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News
The University of Texas Health Science Center at Dallas
5323 Harry Hines Boulevard Dallas, Texas 75235 (214)688-3404

CONTACT: Susan Rutherford
Office: 214/688-3404
Home: 214/349-7820

******Brain researchers probe cause of cerebral palsy as they look at normal brain function.

The five-year-old in the wheelchair jerks with excitement as he's brought into the diagnostic and treatment center.

Unable to right himself posturally, he sits awkwardly in the chair and moves with spastic imprecision in response to those around him. A laugh sends his head backwards and to the side.

Rigidly fisted fingers make it difficult to pick up and put down articles. Curled-in, grasping toes, along with legs that have begun to atrophy from lack of use, hinder his attempts to walk. He still retains the rooting and sucking reflexes of early infancy. These two reflexes make opening the mouth for drinking from a cup and chewing food, exercises in futility.

These are the outward signs of cerebral palsy, a term which means "paralysis of the central nervous system."

But what's going on inside his head?

Researchers in the Department of Cell Biology at The University of Texas Southwestern Medical School are examining the source of the problem--short circuiting of the brain's nerve cells. They hope their laboratory findings on the workings of the normal brain will eventually lead to a more complete understanding of the diseased state.

Working under grants from the National Institute of Neurological and Communicative Disorders and Stroke and the National Science Foundation, a research team led by Dr. Gregory A. Mihailoff is tracing the circuits which link the cerebral cortex and the cerebellum, two of the brain's largest concentrations of nerve cells (neurons).

Mihailoff describes the research as "basic science." The goal is to determine which regions in the cerebral cortex are linked to which specific areas in the cerebellum. And their aim is to add to existing knowledge on how these brain regions participate in the control of our voluntary motor behavior.

As yet, scientists know relatively little about how the different areas of the brain work in concert to form the brain's motor memory. This is the type of memory built up through practice or trial and error, which eventually results in the acquisition of a basic skill. These skills range from the most common head and eye movements to the fine motor coordination skills of a neurosurgeon or an olympic gymnast.

Pieces of the puzzle are beginning to fit together, however, as more research is being done. Ultimately information about the brain's internal circuitry may lead to treatment for the child with cerebral palsy, along with victims of strokes, severe epilepsy and other types of brain damage or brain malformation.

Mihailoff's point of focus is the basilar pons, a portion of the brain that functions as a "relay station" between the cerebral cortex, making up the outer layers of the brain's upper surface, and the cerebellum, located at the back of the brain near the spinal cord. It is theorized that the cortex, the cerebellum and the basilar pons interact and together function as one of the important regulating centers for voluntary motor activity.

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With the use of the light microscope, the team is injecting minute quantities of radioactive amino acids into the cortex of laboratory animals. The cortical neurons transport this traceable material to the basilar pons via long, thin, wire-like extensions of the cell known as axons. At the same time the team is also injecting another observeable drug into the cerebellum. This material travels in the reverse direction since it is taken up by the axons terminals and carried back to the cell of origin in the basilar pons. By carefully experimenting with various cortical and cerebellar injection sites, the crucial cerebro-cerebellar links are being established.

"It was first thought that an area within the cortex initiated motor activity," says Mihailoff, "since muscle contraction can be elicited artificially by electrical stimulation of the 'motor cortex.' But in the normal working brain it's not that simple."

It's now believed that certain motor memories might be stored within the cerebellum, and that there we have a "motor program" from which we can recall, either voluntarily or involuntarily, a motor skill mastered in the past, such as a golf swing. Because of this motor memory we don't have to think about every movement.

In contrast, the motor memory of the cerebral palsied child is impaired. Somewhere within the brain of these children is a damaged or malformed region which is made up of cells which fail to respond to electrical impulses around them. This may result in misfirings, such as seizures, or in a failure to fire at all, as in the case of the "floppy infant" with cerebral palsy, who has little or no muscle response.

Brain cells in cerebral palsied children might be damaged or malformed around the time of birth, perhaps due to an oxygen deficiency at birth. The resulting lesions would therefore interfere from that time forward with normal brain maturation. In this way severe limitations are placed on both primitive and advanced motor programming.

Those with the disease often must face a life with impairment of voluntary movement, seizures, intellectual deficiencies, and visual, hearing and perceptual difficulties--depending on the severity of the affliction. And each year approximately 25,000 victims of the disease are diagnosed.

Mihailoff explains that normally as the brain of the newly conceived fetus develops, its brain cells must migrate to their adult location from the core of the developing brain. Brain cells differ in many respects, and while migrating they arrange themselves in distinct layers according to cell type. If these layers arrange themselves improperly, the disarray can result in a form of cerebral palsy.

"All of the brain develops from tissue surrounding a hollow tube within the embryo," says Mihailoff. "But it's very poorly understood as to how the cells know where to go and how certain connections are established. Much of brain development appears to be genetically determined, although environmental factors can be contributory."

As an infant, the normal brain continues to mature as part of the process known as "myelinization," Mihailoff explains. Brain cell axons are coated by myelin sheaths, which drape around the axons to allow for rapid and efficient transmission of nerve impulses. Normally, the myelinization of axons is incomplete at birth, and it continues until age nine or ten.

Seemingly associated with the myelinization process is the development of a series of reflexes which contribute to the infant's motor behavior. The first reflexes to occur and the most primitive--sucking and rooting, the startle reflex in which arms are flung out to the side, grasping reflexes in the hands and feet, righting of the head, and others--are associated with the internal regions of the brain where myelinization begins.

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Ordinarily these primitive reflexes are concealed as the infant brain matures and the reflexes become integrated into the child's motor memory. A normal child of three to four months of age will no longer root, for example, when his cheek is stroked. And he has lost the startle reflex and the grasp reflex in the hands. But it will be three or four more months before he begins to extend his arms forward in a protective reflex when he starts to fall.

"As the brain continues to develop, certain genetically programmed circuits, or patterns, become functional," explains Mihailoff. "These reflexes are usually consistent from person to person. And they are eventually masked or overridden by other more advanced patterns which develop later."

Lesions in the brain, whether the result of brain damage or brain malformation, can interfere with the integration of reflexes and the acquisition of more advanced motor behavior. And they can therefore cause a cerebral palsied child to retain the most primitive reflexes of infancy, sometimes for a lifetime. Cerebral palsy is not a progressive condition--it doesn't get worse. It only appears to worsen as the child gets older and more is expected from him.

Mihailoff and others point to a brain growth phenomenon known as "axonal sprouting" as a possible direction for future treatment of types of cerebral palsy and other brain disorders. In children and in young adults with brain injuries (particularly in cases where the brain was normal to begin with), neurons from surrounding brain areas may exhibit new growth, much like a pruned plant will grow, and will take over or compensate for the function of the injured part.

Through the use of drugs or surgery, doctors may someday be able to induce sprouting in brain cells and in this way repair disconnected regions in the abnormal brain. Or with further study doctors may be able to promote myelinization if and when that plays a part in brain dysfunction.

Research holds the answer. "Unless we can understand how the brain functions normally, it's difficult to determine what has malfunctioned in various disease states, and it's even more difficult to devise strategies to repair or compensate for the defect, says Mihailoff.

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