Review

SNAREopathy in Neurologic Disorders: From Synaptic Mechanisms to Genetic and Epigenetic Regulation

The Neuroscientist
1–12

DOI: 10.1177/10738584261463537
journals.sagepub.com/home/nro
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Abstract

Synaptic dysfunction is a central feature of many neurologic diseases, and the soluble *N*-ethylmaleimide–sensitive factor attachment protein receptor (SNARE) complex plays a critical role in regulating synaptic vesicle fusion and neurotransmitter release. Despite the rapidly growing body of research on SNAREs, comprehensive reviews addressing their mechanisms, as well as the influence of genetic variants and epigenetic regulation, remain limited. This review aims to address this gap. Disruption of SNARE processes can impair synaptic signaling and lead to neurologic pathology. Genetic variants in SNARE-related genes, including VAMP2, STX1A/STX1B, SNAP-25, STXBP1, UNC13A, SYT1, RIM, and RAB3, have been associated with a broad spectrum of neurologic conditions. In addition to genetic variants, emerging evidence indicates that epigenetic mechanisms can regulate the function of SNARE-related genes in physiologic processes and contribute to disease pathogenesis. Genetic variants are increasingly used as diagnostic markers and may inform the development of targeted therapeutic strategies, whereas epigenetic signatures hold promise as diagnostic, prognostic, and treatment-monitoring biomarkers. Although clinical applications remain limited, advancing knowledge of SNARE genetics and epigenetics may facilitate the development of novel diagnostic modalities, prognostic tools, and precision therapeutic strategies for neurologic diseases.

Keywords

SNARE, neurotransmitter release, SNAREopathy, neurologic disorders, genetic variant, epigenetic