

Strength Training-Induced Changes in Muscle Size and Motor Improvement in Bilateral Schizencephaly: An Experimenter-Blind Case Report With 3-Month Follow-Up

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Abstract

The present case study highlights the effects of a novel Comprehensive Hand Repetitive Intensive Strengthening Training (CHRIST) on morphological changes and associated upper extremity (UE) muscle strength and motor performance in a child with spastic quadriplegic cerebral palsy (CP). The Child, a 10-year-old girl with spastic quadriplegic CP, was treated with CHRIST for 60 minutes a day, five times a week, for 5 weeks. The CHRIST was designed to improve motor function and strength. Clinical tests including the modified Wolf Test, Jebsen-Taylor Hand Function Test, and Pediatric Motor Activity Log questionnaire were used to determine motor function. Ultrasound imaging was performed to determine the changes in the cross-sectional area (CSA) of the extensor carpi radialis (ECR) and triceps brachii (TRI). Muscle strength was measured with a dynamometer at pretest, and post-test, and 3-month follow-up. Ultrasound imaging data showed that the CSAs of both ECR and TRI muscles were enhanced as a function of the intervention. These changes were associated with muscle strength and motor performance and their effects remained even at a 3-month follow-up test. Our results suggest that the CHRIST was effective at treating muscle atrophy, weakness and motor dysfunction in a child with spastic quadriplegic CP.

Key Words: Cerebral palsy; Muscle size; Schizencephaly; Strength training; Ultrasound.

Introduction

Muscle weakness is one of the hallmark motor impairments in children with spastic quadriplegic cerebral palsy (CP) (Damiano and Abel, 1998; Ohata et al, 2008). Clinical studies demonstrated a close relationship between generalized muscle weakness and functional limitations in reaching and grasping, and more specifically, the excessive cocontraction or in-

efficiency and decreased peak linear or angular displacement in elbow kinematics during reaching movement (Chang et al, 2005). This muscle weakness and associated functional limitations further hamper normal development and age-appropriate motor skill acquisitions which include inability to reach and grasp a toy during play activities (You et al, 2005). In addition, it is known that muscle weakness can cause muscle imbalance between agonistic and

antagonistic muscles (Eagleton et al, 2004). In fact, muscle imbalance may become worsen over time if not properly intervened, resulting further muscle weakness and atrophy, and joint contracture (Vaz et al, 2006). Hence, the restoration of muscle strength of the weak muscle group in this population is important to mitigate muscular imbalance and atrophy, thereby improving motor development and age-appropriate skill acquisitions (Eagleton et al, 2004).

Traditional neurorehabilitation of children with CP has been focused on inhibiting spasticity to facilitate normal movement patterns rather than strengthening weak muscles because until recently, spasticity was believed to be exacerbated by muscle strengthening exercise (Bobath, 1971). It was therefore suggested that strength training should be avoided due to the possibility of exaggerating spasticity and associated reaction, which in turn lead to further development of muscle stiffness and joint deformities (Bobath, 1978; Bulter and Darrah, 2001; Koscielny, 2004; Miller, 2007). Conversely, empirical evidence suggests that the positive characteristic of spasticity may not be accountable for functional limitation, but the negative characteristic of muscle weakness is directly implicated with loss of motor skill and function (Carr et al, 1995). Building on this notion, clinical studies demonstrated that strengthening exercises were indeed beneficial for improving muscle strength and associated gait function in children with spastic CP (Damiano et al, 2002; Dodd et al, 2002; McBurney et al, 2003). For example, Kramer and MacPhail investigated the effect of isokinetic strength training (3 times week for 8 weeks) of quadriceps and hamstrings on peak torque and walking speed in 17 children with spastic CP. This study showed that the strength training improved knee joint muscle force and walking speed. Similarly, Damiano and Abel (1998) found that isotonic strengthening exercise (3 times week for 6 weeks) of the lower limb muscles including hip flexors, extensors, and adductors, knee extensors, and ankle dorsiflexors and plantarflexors resulted significant improvements in muscle strength, walking velocity and

cadence, and gross motor function measure (GMFMD) performance. These findings support suggest a positive relationship between muscle strength and motor performance in children with CP, further supporting the notion that the generalized muscle weakness may be a primary impairment affecting motor function (Damiano et al, 2002; Ross and Engsberg, 2002).

