

Rett syndrome in adulthood: the caregiver perspective

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INTRODUCTION

Rett syndrome is a complex, progressive neurodevelopmental disorder that impacts multiple organ systems from childhood into adulthood.¹ A recent report found that 70% of individuals with typical Rett syndrome survived to at least 50 years of age.²

Patient-focused drug development (PFDD)

The US Food and Drug Administration (FDA) established the PFDD initiative to devote attention to gathering patient perspectives.³ Patient experience data are critical to the development of treatments for rare diseases by⁴:

- Providing background and context about the disease
- Informing clinical trial design, including primary endpoints
- Supporting regulatory decision-making, especially the risk-benefit assessment of a potential new treatment

OBJECTIVE

To explore the perspectives of caregivers of adults with Rett syndrome and to inform the clinical development of an investigational gene therapy.

PARTICIPANTS/METHODS

Quantitative insights were gathered through a survey:

- N=142 caregivers of women with Rett syndrome aged ≥ 18 years
- Recruited in partnership with patient advocacy organizations*
- 22 multiple choice and open response questions

Qualitative insights were collected through a workgroup:

- N=7 caregivers of women with Rett syndrome aged ≥18 years
- Recruited in partnership with patient advocacy organizations*
- Daily online survey, including journaling exercises; asynchronous discussion forum; video focus group

RESULTS

THE AGING CAREGIVER EXPERIENCE

As caregivers age, they face unique challenges with mobility and concerns about planning for their loved one's future.

PHYSICAL

- Progressive mobility issues in adulthood increase caregiver burden
- Reports of back pain, fatigue, and falls (for both) were common

EMOTIONAL

- As the disease progresses, continuing with therapy becomes challenging, leaving caregivers to wonder "what can I do?"
- Behavioral or mood disturbances causes caregivers to question attending social activities or to isolate the family

FINANCIAL

- Caregivers' biggest fear: "if something happens" to them who will care for their loved one
- Access to high-quality, affordable day programs for adults is limited

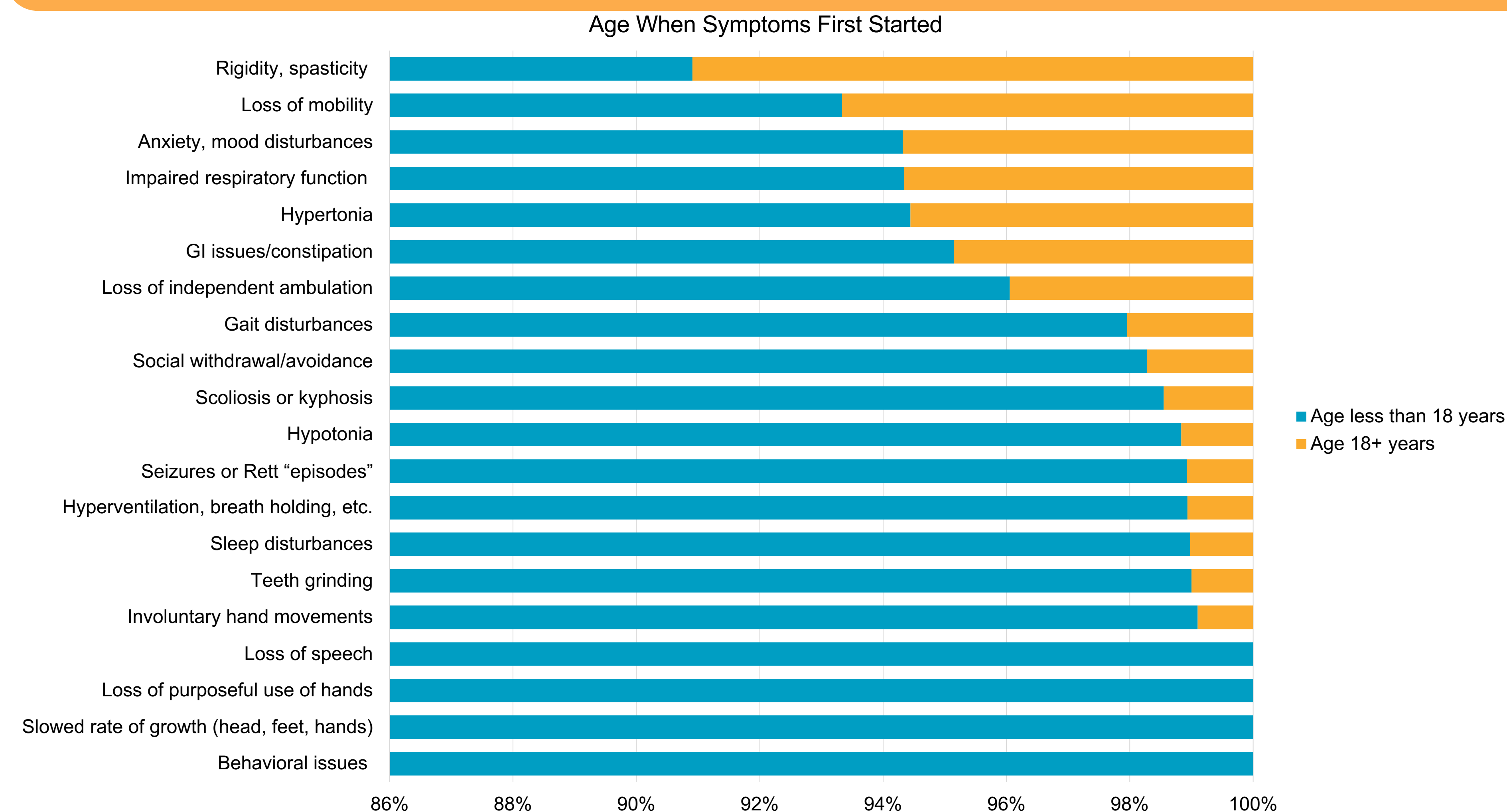
"Who will care for her? Where will she live? Do we have enough money saved for her care?"

