Role of Astrocytes in the Pathophysiology of Lafora Disease and Other Glycogen Storage Disorders

AUTHOR: Jordi Duran

RESEARCH SIMPLIFIED BY: Spencer Nguyen

Duran J. (2023). Role of Astrocytes in the Pathophysiology of Lafora Disease and Other Glycogen Storage Disorders. Cells, 12(5), 722. https://doi.org/10.3390/cells12050722

WHAT ARE ASTROCYTES?

Astrocytes, the abundant type of cell in the central nervous system (CNS), play a crucial role in supporting neurons. These cells undertake various metabolic, structural, and neuroprotective functions. Among their tasks are the clearance of excess neurotransmitters and stabilization and regulation of the blood-brain barrier. Under normal conditions, brain glycogen serves as a supplementary fuel source for heightened neuronal activity. However, genetic mutations can cause glycogen to accumulate in astrocytes, leading to neurological disorders such as Lafora disease (LD).

LAFORA BODIES IN NEURONS AND ASTROCYTES

Lafora bodies (LBs) are misshapen glycogen accumulations found in the brain, present in both neurons and astrocytes. It was previously believed that LD was caused solely by the accumulation of LBs in neurons. However, research indicates that brain glycogen predominantly resides in astrocytes under normal conditions, making it evident that LBs also accumulate in astrocytes. There are two types of LBs: neuronal (nLBs) and Corpora amylacea-like (CAL) LBs, the latter found in astrocytes. CAL LBs are named for their resemblance to Corpora amylacea, which are glycogen aggregates that accumulate in the brain of the elderly. Both types of LBs are present in the early stages of LD in mouse models.

ROLE OF ASTROCYTIC LBS IN THE PATHOPHYSIOLOGY OF LD

The presence of Lafora bodies (LBs) in astrocytes suggests they contribute to Lafora's disease (LD) pathology. Studies in mice show that in regions like the hippocampus, a region of the brain important for memory, astrocytic LBs (CAL) are more prevalent than neuronal LBs (nLBs). Neuroinflammation, a key feature of LD, is associated with excessive astrocytic glycogen accumulation in these mouse models. However, this accumulation does not increase susceptibility to epilepsy, another common early hallmark of LD. Researchers hypothesize that epileptic activity may instead be driven by neuronal LBs.

GLYCOGEN ACCUMULATION IN OTHER NEUROLOGICAL DISORDERS

Glycogen accumulation in nervous tissue is not unique to LD. Similar aggregates, known as Corpora amylacea, are observed in aged human brains and are more prevalent in neurodegenerative conditions like Alzheimer’s, Parkinson’s, Huntington’s, and Pick’s diseases, as well as in temporal lobe epilepsy. The accumulation of Corpora amylacea in the nervous system may contribute to neurological decline associated with aging and neurodegenerative diseases.

CONCLUSION

The study of LD mice has identified the toxic effects of excessive glycogen accumulation in astrocytes, a process that plays a crucial role in the pathophysiology of LD. This process may potentially be relevant to other conditions involving abnormal glycogen accumulation in astrocytes, including common neurodegenerative diseases like Alzheimer's, Parkinson's, Huntington's, and Pick's diseases, as well as normal aging. Further research is needed to understand the mechanisms and the extent to which excessive glycogen accumulation affects neurological activity.