ISSN: 2651-4451 • e-ISSN: 2651-446X

Turkish Journal of Physiotherapy and Rehabilitation

2022 33(1)78-84

Özge ÇANKAYA, Phd, PT[1]
Sinem Asena SEL, Msc, PT[2]
Gökçe GÜRLER, Phd Student, MD[3]
Hira ALTUNBÜKER, MD Student[3]
Mintaze KEREM GÜNEL, Prof., Phd, PT[4]

1 Kütahya University of Health Sciences, Faculty of Health Sciences, Department of Physical Therapy and Rehabilitation Kütahya, Turkey
2 Hacettepe University, Institute of Health Sciences Ankara, Turkey
3 Hacettepe University, Faculty of Medicine Ankara, Turkey
4 Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Department of Cerebral Palsy and Pediatric Rehabilitation, Ankara, Turkey

Correspondence (İletişim):

Sinem Asena SEL, MSc, PT
Hacettepe University,
Institute of Health Sciences, Ankara, Turkey
Phone: +90 538 208 24 60
E-mail: sinem.sel4@gmail.com
ORCID: 0000-0001-6409-5414

Özge ÇANKAYA
E-mail: ozgemuezzinoglu@gmail.com
ORCID: 0000-0002-2116-8924

Gökçe GÜRLER
E-mail: gokce.gurler@hacettepe.edu.tr
ORCID: 0000-0003-3073-4438

Hira ALTUNBÜKER
E-mail: hiraaltunbuker@gmail.com
ORCID: 0000-0002-1556-3477

Mintaze KEREM GÜNEL
E-mail: mintaze@yahoo.com
ORCID: 0000-0003-4942-5272

***Received:** 09.08.2021 (Geliş Tarihi)*
***Accepted:** 03.11.2021 (Kabul Tarihi)*

INVESTIGATION OF PHYSICAL FITNESS AND GROSS MOTOR CAPACITY IN CHILDREN WITH NEUROFIBROMATOSIS TYPE 1

ORIGINAL ARTICLE

ABSTRACT

Purpose: To assess physical fitness, gross motor capacity, their relationship in children with neurofibromatosis type 1 (NF1).

Methods: Children with NF1 (n=40, age 6-17, mean 9.70±3.8 years) and typically developing children (TDC) (n= 28, age 5.5-17.5, mean 11.35±3.0 years) were evaluated by the six-minute walking test, sit-up test, sit-and-reach test, flamingo balance test and body mass index. Gross motor capacity was assessed with the Gross Motor Function Measure-88 D and E subdimensions.

Results: Physical fitness and gross motor capacity (Body Mass Index (BMI) (p=0.007), cardiorespiratory fitness (p=0.001), muscle strength and endurance (p=0.028), flexibility (p=0.011), balance (p=0.031) and items of gross motor capacity: dimensions D (p=0.020 and E (p=0.001) of the GMFM-88) differed significantly between NF1 and TDC. Physical fitness parameters positively correlated with the gross motor capacity to a fair to moderate degree in children with NF1 (r=0.42-0.71; p=0.002 – p=0.001).

Conclusion: Physical fitness and gross motor capacity are correlated and both are impaired in children with NF1. Exercise programs aiming to increase these functions can be recommended: therefore, areas of intervention can be defined from tests described in this study.

Keywords: Neurofibromatosis, Physical Fitness, Physiotherapy

NÖROFİBROMATOZİS TİP 1 TANILI ÇOCUKLARDA KABA MOTOR KAPASİTE VE FİZİKSEL UYGUNLUĞUN İNCELENMESİ

ARAŞTIRMA MAKALESİ

ÖZ

Amaç: Çalışmanın amacı Nörofibramatozis Tip 1 (NF1) tanılı çocuklarda kaba motor kapasite, ve fiziksel uygunluğu ve birbirleri arasındaki ilişkiyi değerlendirmektir.

