

Genetic discovery for hereditary spastic ataxia—rare disease in Newfoundland

September 6 2012

Researchers from the Guy Rouleau Laboratory affiliated with the CHUM Research Centre and the CHU–Sainte-Justine Research Centre have discovered the genetic cause of a rare disease reported only in patients originating from Newfoundland: hereditary spastic ataxia (HSA).

This condition is characterized by lower-limb spasticity (or stiffness) and ataxia (lack of coordination), the latter leading to speech and [swallowing problems](#), and eye movement abnormalities. The disease is not deadly, but people start developing gait problems between 10 to 20 years of age, walk with a cane in their 30s, and in the most severe cases, are wheelchair bound in their 50s. It has been shown that HSA is transmitted from the affected parent to the child in a dominant fashion, which means there is a 50% chance of the child having the mutation.

History of a discovery: collaboration between the University of Montreal and Memorial University

Researchers and clinicians from Memorial University (St. John's, Newfoundland) contacted Dr. Rouleau, who is also a professor of medicine at the University of Montreal, over a decade ago to investigate the genetics behind this disorder occurring in three large Newfoundland families. Dr. Inge Meijer, a former [doctoral candidate](#) in the Rouleau Laboratory, discovered that these families were ancestrally related, and in 2002, identified the locus (DNA region) containing the mutation

causing HSA.

A few years later, Cynthia Bourassa, lead author of the study, took over Meijer's project. "I reexamined some unresolved details using newer and more advanced methods," explains Bourassa, who is a master's student in the Faculty of Medicine at the University of Montreal. She then teamed up with Dr. Nancy Merner, who after obtaining her Ph.D. at Memorial University moved to Montreal to further her career in [genetic research](#). "It is an honour to be a part of this study and impact the lives of my fellow Newfoundlanders. I knew coming into the Rouleau Laboratory that the genetic factors of the HAS families had not yet been identified. In fact, I asked about them on my first day of work, shortly after which I teamed up with Cynthia and we found the gene."

Scientific explanation:

The gene harbouring the mutation is VAMP1, encoding the synaptobrevin protein. "Not only was the mutation present in all patients and absent from all population controls, but also, synaptobrevin is a key player in neurotransmitter release, which made sense at the functional level as well," says Bourassa. In fact, the authors believe that this mutation in the VAMP1 gene may affect neurotransmission in areas of the nervous system where the synaptobrevin protein is located, causing the unique symptoms of HSA. In other words, there are not enough messengers released, so nerves cannot function optimally.

"The discovery will benefit the families affected with this extremely debilitating disorder," says Dr. Rouleau. "A genetic diagnostic test can be developed, and genetic counseling can be provided to family members who are at risk of developing the disease or having children with the condition."

Identification of the VAMP1 mutation was made in the Guy Rouleau

Laboratory in collaboration with investigators from Newfoundland, Nova Scotia, and Ontario. Funding was provided by the Canadian Institutes for Health Research, the Canada Research Chair, and the Jeanne-et-J.-Louis-Levesque Chair for the Genetics of Brain Diseases.

More information: "VAMP1 Mutation Causes Dominant Hereditary Spastic Ataxia in Newfoundland Families." Authors: Cynthia V. Bourassa, Inge A. Meijer, Nancy D. Merner, Kanwal K. Grewal, Mark G. Stefanelli, Kathleen Hodgkinson, Elizabeth J. Ives, William Pryse-Phillips, Mandar Jog, Kym Boycott, David A. Grimes, Sharan Goobie, Richard Leckey, Patrick A. Dion, Guy A. Rouleau. *The American Journal of Human Genetics* (2012), [doi: 10.1016/j.ajhg.2012.07.018](https://doi.org/10.1016/j.ajhg.2012.07.018)

Provided by University of Montreal

Citation: Genetic discovery for hereditary spastic ataxia—rare disease in Newfoundland (2012, September 6) retrieved 11 July 2024 from <https://medicalxpress.com/news/2012-09-genetic-discovery-hereditary-spastic-ataxiarare.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.