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EFFECTS OF ISCHEMIC CONDITIONING ALONG WITH BIMANUAL TASK TRAINING TO IMPROVE SKILL LEARNING IN CHILDREN WITH UNILATERAL CEREBRAL PALSY

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ABSTRACT
Cerebral palsy (CP) comes along with a variety of neurodevelopmental problems, frequently characterized by seizures and musculoskeletal issues. Lesioning of the upper motor neuron (UMN) further disrupts the corticospinal tract (CST) pathways, leading to difficulties and paralysis. Ischemic conditioning and bimanual training are two effective ways to improve motor function in affected adolescents. The purpose of this research is to compare the effectiveness of ischemic conditioning combined with bimanual task training to a sham intervention. 22 children with unilateral cerebral palsy (UCP) aged 8 to 16 participated in the 4 month randomized controlled experiment. MACS levels and the capacity to stack 3 cups in under a minute were among the criteria that were used to identify the participants. Blood pressure was recorded and pressure cuffs were inflated and deflated every 5 minutes during the 45-minute interventions. The ratings from the Assisting Hand Assessment (AHA) were among the data examined using SPSS version-26. Despite variations in demographics, both intervention groups demonstrated enhanced motor function and skill acquisition. These results show that ischemic conditioning combined with bimanual task training greatly improves motor function and task efficiency in children with UCP.

Keywords: Ischemic Conditioning, Bimanual Task Training, Unilateral Cerebral Palsy

INTRODUCTION
Cerebral palsy is characterized by neurodevelopmental problems that impact posture and movement, frequently combined with sensory and cognitive deficits. It usually arises from anomalies or injuries sustained during early brain development; common causes include periventricular white matter damage and other abnormalities of the brain (1, 2). Brain structural abnormalities leading to localized deficits are the cause of cerebral palsy. Complementary medical disorders such as epilepsy and learning disabilities impact a patient's ability to perform after therapy (3). Brain abnormalities or middle cerebral artery infarction are two common causes of unilateral spastic cerebral palsy (CP), which affects the motor regions and corticospinal tract (CST) (4). Problems with the CST make it difficult to perform upper limb movements, which results in poor performance of precise tasks (1).

The assessment of fingertip force determines the hand-motor coordination involved in effective gripping. Children with cerebral palsy frequently exhibit delayed coordination, following that of children, whereas typically growing children attain adult-like coordination by the time they are 6 or 8 years old (5). Upper Motor Neurons (UMN) in the cerebral cortex, spinal cord, brainstem, and cerebellum are how the central nervous system (CNS) regulates movement of the body. The corticospinal and corticobulbar tracts receive messages from these neurons after they leave the pyramidal tract (6). Due to the fact that damage occurs above the cranial nerve nucleus or the anterior horn cells of the spinal cord, UMN lesions result in weakness, spasticity, clonus, and hyperreflexia (7). The pyramidal tract allows the upper motor neurons (UMN) to control movement directly from the cerebral cortex to the spinal cord (8).

Spinal nerves are connected to corticospinal tract fibers, while cranial nerves are connected to the corticobulbar fibers. The cerebral homunculus, which represents motor cortex, places leg control in the center and face control at outermost position (7, 9). Pyramidal tract pathways must be understood in order to comprehend UMN lesions. Lesions above affect contralateral side, causing muscular weakness and stiffness. Symptoms vary depending on where the lesion is in relation to the pyramidal decussation (10). Studies have shown that children who have been diagnosed with cerebral palsy (CP) may face difficulties when trying to perform complex tasks that require exact command of voluntary motions, such as gripping and reaching, using their affected limbs (11). Normally growing adults and children use muscular activities to make smooth and graceful reaching motions when interacting with objects in their environment (12). RIC can improve neurological function, reduce brain edema, and significantly decrease infarct volume (13, 14).

