Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2018, Vol. 46(11) 4669–4677

DOI: 10.1177/0300060518788243
journals.sagepub.com/home/imr
SAGE

Hand strength and dexterity in patients with Prader–Willi syndrome: a pilot intervention study

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Abstract

Objective: The study aim was to examine the hand function (hand strength and dexterity) and intervention effects of training in adults with Prader–Willi syndrome (PWS).

Methods: Six adults with PWS (two females; mean age 26.14 years) underwent hand muscle strength and dexterity training for 3 months (2 hours per week). The following hand function tests were performed pre- and post-intervention: (1) hand grip, lateral pinch, and tip pinch hand strength tests, (2) the Box and Block test (BBT) for gross manual dexterity and (3) the Purdue Pegboard test for finger dexterity.

Results: Before treatment, all subjects showed lower hand grip, lateral pinch, tip pinch strength, and poorer manual/finger dexterity relative to healthy adults. After training, hand function scores improved on many test items, but only the left hand tip pinch and the right hand BBT performance showed significant improvements.

Conclusions: All subjects showed lower hand strength and poorer manual/finger dexterity compared with healthy adults; this should be considered during physical training programs. Owing to limitations in the intervention intensity and possible subject behavioral deficits, further research is needed to clarify the effects of this intervention on hand function in PWS patients.

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Keywords
Prader–Willi syndrome, hand strength, manual dexterity, finger dexterity, intervention effects, Box and Block test, Purdue Pegboard test

Date received: 20 March 2018; accepted: 20 June 2018

Introduction

Prader–Willi Syndrome (PWS) is a rare neurogenetic disorder resulting from a loss of paternally expressed genes in the chromosomal region 15q11-13. Generally, 70% of cases are caused by a paternal deletion, 25% of cases are caused by maternal uniparental disomy and 1% to 5% of cases are caused by an imprinting defect.[1–4] The prevalence of PWS is estimated to be 1 in 10,000 to 30,000 live births.[1,5] PWS is characterized by a wide variety of physical, cognitive, and behavioral deficits. The most important symptoms include hypotonia, muscle weakness, hyperphagia, obesity, short stature, motor developmental delay, small hands and feet (acromicria), mild dysmorphic facial features, cognitive deficits and endocrine disturbances, including hypogonadism, hypothalamic dysfunction and growth hormone (GH) deficiency.[1,4,6,7]

Although not all symptoms are expressed equally in every PWS patient and disability severity differs between patients, motor problems are particularly detrimental, affecting patients as early as infancy and continuing into childhood and even adulthood.[7] A newborn with PWS may present with severe hypotonia, poor sucking ability, and inactivity, followed by later motor developmental delays. Such infants score well below the normal range on standardized motor performance tests owing to poor gross motor skills,[4,8,9] reduced balance capacity, and abnormal gait pattern.[10,11]

Abnormal body composition (increased fat mass and reduced muscle mass) and decreased activity contribute to the development of motor performance problems in patients with PWS.[4,7] Additionally, abnormal body composition in PWS patients may also be related to GH deficiency.[7,12] Moreover, physical activity in patients with PWS has a substantial influence on the growth of lean body mass,[13] gross motor ability and general physical function, such as body composition, muscle strength, fitness levels, motor quality, and exercise tolerance; the use of GH treatment and physical training to improve these factors has been investigated.[14–19]

However, little attention has been paid to hand function in PWS patients. As grip strength is associated with hand size,[20] and PWS patients have smaller hand sizes, concurrently lower muscle mass, and hypotonia, Chiu et al. (2017) successfully predicted that adults with PWS would show lower hand grip and lateral pinch strength in a study with a small sample size.[21] However, Hudgins and Cassidy (1991) have pointed out that although acromicria is often considered a symptom of PWS, many individuals with PWS have hand and foot lengths within the normal range.[22] Therefore, hand size is probably not the only reason for poor grip strength in patients with PWS.

Reduced hand length and muscle strength are insufficient to account for all the differences in hand function and performance between individuals with PWS and those without. Manual dexterity and finger coordination are also important factors, but no studies have focused on this area.

We thus aimed to explore in detail PWS subjects' hand function by measuring hand strength (hand grip, lateral pinch and tip pinch strength) and hand dexterity. As Chiu et al.[21] found that adults with PWS showed poor hand strength, we assumed that hand function in PWS patients is different to that in normal subjects. Furthermore, on the basis of a rehabilitative frame of reference, we predicted that hand strength and finger dexterity functions would improve in patients with PWS after training.