Yöntem: NF1'li çocuklar (n=40, yaş 6-17, ortalama 9,70±3.8 yıl) ve tipik gelişen çocuklar (TGÇ) (n= 28, yaş 5,5-17,5, ortalama 11,35±3,0 yıl) altı dakikalık yürüme testi, mekik testi, otur-uzan testi, flamingo denge testi ile değerlendirildi ve vücut kitle indeksi hesaplandı. Kaba motor fonksiyon, Kaba Motor Fonksiyon Ölçütü-88 D ve E alt boyutları ile değerlendirildi.

Sonuçlar: Fiziksel uygunluk ve kaba motor kapasite (VKİ (p=0,007), kardiyorespiratuar uygunluk (p=0,001), kas kuvveti ve enduransı (p=0,028), esneklik (p=0,011), denge (p=0,031) ve kaba motor kapasite: Kaba Motor Fonksiyon Ölçütü-88 D (p=0,020) ve E (p=0,001) alt boyutları) NF1 ve TDC arasında anlamlı farklılık gösterdi. Fiziksel uygunluk parametreleri, NF1'li çocuklarda kaba motor kapasitesi ile orta derecede pozitif korelasyon gösterdi (r=0,42-0,71; p=0,002- p=0,001).

Tartışma: NF1 tanılı çocuklarda fiziksel uygunluk ve motor kapasite etkilenmiştir ve birbirleri ile pozitif yönde ilişkilidirler. Etkilenen fonksiyonları (fiziksel uygunluk ve kaba motor fonsiyon) arttırmaya yönelik esneklik, denge, kas kuvveti ve enduransı ve kardiyorespiratuvar uygunluğu içeren egzersiz programları önerilebilir. Sonuç olarak; NF Tip-1 tanılı çacuklara yönelik fizyoterapi ve rehabilitasyon müdahale alanları çalışmamızda tanımlanmış testler ile belirlenebilir.

Anahtar Kelimeler: Nörofibramatozis Tip 1, Fiziksel Uygunluk, Fizyoterapi.

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a common genetic disease affecting 1/3000-3500 individuals (1). Its major diagnostic criteria are hyperpigmented spots, neurofibromas, Lisch nodules, bone lesions, optic pathway gliomas, and the presence of a family history (2). Although not included among diagnostic features, cognitive, behavioral, and neuromotor issues are frequently associated with NF1 (3, 4). Motor problems have been described in the areas of strength, balance and coordination, leading to difficulties in controlling voluntary movements and limiting physical activity (PA) (3).

Muscle tone, muscle strength and balance play an important role in the control of voluntary movement (4). Motor problems seen in children with NF1 include muscle weakness, balance and coordination disorders. All these problems cause difficulties in controlling voluntary movements in children with NF1 (3). The repetition of purposeful movements according to motor learning principles enables the development of skills and participation (5). As a result, problems experienced in voluntary and repetitive movements in children with motor problems such as balance problems, weak muscle strength, balance and coordination disorders cause activity and participation limitations (6,7).

Physical activity is defined as any body movement using skeletal muscles that results in energy expenditure (8). Physical fitness (PF), on the other hand, is generally defined as the ability of a person to feel good physically, physiologically, and psychologically, without excessive fatigue and to achieve daily activities (9). It also affects the intensity and duration of children's PA participation (8). It has been stated that the ability to perform activities and participation in children with disabilities has a mutual relationship between motor capacity and PA. Muscle strength and endurance, as well as cardiovascular endurance, were evaluated in children with NF1 in comparison to typically developing children and adults (10,11). However, there is no evidence-based information in the current literature regarding the relationship between PF and motor capacity, specifically for the characteristics of children with NF1. Differentiating from the studies on PF in children with NF1, our current study evaluated the relationship between PF and motor capacity, and compared PF and motor capacity with those of typically developing children.

The aim of this study is to evaluate the relationship between PF and motor capacity in children with NF1 in terms of cardiovascular endurance, muscle strength, muscle endurance, flexibility, balance and gross motor function, and also to compare it with children with typical development.