In both young and old people, the combination of task-specific training with remote ischemic conditioning (RIC) can improve the learning of motor skills, possibly via neuroprotective and neuroplastic mechanisms. More research is necessary to determine the most effective technique to employ RIC to help children with unilateral cerebral palsy (UCP) improve their motor skills (15). In a cup stacking activity, participants used both hands to quickly construct and disassemble pyramids, making corrections as they went (16). For Thailand's aging population, maintaining hand function is a major difficulty that affects 5.8% to 15.3% of elders. For people over 65, research into rehabilitation and alternative methods is required to enhance hand function and quality of life (17).

In this study, the effects of a five-week cup stacking intervention on upper limb coordination are assessed using standardized measurements and kinematic analysis. The results are meant to support the evidence-based inclusion of cup stacking in physical education programs (18). The 1980s phenomenon known as "sports stacking" may benefit senior citizens by enhancing their motor and cognitive abilities. There isn't much research on it, but it might improve coordination, balance, and memory, which could improve quality of life (19). Children with unilateral upper limb disability are measured for bimanual task performance using the Assisted Hand Assessment (AHA). Rasch analysis validates its reliability and accuracy for rehabilitation (20).

Surkar SM, Willson JD, Cassidy JM, et al. investigated how bimanual training using remote ischemic conditioning (RIC) affected children with unilateral cerebral palsy (UCP) between the ages of 8 and 16. With 46 individuals, the study examined corticospinal excitability and movement time to provide treatment insights for UCP (21). Remote ischemic conditioning (RIC) has been studied by Wantong Yu, Changhong Ren, and Xunming Ji for stroke recovery. It is suggested that RIC activates neuroprotective pathways. RIC has potential, but further studies are required to fully grasp how it affects healing (22). Researchers Wu, Yu-Kuang and Wecht, Jill M. discovered that, Remote Ischemic Conditioning (RIC) may improve corticospinal transmission. Further research is necessary to validate the safety and effectiveness of RIC, as preliminary findings suggest that it may boost corticospinal excitability when combined with task-specific training (23).

Studies on motor learning investigate elements such as practice sequencing and learning strategies to improve retention of skills. In a follow-up study, which involved 48 participants practicing cup stacking and taking a retention test, the effects of interaction and observation were investigated (16). Prasomsri and Wadbanjerd discovered that practicing cup stacking enhanced the hand-eye

coordination of older persons, with physical practice exceeding mental exercise in terms of movement time reduction. Both training modalities improved performance, but more study is required to fully understand the impacts of retention and training strategies (17). 5 weeks of cup stacking instruction increased bilateral coordination, concentration, and hand-eye coordination in 6th grade students, according to Rhea's research. Significant post-test gains were found using motion analysis and standardized testing (18).

Greaves examined bimanual skill assessment instruments for children with hemiplegic cerebral palsy under 3 years old. It is evident that infant-specific assessments are necessary to enable early intervention because only the Assisting Hand Assessment demonstrated adequate validity and reliability (24). The Assisting Hand Assessment (AHA) assesses young children with hemiplegic cerebral palsy on their ability to complete bimanual tasks (20). Based on MACS levels, Klevberg and Jahnsen's study of 166 children with unilateral cerebral palsy (CP) ages 18 months to 13 years showed notable differences in development of hand usage. Before age of 6 many children could operate their hands steadily, however this varied based on their starting skill level (25).

Bimanual training in combination with traditional physical treatment significantly improved hand-eye coordination and everyday activities in patients with unilateral spastic cerebral palsy, according to a study conducted in Kasur, Pakistan by Ejaz, Tanveer, and Ahmad (26). The combined intervention appears to have a large favorable impact, according to hypothesis. The study has potential to improve UCP patients' motor function and skill acquisition by providing evidence-based therapy protocols. In order to evaluate combined therapies' beneficial impact on skill learning outcomes, a challenging randomized control trial is utilized, which addresses lack of evidence on combination interventions. The objectives are to assess the effects of ischemic conditioning and bimanual task training, evaluate the sham intervention, and enhance skill learning and coordination in UCP. The rationale highlights that bimanual function coordination is a significant problem that inhibits children with UCP from being independent in their day-to-day activities.

