v. 5, n. 24, 2025

International Journal of Health Science

MOTOR AND FUNCTIONAL OUTCOMES OF A CHILD WITH TUBULINOPATHY UNDERGOING INTENSIVE TRAINING: A CASE REPORT

Acceptance date: 24/06/2025
Submission date: 10/06/2025

Bruna Justino de Morais
Physiotherapy student at Christus University Center (UNICHRISTUS)
Fortaleza, Ceará, Brazil.
https://lattes.cnpq.br/0641237542841247

Maria Valdeleda Uchoa Moraes Araújo
Physiotherapist at the César Cals General Hospital (HGCC); Professor at the Christus University Center (UNICHRISTUS).
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/7314440835465770

Mara Marusia Martins Sampaio Campos
Physiotherapist at the Federal University of Ceará (UFC)/Brazilian Hospital Services Company (EBSERH)/Assis Chateaubriand Maternity School (MEAC).
Lecturer at the Christus University Center (UNICHRISTUS).
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/6515305320777878

Gianini Portela Teixeira Albuquerque
Physiotherapist and Director of the Evolud Clinic
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/1335622403061367

Ana Lúcia do Carmo Delmiro
Physiotherapist at the César Cals General Hospital (HGCC)
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/3079727871331828

Auralice Maria Rebouças Machado Barroso
Physiotherapist at the César Cals General Hospital (HGCC)
Fortaleza, Ceará, Brazil.
https://lattes.cnpq.br/2397451490483595

Wanda de Andrade Câmara
Physiotherapist at the César Cals General Hospital (HGCC)
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/2515452430736959

Maria Goretti Alves de Oliveira da Silveira
Physiotherapist at the César Cals General Hospital (HGCC)
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/8731216620050793

Cristianne Melo de Mendonça
Doctor at the César Cals General Hospital (HGCC)
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/0053687342755649

Sandra Mara Benevides Caracas
Physiotherapist at the César Cals General Hospital (HGCC)
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/7785982363462530

Lucia Goersch Fontenele
Physiotherapist at the César Cals General Hospital (HGCC)
Fortaleza, Ceará, Brazil.
http://lattes.cnpq.br/1452578609885169

Sandra Imaculada Souza Frota
Physiotherapist at the César Cals General Hospital (HGCC)
Fortaleza, Ceará, Brazil.
https://lattes.cnpq.br/7129935404643450

Abstract: Introduction: Tubulinopathies are a group of cortical and subcortical brain malformations characterized by various clinical alterations. Children with tubulinopathies can present variable clinical manifestations, such as cognitive alterations, developmental delays, motor impairment, hypotonia, intellectual disability of varying degrees and strabismus. Intensive approaches are essential for a better prognosis, such as the Training Program in Intensive Neurological Rehabilitation (TRAINI®) **Objective: To** analyze the motor and functional outcomes of a child with tubulinopathy who underwent TRAINI®**. Methods:** This is a case study carried out in a pediatric clinic in Fortaleza-CE, with a 1 year and 1 month old child diagnosed with a mutation in the TUBA1A gene. Intensive treatment was carried out for six months, with sessions from Monday to Friday, using resources such as therapeutic clothing, strength training and task-oriented training. Assessments were carried out using the Gross Motor Function Measure (GMFM-88) at two points in time: January and June 2024. **Results:** There was an overall improvement of 15.1% in the GMFM-88 score, from 19.6% to 34.7%. The greatest gains were seen in dimensions A (lying down and rolling over) and B (sitting). There was also an improvement in eye fixation and visual perception with the use of optical correction. **Conclusion:** The TREINI® program, with its interdisciplinary approach and therapeutic strategies based on the ICF, proved to be effective in promoting the child's functionality and independence, contributing to their engagement with the environment and improving their quality of life.