Materials and methods

Participants

Adults over 18 years of age and with a genetically confirmed diagnosis of PWS were enrolled from the Prader–Willi Syndrome Association in Taiwan. Subjects had to have a sufficient command of Mandarin to understand the study information and the guidewords in the training program. Subjects with orthopedic conditions that potentially limited their movement capacity (such as hand malformation) and those receiving other simultaneous treatments (such as GH treatment or testosterone replacement) were excluded. This study followed the principles of the Declaration of Helsinki and all participants provided written informed consent prior to participating in the study. The study protocol was approved by the research ethics committee of Buddhist Taipei Tzu Chi General Hospital (approval no. 05-XD39-071).

Study design

In the first part of the study, all subjects received a detailed hand function assessment comprising hand strength (hand grip, lateral pinch and tip pinch tests) and hand dexterity tests (manual and finger dexterity). In the second part, according to the assessments, subjects with poorer hand function were referred for the further training program. After the training, all participants received the same evaluation to assess the training effect.

Following previous studies[14,15] and in line with the timetable of the PWS Association, a 12-week training program was conducted with a small group of six participants. To ensure compliance and safety, participants were supervised and guided by three trained and certified occupational therapists. The program was conducted once a week over 12 weeks. Each session lasted 120 minutes and was subdivided into two subsessions, consisting of hand muscle strength training (such as using therapeutic putty, using a clamp, and engaging in TheraBand activities) and gross manual and finger dexterity training (such as using scissors, painting, cutting/pasting, and two-hand coordination activities). There was a 10-minute break between the two subsessions. During the 3-month intervention period, none of the participants' daily activities changed, and all participants were able to complete the study protocol.

Hand function assessments

Hand function was evaluated by a certified and trained occupational therapist. It was also assessed by a medical doctor at baseline and at follow-up after the 12-week intervention. The hand function evaluations were undertaken in three parts: (1) hand grip, lateral pinch, and tip pinch tests for hand strength, (2) the Box and Block test (BBT) for gross manual dexterity, and (3) the Purdue Pegboard test for finger dexterity.

Hand grip, and lateral pinch and tip pinch strength, were assessed in both hands using a Baseline® Hydraulic Hand Dynamometer (Fabrication Enterprises, New York, USA) and a pinch gauge (B&L Engineering, California, USA), respectively. These two instruments have

shown very high inter-rater and test–retest reliability in all tests and are therefore highly accurate.[23] Three successive trials with the hand grip, lateral pinch and tip pinch were conducted, and only the highest of the three handgrip and lateral pinch measurements was recorded for analysis.

BBT is a simple and efficient test of gross manual dexterity used by occupational therapists in clinical practice.[23] The BBT is administered by asking subjects to move, one by one, the maximum number of cubes (1 inch square) from one compartment of a box to another within 60 s. This study tested both the dominant and non-dominant hands simultaneously. The test–retest reliability of the BBT is high (intraclass correlation coefficients of 0.89 to 0.97) and BBT scores correlate significantly with measures of upper limb performance and functional independence.[24]

The Purdue Pegboard test measures unimanual and bimanual finger and hand dexterity. We conducted each of the four subtests twice. These consisted of a right hand test, left hand test, both hand test, and assembly test. We then calculated the average scores for analysis. In the first three subtests, the subject was asked to place as many pins as possible in the given holes within a 30-s period; in the fourth subtest, the subject was asked to use both hands alternately to construct "assemblies" of a pin, a washer, a collar, and another washer as many times as possible within 60 s. The Purdue Pegboard has shown good reliability (correlations range from .60 to .91) and validity (coefficients for 14 studies range from .07 to .76).[25]

Statistical analysis

IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA) was used to analyze the data. We used the baseline scores of all tests on admission (pretest) to determine participants' hand functional performance. We then compared the pretest and posttest results to determine the effect of the intervention on hand function. Nonparametric statistical methods, including the Wilcoxon signed-rank test, were used to analyze all the variables owing to the small sample size and non-standardized normal distribution. P-values of less than 0.05 were considered to indicate rejection of the null hypothesis.