MATERIALS & METHODS

In children with unilateral cerebral palsy (UCP), this randomized controlled experiment examined the potential benefits of ischemic conditioning and bimanual task training for improving skill development. After receiving approval from the ethical review committee, data was obtained over a four-month period from Children Hospital in Faisalabad, Punjab, Pakistan. In order to reduce bias, participants were divided into two groups at random using the chit and draw method, and patients were recruited using purposive sampling. Children with UCP were the target group, and a sample size of 22 was determined with a 95% confidence level using OpenEpi. UCP children with bimanual coordination issues were identified using a self-generated screening form consisting of 10 questions. The participants were 8 to 16-year-old children with unilateral cerebral palsy (UCP), categorized as Levels I–III on Manual Ability Classification System (MACS), who could stack three cups in almost 60 seconds. Children with developmental disorders (such as autism or ADHD), absence of active motor threshold, cardiorespiratory, metabolic, or vascular diseases, hydrocephalus, neoplasm, recent adjunct therapy, active or recent seizures, use of anti-seizure medications, and incompatible medical devices or metal implants were excluded in this study (21). Children with unilateral cerebral palsy (UCP) are assessed for bimanual coordination and hand function using Assisting Hand Assessment (AHA). The arm use score on AHA ranges from 1 ("no arm use") to 4 ("effective arm use") based on 22 components. The BP Apparatus and AHA Question Scale were used as outcome collection instruments. Physical materials such as stacking cups, physio mats, and BP apparatus were utilized in addition to printed consent forms and screening questions.

Remote Ischemic conditioning

Pre- and post-assessments were used to divide individuals into two groups at random over the course of 6 weeks: Ischemic Conditioning with Bimanual Task Training and Sham Intervention with Bimanual Task Training. Cycles of cuff inflation and deflation were used in ischemic conditioning, whereas equivalent procedures were performed on the sham group without requiring artery constriction. Participants completed 15 trials per day over the course of 5 training days in order to evaluate their timing and coordination using speed stack exercises. To guarantee security, vital signs were tracked. The AHA assessed hand function in great detail, and scores indicated efficiency and coordination in bimanual activities.