Keywords: Physiotherapy; Neurological disorders; Development; Genetic diseases; Pediatrics

INTRODUCTION

Tubulinopathies are a group of cortical and subcortical brain malformations characterized by various clinical alterations, resulting from pathogenic variants in the genes that regulate different tubulin isotypes. The main cortical anomalies include lissencephaly and polymicrogyria, while subcortical anomalies affect structures such as the corpus callosum, cerebellar vermis, brainstem, basal ganglia and cerebellum (Cushion *et al*., 2023; Hagege *et al*., 2022; Hebebrand *et al*., 2019).

Children with tubulinopathies can present variable clinical manifestations, such as cognitive alterations, developmental delays, motor impairment, hypotonia, intellectual disability of varying degrees, epilepsy, visual alterations and strabismus. Diagnosis is made using magnetic resonance imaging and genetic tests. The assessment of these children should be comprehensive, including the analysis of neuropsychomotor development in order to verify their abilities and functionalities (Cushion *et al*., 2023; Pavone *et al.*, 2023).

Treatment should involve a multidisciplinary approach, capable of covering all the clinical manifestations of the disease. The follow-up team should include doctors, occupational therapists, speech therapists, nutritionists and physiotherapists who work in different areas, such as motor skills, respiratory function, vision and hearing. Intensive approaches are essential for a better prognosis, such as the Training Program in Intensive Neurological Rehabilitation (TRAINI®) (Bahi-Buisson, 2016; Pavone *et al.*, 2023).

TREINI® consists of a global approach aimed at the rehabilitation process, with interventions centered on the patient's needs. The program relies on an interdisciplinary team that applies evidence-based knowledge to pediatric rehabilitation, addressing motor, cognitive, emotional and social aspects. The program is aimed at children and adolescents undergoing neurological rehabilitation with delayed neuropsychomotor development, with the aim of maximizing their functionality and independence (Flores Cruz *et al*., 2024; Loffi *et al.,* 2024).

TREINI® uses strategic interventions aligned with the domains of the International Classification of Functioning, Disability and Health (ICF). Its intensive approach, with high-frequency, long-duration activities, aims to stimulate neuroplasticity and promote tissue remodeling. During training, the child wears a flexible therapeutic garment, called an exoskeleton, which provides support for the musculoskeletal system, favoring postural control, proprioception and the transmission of forces, without restricting movement. In this way, the program contributes to improved functionality and independence in activities of daily living (Flores Cruz *et al*., 2024; Loffi *et al.,* 2024).

The brain has the ability to adapt to new stimuli, and these external and internal stimuli can cause the brain to adapt structurally and functionally, known as neuroplasticity. Intensive treatment for children with alterations in neuropsychomotor development is of great importance for motor gains associated with cognitive gains (Chaves, 2023; Morgan *et al.*, 2023).

Given the complexity of tubulinopathies and the significant impact these alterations have on children's motor and functional development, it is essential to understand and evaluate effective therapeutic strategies. Intensive physiotherapy has been identified as a promising approach to improving the functionality and quality of life of these patients, although there is still a lack of studies documenting its effects in detail.

The aim of this study was to analyze the motor and functional outcomes of a child with tubulinopathy who underwent TRAINI®.

METHODOLOGY

This is an observational and descriptive case report study carried out in a pediatric clinic in Fortaleza-CE, involving a child aged 1 year and 1 month, diagnosed with tubulinopathy associated with the TUBA1A mutation. The legal guardian signed the Informed Consent Form (ICF), authorizing data collection and the disclosure of information in an anonymized form. The study was approved by the Research Ethics Committee (CEP) of the Christus University Center, located at Rua João Adolfo Gurgel, 133, Cocó, Fortaleza - CE, with opinion: 7.608.051.

A case report is a type of study that aims to report in detail the clinical assessments, the interventions carried out and the results observed.

The intensive training lasted six months, with sessions from Monday to Friday.

Treatment Protocol

- Environmental enrichment activities
- Task-oriented training
- Mobility training
- Strength training
- Use of Treini Flex clothing to improve muscle activation.

