SOUTHWESTERN NEWS

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PROTEIN LINKED TO 'MIRROR MOVEMENT' DISORDER; RESEARCH PROVIDES INSIGHT INTO BRAIN/SPINAL CORD CONNECTION

DALLAS – Jan. 25, 2001 – A UT Southwestern Medical Center at Dallas researcher has found that mutated mice bred without an essential protein exhibit symptoms of a rare disorder that causes involuntary "mirror movement" in people.

The findings, published in the January issue of *Neuron*, demonstrate the importance of the protein ephrin-B3 in making the connection between the brain and the spinal cord.

Dr. Mark Henkemeyer, assistant professor in the Center for Developmental Biology, said the findings should help researchers understand how the brain forms its axonal connections with the spinal cord. Such knowledge could someday prove helpful in the regeneration of nerves in people with spinal-cord injuries. More immediately, the research elucidates how the brain becomes "hard-wired" to the spinal cord.

First described in 1889, mirror-movement disorder is characterized by an involuntary symmetrical movement of limbs. For example, when people with the disorder move their right hand, their left hand involuntarily moves with it. Typically, they cannot perform complex activities like tying shoes and typing, and even running and walking can be difficult. Mirror movement is natural in infants, but over time people normally develop the motor coordination to control their limbs and digits more independently.

Researchers have believed for some time that mirror movement is caused by defects in the corticospinal tract, which connects the brain's cortex with motor neurons and interneurons in the spinal cord. Playing pivotal roles in forming these connections are ephrins, which regulate cortical nerve growth to help form their proper circuits with the spinal cord.

"Ephrin-B3 is a very important molecule as it is expressed down the middle of the spinal

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column," Henkemeyer said. "It serves as a repulsive barrier that keeps the left axons on the left side of the nervous system and the right axons on the right."

The mice used in the study were genetically engineered to completely lack ephrin-B3 protein, which caused each side of the motor cortex to connect to both sides of the spinal cord. These mice display a kangaroo-like hopping gait involving both their forelimbs and hind limbs. In addition to such unusual locomotion, other mirror movements are evident, such as when the mutant mice groom themselves and swim.

Henkemeyer's research was funded by the Christopher Reeve National Paralysis Foundation, the Muscular Dystrophy Association and the National Institutes of Health.

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