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Nerve fibers need specific growth factor chemical to form connections within the brain

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A discovery on how neural circuitry develops to aid proper cerebral cortex activity may help explain the memory and cognitive decline seen in Alzheimer's disease patients – a discovery that could point toward potential treatments, according to UC Irvine scientists.

The study uncovers how cholinergic neuronal circuits, which help the cerebral cortex process information more efficiently, rely on neurotrophin-3, a chemical that stimulates nerve growth. The scientists have determined the circuits need this chemical in order to recognize and reach their target nerve cells in the brain.

Richard Robertson, professor of anatomy and neurobiology, and other researchers from UCI's School of Medicine found that cholinergic nerve fibers grow toward sources of neurotrophin-3 during early development. In experiments with mice, without neurotrophin-3 to direct growth, the developing cholinergic nerve fibers appeared to not recognize their normal target cells in the brain. Because of this, the axon nerve fibers aided by these circuits grew irregularly and missed their specific target neural cells.

This finding, according to Robertson, has significant implications for neurodegenerative diseases like Alzheimer's. Cholinergic neuronal circuits play a key role in the proper information processing by the cerebral cortex and other areas of the brain. The cerebral cortex is the

part of the brain that determines intelligence, personality, and planning and organization, and these actions are compromised by neurodegenerative diseases.

"Studies on the brains of Alzheimer's patients have shown a marked decline in these cholinergic circuits. Our work demonstrates that neurotrophin-3 is essential to maintain the connections to cerebral cortex neurons," Robertson said. "This study shows that a neurotrophin-3 therapy may be able to induce nerve fibers to regrow in the cerebral cortex, which would be beneficial to people with Alzheimer's."

Study results appear in the Dec. 1 issue of the journal *Neuroscience*.

In further studies on this subject, supported by a recently awarded three-year grant from the Alzheimer's Association, Robertson and his colleagues are testing the respective roles of nerve growth factor and neurotrophin-3 in a laboratory model of Alzheimer's disease. Laboratory rats with experimental damage to forebrain cholinergic circuits will be treated with either nerve growth factor or neurotrophin-3, or a combination of both, to determine their ability to produce anatomical, molecular and behavioral recovery.

Source: University of California - Irvine