METHODS

Participants

Forty children with NF1 (20 male, 20 female, aged 6-17 years) diagnosed according to the NIH clinical diagnostic criteria for NF1 and 28 typically developing children (TDC) (14 male, 14 female, aged 5,5-17,5 years) participated to the study (12). Patients were being followed-up in Hacettepe Faculty of Physical Therapy and Rehabilitation Division of Cerebral Palsy and Pediatric Rehabilitation and the Department of Paediatric Neurology of Hacettepe University Hospital. Children were assessed during routine control and randomly recruited to study. TDC were randomly recruited from NF1 patients' siblings of closest age or from healthy volunteers. Inclusion criteria were being aged between 5-18 years. Exclusion criteria were the presence of any concurrent disease, impairment in hearing, vision, or cognition, orthopedic problems and participation in elite-level sport activities (Figure 1). Informed consent was obtained from children and their parents. The study was approved by the Non-Interventional Clinical Research Ethics Committee of Hacettepe University (Approval Date: 02.01.2018

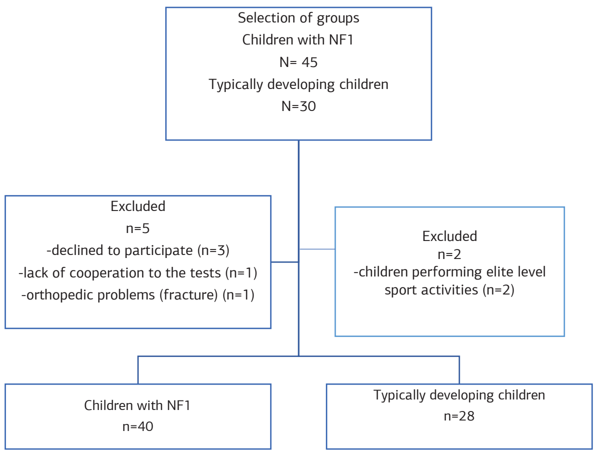

Figure 1. Flow diagram

and Approval Number: GO: 17/935). Evaluations were made between 04.01.2018 and 05.10.2018. The Helsinki Declaration Principles were followed during the study process.

Measurements

Health-Related Physical Fitness

Body composition: Body mass index (BMI) calculated as weight (kilograms)/height2 (m2) was used to reflect body composition (13).

Cardiovascular endurance (Six-minute walking test, SMWT): This test measures the distance (m) covered in 6 minutes by applying submaximal cardiovascular exercise capacity and indirectly shows PF. It is valid and reliable in the pediatric population. The test was applied by a physiotherapist in a 30-meter corridor according to the recommendations of the American Thoracic Society. Participants were instructed to walk (not run) the longest distance as fast as possible for 6 minutes. All participants received standard encouragement ('you are doing well') and an announcement of time ('last one minute'). Transcutaneous oxygen saturation was measured and heart rate was recorded before and immediately after the SMWT using a finger pulse oximeter (14).

Muscular strength and endurance (sit-up test): The child lies on a mat in a supine position, hands locked on the nape, sole of the feet on the mat and knees bent at 90°. The number of sit-ups performed in 30 seconds is recorded (15).

Flexibility (sit-and-reach test): The child sits on a mat where a standard box and a scale are placed, and bends forward three times with knees extended. The most distant point reached with fingertips is determined (16).

Performance Related Physical Fitness

Balance (Flamingo balance test): This test measures the ability to maintain balance on one leg (17). On a standard test board, subjects are asked to lift one foot, bend the knee backward and grip their foot with their hand on the same side. Support from the physiotherapist is allowed initially to reach the balance position. The posture is maintained as long as possible and up to one minute. Both legs are evaluated and the longest time (seconds) is recorded (17).

Gross Motor Capacity

Gross Motor Function Measurement (GMFM-88): GMFM-88 is a standardized functional assessment tool frequently used by physical therapists to assess the achievements and limitations of gross motor function of children with cerebral palsy. It is sensitive to changes in motor functioning. Five-year-old children with normal motor abilities can accomplish all items (18). The dimensions D (standing) and E (walking, running and jumping) of GMFM-88 were applied because all our subjects in the study being ambulatory, only the dimensions containing advanced motor skills would be informative.

