JOURNAL NEWS

Mapping toxic lipid buildup in a rare neurological disease

By Stella Ekaputri
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Globoid-cell leukodystrophy, or GLD, is a rare genetic condition that causes severe damage to the nerve myelin sheath and leads to drastic neurological decline. Symptoms of GLD include blindness or deafness, severe motor skill loss and intellectual disability, which can manifest in individuals between one and seven months of age, in childhood or in adulthood. This condition stems from impaired activity of Galc, an enzyme that breaks down two sphingolipids found in the nervous system: galactosylceramide, or HexCer, and psychosine, or HexSP. Without functional Galc, these lipids accumulate to toxic levels in the brain and damage cells that form myelin. While several studies have measured the levels of these two lipids in GLD, their distribution across different brain regions during the disease remains largely unknown.

In a recent paper published in the Journal of Lipid Research, Tingting Yan and colleagues from Columbia University and the University of Florida developed a novel method to detect and visualize HexCer and HexSP in brain sections with high sensitivity and minimal processing. The researchers used an imaging mass spectrometry to map and quantify these two toxic lipids across brain regions from birth to the onset of disease in a GLD mouse model lacking Galc. As the mice gradually developed neurological symptoms, the researchers observed a gradual increase in HexCer and HexSP across multiple brain regions, with HexSP buildup beginning earlier than HexCer accumulation. Using immunohistochemistry, they also found that brain regions with high HexSP levels were especially associated with disrupted myelin, neuronal damage and inflammation.

Although this method cannot distinguish lipids from their isomers, it enables researchers to map and quantify toxic lipid accumulations spatially and to observe how they relate to declining brain function as the disease progresses. This study supports drug development for GLD by offering a novel approach that directly links toxic lipid levels to neuronal damage over the course of the disease.

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