

## MitoInsights

### ***Bringing mitochondrial science closer to the people it matters to most***

Science moves fastest when everyone can take part. That's why MitoCanada is committed to empowering our community with knowledge. By translating cutting-edge mitochondrial research into clear, easy-to-understand summaries, we aim to nurture curiosity, strengthen understanding, and build confidence in the science driving hope and progress.

## Lay Summary: Signs, symptoms, and health-related quality of life in MELAS: measuring what's important from the patient and clinician perspectives

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### **What's this research about?**

This study focuses on *mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS)*, a rare genetic condition caused by changes in mitochondrial DNA that disrupt how cells make energy. MELAS often affects organs that need lots of energy, like the brain and muscles, leading to symptoms such as seizures, stroke-like episodes, fatigue, hearing loss, and memory problems.

While many scientific papers describe MELAS from a clinical or biological standpoint, few have explored what it's actually *like* to live with this disease. To fill that gap, researchers from the U.S. conducted in-depth interviews with both expert clinicians and adults living with MELAS. Their goal was to understand the most important symptoms, life impacts, and daily challenges from the patient's perspective, and to identify which aspects of the condition matter most when designing future treatments and clinical trials.

### **Why is this important?**

For people with MELAS, medical progress has long been limited by a lack of treatments and by how little patient experience was captured in research. By directly asking patients to describe their symptoms, limitations, and quality of life, this study ensures that future therapies and outcome measures reflect what truly matters, not just what can be measured in a lab.

Importantly, regulatory agencies like the FDA and EMA now encourage patient-reported outcomes in rare-disease research. Understanding how MELAS affects physical, emotional, and cognitive well-being helps researchers design more meaningful clinical trials and better tools to measure improvement over time.

## How did they study this?

The study was carried out in two phases. First, researchers interviewed five clinicians with years of experience treating mitochondrial diseases. These experts described the range of symptoms and life impacts they observe in MELAS and provided input on whether patients could reliably share their own experiences.

Next, the researchers conducted 45–60 minute interviews with 16 adults living with MELAS, all of whom had the common m.3243A>G variant. Participants were asked to describe their signs, symptoms, and how MELAS affects their daily lives, work, and emotions.

All interviews were recorded, transcribed, and analyzed for recurring themes. Researchers looked for *saturation* (the point where no new information emerges) to confirm that the sample size captured the full scope of patient experience. Ultimately, 35 unique symptoms and 68 life-impact themes were identified across 15 categories.

## What did they find?

### 1. The most common and burdensome symptoms

Patients most frequently described:

- Physical fatigue (94%): a deep, unrelenting tiredness that goes beyond sleepiness.
- Hearing loss (81%): often requiring hearing aids or cochlear implants.
- Mental fatigue (75%): feeling mentally “drained” and unable to concentrate.
- Exercise intolerance and memory problems (69% each): struggling with stamina, word-finding, or remembering everyday details.

Many patients described fatigue as “hitting a wall,” suddenly running out of energy even during small tasks like walking or cooking. Memory issues, brain fog, and speech difficulties were also major sources of frustration and anxiety.

### 2. The biggest life impacts

The most affected areas of life were:

- Adaptive behaviours: needing mobility or hearing aids, or adjusting eating habits.
- Work and independence: half of participants were unable to work due to fatigue and cognitive difficulties.
- Emotional well-being: feelings of frustration, sadness, and anxiety were common.

Patients often described how fatigue and cognitive issues limited their ability to work, socialize, and care for themselves, turning routine activities into daily challenges.

### 3. Clinician vs. patient perspectives

Clinicians tended to emphasize acute, organ-specific symptoms (like seizures or stroke-like episodes), while patients highlighted chronic, ongoing problems such as fatigue, mental exhaustion, and memory loss. This difference underscores why patient-reported data are essential, they reveal the lived reality behind the medical picture.

## **What does this mean for mitochondrial disease research?**

This study provides one of the most detailed portraits to date of what it's like to live with MELAS. It confirms that patients can meaningfully self-report their symptoms, even when experiencing fatigue or cognitive impairment, and that their insights are crucial for designing effective treatments.

The findings also call attention to the need for new clinical trial measures that better capture fatigue, cognition, and daily function. By focusing on what patients identify as most impactful, future therapies can be designed to target the symptoms that truly limit independence and quality of life.

Finally, the study highlights the power of partnership between clinicians, researchers, and patient communities, to drive forward the next phase of progress in mitochondrial medicine.

## **The research in simple terms**

This research asked people living with MELAS to share their honest experiences, how the disease affects their energy, memory, emotions, and daily lives. Their stories reveal that fatigue and cognitive struggles are at the heart of the condition. By documenting these experiences, the study ensures that the patient voice shapes how treatments are measured and developed in the future.

## **Why this study matter to the mito community**

For families affected by MELAS, this research is a reminder that every lived experience has value in shaping scientific progress. It shows that the global mito community, from patients and caregivers to researchers and clinicians, is united in building knowledge that leads to better care and, one day, effective treatments.

It also demonstrates how important patient participation is. Joining registries, participating in studies, contributing to interviews, and sharing experiences helps researchers understand the true impact of mitochondrial disease, and speeds the path to new therapies.

## **Acknowledgment**

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Their work stands as an important milestone in mitochondrial research, one that reminds us that understanding begins by listening. By elevating patient voices, this team has brought the lived experience of MELAS to the forefront of scientific progress, helping ensure that future research measures what truly matters most to those living with the disease.