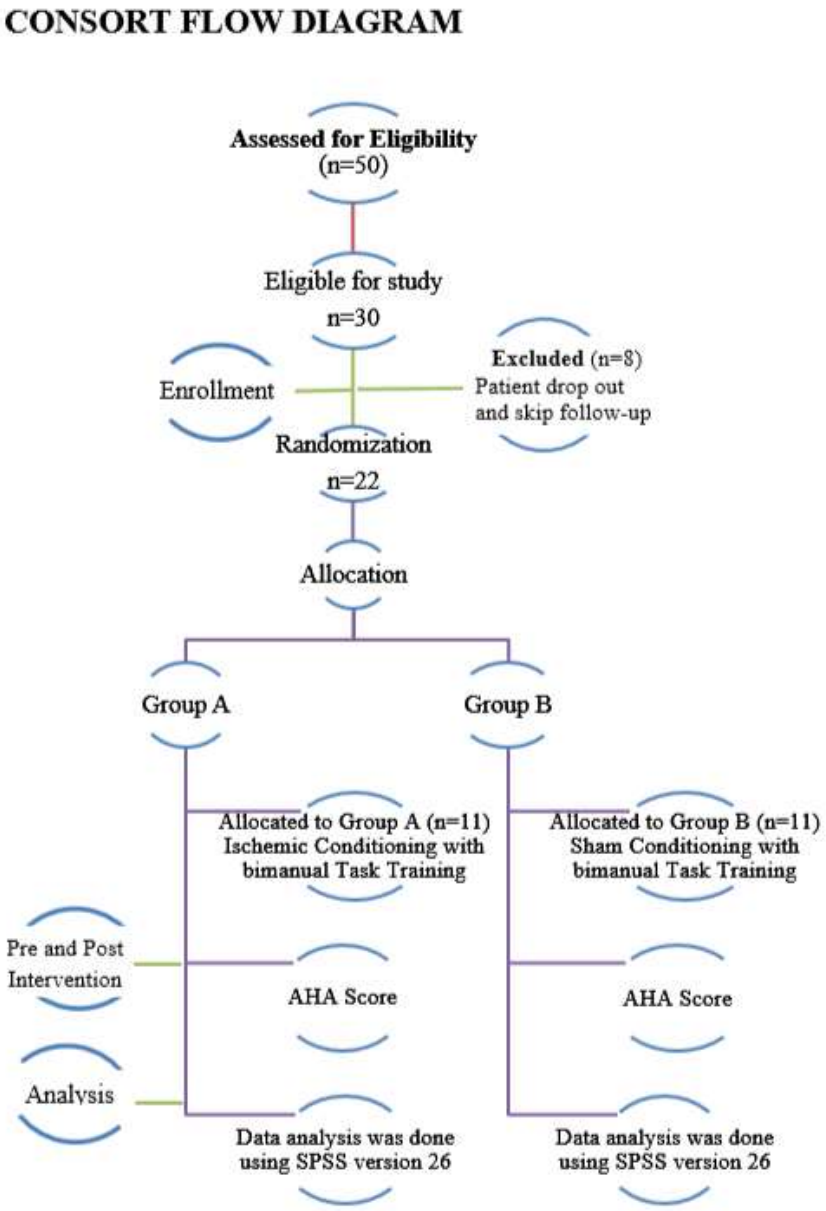
Bimanual Speed Cup Stacking Task

5 days following the 5th treatment session, follow-up evaluations were carried out to determine whether ischemic conditioning and bimanual task training were beneficial for children with unilateral cerebral palsy (UCP). Future clinical techniques for children with UCP will be guided by outcome, such as the Assisting Hand Assessment (AHA). The study was approved by the University of Faisalabad's Ethical Committee, and the guardians of the subjects provided informed consent. Strict data coding guaranteed privacy, and data was securely maintained with participant safety as the top priority.

Statistical Analysis

In two groups, ischemic conditioning with bimanual task training and sham conditioning with bimanual task training, the significance of the interventions was assessed statistically using SPSS version 26. Data normality was confirmed by the Shapiro-Wilk test, which produced significant

findings. A normal distribution was indicated by the AHA score. Significant conclusions regarding the effectiveness of treatment for bimanual task function rehabilitation were obtained from this investigation.



RESULTS

This study investigated at how bimanual task training and ischemic conditioning affected the acquisition of skills in children with unilateral cerebral palsy. The study, which was carried out at Children Hospital Faisalabad in Punjab, Pakistan, aimed to determine whether this combination significantly improved learning over a Sham intervention. After allowing for a 20% dropout rate, 22 of the 30 participants who had initially been assessed for eligibility were enrolled and divided into two groups at random. Group B had the same training regimen but with sham conditioning, while Group A received ischemic conditioning and bimanual task training. The Assisting Hand Assessment (AHA) ratings were used to evaluate the outcomes, and SPSS version 26 was used to thoroughly analyze the data.

Age, gender, and side of disability were among the demographic factors that were considered; the median age was 9 years old, and the approximate mean age was 9.59 years old. Age, gender, and side

all had non-normal distributions according to the Shapiro-Wilk test, which indicated substantial departures from typical distribution patterns. In particular, a higher incidence of right-side participation was indicated by the side variable's mean of 1.41, and a larger prevalence of males was suggested by the gender variable's mean of 1.5. Non-parametric statistical tests had to be used in order to further analyze these data.