"My biggest fear is not being able to take care of her. I worry about something happening to me or my husband."

RESULTS

RETT SYNDROME SYMPTOMS AND AGE OF ONSET

- Some patients developed new symptoms in adulthood, including rigidity and spasticity, loss of mobility, anxiety, impaired respiratory function, hypertonia, and gastrointestinal issues
- In addition to development of new symptoms, caregivers reported that some existing symptoms worsened in adulthood, such as loss of mobility, anxiety, and sleep disturbances



CHALLENGING SYMPTOMS THAT AFFECT QUALITY OF LIFE

Caregiver-rates symptoms with greatest impact on quality of life in adulthood. The top 5 are listed below in order, starting with the most challenging:

Loss of speech

- The inability for a caregiver to know what their daughter needs or is feeling is the most challenging symptom
- "If our daughter could speak, she would assist us with her care, needs, desires, etc."

Loss of purposeful use of hands

- The inability to perform daily living activities, such as eating and grooming, are the most impactful to both patients and caregivers
- "Hand movements have controlled her completely. She can't think properly – it takes over her."

Seizures or Rett "episodes"

- Although not all patients experience seizures or "Rett episodes", when these symptoms are present, they have a significant impact on quality of life
- "Some days she seizes so much that she's too tired for any of her therapies."

Loss of independent ambulation

- Ability to stand and take steps decreases as patients age, and it is increasing difficult for caregivers to assist with standing and transfers
- "She is now unable to bear weight, so she's totally dependent on a wheelchair."

GI issues/constipation

- GI issues cause anxiety, pain, bloating and were often the culprit behind "bad days"; managing constipation is time-consuming and frustrating
- "We have to build a schedule around bowel issues as sometimes she goes very frequently and other times she only goes with a suppository. We cannot go anywhere without a change in plan in place."

SYMPTOM MANAGEMENT

- Symptom management involves medication, therapies, mobility aids, and communication devices

Approach to the management of Rett syndrome in adults across 4 countries (% caregivers reporting use of intervention)				
Medicines and Supplements	US	Canada	Israel	UK
Anti-seizure medicine or treatments	76%	57%	58%	74%
Gastrointestinal medications/supplements	61%	43%	47%	49%
Acid reflux medication	43%	48%	5%	54%
Sleep medication	42%	19%	16%	17%
Anxiety medicine	36%	24%	11%	31%
Feeding tube	52%	14%	11%	31%
Nutritional supplements	45%	38%	42%	37%
Special diet (eg, ketogenic diet)	15%	14%	16%	17%
Therapy	US	Canada	Israel	UK
Ankle-foot orthosis	46%	29%	32%	31%
Physical therapy	42%	29%	68%	46%
Surgery (to correct scoliosis)	40%	19%	26%	23%
Communication therapy	36%	38%	63%	49%
Positioning aids	33%	29%	26%	49%
Splints (hands, legs, or elbows)	31%	33%	58%	29%
Occupational therapy	27%	19%	16%	49%
Manual therapy	25%	24%	21%	29%
Music therapy	15%	19%	68%	51%
Hydrotherapy	9%	19%	63%	54%

Note: Green boxes represent those treatments or interventions used by 40% or more of respondents in each respective age group

CAREGIVER EXPECTATIONS FOR GENE THERAPY ARE HIGH

Desired improvements include:

- **Mobility:** Ability to stand and take steps
- **Communication:** Ability to express needs and opinions (eg, hunger, discomfort, preferences)
- **Hand use:** Ability to perform daily living activities, such as eating, grooming, and age-appropriate play
- **GI issues:** Reduced pain and dependence on medication. Increased predictability of bowel movement
- **Overall anxiety:** Fewer crying and screaming episodes and more predictable moods to ease public outings
- **Breathing:** Reduced breath-holding and hyperventilation

CONCLUSION

- While individuals tend to stabilize clinically over time², women with Rett syndrome experience new and worsening symptoms well into adulthood
- The most challenging symptoms are inability to communicate, lack of hand use, GI symptoms, seizures, and loss of ambulation
- For older caregivers, declining mobility made lifting more challenging and future care was a concern
- Caregivers of adults with Rett syndrome are willing to participate in a gene therapy trial; they desire improvements, even slight ones, in the most challenging symptoms
- Caregiver insights were critical to the selection of endpoints in Taysha's Phase 1/2 clinical trial of a gene therapy for adult females with Rett syndrome, also known as the REVEAL Adult Study

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*RettSyndrome.org, Reverse Rett UK, Ontario Rett Syndrome Association, Israel Rett Syndrome Foundation, Rett Syndrome Research Trust.