While strengthening exercise has recently gained widespread support among the clinicians to improve gait performance, there is however a dearth of clinical evidence about its efficacy on reaching and grasping. Hence, we developed the Comprehensive Hand Repetitive Intensive Strengthening Training (CHRIST) technique, which is designed to improve upper extremity (UE) muscle strength and performance for important reaching and grasping skills. This approach is based on the integration of the best clinical evidence (Naylor and Bower, 2005; Renner et al, 2005; Taub et al, 2004; Woldag et al, 2006; Wright and Granat, 2000). The specific aim of this study was to determine the long-term effect of CHRIST on muscle size and associated strength and performance using ultrasound imaging and clinical tests, respectively. Our basic premise was that the CHRIST technique would lead to increases in muscle size, associated muscle strength, and functional motor performance in reaching and grasping.

Methods

Subject

The subject was a 10-year-old girl delivered by normal spontaneous vaginal delivery (NSVD) at 40 weeks of gestation. She did neither present with any perinatal asphyxia nor neonatal seizure and discharged. She was diagnosed with spastic quadriplegic CP at 23 months, which was associated with the primary diagnosis of bilateral schizencephaly. Schizencephaly is an extremely uncommon congenital, cortical developmental disorder, defined as abnormal (gray matter-lined) clefts in the cerebral hemispheres (Koç et al, 2005) and was

confirmed by brain magnetic resonance imaging (MRI) (Figure 1). She was able to control her head at 9 years old. She was unable to perform functional reaching and grasping tasks although she attempted to use her less involved left hand for reaching and grasping tasks. The clinical and demographic characteristics are presented in Table 1.

Design

The study employed a single case report design. Training was conducted in one-hour session fifth a week for five weeks. Subject was pre-/posttest with a follow-up test taken three weeks later. Conditions and procedures of examination and intervention were standardized across all measurement sessions.

Examination

Ethical approval for the study was granted by the institutional review board at a local community

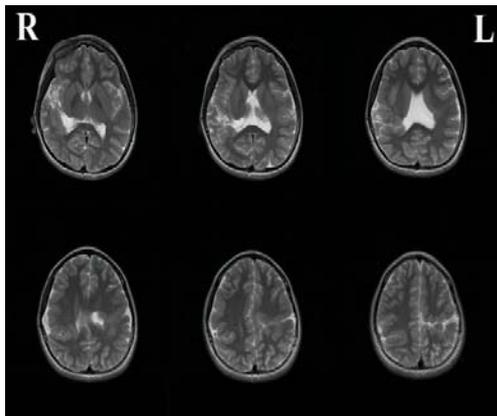


Figure 1. T2-weighted diagnostic brain magnetic resonance imaging.

hospital. The child's mother gave informed consent. A board-certified radiologist performed the ultrasound scanning and a licensed occupational therapist implemented the clinical tests; both were blinded to the study. Clinical measures included Wolf Motor Function Test (WMFT), Jebsen-Taylor Hand Function Test (JHFT), Pediatric Motor Activity Log (PMAL) questionnaire, modified Ashworth scale, a real-time ultrasound imaging. Pre-test was initially administered; a 5-week of intervention was provided, and followed by the post-test and 3-month follow up test. The outcome measures were emphasized on the shoulder, elbow, wrist, and hand gross movement because the CHRIST was designed to improve these proximal components.