Results

Six adults with PWS were recruited through the Prader–Willi Syndrome Association in Taiwan (two females and four males; mean age 26.14 years, age range 20 to 32 years, standard deviation 5.02 years; body mass index [BMI] 20.7–38.4 kg/m^2). All PWS subjects showed lower handgrip, lateral pinch, and tip pinch strengths, and could assemble fewer cubes and pins in the BBT and Purdue Pegboard test compared with the normative data of healthy adults.[26–28] Subject characteristics and pretest scores at baseline are shown in Table 1. Almost 90% of the population is right-handed; as all of our subjects were right-handed dominant, it is appropriate to compare our data with population norms. Although all subjects had received GH treatment, this had occurred in adolescence; therefore, we assumed that GH effects would not influence their performance.

Table 2 shows the means and standard deviations of the baseline and post-intervention scores on the three hand function tests. Performance on each test was better after treatment (posttest), but the improvements were significant only for the left hand tip pinch strength test and the right hand BBT test (left hand tip pinch: pretest, 5.6 ± 2.19, posttest, 7.57 ± 2.718, $p = .046$; right hand BBT: pretest, 49.16 ± 12.36, posttest, 54.33 ± 15.98, $p = .046$).

Table 1. Characteristics and pretest scores of subjects with Prader–Willi syndrome.

Age (years)	Sex	Gene	GHTX	Dominant hand	Grip (lbs)		Lateral pinch (lbs)		Tip pinch (lbs)		BBT (score)		Purdue (score)			
					R	L	R	L	R	L	R	L	R	L	B	Ass
32	M	UPD	+	R	45	47	14.6	12.2	7.2	6.0	69	58	14	12	10.5	22
28	M	U/K	+	R	55	55	11.6	11.4	4.8	6.0	55	53	13	13.5	10	21.5
32	M	Del	+	R	35	35	7.2	8.8	7.0	9.4	43	43	10	8	6.5	11
20	F	Del	+	R	25	21	4.4	3.2	3.8	3.2	32	39	5.5	5.5	2.5	8
26	F	Del	+	R	32	30	6.6	5.8	3.6	3.8	47	49	9	9	8	22
20	M	U/K	+	R	56	46	12.8	14.8	10.8	5.2	49	48	9.5	10	9.5	25.5

Note: Gene: genetics; GHTX: growth hormone treatment; Del: paternal deletion type; UPD: maternal uniparental disomy type; U/K: unknown; BBT: Box and Block test; Purdue: Purdue Pegboard test; R: right hand; L: left hand; B: both hands; Ass: assembly.

Table 2. Effect of the intervention on hand function in subjects with Prader–Willi syndrome.

	Grip (lbs)		Lateral pinch (lbs)		Tip pinch (lbs)		BBT (score)		Purdue (score)			
	R	L	R	L	R	L	R	L	R	L	B	Ass
Pre	41.33±12.72	39.0±12.57	9.53±4.03	9.37±4.31	6.2±2.73	5.6±2.19	49.16±12.36	48.33±6.8	10.17±3.04	9.67±2.86	7.83±3.0	18.33±7.05
Post	45.17±13.67	42.25±12.69	9.83±3.0	9.9±3.13	7.7±2.74	7.57±2.71	54.33±15.98	53.17±10.52	10.67±2.68	10.42±2.64	9.42±4.04	19.92±6.37
P value	0.115	0.225	0.673	0.461	0.173	**0.046***	**0.046***	0.058	0.357	0.102	0.058	0.343

Note: Data are means and standard deviations. Pre: pretest; Post: posttest; BBT: Box and Block test; Purdue: Purdue Pegboard test; R: right hand; L: left hand; B: both hands; Ass: assembly. *$P < .05$.

Discussion

PWS is a neurogenetic disorder characterized by decreased motor performance from birth through adulthood. Few studies have examined and discussed hand function performance in PWS patients. Research indicates that hand grip strength is associated with functional limitations.[29] Hand muscle function also correlates well with functional dependency in older people,[30] and patients with PWS have lower hand strength. Grip strength of patients with PWS negatively correlates with bodily pain scores on the Short-Form 36 Health Survey Questionnaire (SF-36), which is used to evaluate health-related quality of life (QoL).[21] Hand dexterity affects a range of different hand abilities and is critical for activities of daily living,[31] such as bathing and showering, dressing, self-feeding, personal hygiene, and toileting; total manual function is also highly correlated with SF-36 and instrumental activities of daily living scores.[30] Hand function should be considered when caring for PWS patients; however, there is little research on this ability in patients with PWS.

The goal of this study was to examine the effects of a training intervention on hand function and performance (hand strength and manual/finger dexterity) in adults with PWS. We hope that this type of programmed intervention could be used to improve both hand function and overall QoL in such patients.