Procedure

All children who participated in the study were tested by a pediatric physiotherapist blinded to the child's diagnosis. The child's tests were completed in one day. The methods used to determine PF are known as valid and reliable in the pediatric age group.

Statistical analysis

The distribution of the data was checked for normality by the Kolmogorov–Smirnov test and some measurements were found to differ from the normal distribution. The "p" value was determined as 0.05. In the power analysis, the error level of α: 0.05 was determined with 80% power and the sample size was determined. Mean and standard deviation were calculated for parametric data (age). Median and minimum-maximum range were calculated for non-parametric data (body composition, cardiorespiratory fitness, muscular strength and endurance, flexibility, balance and gross motor capacity). Mann Whitney-U test was used to compare the results of PF and gross motor capacity in NF1 and TDC. Spearman's correlation test was used to assess the relation between PF and dimensions D and E of the GMFM-88. The correlation coefficient was graded as: 0.10–0.30 weak (positive/negative), r = 0.30–0.70 moderate (positive/negative), r = 0.70–1.00 strong (positive/negative) correlation (19). $p<0.05$ was accepted as statistical significance. Statistics were done using Statistical Package for Social Sciences, version 20.0 (SPSS, Chicago, IL, USA).

RESULTS

The mean ages of the NF1 (9.7±3.8 years) and TDC (11.3±3.0 years) were not different statistically.

Table 1. Characteristics of children with NF1 and TDC

	NF1 (n=40)		TDC (n=28)	
Age (year)	9.7±3.8		11.3±3.0	
Gender	**Girl (n=20) %50**	**Boy (n=20) %50**	**Girl (n=13) %46.5**	**Boy (n=15) %53.5**
Height (cm)	131.33±21.23		142.26±18.67	
Weight (kg)	32.09±14.39		42.70±17.84	
BMI (kg/m²)	32.09±14.39		42.70±17.84	

NF1: Neurofibromatosis type 1; TDC: Typically developing children; cm: centimeter, BMI: Body Mass Index kg: kilogram.

Table 2. Comparison of Physical Fitness and Gross Motor Capacity Between NF1 and TDC

Physical Fitness Components	NF1 (n=40)		TDC (n=28)		Mann Whitney U test	
	Median	**Range**	**Median**	**Range**	**z**	**p**
Body composition						
Height (cm)	131.50	84-172	116.50	114-118	-2.756	0.006*
Weight (kg)	28	16-63	40.50	18-93	-3.036	0.002*
BMI (kg/m²)	17.25	11.11-24.65	19.21	13.85-29.48	-2.685	0.007*
Cardiorespiratory fitness						
SMWT (m)	506	313-787	606	450-728	-4.001	0.001**
Muscular strength and endurance						
Sit-ups (reps)	13	0-26	18	0-28	-2.203	0.028*
Flexibility						
Sit and reach test (cm)	12	0-18.50	7.50	0-15.50	-2.557	0.011*
Balance						
Flamingo balance test (sec)	5.31	0-60	8.33	2.76-60	-2.151	0.031*
Gross motor capacity						
GMFM-88 dimension D (standing)	84.5	69-100	96	92-100	-2.323	0.020*
GMFM-88 dimension E (walking, running, jumping)	80.5	61-100	97	94-100	-3.361	0.001**

cm: centimeter, BMI: Body Mass Index; GMFM: Gross Motor Function Measurement; kg: kilogram; m: meter; NF1: Neurofibromatosis type 1; reps: repetitions; SMWT: Six Minutes Walking Test; sec: second; TDC: Typically developing children; *p<0.05; **p<0.001.