Motor function tests

The WMFT is a time and force-based measurement to examine the unimanual (more-involved) upper extremity motor function, which involves 15 timed functional motor tasks and 2 strength based tasks. The performance time and functional ability scale on the functional tasks were implemented in this study. The speed at which functional tasks was successfully accomplished was determined by performance time whereas the movement quality was assessed by functional ability. The maximum time allotted to complete each item was 120 seconds. For functional ability scoring system, a 6-point ordinal scale, where 0=No attempt and 5=normal, was used.

The JHFT was a staff-timed measure which contains 7 major hand activities including feeding, writing, turning pages, stacking checkers, picking up small objects or large light objects or large heavy objects. Both hands are tested to evaluate the effectiveness of

Table 1. Clinical and demographic characteristics of the child

Age	School grade	Lesion (topography)	Diagnosis	Functional status
10	4th grade in elementary school	Open lip schizencephaly at the right hemisphere (frontoparietal region). Closed lip schizencephaly at the left hemisphere (parietal region).	Quadriplegic cerebral palsy	Limited reaching and grasp No functional use of upper extremity

the intervention. Time to complete each task was counted. The JHFT was modified by adopting the simulated page turning task and stacking task.

The PMAL is a parent-report measure of the amount of use and quality of movement of the affected upper extremity in children with hemiplegic cerebral palsy (CP) in everyday activities. PMAL consists of 22 motor tasks which involve fine motor (i.e. Pick up and hold a small object), gross arm motor items (i.e. Reaches to be picked up), unilateral (i.e. Turns a knob), and bilateral tasks (i.e. Holds a handle on a riding, pulling or push toy). The scoring system ranges from 0 (no use) to 5 (normal). The validities and reliabilities of the selected clinical motor tests are well established (Eliasson et al, 2006; Jebsen et al, 1969; Kim et al, 1987; Senesac, 2007; Sutcliffe et al, 2007; Taub et al, 2004; Wallen et al, 2008).

Spasticity measurement

Spasticity for extensor carpi radialis (ECR) and triceps brachii (TRI) muscles were determined by the modified Ashworth Scale (MAS) (Bohannon and Smith, 1987; Wallen et al, 2007).

Ultrasound imaging

A real-time ultrasound imaging is a powerful vehicle to accurately determine morphological changes in muscle thickness or cross-sectional area (CSA)

associated with pathology or exercise, representing an index of muscle strength (or weakness) and atrophy or hypertrophy (Hides et al, 1992) Ultrasound imaging was performed on an iU22 ultrasound system¹⁾ with a 7~12 MHz linear array transducer using a block paradigm of the 3 consecutive rest-maximal voluntary isometric contractions (MVICs) of wrist and elbow extension movement (3-sec rest and contraction) and a 10-sec resting interval between the testing blocks (Figure 2a).

For ECR imaging, the child was positioned in supine with the head and neck in neutral position and the arm supported on a pillow. The shoulder was abducted to 30° and internally rotated with full elbow extension and forearm pronation. The head of the radius was palpated and marked as a reference point. The exploratory ultrasound scanning of the ECR was first placed longitudinally in its relaxed state over the previously marked reference point to orient and confirm the mark. The transducer was then rotated through 90° to align transversally and moved distally 2 cm from the tip of the radius head until the sharpest and the largest CSA of the entire ECR was identified. The entire CSA of the ECR were then captured for the resting condition and an electronic onscreen caliper was used to trace around the muscle border or the region of interest (ROI). After ultrasound scanning of the ECR at rest, the subject was asked to maximally