Interpretation of Normality Tests on pretest variable
Tests of Normality on pretest variable

Tests of Normality						
	Kolmogorov-Smirnov[a]			**Shapiro-Wilk**		
	Statistic	df	Sig.	Statistic	df	Sig.
TOTAL AHA score (PRE Intervention)	.215	22	.009	.860	22	.005

The data is not normally distributed, as seen by the considerable deviations from normal distribution found in the TOTAL AHA score (PRE Intervention) normality testing. For reliable data analysis, non-parametric statistical tests are therefore required.

Non-Parametric Tests finding of Ischemic Conditioning Combined with Bimanual Task Training Group
Within-group Analysis (Wilcoxon Signed Ranks Test) of RIC + Bimanual Task Training

Ranks				
		N	Mean Rank	Sum of Ranks
TOTAL AHA score (POST Intervention) - TOTAL AHA score (PRE Intervention)	Negative Ranks	0	.00	.00
	Positive Ranks	11	6.00	66.00
	Ties	0		
	Total	11		

Following the intervention, the TOTAL AHA score of all 11 paired observations significantly improved, with each observation receiving a positive rank and no scores declining or equal.

Test Statistics	
	TOTAL AHA score (POST Intervention) - TOTAL AHA score (PRE Intervention)
Z	-2.937
Asymp. Sig. (2-tailed)	.003

Wilcoxon Signed Ranks Test yields a test statistic of -2.937 with a significance level of 0.003. This suggests that following the intervention, scores significantly improved.

Non-Parametric Wilcoxon Test on Sham Combined with Bimanual Task Training Group
Within-Group Analysis (Wilcoxon Signed Ranks Test) of Sham + Bimanual Task Training

Ranks				
		N	Mean Rank	Sum of Ranks
TOTAL AHA score (POST Intervention) - TOTAL AHA score (PRE Intervention)	Negative Ranks	2	3.00	6.00
	Positive Ranks	9	6.67	60.00
	Ties	0		
	Total	11		

According to statistics on the Total AHA Score, 18.2% of cases showed a drop following the intervention, whilst 81.8% of cases improved.

Test Statistics	
	TOTAL AHA score (POST Intervention) - TOTAL AHA score (PRE Intervention)
Z	-2.404
Asymp. Sig. (2-tailed)	.016

The Total AHA Score had a significant change at a 98% confidence level, with a Z-score of -2.404 and a p-value of 0.016, or less than 0.05.
After the intervention, the TOTAL AHA score in Group A improved statistically significantly in all 11 paired observations, with no ties or reductions noted. At a 2-tailed significance level of 0.003, the variations in the TOTAL AHA Score were statistically significant. Group B, on the other hand, demonstrated a significant improvement in the Total AHA Score (Z-score of -2.404, p = 0.016), with 81.8% of cases improving and 18.2% showing a fall.

Total AHA Score
Between-Group Analysis (Mann Whitney U) of Total AHA Score

Ranks				
	Group	N	Mean Rank	Sum of Ranks
TOTAL AHA score (PRE Intervention)	RIC + Bimanual Task	11	12.09	133.00
	Sham + Bimanual Task	11	10.91	120.00
	Total	22		
TOTAL AHA score (POST Intervention)	RIC + Bimanual Task	11	12.09	133.00
	Sham + Bimanual Task	11	10.91	120.00
	Total	22		

Mann Whitney U Test reading on Total AHA Score between group A and Group B. On pre-intervention, for group A, the mean rank was 12.09 and for group B, the mean rank was 10.9. However, post-intervention results of both group A and B remained unchanged.

Mann Whitney U test statistics between both groups

Test Statistics[a]		
	TOTAL AHA score (PRE Intervention)	TOTAL AHA score (POST Intervention)
Mann-Whitney U	54.000	54.000
Wilcoxon W	120.000	120.000
Z	-.431	-.428
Asymp. Sig. (2-tailed)	.666	.669
Exact Sig. [2*(1-tailed Sig.)]	.699	.699

When comparing the both groups for the effectiveness of results, the Mann Whitney U test statistics shows that P-value of post-intervention between both groups was 0.66, higher than 0.05, showing that there is no statistically significant difference between both groups in bimanual hand task improvement.