Visual treatment plan

- Visomotor coordination
- Visomotor activities
- Use of occlusion for 30 minutes a day in the left eye.

RESULTS

During pregnancy, alterations were observed on the second morphological ultrasound, prompting specialized prenatal follow-up. The female child was born by caesarean section, with a gestational age of 39 weeks and 2 days, an APGAR index of 9/9, a height of 48cm and a weight of 3,195g. The neonatal tests (little eye, little heart, little ear and little tongue) showed normal results. After birth, strabismus and head bobbing were observed. The ophthalmological assessment identified hyperopia and nystagmus, indicating optical correction.

A functional physiotherapy assessment of vision was carried out on 29/08/2023, before the use of optical correction, with observation of convergent strabismus to the right (exotropia), bilateral nystagmus, decreased ocular fixation latency (around two seconds), better visual response to light stimuli in a dark environment and visual preference for the color red. In the visual tracking tests, the child had difficulty moving the left eye horizontally and showed a preference for looking downwards. With the use of optical correction, there was an improvement in visual perception and eye fixation time to the light object.

In the assessment of neuropsychomotor development, the following were observed: Brachycephaly (posterior flattening of the skull); Spontaneous movement inadequate for age; Communication based on crying, with a demonstration of disorganization and difficulty in soothing. Postural pattern with head tilted to the right, right hand open with elbow flexion and wrist rotation, and left hand closed and thumb adducted.

The assessments were carried out at two points in time: at the beginning (January 2024) and after six months of treatment (June 2024). To analyze motor development, we used the Gross Motor Function Measure (GMFM-88), a quantitative instrument made up of 88 items divided into five dimensions: A: Lying and rolling (17 items); B: Sitting (20 items); C: Crawling and kneeling (14 items); D. Standing (13 items); E: Walking, running and climbing (24 items): Standing (13 items); E: Walking, running and jumping (24 items). Each item scored varies from 0 to 3: 0: Does not perform; 1: Starts the movement, but does

not perform it completely; 2: Performs it partially; 3: Performs it completely. The scores are converted into percentages per dimension, ranging from 0 to 100% (Choi, 2024).

Motor development assessments were carried out in January 2024 (initial) and June 2024 (after six months of treatment) using the (GMFM-88). In addition, observations on the child's visual function were recorded.

The comparative assessment of the percentage scores of the GMFM-88 revealed an overall improvement of 15.1% when comparing the assessment with the reassessment; in the assessment the child obtained a score of 19.6% and a score of 34.7% in the reassessment. Table 1 shows the percentages per dimension of the GMFM-88 in the initial and final assessments.

Dimension GMFM-88	Initial Assessment (%)	Reassessment (%)
A - Lie down and roll over	74.5%	100%
B - Sitting	23.3%	56.7%
C- Crawling and kneeling	0%	11.9%
D - Standing	0%	5.1%
E - Walking, running and jumping	0%	0%
Overall score	19.6%	34.7%

Table 1 - Percentage Scores by GMFM-88 Dimension

There was motor progress in the domains assessed by the GMFM-88 between the initial assessment and the reassessment. In dimension A (lying down and rolling over), the child started to roll over completely to the prone position on both sides (items 8 and 9) and to lift the trunk in prone with cervical extension and elbows extended (item 11), reaching the maximum score. She also improved when rolling from prone to supine (items 14 and 15) and started to pivot to both sides (items 16 and 17), skills not previously tested.

In the sitting position, there was progress in postural control and balance. The child started to sit with their arms free (item 24), lean and return without support (item 25), as well as reaching backwards (items 26 and 27) and sitting sideways (items 28 and 29). She also demonstrated the start of postural transitions, such as going from a seated position to prone (item 30) and starting the four-legged stance (items 31 and 32).