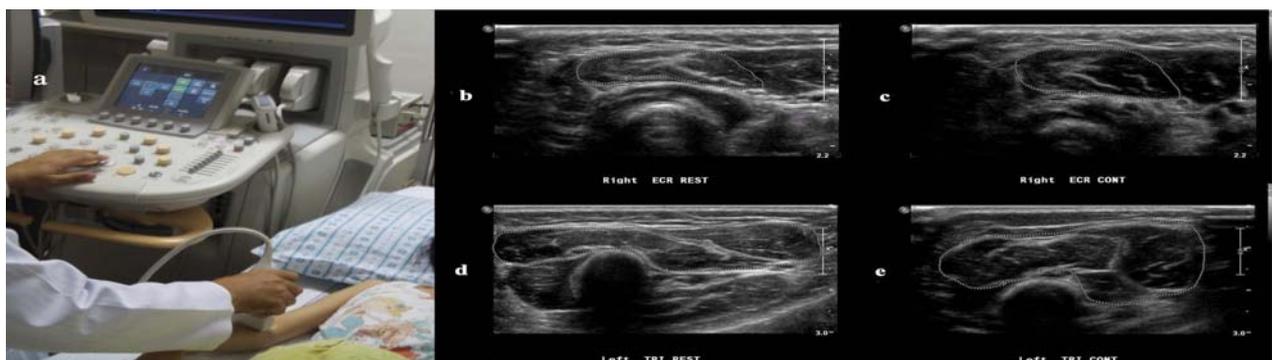


Figure 2. Ultrasound imaging set up and cross-sectional area (CSA) data. (a) Sonographic images were acquired with Philips iU22 ultrasound system using linear transducer (L7-12 MHz); (b) CSA of Rt. ECR at rest; (c) CSA of Rt. ECR at contraction; (d) CSA of Lt. TRI at rest; (e) CSA of Lt. TRI at contraction.

1) iU22, Philips, Bothell, U.S.A.

contract her ECR muscle at the radial deviation and wrist extension position. At this point, we measured the actual muscle force value (N) of MVICs with the dynamometer²⁾ and monitored to ensure a consistent MVICs at the same scanning location during over the 3 repeated scanning at the same scanning location. The entire CSA on bothsides were then captured for the contraction condition and an electronic on screen caliper was used to trace around the muscle border or the region of interest (ROI). The reliability and validity of the ultrasound imaging and dynamometer measurements is well established (Berry et al, 2004; Chi-Fishman et al, 2004; Crompton et al, 2007).

For TRI scanning, the subject was instructed to lie in prone with head rotated to the tested side and the arm supported on a pillow, shoulder abduction to 90° and the elbow flexion and hanging vertically over the side of the plinth. The olecranon process of ulna was palpated and used as a consistent landmark. The exploratory ultrasound imaging of the TRI was again placed longitudinally in its relaxed state over the predetermined landmark to confirm the landmark. The transducer was then rotated through 90° to position transversally and moved cephalically 10 cm from the olecranon process where the largest CSA of the entire TRI was clearly measured. The entire CSA and of TRI were captured for the resting condition and an electronic onscreen caliper was used to trace around the muscle border or the region of interest (ROI). Following the scans at the resting condition, the subject was asked to maximally contract her TRI muscle at maximal elbow extension. MVICs of the triceps muscle was measured with the dynamometer and monitored to ensure consistent MVICs at the same location. The three scans of the entire CSA of TRI on both sides were captured for the contraction condition.

The muscle testing method was adapted from Daniels and Worthingham whereas ultrasound imaging method was adapted from Chi-Fisherman et al (2004), Hislop and Montgomery (2007) and Rankin et

al (2005). Muscle strength for ECR and TRI was determined by measuring the actual muscle force value (N) of MVICs with the dynamometer. An immediate readout of the computed muscle dimension in CSA was stored for further analysis. The data that were not acceptable due to movement artifact were discarded and the scan was then repeated. For data analysis, the mean of the two representative scans out of three scans recorded on both sides were used.

Intervention

The CHRIST utilizes the BESTOP k-max-720 treadmill with customized suspension belt and supporting frame in the treadmill, elbow immobilizers, and customized gloves, and NMES (Figure 3). The treadmill belt speed was set at .5 mph, which was sufficient to accommodate the child's slow arm movement in this study (Daly and Ruff, 2004). The child was instructed to advance their upper limbs as they would for crawling, keeping up with the belt as it moved backwards.

