With potential advancements on the horizon for Hunter syndrome, read on to learn more and stay updated.

IN HUNTER SYNDROME

GAG buildup never stops, so neither will I.

For individuals living with Hunter syndrome, or mucopolysaccharidosis type II (MPS II), there is an unmet need to completely remove glycosaminoglycan (GAG) buildup in the brain and the body to address symptoms.

What role do GAGs play in Hunter syndrome?

Chain-like molecules called glycosaminoglycans (GAGs) accumulate in the body and brain of individuals living with Hunter syndrome. Continued GAG buildup leads to symptoms appearing and worsening over time.

GAG levels are elevated in the brain, regardless of disease severity

GAG levels in the brain can be measured through the cerebrospinal fluid (CSF), the liquid that protects the brain and spinal cord.

Individuals with attenuated or severe Hunter syndrome consistently had higher GAG levels in the brain compared to those without the condition.[a]

Attenuated Hunter syndrome

Children with attenuated Hunter syndrome have UP TO

10x

HIGHER GAG LEVELS IN THE CSF

vs children without Hunter syndrome

Adults with attenuated Hunter syndrome have UP TO

32x

HIGHER GAG LEVELS IN THE CSF

vs adults without Hunter syndrome

Severe Hunter syndrome

Children with severe Hunter syndrome have UP TO

93x

HIGHER GAG LEVELS IN THE CSF

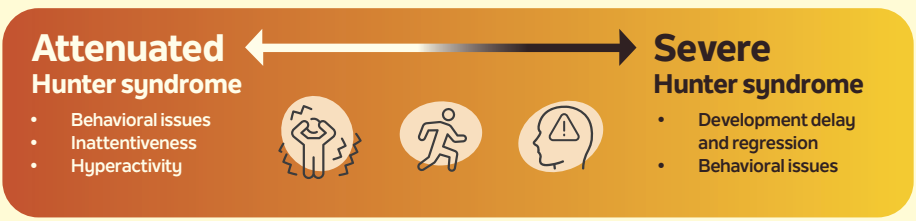
vs children without Hunter syndrome

[a]Based on an analysis from 4 studies of GAGs in the CSF of 257 individuals, including 25 with Hunter syndrome.

The impact of GAG buildup

It's commonly understood that individuals with severe Hunter syndrome experience cognitive and behavioral symptoms due to GAG buildup. **Individuals with attenuated Hunter syndrome, however, also experience brain-related symptoms such as behavioral issues, difficulty focusing, and hyperactivity.**

Central nervous system manifestations exist across the spectrum of disease



Biomarkers and their role in Hunter syndrome management

Biomarkers are natural substances in bodily fluids, such as blood or urine, that can be signs of disease activity. **Urine GAG (uGAG) level, for example, is one commonly measured biomarker for tracking GAG levels in the body,** but other biomarkers may become useful as science advances.

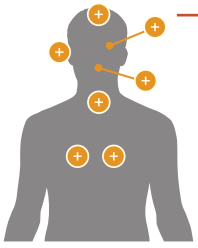
Biomarkers for the brain

We are learning more about biomarkers that may be useful in the future for understanding how Hunter syndrome affects the brain.

Heparan sulfate (HS) is the primary GAG found in high levels in the brain of individuals with Hunter syndrome.

HS levels can be measured in the CSF. It is currently used in Hunter syndrome clinical studies to help assess impact of disease and treatment on the brain.

Another biomarker for the brain is called neurofilament light (NfL), which can be measured through a blood test. NfL is a protein that is released when brain cells are damaged and could signal changes in cognitive function.



Explore the areas of the body impacted by Hunter syndrome and learn more about the role of biomarkers in understanding Hunter syndrome at **GAGsinHunterSyndrome.com**

What's next for Hunter syndrome

There are investigational treatments in development designed to **treat both the brain and the body**. As the science advances and the use of biomarkers evolves, Hunter syndrome management will continue to change.

In the future:

New therapies may offer alternative options that better meet the needs of both individuals with attenuated or severe Hunter syndrome.

Reducing GAG levels to those seen in individuals without Hunter syndrome may become a more important treatment goal.

Emerging biomarkers may provide additional information on the impact of Hunter syndrome on the brain and the management of related symptoms.

Scan the QR code or visit **GAGsinHunterSyndrome.com** to sign up and stay updated on what's next in Hunter syndrome

DENALI THERAPEUTICS

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