The Total AHA Score for Groups A and B was compared using the Mann-Whitney U test, which showed mean ranks of 12.09 and 10.9, respectively, before to intervention. The post-intervention outcomes for both groups did not improve. After the intervention, the P-value for the Mann-Whitney U test was 0.66, which was greater than the 0.05 cutoff point and meant that there was no statistically significant difference in the groups' performance on the bimanual hand task.

DISCUSSION

The purpose of this randomized clinical study was to find out how ischemic conditioning when combined with bimanual task training improves the learning of skills in children with unilateral cerebral palsy who are between the ages of 8 and 16. 22 individuals were split into two groups: Group B performed a sham intervention along with bimanual task training, whereas Group A got ischemic conditioning. For 5 days in a row, participants got treatments at a frequency of 15 trials per day and an intensity of 10 to 35 minutes per day. The bimanual task functioning was assessed using the Assisting Hand Assessment Scale. Prior to any conditioning, baseline measurements of nine stacking sequences were made. In order to ensure safety, pain levels were recorded prior to, during, and following each session, as well as vital indicators like blood pressure, heart rate, and oxygen saturation in the non-conditioned arm.

Previous research primarily examined specific treatments for children with unilateral cerebral palsy (UCP). According to Surkar et al., bimanual training combined with remote ischemic conditioning (RIC) enhanced the acquisition of new skills. The potential benefits of RIC in rehabilitation was indicated by Yu et al. and Wu et al.'s demonstration of the neuroprotective advantages of RIC in stroke recovery and spinal cord injuries (21, 27).

We investigated the possible advantages of ischemic conditioning when combined with bimanual task training, and noticed significant enhancements in multiple important statistics, mainly in the total AHA score following the intervention. These findings imply that the combination strategy can improve motor learning and functional outcomes for UCP patients. Previous studies concentrated on providing individualized therapies to improve motor function in children with UCP. By examining the combined effects of ischemic conditioning and bimanual task training, this study raises the possibility that an integrated strategy may be more advantageous than each intervention used alone (28).

The results show the importance of modified and effective rehabilitation techniques and offer important new information. We provide strong evidence for the approach's efficacy through comprehensive analysis, indicating that it can enhance children with UCP's motor function and quality of life and demonstrating the potential of multifunctional therapies in neurorehabilitation. The intervention's effectiveness is demonstrated by the statistically significant increase in AHA scores, which indicates a notable and lasting improvement that may be attributed to the intervention. These findings are essential for comprehending how the intervention affected bimanual function and for directing future interventions meant to enhance bimanual task performance.

Although the current study's limited data and lack of published journals may limit conclusive proof of progress, it creates opportunities for future research by pointing out gaps and producing early results. More thorough study is required to expand on our knowledge and make important strides in the discipline, which will ultimately result in notable developments in neurorehabilitation.

CONCLUSION

These results demonstrate the intervention's significant impact on improving motor function. Children with unilateral cerebral palsy, aged 8 to 16, who took part in randomized clinical research on bimanual task training and ischemic conditioning showed appreciable improvements in bimanual task performance, as indicated by a statistically significant increase in Total Assisting Hand Assessment (AHA) scores post-intervention.

Strength

- In order to improve motor learning in children with unilateral cerebral palsy, the study uses a novel technique called remote ischemic conditioning (RIC).
- Requiring only a blood pressure cuff and a minimum level of technical competence, RIC is simple, affordable, and practical for use in clinical, research, or home settings.
- Safety precautions guarantee participant wellbeing and uphold ethical standards. These include monitoring vital signs and pain thresholds.