Table 3. Correlation Coefficients Between Gross Motor Capacity and Physical Fitness Measures in Children With NF1 and TDC

	NF1		TDC	
Physical Fitness Components	**GMFM-88 dimension D (standing)**	**GMFM-88 dimension E (walking, running, jumping)**	**GMFM-88 dimension D (standing)**	**GMFM-88 dimension E (walking, running, jumping)**
Body composition				
BMI (kg/m²)	0.32	0.26	-0.11	0.33
Cardiorespiratory fitness				
SMWT (m)	0.42**	0.54**	0.25	0.20
Muscle strength and endurance				
Sit-ups (reps)	0.65**	0.71**	0.29	0.49**
Flexibility				
Sit and reach test (cm)	-0.18	-0.01	0.32	0.30
Balance				
Flamingo balance test (sec)	0.45**	0.65**	0.27	0.41*

cm: centimeter, BMI: Body Mass Index; GMFM: Gross Motor Function Measurement; kg: kilogram; m: meter; NF1: Neurofibromatosis type 1; reps: repetitions; SMWT: Six Minutes Walking Test; TDC: Typically developing children *p<0.05; **p<0.01

Characteristics of children with NF1 and TDC were given in Table 1. All tests of PF: BMI, cardiorespiratory fitness, muscle strength and endurance, flexibility, balance and items of gross motor capacity: dimensions D and E of the GMFM-88 yielded significantly different results between NF1 and TDC ($p<0.05$) (Table 2).

In the NF1 group, gross motor capacity correlated with cardiovascular endurance, muscular strength and endurance and balance. The correlations were positively moderate degree (r: 0.42-0.71) (p=0.002-p=0.001). Gross motor capacity did not correlate with BMI and flexibility. In TDC, gross motor capacity correlated with muscular strength and endurance and with balance (r: 0.41-0.49), but not with BMI, flexibility and cardiovascular endurance (p=0.002) (Table 3).

DISCUSSION

In this study we observed children with NF1 had lower PF and gross motor function than TDC and these two measurements were positively correlated.

Physical fitness comprises health-related fitness (HRF) and performance-related fitness (PRF), a classification equally applicable to children. Health-related fitness includes body composition, cardiovascular endurance, strength and endurance, and flexibility, as evaluated in this study (20). We found that children with NF1 were limited in all of these aspects compared to TDC.

Cardiovascular endurance measured using the 6MWT in the current study was lower than TDC. When impaired as in cerebral palsy, cardiovascular endurance can affect gross motor capacity but such a relation has not been studied in healthy children (21, 22). In general, cardiovascular endurance is related to gross motor capacity and can be impaired in children with developmental coordination disorder (23). It had not been studied in NF1 before, and might be one of the factors underlying the coordination problems experienced by some children with NF1.

Performance-related fitness involves balance, power, agility, coordination, speed and reaction time (20). Regarding PRF, children with NF1 differ from their unaffected siblings by lower jumping power and force (24). Souza et al. reported maximal voluntary muscle force was reduced in a group of pediatric and adult NF1 patients and attributed it to genetic and neurological abnormality or to altered calcium metabolism (25). Johnson et al. examined the strength of lower extremities and the relationship between isometric strength and functional activities in 28 children with NF1 and 48 TDC; they found less force production in hip extensor muscles (10). Ground reaction force in hopping and jumping and force in knee extensors were inter-related in the NF1 group. The authors of these studies deduced decreased muscle strength could result in reduced PF. In fact, physical capacity in various neuromuscular diseases is limited by factors such as low muscle strength, low endurance, high submaximal oxygen demand or low maximal heart rate rather than muscle function (26). We evaluated balance within the framework of PRF and found they were significantly limited in NF1 compared to TDC. This has been studied by Johnson et al who observed poorer postural control on single leg standing test in 5-18-year-old children with NF1 compared to TDC, suggesting a possible effect on their gross motor performance and proposed adding balance tests into the motor examination (27). The method and results of our study are comparable with this study.