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To augment the therapeutic effect, the electrodes of NMES³⁾ were applied on the predetermined motor points of the ECR and TRI of both upper limbs according to the manufacturer's guideline. Foreexample, NMES was used to evoke muscle activation to produce adequate joint movement throughout the entire or maximal possible range of motion at the appropriate time so that normal arm swing flexion and stance extension pattern can occur and become internalized with repetitive practice. Specific parameters of the NMES used encompassed: waveformtype, biphasic; frequency,

2) PowerTrack II, JTECH Medical, Salt, UK.

3) PROMED-205, D.M.C Co., Gyunggi, Korea.

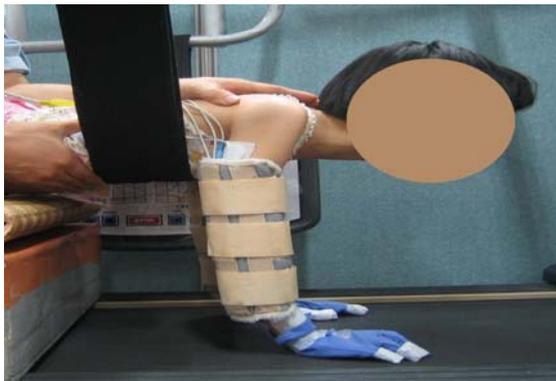


Figure 3. Intervention set-up for CHRIST. A customized suspension belt and supporting frame in the upper extremity weight treadmill system, elbow immobilizers, and customized gloves were used to improve muscle strength of the upper extremity muscles and facilitate appropriate arm stepping and reaching movement in coordinated fashion.

35 Hz; amplitude, 20 mA; pulsewidth, 250 seconds; and on/off ratio, 1:1 (Carnick, 1993; Park et al, 2001). NMES was discontinued after 2 weeks when the child was able to fully extend her elbows independently.

As with the body weight supported treadmill training, the child was instructed to advance the upper limbs with maximal elbow and wrist extension and shoulder flexion (160°) during the arm swing phase and to bear weight on the elbow and palmar surface of the hand and metacarpal heads during the arm stance phase with shoulder flexion (90°) in quadruped position. This repetitive, intensive hand weight bearing during arm stepping task was designed to facilitate normal rhythmic flexion and extension pattern and muscle strength in the involved musculatures, particularly triceps and wrist extensors. Initially, the child was unable to extend her elbow and wrist; the therapist guided the proper advancement and weight bearing movements of the affected limb using verbal and tactile cues along with deep proprioceptive stimulation via approximation as needed. However, the NMES and additional verbal and proprioceptive stimuli were gradually withdrawn

as the child was able to generate appropriate arm stepping movement in coordinated fashion (i.e., wrist extension at swing and elbow extension at stance), which consistently occurred after 12 sessions of intervention. The intervention was provided 60 minutes (10-minute exercise, 5-minute rest) a day, 5 times a week over a 5-week period.

Results

Motor Function

Descriptive statistics of functional motor scores at the pretest, post-test, and follow-up test are presented in Table 2. In particular, the right and left UE movement performance time in the JHFT improved about 65% and 39%, respectively.

Spasticity Data

MAS of the right and left in both ECR and TRI muscles after the intervention reduced 2 and 1.5 to .0 respectively.

Ultrasound Imaging

Excellent images were obtained in all scans. The CSAs of the ECR and the TRI during relaxation-contraction for the pretest, post-test, and follow-up test are presented in Table 3. Specifically, the right and left ECR-CSAs at contraction increased about 67% and 79%, respectively while the right and left TRI-CSAs at contraction improved approximately 38% and 67%, respectively. These increases in muscle size still remained stable at the 3-month follow-up test.