Limitations

- The study might have been limited by a comparatively small sample size, which might have had an impact on how broadly the results might be applied.
- Measurement error or judgment may have resulted from limitations in the measurement instruments employed to evaluate the variables under consideration.
- There wasn't enough statistical power in the research study to distinguish between people who responded well to the treatment and people who didn't. As such, it was unable to fully understand how the treatment affected various individuals.

Recommendations

- More multiple individuals should be included in future studies to increase the validity of the findings and their applicability.
- To increase the accuracy of the data, researchers should measure variables using better and more reliable tools.
- In order to get a better understanding of how variables interact and change, long-term studies can be used to study changes over time.

Conflict of Interest

The authors declare no conflict of interest.

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Compliance with Ethical Standards

Ethical approval was obtained from The University of Faisalabad under Ref. no. Tuf/IRB/345/24.

REFERENCES

1. Reid LB, Rose SE, Boyd RN. Rehabilitation and Neuroplasticity in Children with Unilateral Cerebral Palsy. Nature Reviews Neurology. 2015;11(7):390-400.
2. Towsley K, Shevell MI, Dagenais L, Consortium R. Population-Based Study of Neuroimaging Findings in Children with Cerebral Palsy. European journal of paediatric neurology. 2011;15(1):29-35.
3. Novak I, Hines M, Goldsmith S, Barclay R. Clinical Prognostic Messages from a Systematic Review on Cerebral Palsy. Pediatrics. 2012;130(5):e1285-e312.
4. Gordon AM, Bleyenheuft Y, Steenbergen B. Pathophysiology of Impaired Hand Function in Children with Unilateral Cerebral Palsy. Developmental Medicine & Child Neurology. 2013;55:32-7.
5. Gordon A. Development of Hand Motor Control. Handbook of brain and behaviour in human development. 2001:513-37.
6. Emos MC, Agarwal S. Neuroanatomy, Upper Motor Neuron Lesion. Statpearls [Internet]: StatPearls Publishing; 2022.
7. Champney TH. Essential Clinical Neuroanatomy: John Wiley & Sons; 2023.
8. Oliveira Santos M, Swash M, de Carvalho M. Current Challenges in Primary Lateral Sclerosis Diagnosis. Expert Review of Neurotherapeutics. 2024;24(1):45-53.

