Many Benefits Expected From Neuroscience Research

Ninety percent of what we know about the brain we have learned in just the past 10 years. Thanks to such extraordinary progress, brain researchers are discovering effective new treatments for such devastating and expensive mental disorders as schizophrenia and depression, as well as mapping the physical underpinnings of the mind.

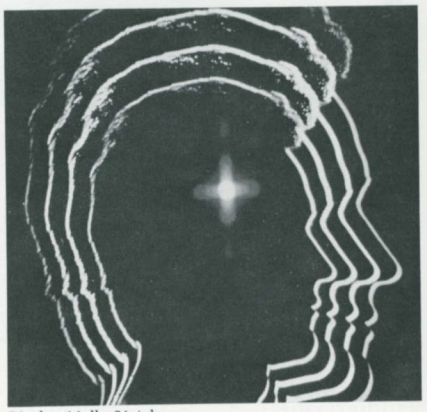
Recognizing that "a new era of discovery is dawning in brain research," President Bush signed a proclamation declaring the 1990s as a "Decade of the Brain."

An impressive array of neuroscientists and government officials met to usher in a decade-long emphasis on neuroscience research. During a two-day symposium, sponsored jointly by the National Institute of Mental Health (NIMH) and the Institute of Medicine, researchers and federal policymakers discussed topics ranging from recent advances in understanding how the brain works, some of which are described below, and initiatives for providing resources to accelerate research efforts.

"In this country more people are hospitalized with mental and neurological disorders," noted Louis W. Sullivan, the secretary of health and human services, "than any other major disease group including cardiovascular disease and cancer." Relying on statistics collected from a recent NIMH survey, director Lewis L. Judd pointed out that "one in five people in this country at some point in their lifetime will experience a mental disorder."

Physical Defects

Just 30 years ago, Judd pointed out, psychiatrists were basing causes and treatments of mental illness on Freud's theoretical model of the mind, rather than pursuing the brain for any physical evidence of defects in brain function. Now neuroscientists have turned up some tantalizing clues to the causes of several mental disorders. Effective treatments for some, such as for manic depression, are already in use.



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Evidence for a physical basis of mental illness came from the positron emission tomography (PET) research presented by Marcus E. Raichle, a neurologist at Washington University School of Medicine in St. Louis. PET scans dynamically reveal those parts of the brain that are active during stress or other mental processes by showing in a color-coded map how much of a radioactive sugar is consumed by brain cells.

A book on the Decade of the Brain symposium will be published by National Academy Press in spring of 1991.

When Raichle compared the PET scans of depressed patients to those of normal individuals, who were asked to think a sad thought, he discovered some striking differences. Although one area of the brain was equally active in both the depressed and normal subjects, another area of the brain was active only in normal subjects. The upper tip of this area, known as the caudate nucleus, plays a role in regulating emotions. It continued to be underactive in depressed patients even when they recovered from their current depression.

The findings suggest, said Raichle, that although depressed and normal individuals use some of the same parts of their brains when feeling sad, depressed patients may be more susceptible to having such sad feelings because of an underlying brain defect — perhaps a malfunctioning caudate nucleus.

Anatomy of Memory

On a smaller anatomical scale, Patricia Goldman-Rakic of Yale University showed how, in rhesus monkeys, the neurons of the thinking portion of the brain — called the prefrontal cortex — work together literally to keep an image in mind.

Goldman-Rakic flashed a target on a television screen in front of rhesus monkeys. After the target disappeared, the trained animals indicated its location by moving their eyes to where the target had been. In order to carry out this task, the monkeys had to keep an image of the target's position in mind, even though they could no longer see it.

By systematically rotating the position of the target along the circumference of a circle while monitoring the activity of a monkey's various prefrontal cortex neurons, Goldman-Rakic discovered that each neuron is dedicated to remembering or bringing to mind only a particular portion of what the monkey has seen. For example, when the target appeared at the 3 o'clock position, the neuron sensitive to that position fired after the target disappeared from the screen. When the target was moved to the 9 o'clock position, the neuron that fired previously stayed silent, but the neuron tied to that position fired. When Goldman-Rakic surgically removed a neuron, the monkey couldn't remember the target when it appeared at that neuron's particular spot.