Other gains included remaining seated on a bench with arms and feet free (item 34), supporting herself on all fours for a few seconds (item 39), reaching a seated position from all fours (item 40), starting from a prone position on all fours (item 41) and remaining kneeling with support (item 48). In the standing position, she held on with just one hand for 3 seconds (item 53), and on her knees she demonstrated the start of the standing position (item 60), skills not previously tested.

In the functional physiotherapy vision assessment carried out on 29/08/2023 (before the start of TREINI® and the use of optical correction), convergent strabismus to the right (exotropia), bilateral nystagmus, decreased ocular fixation latency (around two seconds), better visual response to light stimuli in a dark environment and visual preference for the color red were observed. In the visual tracking tests, the child had difficulty moving the left eye horizontally and showed a preference for looking downwards.

With the use of optical correction, introduced before the initial intensive training assessment, there was an improvement in visual perception and in the time it took for the eyes to fixate on the luminous object. During the TREINI® treatment period, there was an increase in the child's interest in visual stimuli, an increase in the search for light sources and a greater frequency in the visual tracking of objects in different planes.

DISCUSSION

Tubulinopathies, such as the one caused by a mutation in the TUBA1A gene, represent a rare group of neurodevelopmental disorders characterized by alterations in the process of brain formation and organization. These conditions compromise motor, cognitive and visual development, requiring specific and intensive therapeutic approaches (Hagege et al.,2022; Hebebrand et al., 2019).

In this case report, the child with TUBA1A tubulinopathy showed significant functional progress after six months of intensive TRAINI® intervention. The gains were especially evident in dimensions A (Lying and rolling) and B (Sitting) of the GMFM-88, with a total increase of 15.1% in the overall score of the scale, indicating concrete advances in motor functionality.

The higher scores obtained in basic postural skills, such as rolling, maintaining a seated position with support and pivoting on the ground, are consistent with the literature which describes the first motor gains in children with severe neurological injuries as occurring in less complex functions (Loffi et al., 2024). The lack of progress in the E dimension (walking, running and jumping) may be related to the severity of the condition and the age of the child, who is still in the process of acquiring more advanced motor skills.

The use of Treini Flex therapeutic clothing may have contributed to the positive results by offering postural support and proprioceptive stimulation during the execution of motor tasks. The literature shows that this tool helps with body alignment, reduces postural compensations and favors active motor practice (Flores Cruz et al., 2024).

In addition, the combination of techniques used in the program - such as environmental enrichment, strength training, task-oriented training, mobility training and task-oriented training - provided a multimodal approach that intensified the child's sensorimotor stimulation. The diversity of strategies applied in a structured sequence favors neuroplasticity, which is essential for the development of new neural connections (Pavone et al., 2023).

Another relevant aspect was the use of visual stimulation combined with optical correction, which improved visual attention and interaction with the environment. Children with TUBA1A mutations often have significant visual alterations, and early intervention in this area can be decisive for motor and cognitive progress (Cushion et al., 2023).

Family involvement throughout the therapeutic process also stands out as an essential factor. Guidance for caregivers and stimulation at home complement the work carried out in the clinic and expand the opportunities for motor learning in a variety of contexts. Family-centered care is an important guideline in pediatric rehabilitation and has a direct impact on functionality (Flores Cruz et al., 2024).

The gains observed in the GMFM-88 reflect not only the effect of the techniques applied, but also the intensity of the program. A high frequency of visits over a short period of time is associated with better functional outcomes in children with neurological injuries (Loffi et al., 2024), as it allows for greater repetition of tasks, increased motivation and continuous positive reinforcement.

The organized structure of the TREINI® program, with weekly objectives, continuous assessments and readjustment of therapeutic goals, allowed for effective monitoring of the child's progress. This dynamic approach contributes to the engagement of the interdisciplinary team and constant adaptation to the child's needs.