Muscle strength

Table 4 presents muscle strength data obtained from the handheld dynamometer at the pretest, post-test, and follow-up test. The improvements of muscle forces for the right and left ECRs were approximately 525% and 87%, and the improvements of muscle forces for the right and left TRIs were ap-

Table 2. MAS and Motor function tests

	MAS ^a		PMAL ^d		JHFT ^g				WMFT ^h
	Rt. ^b	Lt. ^c	AOU ^e	QOU ^f	Rt.	Improved	Lt.	Improved	Upper limb
			Median	Median	Value (sec)	(sec)	Value (sec)	(sec)	Median
Pretest	2.0	1.5	.0	.5	101.70		28.80		2
Post-test	.0	.0	1.0	2.0	36.00	-65.70	17.60	-11.20	3
3-mon follow-up	.0	.0	.75	2.0	61.30	-40.40	18.10	-10.70	3

^aModified Ashworth Scale, ^bright hand, ^cleft hand, ^dPediatric Motor Activity Log, ^eamount of use, ^fquality of use ^gJebsen-taylor hand function test, ^hWolf Motor Function Test scores.

Table 3. Cross-sectional area (cm²) of the affected upper limbs for the pretest, post-test, and 3-month follow-up tests obtained from a real-time ultrasound imaging

Affected Limb	Rest ^c		Cont ^d		ECR ^a			
	Rt.	Lt.	Rt.	Lt.	Cont-Rest			
					Rt.	Improved(%)	Lt.	Improved(%)
Pretest	.96	1.04	.99	1.18	.03		.14	
Post-test	1.07	1.11	1.12	1.36	.05	67	.25	79
3-mon follow-up	.99	1.12	1.03	1.28	.04	33	.16	14

Affected Limb	Rest		Cont		TRI ^b			
	Rt.	Lt.	Rt.	Lt.	Cont-Rest			
					Rt.	Improved(%)	Lt.	Improved(%)
Pretest	3.90	3.77	4.22	4.01	.32		.24	
Post-test	4.27	3.95	4.71	4.35	.44	38	.40	67
3-mon follow-up	4.43	3.95	4.99	4.66	.56	75	.64	125

^aextensor carpi radialis, ^btriceps brachii, ^crest, ^dcontraction.

Table 4. Muscle strength (N) of the affected upper limbs for the pretest, post-test, and 3-month follow-up tests.

	ECR ^a				TRI ^b			
	Rt.	Improved (%)	Lt.	Improved (%)	Rt.	Improved (%)	Lt.	Improved (%)
Pretest	1.78		7.12		1.78		7.78	
Post-test	11.12	525	13.34	87	20.02	1025	26.69	243
3-mon follow-up	8.59	383	11.25	58	18.99	967	21.92	182

^aextensor carpi radialis, ^btriceps brachii,

proximately 1025% and 243%, respectively. These increases in muscle strength were also maintained at the 3-month follow-up test. These data suggest that the intervention was effective in restoring muscle strength and this effect continued to exist even after the 3-month post-intervention.

Discussion

To our best knowledge, our case report represents the first clinical trial highlighting the effect of CHRIST on muscle size, strength, and functional motor performance and skills in a child with spastic quadriplegic CP.

As anticipated, CHRIST increased the muscle size, strength, and functional motor performance at the post-test and even at the 3-month follow-up test.

Certainly, our real-time ultrasound imaging data demonstrated that the muscle sizes of ROIs for the ECR and TRI muscles were increased as a function of the intervention. Moreover, the CSA measurements using ultrasound imaging were useful for accurately determining the intervention-related morphological changes in the underlying musculature. Comparing our results with previous studies was not possible in this regard because the literature does not contain comparable imaging data. One possible mechanism is that the muscle size gain represents an increase in muscle strength that may have resulted from the intensive strength training (Charette et al, 1991; Trappe et al, 2001). Perhaps, our finding in muscle size gain supports empirical evidence that resistance strength training can produce significant increases in size and number of myofilaments via protein synthesis, thereby increasing the cross-sectional area or diameter (hypertrophy) of the individual muscle fibers (Paul and Rosenthal, 2002).

