

# Mechanisms by which Afferents Regulate Striatal Neuronal Loss and Motor Activity in Movement Disorders

<https://neurodegenerationresearch.eu/survey/mechanisms-by-which-afferents-regulate-striatal-neuronal-loss-and-motor-activity-in-movement-disorders/>

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## Title of project or programme

Mechanisms by which Afferents Regulate Striatal Neuronal Loss and Motor Activity in Movement Disorders

## Source of funding information

CIHR

## Total sum awarded (Euro)

€ 397,963

## Start date of award

01/04/2014

## Total duration of award in years

5

## Keywords

### Research Abstract

A part of the brain known as the striatum is a key structure that helps coordinate movement and thought in humans and other mammals. Progressive loss of nerve cells in the striatum occurs in Huntington's disease, and results in abnormal movements and disorders of thought and mood. We propose that the nerve supply to the striatum, also known as its afferent input, is an important factor in producing the abnormalities seen in Huntington's diseases. Specifically, we

propose that afferents that provide information to striatum nerve cells by using the chemical messenger glutamate, work with a survival or growth factor, brain derived neurotrophic factor (BDNF), to sustain subgroups of neurons in normal striatum, and this function is impaired in Huntington's disease. Loss of trophic support produces a specific form of cell death known as apoptosis, which can be studied in developing cells. Finding out how glutamate and BDNF control survival of striatum neurons may provide important clues to how cells may be rescued in Huntington's disease and other degenerative disease of the brain. We will use 3 main approaches: 1) Examine how glutamate and growth factors produced by input connections to the striatum cooperate to regulate survival of specific populations of vulnerable striatum neurons in rodents. 2) Examine how absence of specific inputs to the striatum, with resulting loss of specific neuronal subpopulations influences motor behavior. 3) Determine how impaired delivery of BDNF produces loss of striatal neurons in animal models of Huntington's disease. 4) Develop a unique gene therapy method to rescue striatal neurons and improve motor behavior in an animal model of HD. Our work will have important implications for understanding how nerve cells die in Huntington's disease, and in other neurodegenerative diseases of motor systems, such as Parkinson's disease. This work may eventually lead to novel therapies using growth factors to treat neurodegenerative diseases.

**Further information available at:**

**Types:**

Investments < €500k

**Member States:**

Canada

**Diseases:**

N/A

**Years:**

2016

**Database Categories:**

N/A

**Database Tags:**

N/A