It is worth noting that, even in the face of a genetic condition with significant structural brain alterations, such as lissencephaly and hypoplasia of the corpus callosum, the child

showed measurable functional improvement. This reinforces the idea that functional prognosis is not determined solely by anatomical changes, but also by the quality and intensity of interventions (Hebebrand et al., 2019; Pavone et al., 2023).

Despite the positive results observed, this study has important limitations, such as the single case study design and the absence of a control group, which restricts the generalization of the findings and makes it difficult to accurately attribute the effects to the interventions applied. In addition, the relatively short post-intervention follow-up time limits the analysis of the long-term maintenance of gains. However, the advances seen in motor skills, especially in rolling and sitting, suggest the potential of TRAINI as a rehabilitation strategy for children with TUBA1A tubulinopathy. These findings contribute to expanding knowledge about the role of intensive physiotherapy in rare genetic diseases and reinforce the importance of structured, individualized and evidence-based programs for the management of children with severe motor impairment.

CONCLUSION

This study showed that physiotherapy using TREINI® can promote progress in the motor development of children with tubulinopathy, especially in the skills of rolling over and sitting down. The improvement in the GMFM-88 score after six months of intervention shows the potential for neuroplasticity even in severe and genetically determined neurological conditions.

The TREINI® program, with its interdisciplinary approach and therapeutic strategies based on the ICF, proved to be effective in promoting the child's functionality and independence, contributing to his engagement with the environment and improving his quality of life. Progress in visual function may also have favored motor development, reinforcing the importance of integrated action between the different areas of rehabilitation.

In view of the results observed, it is recommended that studies be carried out with larger samples and more robust methodological designs, such as controlled clinical trials, in order to strengthen the scientific evidence on the effectiveness of intensive physiotherapy in children with tubulinopathy associated with the TUBA1A gene.

REFERENCES

BAHI-BUISSON, Nadia; MAILLARD, Camille. Tubulinopathies Overview. In: ADAM, Margaret P. et al. (ed.). **GeneReviews®** [Internet]. Seattle (WA): University of Washington, 2016.

CHAVES, José Mário. Neuroplasticidade, memória e aprendizagem: Uma relação atemporal. **Revista Psicopedagogia**, v. 40, n. 121, 2023.

CHOI, Ja Young. Motor Function Measurement in Children: Gross Motor Function Measure (GMFM). **Annals of Rehabilitation Medicine**, 2 out. 2024.

CUSHION, Thomas D.; LECA, Ines; KEAYS, David A. MAPping tubulin mutations. **Frontiers in Cell and Developmental Biology**, v. 11, 15 fev. 2023.

FLORES CRUZ, Thalita Karla *et al.* **Efeitos do Programa TREINI® no desempenho e satisfação de metas funcionais de crianças e adolescentes com paralisia cerebral: Uma análise preliminar. Fisioterapia Brasil**, v. 25, n. 3, p. 1481-1496, 16 set. 2024.

HAGEGE, R. *et al.* Spectrum of brain malformations in fetuses with 'mild' tubulinopathies. **Ultrasound in Obstetrics & Gynecology**, 9 dez. 2022.

HEBEBRAND, Moritz *et al.* **The mutational and phenotypic spectrum of TUBA1A-associated** tubulinopathy. **Orphanet Journal of Rare Diseases,** v. 14, n. 1, 11 fev. 2019.

MORGAN, Catherine *et al.* Harnessing neuroplasticity to improve motor performance in infants with cerebral palsy: a study protocol for the GAME randomised controlled trial. **BMJ Open**, v. 13, n. 3, p. e070649, mar. 2023.

LOFFI, Renato Guimarães *et al.* Narrative Review of the Theoretical–Methodological Foundations of the TREINI Program. **Children**, v. 11, n. 10, p. 1181, 27 set. 2024b.

PAVONE, Piero *et al.* **Case** report: Structural brain abnormalities in TUBA1A-tubulinopathies: a narrative review. **Frontiers in Pediatrics**, v. 11, 8 set. 2023.