOGY, Chugani and his colleagues report that PET data, combined with more traditional measures such as electroencephalographic (EEG) recording of brain electrical activity, greatly increased the ability to distinguish between epileptic and healthy brain tissue in eight such youngsters, including Ryan, ranging in age from 18 days to 5 years. Six of the children had epileptic tissue confined to one side of the brain, making them good candidates for surgery.

PET has a bright future both as a diagnostic tool for identifying diseased parts of the brain and as a surveyor of normal brain functions, says Chugani. He and his co-workers have already used this technology to chart a tremendous burst of brain activity occurring only during childhood, which may be related to the considerable learning and recuperative powers of the young brain.

In PET studies of the brain, biologically important elements, such as glucose and oxygen, are labeled with harmless, short-lived radioactive isotopes that are produced in a cyclotron. These substances are injected or inhaled and serve as tracers of normal physiological activity. As the isotopes decay, they emit positively charged electrons, or positrons, which combine with electrons to produce gamma rays. A circular array of tubes around the head records the emission of gamma rays and localizes their source. A computer transforms this information into color-coded images of brain function.

The UCLA scientists used radioactively labeled glucose to examine activity in specific brain regions. "Since the brain runs on internal combustion by burning up sugar, these PET scans look directly at the brain's energy requirements," says UCLA radiologist Michael E. Phelps, a participant in the epilepsy study.

For 3 of 4 children in the study who have undergone surgery to remove all or part of one hemisphere, PET was the only brain-imaging test that homed in on seizure-producing tissue. Two techniques that provide pictures of brain anatomy but not brain chemistry — computerized tomography (CT) and magnetic resonance imaging (MRI) — failed to locate epileptic areas. PET's advantage is its ability to pick up microscopic areas where neurons are in the early stages of disorganization, says Chugani, whereas CT and MRI can identify tissue degeneration that occurs later on.

No less important, he adds, is the ability of PET to map out normally functioning brain regions to be spared in potential surgery.

PET is not infallible on its own, though. A baby girl with uncontrolled seizures was given a PET scan at age 4 months that identified abnormally high metabolism only in the left hemisphere, but EEG revealed epileptic centers on both sides of her brain. The latter test confirmed that seizure activity was too widespread for surgery to be considered.

But why, in a case such as Ryan's, would epileptic activity covering virtually half of the brain necessitate surgery? First, several studies of humans, cats and other animals have documented a remarkable recovery of most mental and physical abilities after removal of a brain hemisphere early in life. The human cases involved treatment for uncontrolled epilepsy, brain tumors and other life-threatening conditions, but PET was not used in evaluating these patients for surgery.

The resilience of a young brain appears to relate in part to the overproduction of neurons during infancy and an excess of synapses that make neuronal connections throughout childhood. Researchers have found that the concentration of synapses in the brains of children up to 11 years of age is markedly greater than what is found in adult brains, although by about age 7 the child's brain is nearly the same size and weight as that of the adult.

Add to this the observation of Chugani and his colleagues, in the October 1987 ANNALS OF NEUROLOGY, that the brain's energy requirements rise steeply during childhood. They again used PET to study 29 children between the ages of 5 days and 15 years. The youngsters had suffered temporary neurological problems, including seizures, "but they are [otherwise] reasonably representative of normal children," says Chugani.

In infants less than 5 weeks old, only a few structures deep within the brain actively use glucose. Over the next few months, one region after another lights up in the PET images as more brain functions mature. By 2 years of age, glucose use throughout the brain reaches adult values.

"Then, something strange and dramatic happens," says Phelps. Energy production continues to rise until, by 3 to 4 years of age, it is at least twice the normal adult rate, where it continues to burn for about seven years. At that point, the rate of glucose metabolism tapers off and stabilizes at adult levels during the teens.

The overdevelopment and heightened activity of the brain between ages 3 and 10 suggest that it is capable of reorganizing itself in radical ways during childhood, says Phelps, even to the extent that one hemisphere can learn to function as two. By contrast, the loss of an entire hemisphere or the severing of communication between hemispheres causes severe, irreparable damage in adults.

