**Background and Objectives**

GM2 Gangliosidoses

GM2 gangliosidoses are a group of lysosomal lipid storage disorders caused by mutations in at least 1 of 3 recessive genes (HEXA, HEXB, and GM2A), resulting in accumulation of GM2 ganglioside substrate inside neuronal lysosomes, leading to cell death.

Research Goal:

Understand the patient’s and caregiver’s perspective of living with late-onset GM2 gangliosidosis (Tay-Sachs disease and Sandhoff disease).  

**Key Objectives:**

- Explore and understand the symptoms of patients who are living with late-onset GM2, their experience with treatment, and the impact of the disease on their lives. 
- Understand possible differences in experience over time. 
- Understand the impact of providing care and support to the adult patient with late-onset disease from the perspective of the caregiver.

**Project Approach:**

- Adult patients with GM2 (n=12) and caregivers (n=7) were contacted and recruited through their membership in the National Tay-Sachs & Allied Diseases Association (NTSAD). 
- Two patient focus groups and one caregiver focus group were conducted with attendees at NTSAD’s 37th Annual Family Conference in Reston, Virginia, April 18, 2018.

**Major Topics of Discussion**

- Background information in terms of age, relationship with adult GM2 patient.  
- Career-roles and responsibilities in caring for the GM2 patient. 
- Formal training in caregiving and relationship with medical community.  
- Impacts and burdens of caregiving.  
- Perspective on the impact of the disease on the patient.

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**Patients' Experience & Perspective**

**Who Are GM2 Patients?**

GM2 patient groups differed greatly by age distribution, time since living, and living situation.

Group 1: 29% Living alone: 20–35 years old (26%); 3–10 years ago (26%); 71% ganglioside (hemizygous) patients. 

Group 2: 40% Living with and caring for adult child patient: 29% 40–60 years old (30%); 20–25 years ago (30%); 60% ganglioside (heterozygous) patients.

- Problems with limited mobility and “clumsy” (stumbling) are common among these GM2 patients. 
- Patients are often unable to walk long distances, have adjusted their strides to accommodate their difficulty with walking, and fall frequently. 
- Muscle Weakness, Speech Changes
  - Additionally, patients cite muscle weakness and changes in speech as among the most common symptoms.

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**Key Symptoms**

- Lack of Sustained Mobility: “Clumsy” Gait, Falling
  - Problems with limited mobility and “clumsy” (stumbling) are common among these GM2 patients.
  - Patients are often unable to walk long distances, have adjusted their strides to accommodate their difficulty with walking, and fall frequently.

- Muscle Weakness, Speech Changes
  - Additionally, patients cite muscle weakness and changes in speech as among the most common symptoms.

**Results**

**Preliminary Conceptual Model of GM2 Concepts**

Model is based primarily on patient interviews, but uses caregiver input when confirmatory.

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**Caregivers’ Experience & Perspective**

Caregivers in this sample are typically close family members (spouses or parents); the majority are employed, live with the GM2 patient, and have been caregivers for more than a decade.

Impact and Burdens of Caregiving

Deep emotional investment in the well-being of the patient, deep uncertainty about the future, and a high level of patient need as the disease progresses combine to create a high level of unmet, yet understandable, stress in the day-to-day lives of these caregivers.

Caregivers’ Perspective of GM2 Patients’ Experience

When asked how the disease has affected other people, patients most often express concern that their increased level of reliance on others due to limited/complete lack of mobility impacts other people’s interactions with them. They feel their disease is “socially burdensome” to others.

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**Conclusions**

This research highlighted key needs for additional support for both patients and their caregivers:

- For patients, there is a need for solutions that would enable more independence and management of their own lives as long as possible. 
- Patients would like to be able to move more, reduce falling, and maintain their ability to communicate.
- For caregivers, there is a need for training, social support, and activities that reduce or help manage their burdens.
- Many noted a lack of social opportunities to exchange ideas and share experiences, (and NTSAD conference as a welcomed exception. 
- Caregiver organizations and/or forums that help learn more about the disease, their roles, and what to expect in the near and long terms (even though disease experience is not formal) as well as social opportunities to meet other caregivers, would greatly enhance their experience.

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**References**


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**Patient-reported GM2 symptoms align with published literature**

The most frequent and impactful symptoms reported (lack of limited mobility, odd gait, frequent falling, speech changes, etc.) align well with published literature.

- In both late-onset Tay-Sachs and Sandhoff disease, patients are often described as "clumsy and awkward", which is directly in line with how these patients described their balance and frequent falling issues.

The patients mentioned experiencing symptoms of frequent muscle tremors, [progressive] muscle weakness, as well as changed speech (slurred speech, talking fast), all of which are cited to be more apparent in the first decade of disease manifestation, indicating underlying neuroplogic problems.

Development of a broad-basediatric gait that makes walking difficult, and described by these patients as “having an old soul,” is well documented and leads to patients almost always losing ambulatory ability by the sixth decade of disease.