

Beyond contractures: Neurological and neuromuscular findings in Arthrogryposis Multiplex Congenita

My Vuong Hermansen^{1,2,3}, Kristin Ørstavik², Unni Steen¹, Mathias Toft^{3,4}, Cathrine Brunborg⁵, and Lena Lande Wekre¹

- 1. Norwegian Centre for Rare Diseases, Sunnaas Rehabilitation Hospital, Nesodden, Norway
- 2. Section for Rare Neurological disorders and EMAN, Department of Neurology, Oslo University Hospital, Oslo, Norway
- 3. Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway
- 4. Department of Neurology, Oslo University Hospital, Oslo, Norway
- 5. Oslo Centre for Biostatistics and Epidemiology (OCBE), Oslo University Hospital, Oslo, Norway

1 BACKGROUND

Arthrogryposis multiplex congenita (AMC) is a group of congenital conditions defined by multiple joint contractures, often accompanied by underdeveloped muscles. Historically regarded as a non-progressive and primarily orthopedic condition, AMC is now understood as a heterogenous spectrum in which underlying neurological and neuromuscular mechanisms may play an important role. Despite this shift, the extent and nature of neurological involvement remain largely unexplored. The EXPLAIN study (Exploring Arthrogryposis multiplex congenita in adults in Norway) provides the first systematic neurological assessment of adults with multiple congenital contractures and represents the largest adult AMC cohort to date.

2 METHODS

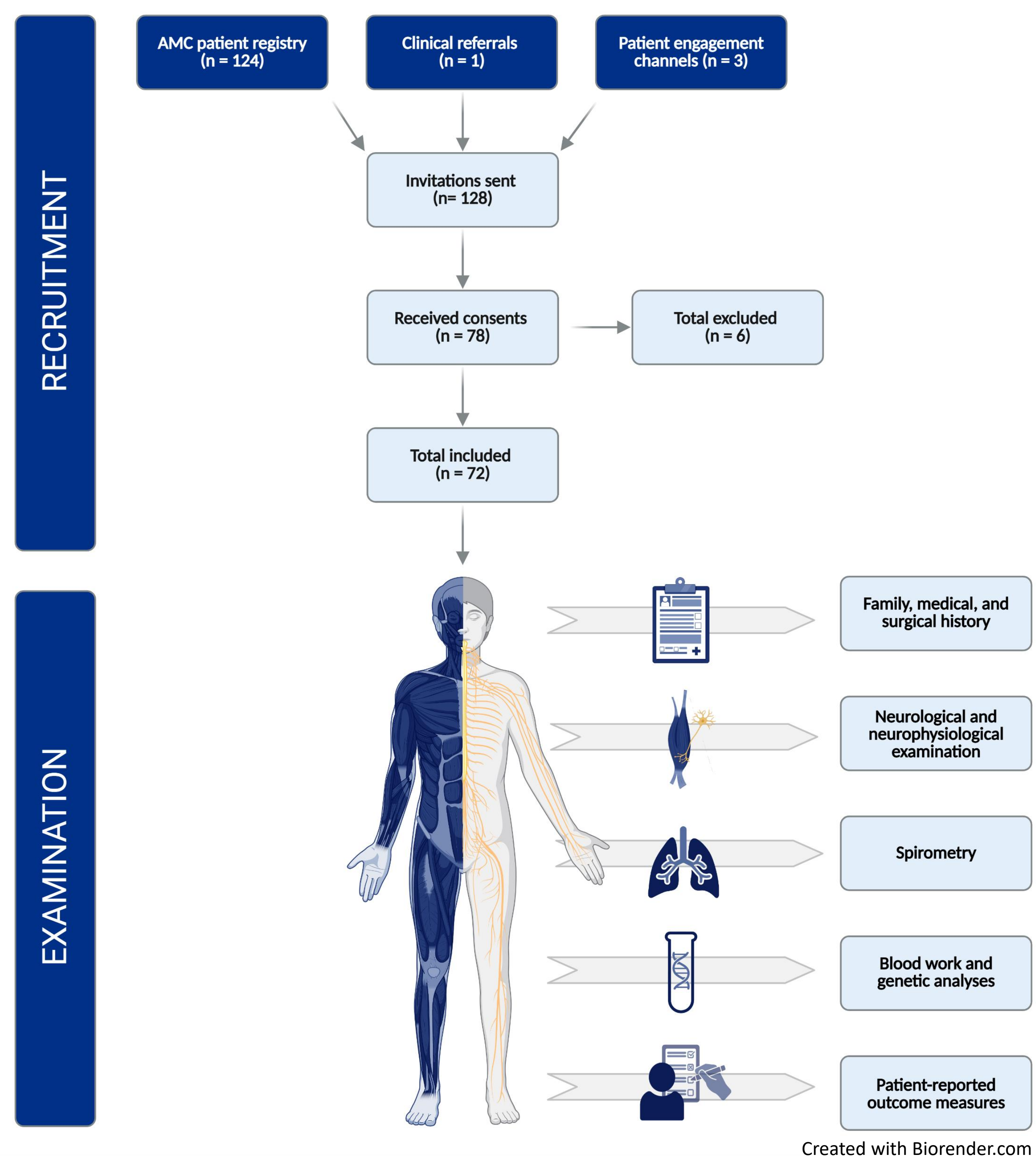


Figure 1: The EXPLAIN study is a patient-oriented and cross-sectional study, conducted from June 2023 to March 2025. Adults with AMC underwent structured interviews addressing symptoms and age-related changes, neurological examination, nerve conduction studies, electromyography, and biochemical analyses. Phenotypes were described using Human Phenotype Ontology (HPO) terms.