Gross motor capacity was also lower in children with NF1 than TDC. Soucy et al. reported motor delay in 68% of children <8 years old with NF1 using a parental evaluation scale (28). Others reported low scores in gross motor function areas such as walking backward, walking in a straight line, kicking the ball, running, standing and jumping in 21-30-month-old children with NF1 using the Bayley Scales of Infant Development-II (BSID-II9, and attributed these findings to muscle weakness and decreased muscle tone (29). The Bruininks-Oseretsky Test of Motor Proficiency (BOT 2) demonstrated a lower motor profile in children with NF1 aged 4-15 years compared to norms based on age and gender: significant differences existed in strength, balance, running speed and agility subscores (30). Another study using BOT 2 and gait analysis with GAITRite electronic instrumented walkway showed motor and gait impairments in 7-17-year-old children with NF1, particularly in velocity, cadence, stride length, single support, double support and step time. This walking pattern was directed at maintaining balance at the expense of velocity (30). We consider balance might affect motor capacity because the dimensions D and E of the GMFM-88 applied in our study contain items similar to Bayley Scales of Infant Development (BSID-II) and the BOT 2 such as standing on one leg, jumping on one leg, jumping down the step, running, kicking the ball (29,30). The correlation between PF components and gross motor capacity in our patient group indicates these advanced motor skills are affected by muscle weakness, decreased muscle tone and loss of coordination.

Also, the correlation shown between these two measurements suggested an interaction between fitness and gross motor capacity, and that they could be limited by each other.

This study has a number of strengths. First, children were evaluated in terms of both physical fitness and motor function and compared with TDC. Second, results points to the right exercise choices for better intervention in children with NF1 may improve physical fitness. The first limitation of this study was physical activity levels could be measured by an accelerometer for both groups for more objective results. The second was reaching an efficient number of children with NF type 1. This situation prevented us from performing further statistical analysis such as regression analysis.

Knowing the level of PF in children with developmental problems helps to create an efficient training program (31). We think that in order to support children with NF1, physical therapists should focus on a PF training program combined with gross motor function. Children with NF1 are frequently referred to special education programs because of well-known attention and learning problems. According to our results, these children may also need physiotherapy programs to improve their gross motor capacity and PF. Besides clinical significance, motor limitations may affect the social life, play and sports activities of these children. Another point of clinical interest would be an investigation of the effect of such intervention on the incidence or severity of osteoporosis and scoliosis, other frequent problems in NF1.

CONCLUSION

Children with NF1 participate less to performance-based activities, preferring sedentary activities. In children with NF1 the muscle strength and balance required for PF and total motor capacity may be suboptimal. This observation has clinical implications, particularly for the success of habilitation efforts in children with NF1. The relation between PF, in particular, cardiorespiratory fitness and gross motor capacity in NF1 may suggest targets for interventions, assist physiotherapists and researchers in the planning of exercise training programs. Testing for these functions as part of the routine management of this disorder may also help to draw the attention of parents to the motor development of the child with NF1. Fitness contributes to physical, physiological and psychological well-being.

Author Contributions: Concept – Ö. Ç., S.A.S., G.G. H.A., M.K.G.,; Design – Ö.Ç., S.A.S., M.KG; Supervision – M.K.G.; Data Collection and/or Processing – Ö.Ç., S.A.S, G.G., H.A.; Analysis and/or Interpretation – Ö.Ç., S.A.S, G.G., H.A.; Literature Review – Ö.Ç., S.A.S, G.G., H.A; Writing – Ö.Ç., S.A.S.; Critical Review – M.K.G.

Declaration of interests: The authors declare no conflicts of interest.

Acknowledgments: The authors are grateful to the parents and children for participating in the study. Also, we would like to thank Sefa Üneş, Merve Tunçdemir and Kübra Seyhan Bıyık.

Funding: None. The authors received no financial support for the research, authorship, and/ or publication of this article.

Informed Consent: A written informed consent form was obtained from the participants' families. All the families signed a declaration of informed consent.

Ethical Approval: Hacettepe University, Non-Interventional Clinical Researches Ethics Board approved the study (Approval Date: 02.01.2018 and Approval Number: GO: 17/935).

Peer-Review: The authors will comply with the editor's decision on this matter.

The subjects in this study are also included in the article titled "Evaluation of skeletal muscles and speech in Neurofibromatosis type 1: a clinical and laboratory study" (manuscript in preparation)

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