At baseline, subjects showed decreased hand strength and poor gross manual and finger dexterity compared with healthy adults. Hand function decreases with age in both men and women,[31] and there are negative correlations between age and grip strength/hand dexterity.[32] Our subjects' baseline hand function scores were similar to those recorded in an older population.[26–28] Our findings indicate that both hand strength and dexterity should be considered as part of physical training programs for individuals with PWS.

PWS demonstrates a unique congenital model of sarcopenia characterized by lower muscle function and muscle mass[33] and smaller hand size;[1,22] these characteristics may explain why patients with PWS have poorer hand function. Grip strength is substantially correlated with hand length in PWS patients.[20] Furthermore, muscle strength also contributes to aiming and tapping dexterity, which requires both fast actions and precise coordinated movements of the hand, wrist, elbow, and shoulder.[32]

Dexterous movements require large muscle activations, rapid accelerations of movement, and precise coordinated movements of the hand, wrist, elbow, and shoulder to respond to tasks.[32] Dexterity seems to be directly associated with hand grip strength, muscle mass, and force steadiness.[31,34,35] Poor hand strength in individuals with PWS is likely to influence their hand dexterity.

However, poor dexterity and poor hand grip strength are not always correlated in individuals with PWS, as Martin et al. (2015) found that strength had little predictive value for the hand dexterity measures of steadiness variance and line tracking.[32] Steadiness and line tracking both rely on stable arm and hand control and on hand–eye coordination with visual guidance. Other factors, such as vision or cognitive capacity for online visual guidance, may also influence dexterity. Patients with PWS have poor visual–motor integration, poor motor coordination and visual capacity problems,[36–39] which could also explain their poorer dexterity performance. Hand dexterity in individuals with PWS may be influenced by physical dysfunction (hand size, lower muscle mass, lower muscle strength and hypotonia), hand–eye coordination, and other visual or cognitive problems.

In the present study, we provided a 12-week hand muscle strength and dexterity

training program to individuals with PWS. Although all subjects showed improvements in post-treatment scores, the improvement was significant for only two tests (left hand tip pinch strength and right hand BBT). One possible study limitation was the low training frequency. Our training program was not long term and was of a lower intensity than previous study programs.[13–15,18,40] To accommodate the PWS Association timetable, we provided one 2-hour treatment per week for 12 weeks, which might have been insufficient to achieve significant hand muscle strength and dexterity improvements. Future studies should consider the use of higher intensity and higher frequency muscle strength training, such as once per day for 12 weeks, or the addition of simple, effective, and feasible home-based training programs. It should be noted that individuals with PWS, particularly young adults, show prominent cognitive, behavioral and psychiatric problems, and high rates of temper tantrums, oppositionality, aggression, skin-picking, and compulsive-like behaviors;[41,42] these characteristics could have affected the compliance and motivation of our sample. During the training period, the occupational therapists reported behavioral characteristics of inattention, compulsive-like behaviors, impulse control disorders, and cognitive problems in subjects, which might have reduced the effectiveness of the training program. This may explain the limited significance of the intervention effects. Further studies to develop a more specific training protocol to improve hand function are warranted.

The study has several limitations, such as the small sample size and non-randomized control design, which makes it difficult to generalize these results. However, PWS is a rare syndrome and large-scale studies are therefore difficult to perform. Additional studies with more participants, higher intensity training programs and longer-term follow-up are warranted to reduce data heterogeneity and to generate a better understanding of the effects of the training program on hand function. Furthermore, the addition of a control group with similar physical characteristics (such as hand length, BMI, age and gender) is desirable in future studies, as this could clarify the impact of physical dysfunction on hand performance.

Conclusions

To our knowledge, this is the first study to explore hand function and intervention effects in individuals with PWS. All our PWS subjects showed decreased hand muscle strength and poorer manual and finger dexterity performances compared with healthy adults. Both hand strength and dexterity tasks should be included in physical training programs for individuals with PWS. Limited positive benefits were observed after treatment; this could be attributed to the lower intensity and duration of our intervention and to possible cognitive and behavioral deficits, which may have limited participants' motivation and cooperation during the training sessions. Therefore, additional research is needed to clarify the effects of this intervention on hand function in patients with PWS.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

The study was supported by a grant from the Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, No. TCRD-TPE-107-RT-2(1/3). The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of this manuscript.

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