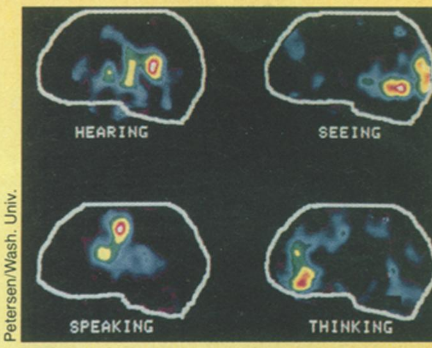
The ways in which a child's brain adapts to extensive surgery and recoups most normal functions are not, however, clearly understood. Chugani plans to follow children from the epilepsy study with PET to see, for example, if Ryan's right hemisphere undergoes the metabolic burst found in children with intact brains and if any specific areas take charge of reorganizing his brain function.

The UCLA researcher is also in touch with a 22-year-old man who had his left hemisphere removed as a child because of uncontrolled epilepsy. "He graduated from high school and is operating fairly normally now except for some weakness on his right side," says Chugani. "We want to use PET to see what [mental and physical] tasks are represented where in his right hemisphere." □

Lighting language lanes in the brain

Positron emission tomography (PET), developed in the early 1970s, is just beginning to illuminate the brain centers and connections involved in language, intellect and other areas of mental life. Preliminary findings are providing scientists with a few surprises.

In the Feb. 17 NATURE, investigators at Washington University in St. Louis report that PET scans of 17 healthy volunteers reveal separate processing routes in the brain for words that are read and words that are heard. The findings support recent theories in cognitive psychology that are based on "parallel pathways" for information processing in the brain, but they contradict the traditional neurological view that there is a single brain pathway for language comprehension.



Petersen/Wash. Univ.

Side-view PET images show left-brain activity while subject is hearing a word (upper left), seeing a word (upper right), repeating a word (lower left) and saying a word related to the one presented.

Steven E. Petersen and his colleagues mapped blood-flow changes in precise areas of the brain by injecting subjects with water containing minute amounts of a radioactively labeled oxygen compound. This tracer remains active in the body for only a few minutes (compared with several hours for the glucose compound used in the UCLA researchers' epilepsy study), allowing a rapid series of scans to be taken. First, subjects read or heard a list of 40 common nouns. Next, they repeated each noun aloud. Finally, they repeated a use for each noun. Computer software developed at Washington University was used to subtract each PET image from the image following to reveal only those brain areas involved in each task. In this way the researchers generated a standardized PET image for each trial, based on average brain activity across all subjects.

The results show that brain areas where sounds are associated with words, and meaning is then added on, are activated only when a word is heard. Words that are read bypass those areas and appear to gain meaning almost immediately after entering the brain, then traveling to speech articulation and production areas. Surprisingly, when associations are generated for a noun, the brain does not light up in Broca's area, a region long thought to govern speech production, but instead about 2 centimeters in front of it.

Broca's area, say the scientists, is a generalized motor-control center not solely connected to speech. It is active if you speak, but also if you wriggle your tongue, if you wriggle your fingers or if you think about wriggling your fingers.

"I hadn't expected to see such exquisite anatomical specificity in word processing," says psychologist and study participant Michael I. Posner. Further PET studies, he notes, may examine brain areas associated with grammar and emotional aspects of language.

In a related PET study charting glucose use, psychiatrist Richard Haier of the University of California at Irvine finds that the brains of people who score well on a test of abstract reasoning expend less energy than the brains of those with low scores, suggesting that circuits of neurons involved in intelligence work more efficiently in smarter people (SN: 2/27/88, p.137).

"Investigators are no longer dependent on lesioned brains or nonhuman animals to study higher brain function," says neurologist Peter T. Fox of Washington University in St. Louis. "We're breaking into a new era of human brain research." *— B. Bower*