The present results demonstrated that repetitive bilateral arm strengthening exercise combined with NMES in a weight-bearing quadruped position improved muscle strength and performance in reaching. This finding supports previous evidence that muscle strengthening exercise combined with NMES is beneficial for children with CP and adults with stroke (Kerr et al, 2004).

The observable reduction in spasticity after the intervention was consistent with a previous finding that NMES may have reciprocally inhibited spasticity on the antagonistic muscle while effectively stimulating the agonistic muscles (Postans and Granat, 2005). This decreased spasticity helped improving the efficiency and smoothness of movement, thereby strengthening normal motor development in reaching and grasping.

The WMFT and JHFT showed improvements in fine and gross motor skills in the affected UEs for activities such as lifting a pencil from table, stacking 3 checkers, flipping 3 card, lifting a basket with 1.35

kg of weight from a chair to a bedside table. The improvement in gross motor skills was apparently greater than the improvement in fine motor skills because our CHRIST intervention was designed to improve elbow and hand motor function as reflected in the WMFT. These enhanced UE motor functions were continuously evident in the PMAL questionnaire. The PMAL questionnaire was adapted from the Motor Activity Log (MAL) and obtained from the child's mother suggested that the child was initially unable to use the more-affected arm functionally, but now is able to perform her reaching and grasping tasks using both UEs.

Of clinical importance is that our novel CHRIST approach was effective in treating a child with severe muscle atrophy and functional motor impairment secondary to spastic quadriplegia. In clinical setting, our CHRIST approach may shed new light on other neuro-rehabilitation options for children with CP and can be incorporated into the current intervention. Alternatively, CHRIST can easily implemented by parents or family members at home. A wheelbarrow walking with legs support or ball (for advanced case) may be a good home exercise where the child slowly walks forward and backward with his or her hands. Steady breathing, proper upper extremity alignment, and core stabilization are desirable. If the child requires additional support, a suspension belt around the chest and anterior superior iliac spine areas can be provided.

Several shortcomings have been identified in this research, and their consideration would enhance the experiment if carried out in a more robust, large-scale clinical study in future. First, the case study we present is a preliminary experiment that was intended to investigate the effect of the CHRIST approach on morphological changes, and associated motor performance and skills, in a child with spastic quadriplegia. Although the approach showed promising results, further research with a larger sample size is required to allow the generalization of our findings.

Second, recent evidence suggests that the Ashworth scale is a less appropriate measure of spasticity than the Tardieu scale because it fails to

differentiate between the neural and mechanical (altered muscle properties such as contracture) components of increased resistance to passive movement. In our case, however, contracture, which could potentially have threatened the validity of the Ashworth scale, was not evident. The Tardieu scale would be a more appropriate measure of spasticity, though, which is confounded by contracture. Lastly, it would be of great interest to probe the neuroplasticity and neural substrates underlying motor relearning following treatment with the CHRIST approach using functional MRI. Nevertheless, our findings on CHRIST make an important contribution to the existing body of knowledge on therapeutic exercises for upper extremity muscle strengthening and motor relearning in children with spastic quadriplegia for whom current neurorehabilitation approaches have limited efficacy due to such severe neuromuscular impairments as muscle weakness and spasticity.

Conclusion

As a first step in developing an innovative and effective neurorehabilitation technique, our findings demonstrated the efficacy of CHRIST for improving muscle structure and strength as well as motor performance and skills in a child with quadriplegic CP. Our results provide evidence that the integration of strength training with weight bearing and NMES can produce major functional gains and therapeutic advantages not afforded by conventional rehabilitation. Our results may provide conceptual and clinical insights into the examination and management of affected muscles for reaching and grasping in children with CP.

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