

Original Investigation | Neurology

Huntington's Disease – Causes and Treatment

Kshitij Ramesh Dhokne.¹

MD Alte University, Tbilisi, Georgia¹

Key Points

Question:

What causes Huntington's disease, and how can it be effectively treated?

Findings:

HD results from expanded CAG repeats in the Huntington gene, producing toxic protein. Splicing modulators are emerging therapies aimed at halting toxic protein synthesis. FDA-approved drugs effectively treat chorea, HD's most common symptom.

Meaning:

Research on splicing modulators and symptom management offers hope for better HD treatments, addressing both causes and symptoms of the disease.

Abstract

Importance:

Huntington's disease (HD) is a fatal autosomal dominant neurodegenerative disease with profound impacts on individuals and families. It is caused by an expansion of CAG repeats in the Huntington gene, leading to toxic protein production that damages neurons.

Objective:

To explore the causes of HD and evaluate current and emerging treatments, including splicing modulators and symptom management strategies.

Evidence Review:

The Huntington gene encodes the Huntington protein, essential for neuronal function. Excessive CAG repeats result in mutant Huntington protein, causing neuronal dysfunction and death. Emerging therapies like splicing modulators aim to reduce toxic protein production, while symptom management focuses on FDA-approved drugs for chorea.

Findings:

HD manifests when CAG repeats exceed 40, intermediate repeat ranges influence risk and inheritance. Mutant Huntington protein disrupts neuronal networks and gene regulation. Splicing modulators introduce stop codons in RNA to halt toxic protein production. FDA-approved drugs effectively manage chorea, the most common HD symptom.

Conclusions and Relevance:

Advances in HD research highlight promising treatments targeting the disease's root causes and symptoms. While splicing modulators are under investigation, current therapies effectively manage symptoms, offering hope for improved patient care.

References

- Ross CA, Tabrizi SJ. Huntington's disease: From molecular pathogenesis to clinical treatment. *Lancet Neurol*. 2011;10(1):83-98. doi:10.1016/S1474-4422(10)70245-3.
- Bates GP, Dorsey R, Gusella JF, et al. Huntington disease. *Nat Rev Dis Primers*. 2015;1:15005. doi:10.1038/nrdp.2015.5.
- Kumar A, Ratan RR. Oxidative stress and Huntington's disease: The good, the bad, and the ugly. *J Huntingtons Dis*. 2016;5(3):217-237. doi:10.3233/JHD-160211.
- Frank S. Tetrabenazine as anti-chorea therapy in Huntington disease: An open-label continuation study. *BMC Neurol*. 2014;14:26. doi:10.1186/1471-2377-14-26.

Article Information

Accepted for Publication: December 24-2024

Published: February 13-2025.

Open Access: This is an open-access article distributed under the terms of the Creative Commons Attribution license.

Corresponding Author: Kshitij Ramesh Dhokne, MD Alte University, Tbilisi, Georgia.

Acknowledgment: - MedVentures (CPD no.-#784331) for providing financial support for Publishing, Alte University.