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In this case, said Goldman-Rakic, "when the target goes out of sight, it also goes out of mind," and the animal is left with a "hole in memory."

The prefrontal cortex is highly enlarged in humans in comparison to other animals and is perhaps the most important determinant of human nature. Goldman-Rakic noted that individuals who have lost their prefrontal cortex are unable to plan ahead or carry out even the simplest behaviors that require them to use mental images akin to what she studied in monkeys.

Many of these handicaps are seen in schizophrenic patients, she added. PET scan studies done by other investigators reveal that some areas of the prefrontal cortex fail to activate in schizophrenics given tasks that require them to use this part of their brains. Further studies on the prefrontal cortex hold promise for not only elucidating the mechanisms behind thinking, but also the abnormalities that might be responsible for schizophrenia, she said.

Role of Genes

Another way of probing the brain for defects responsible for mental disorders is to find the gene that predisposes a person to the disorder. Once that gene is pinpointed, researchers can explore what role the gene's protein product plays in brain functions and possibly in the cause of a disorder.

"There are so many components to any given cell, and even more in the

Cheers From Barbara Bush

First Lady Barabara Bush gave a warm welcome to the participants at the Institute of Medicine and National Institute of Mental Health "Decade of the Brain" symposium. "Every one of us has a friend or relative that suffers from a disease of the brain," she said. Many of these illnesses often are ignored, feared or misunderstood, she added. "By revealing the problems of brain structure and function that play such an enormous role in mental illness," Bush said, "you [brain researchers] are helping to free patients and their loved ones from a really wrongful burden of guilt and shame."

"Your work will help us better understand ourselves and our behavior, and will help us become a healthier and more productive nation." —*M.P.*

brain, that we won't know what went wrong in most cases of mental disease until we can find the gene that sets it off," said James Watson, director of Cold Spring Harbor Laboratory and director of the National Center for Human Genome Research. He predicted that researchers will uncover the gene that predisposes for Alzheimers disease on chromosome 21 within five years. The technology is already in place, he added, to find the genes for schizophrenia and other major mental diseases, even if they each are caused by more than one genetic defect.

Insights into Learning

Focusing on the neuron, psychiatrist and neurobiologist Eric Kandel of Columbia University and his colleagues have discovered a molecule that not only plays an important role in the development of the sea snail embryo but may also influence the animal's ability to learn once it becomes an adult.

When sea snails are repeatedly stroked on their tails, they learn to retract their siphons quickly the next time they are touched. The Kandel team discovered that during this learning process, production in the neuron of a cell adhesion molecule called *Aplysia* CAM is suppressed. It would seem that inhibition of *Aplysia* CAM may be an early step that is necessary for the growth of connections (synapses) between nerve cells. "The network growth of synapses is the anatomical 'signature' of long-term memory, Kandel said.

Although *Aplysia* CAM is active in all tissues in the developing sea snail embryo, in the adult its influence is restricted to the nerve cells.

"Some of the same [biochemical] steps involved in development," Kandel said, "seem also to be reutilized later on for the growth process of learning."

Looking Ahead

"What does it mean for our patients that Congress has passed a resolution declaring the 1990s the Decade of the Brain?" was the question Joseph B. Martin, dean of the University of San Francisco, posed to a panel of representatives from government, industry and private foundations. "How can we make the most of it?"

Although no plan of action emerged, the speakers left no doubt that all interested parties can help make the Decade productive. Perhaps the enthusiasm for the Decade was expressed best by Massachusetts Congressman Silvio O. Conte, a sponsor of the declaration: "We all know now that the heart is just a pump. That leaves only one place to go to discover our soul, the essence of our humanity. Here we are, poised on the brink of a new frontier, every bit as exciting and challenging as the journey to space or to the moment of creation of the universe."

—*Margie Patlak*

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