9. Hooks BM, Papale AE, Paletzki RF, Feroze MW, Eastwood BS, Couey JJ, et al. Topographic Precision in Sensory and Motor Corticostriatal Projections Varies across Cell Type and Cortical Area. Nature communications. 2018;9(1):3549.
10. Pimer LJ, Leslie RA, Phillips G, Newman AJ, Rusak B, Rolheiser TM, et al. Aberrant Corticospinal Tract Characteristics in Prodromal Pd: A Diffusion Tensor Imaging Study. Clinical Parkinsonism & Related Disorders. 2023;8:100182.
11. Bagesteiro LB, Tellini TL, Brown LE. Analysis of Motor Characteristics of Reaching Movements in Children with Cerebral Palsy. Heliyon. 2023;9(2).
12. Kukke SN, Curatalo LA, de Campos AC, Hallett M, Alter KE, Damiano DL. Coordination of Reach-to-Grasp Kinematics in Individuals with Childhood-Onset Dystonia Due to Hemiplegic Cerebral Palsy. IEEE Transactions on Neural Systems and Rehabilitation Engineering. 2015;24(5):582-90.
13. Wang L, Ren C, Li Y, Gao C, Li N, Li H, et al. Remote Ischemic Conditioning Enhances Oxygen Supply to Ischemic Brain Tissue in a Mouse Model of Stroke: Role of Elevated 2, 3-Biphosphoglycerate in Erythrocytes. Journal of Cerebral Blood Flow & Metabolism. 2021;41(6):1277-90.
14. Basalay MV, Wiart M, Chauveau F, Dumot C, Leon C, Amaz C, et al. Neuroprotection by Remote Ischemic Conditioning in the Setting of Acute Ischemic Stroke: A Preclinical Two-Centre Study. Scientific Reports. 2020;10(1):16874.
15. Gonzalez NR, Connolly M, Dusick JR, Bhakta H, Vespa P. Phase I Clinical Trial for the Feasibility and Safety of Remote Ischemic Conditioning for Aneurysmal Subarachnoid Hemorrhage. Neurosurgery. 2014;75(5):590.
16. Granados C, Wulf G. Enhancing Motor Learning through Dyad Practice: Contributions of Observation and Dialogue. Research quarterly for exercise and sport. 2007;78(3):197-203.
17. Prasomsri J, Wadbanjerd J, Suttinon T, Keereena S. Comparison between the Effectiveness of Mental Practice and Physical Practice Using Cup Stacking on Hand Function in the Elderly. Journal of Health Science and Medical Research. 2021;39(6):481-9.
18. Rhea CK. Changes in Upper Limb Coordination and Kinematics Following a Five Week Instructional Unit in Cup Stacking. Journal of Motor Behavior: Barry University; 2004.
19. Moodley K. The Short-Term Effects of a Sports Stacking Intervention on the Cognitive and Perceptual Motor Functioning in Geriatrics 2016.
20. Krumlinde-Sundholm L, Eliasson A-C. Development of the Assisting Hand Assessment: A Rasch-Built Measure Intended for Children with Unilateral Upper Limb Impairments. Scandinavian Journal of Occupational Therapy. 2003;10(1):16-26.
21. Surkar SM, Willson JD, Cassidy JM, Kantak S, Patterson CG. Protocol: Remote Ischaemic Conditioning Combined with Bimanual Task Training to Enhance Bimanual Skill Learning and Corticospinal Excitability in Children with Unilateral Cerebral Palsy: A Study Protocol of a Single Centre, Phase Ii Randomised Controlled Trial. BMJ Open. 2023;13(9).
22. Yu W, Ren C, Ji X. A Review of Remote Ischemic Conditioning as a Potential Strategy for Neural Repair Poststroke. CNS Neuroscience & Therapeutics. 2023;29(2):516-24.
23. Wu Y-K, Wecht JM, Bloom OE, Panza GS, Harel NY. Remote Ischemic Conditioning as an Emerging Tool to Improve Corticospinal Transmission in Individuals with Chronic Spinal Cord Injury. Current Opinion in Neurology. 2023;36(6):523-30.
24. Greaves S, Imms C, Dodd K, Krumlinde-Sundholm L. Assessing Bimanual Performance in Young Children with Hemiplegic Cerebral Palsy: A Systematic Review. Developmental Medicine & Child Neurology. 2010;52(5):413-21.
25. Klevberg GL, Jahnsen R, Elkjær S, Zucknick M. Hand Use Development in Children with Unilateral Cerebral Palsy. Developmental Medicine & Child Neurology. 2021;63(12):1462-8.
26. Ejaz F, Tanveer F, Shoukat F, Fatima N, Ahmad A. Effectiveness of Routine Physical Therapy with or without Home-Based Intensive Bimanual Training on Clinical Outcomes in Cerebral Palsy Children: A Randomised Controlled Trial. Physiotherapy Quarterly. 2024;32(1):78-83.

27. Jia J, Hu Y-S, Wu Y, Liu G, Yu H-X, Zheng Q-P, et al. Pre-Ischemic Treadmill Training Affects Glutamate and Gamma Aminobutyric Acid Levels in the Striatal Dialysate of a Rat Model of Cerebral Ischemia. Life sciences. 2009;84(15-16):505-11.
28. Nemanich ST, Rich TL, Chen C-Y, Menk J, Rudser K, Chen M, et al. Influence of Combined Transcranial Direct Current Stimulation and Motor Training on Corticospinal Excitability in Children with Unilateral Cerebral Palsy. Frontiers in Human Neuroscience. 2019;13:137.