



## MEDIA RELEASE | JANUARY 27, 2010

### Discovery of new mechanism of brain cell injury in Huntington's disease offers new approaches to treatment

Scientists at the Brain Research Centre and Centre for Molecular Medicine and Therapeutics have uncovered a key cellular mechanism that alters brain cell function in Huntington's disease, and identified a possible treatment for the disease.

The results of the study were published online today and will appear in the January 28 edition of the journal *Neuron*.

Huntington's disease is an inherited degenerative brain disease that causes cognitive and motor impairment, and eventually death. One in 10,000 Canadians suffers from Huntington's disease.

The researchers found that, in mouse models, the genetic mutation that causes Huntington's disease results in an excessive number of NMDA receptors—special receptors found at the surface of brain cells—to accumulate and be active outside synapses, which are the connections between brain cells. In healthy conditions, there should be few NMDA receptors outside the synapse.

The researchers also found that the over-activation of the NMDA receptors outside the synapse leads to a reduction in brain cell survival signals and disruption in brain function.

“Previous work in cell cultures showed that NMDA receptors located within the synapse can have beneficial effects on brain cells, whereas NMDA receptors outside the synapse, called ‘extra-synaptic NMDA receptors,’ have a detrimental effect,” says Dr. Lynn Raymond, a professor in the UBC Department of Psychiatry, a member of the Brain Research Centre at UBC Hospital, and co-director of the Huntington's Disease Medical Clinic.

“Our study shows an increase in the number of extrasynaptic NMDA receptors, shifting the balance between these opposing cellular mechanisms in animal models of early stages of Huntington's disease,” Raymond says.

While further work still needs to be done to determine how the genetic mutation causes the excessive number and activity of NMDA receptors to localize outside the synapses, the researchers did find a way to mitigate damage and slow disease progression at early stages of the disease—using Memantine, a drug currently used to treat Alzheimer's disease.

“Memantine in low dose works by preferentially blocking the activity of NMDA receptors outside the synapse,” says Dr. Michael Hayden, director of the Centre for Molecular Medicine and Therapeutics, professor in the UBC Department of Medical Genetics, and co-author on the study.

“It was previously shown to reverse deficits and damage in late stages of animal models of Huntington's disease, but we found it could improve learning and cell survival signaling even at early stages of the disease,” says Hayden. “A small human clinical trial of Memantine for Huntington's disease has also recently shown positive effects. Larger, international clinical trials are now being planned.”

“Memantine's beneficial effects appear to be dose-specific,” Raymond adds. “Before it can be prescribed to treat Huntington's disease, we need to know how to determine appropriate dosing and whether it interferes with other essential cellular and brain functions.”



This study was funded by the Canadian Institutes of Health Research, Cure Huntington Disease Initiative, Michael Smith Foundation for Health Research, Heart & Stroke Foundation of BC & Yukon, Huntington's Disease Society of America, and the Huntington Society of Canada.

The **Brain Research Centre** comprises more than 225 investigators with multidisciplinary expertise in neuroscience research ranging from the test tube, to the bedside, to industrial spin-offs. The Centre is a partnership of the UBC Faculty of Medicine and Vancouver Coastal Health Research Institute. [www.brain.ubc.ca](http://www.brain.ubc.ca)

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