4 RESULTS

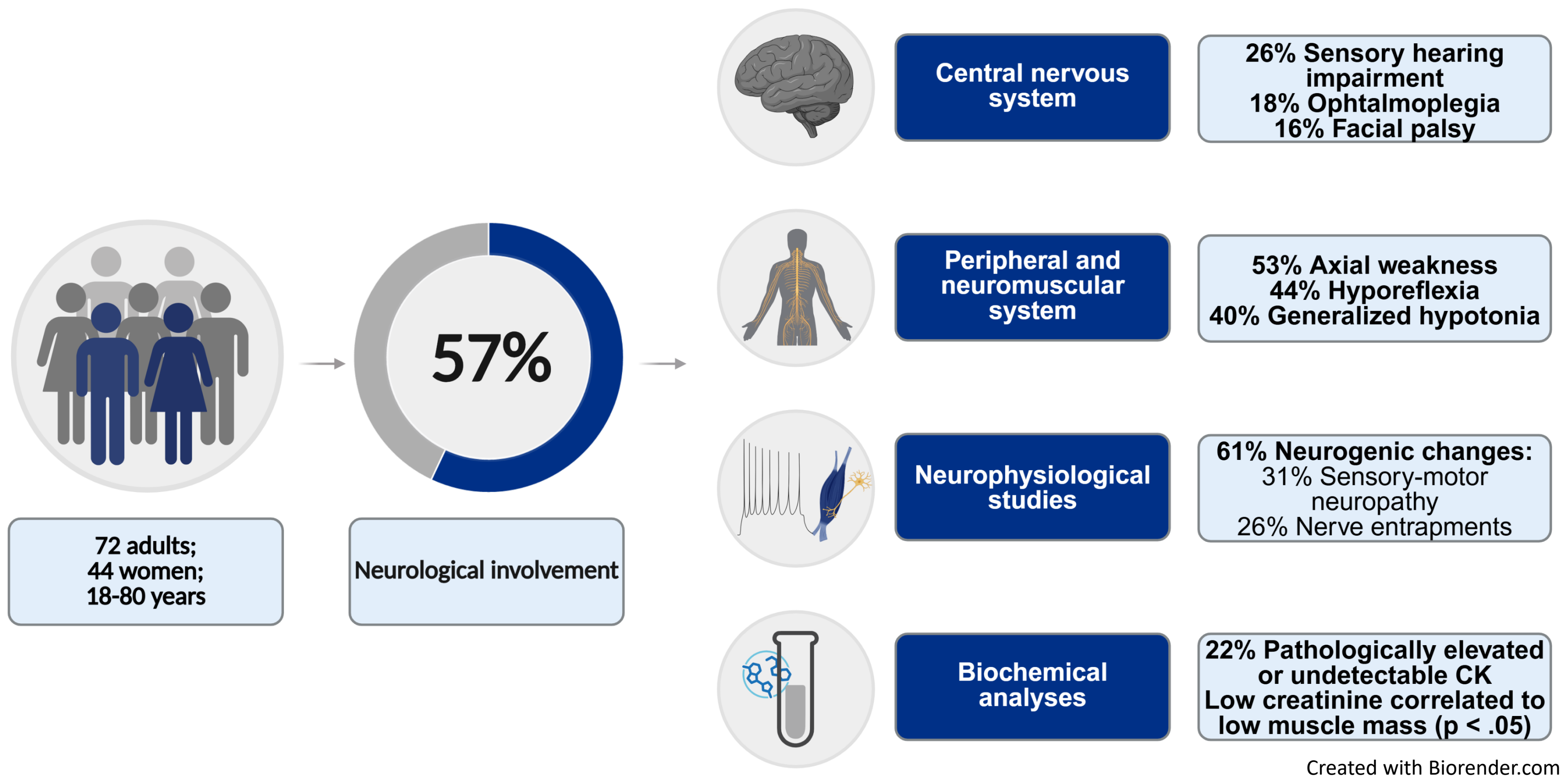


Figure 2: Most common neurological and neuromuscular findings in 72 adults with congenital contractures. In total, 41 participants (57%) reported neurological disease or symptoms. Neuropathies were most prevalent ($n = 27$). Headache disorders ($n = 8$), especially migraine, was the second most common neurological disorder. Clinical examination of muscle morphology revealed localized muscle hypoplasia in 73% of the patients, while generalized muscle hypoplasia was observed in 22%. Supplementing magnetic resonance imaging (MRI) of musculature in twelve participants revealed clinically relevant muscle atrophy and fat infiltration in three participants.

Medical history revealed that nearly half of the subjects reported early progressive functional decline, including stiffness, weakness, fatigue, and reduced mobility. Neuropathic pain was common (50%). Among participants reporting continuous use of analgesics ($n = 36$), 71% needed drugs for neuropathic pain.

5 CONCLUSION

The EXPLAIN study represents the largest clinical cohort of adults with AMC to date. The presented findings challenge the notion of AMC as a static condition primarily defined by joint contractures. Adults with AMC exhibit broader neuromuscular involvement and more premature functional decline than previously acknowledged. These progressive features, particularly muscle weakness and neuropathic symptoms, indicate that myopathic and neurogenic AMC may follow a more dynamic course across the lifespan. These findings highlight the need for neurological assessment and lifelong multidisciplinary follow-up. Underlying neurological or neuromuscular etiology should be explored through future phenotype-genotype approaches.

SCAN ME

