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New Discovery Could Rejuvenate the Brain

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(PhysOrg.com) -- Researchers at The University of British Columbia have discovered why the brain loses its capacity to re-grow connections and repair itself, knowledge that could lead to therapeutics that "rejuvenate" the brain.

The study, published today in *The EMBO Journal,* identified a set of proteins -- calpain and cortactin, which regulate and control the sprouting of neurons -- a mechanism known as neural plasticity.

Neurons, or nerve cells, process and transmit information by electrochemical signalling and are the core components of the brain and spinal cord. During development, growing neurons are relatively plastic and can sprout new connections, however their plasticity levels drop rapidly as they mature and become integrated into neuronal networks.

This process is the mechanism by which the brain regulates these networks from uncontrolled growth, however; as a consequence, the central nervous system is unable to reorganize itself in response to injury or disease.

"This discovery is exciting because we now know that neurons haven't lost their capacity to re-grow connections, but instead are under constant repression by the protein calpain," says Ana Mingorance-Le Meur, postdoctoral fellow in UBC's Department of Cellular and Physiological Sciences, who has led the investigation along with UBC Professor Timothy O'Connor. "If we can target therapies that block this mechanism, then neurons should be able to sprout new connections,

therefore stimulating the brain's ability to repair its wiring network."

The research reveals that the loss of plasticity is due to the protein calpain actively blocking the protein cortactin, which is responsible for the sprouting of new connections. The researchers reduced calpain activity in animal models to unlock the sprouting potential of neurons and found that when calpain activity is reduced neural plasticity is enhanced.

"The maintenance of neuronal connections is an active process that requires constant repression of the formation of nerve sprouts by the protein calpain to avoid uncontrolled growth," says Mingorance-Le Meur, who is also a member of the Brain Research Centre at UBC and VCH Research Institute. "But a consequence of this role is that calpain limits neural plasticity and the brain's ability to repair itself. The next step is to find a way to enhance neural plasticity without interfering with the good connections that are already in place. The next step is to find a way to enhance neural plasticity without interfering with the good connections that are already in place."

According to Mingorance-Le Meur, who is also a member of International Collaboration on Repair and Discovery (ICORD), the results are very promising because they help us understand how neural plasticity is regulated. Drugs that could promote neural plasticity could potentially treat a wide range of neurological disorders, as well as boost the effects of other treatments under investigation.

Provided by University of British Columbia