ARTICLE IN PRESS

Journal of Hand Therapy xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Journal of Hand Therapy

journal homepage: www.elsevier.com/locate/jht

Research Paper

A randomized controlled trial on the effectiveness of mirror therapy in improving strength, range of movement and muscle activity, in people with carpal tunnel syndrome

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A R T I C L E I N F O

Article history:
Received 7 September 2023
Revised 7 January 2024
Accepted 9 February 2024
Available online xxxx

Keywords:
Hand
Mirror therapy
Cross-education
Carpal tunnel syndrome
Strength

A B S T R A C T

Background: There is little information on the potential effects of mirror therapy (MT) on motor recovery in individuals with Carpal Tunnel Syndrome (CTS).
Purpose: To compare the effectiveness of a MT protocol versus a therapeutic exercise (TE) protocol, in improving strength, range of motion (ROM), muscle activity, pain, and functionality in patients with CTS.
Study design: Randomized clinical trial.
Methods: Thirty-nine participants with unilateral CTS were divided into two groups: (i) MT group (n = 20) that followed an exercise protocol applied to the unaffected hand reflected in a mirror, and (ii) TE group (n = 19) that followed the same exercise protocol using the unaffected hand but without a mirror. Strength, wrist ROM, muscle activity, pain and functionality, were assessed at baseline (T0), after treatment (T1) and one month after treatment (T2).
Results: At T1, the MT group showed significantly higher wrist flexion-extension ROM compared to TE (p = 0.04, d = 0.8), maintained at T2 (p = 0.02, d = 0.8). No significant changes were observed in ulnar-radius deviation, pronosupination, or fatigue following either MT or TE ($p > 0.05$). MT exhibited enhanced handgrip strength at T1 (p = 0.001, d = 0.7), as well as an increase in the extensor carpi radialis (ECR) and flexor carpi radialis (FCR) maximum muscle activity (p = 0.04, d = 1.0; p = 0.03, d = 0.4). At T1, both groups decreased pain (p = 0.002, d = 1.1; p = 0.02, d = 0.7), and improved functionality ($p < 0.001$, d = 0.8; p = 0.01, d = 0.5) (MT and TE respectively).
Discussion: MT led to enhancements in wrist flexion-extension movement, handgrip strength and functionality unlike TE. MT notably increased muscle activity, particularly in the ECR and FCR muscles.
Conclusions: MT is a favorable strategy to improve wrist flexion-extension ROM, handgrip strength, ECR and FCR muscle activity, and functionality in people with unilateral CTS.

Introduction

Carpal Tunnel Syndrome (CTS) is a highly prevalent neuropathy caused by the entrapment of the median nerve in the carpal tunnel at the level of the wrist.[1] Patients with CTS experiment chronic pain, paresthesia, sensory disturbances along the median nerve territory, and at a more advanced stage, loss of strength,[2] and functional impairment, leading to upper limb disability.[3] Due to its increasing prevalence and incidence in recent years, CTS has become an occupational disease with a considerable health care cost.[4] Conservative treatment, based on splinting, steroid injections, electrotherapy, and manual therapy, is the most recommended approach to manage symptoms and loss of function in patients with mild to moderate CTS.[5]

Although it is a peripheral neuropathy, recent studies affirm that CTS has a profound impact on brain structures in terms of structural connectivity.[6] Other studies consider the existence of a form of maladaptive neuroplastic response to CTS-associated afference and

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https://doi.org/10.1016/j.jht.2024.02.007

motor control deficits.[7] Such insights may be helpful in developing new conservative strategies for the treatment of CTS based on brain neuroplasticity.

An important neural mechanism involved in the induction of neuroplasticity is the modulation of the primary motor cortex (M1) excitability.[8,9] It is also known that voluntary unilateral arm/hand movement induces changes in excitability in both the contralateral and ipsilateral M1.[10,11] This finding suggests that movement of the unimpaired limb might benefit functional recovery of the impaired limb, which constitutes a basis for post-stroke motor recovery of the paretic arm.[12]

In this regard, cross-education is defined as the transfer of strength or motor skill gains to the contralateral untrained limb following unilateral motor training.[13,14] Its effects are commonly accompanied by neural adaptations within the corresponding motor areas in healthy individuals[15,16] and in post-stroke.[17] Specifically, electrophysiological studies have demonstrated that simple motor task training increases the corticomotor excitability and reduces intracortical inhibition in the untrained hemisphere, while decreasing interhemispheric inhibition from the trained to the untrained hemisphere.[18,19]

Other therapeutic approaches that have proven to be effective in increasing ipsilateral excitability of M1 in healthy people is mirror therapy (MT), promoting improved motor function.[20] Further, it has also been used as a rehabilitation technique for pain relief in several populations[21] and reported to be effective for improving functionality in post-stroke individuals.[22] The mirror placed in the patients' midsagittal plane reflects the movements of the unaffected limb creating the visual illusion that the impaired limb moves normally and without pain. Mirror visualization leads to an additional facilitation of M1 beyond that produced by ipsilateral hand movement alone.[23]

Despite the promising clinical relevance of MT and cross-education effects of unaffected limb training, there is little information on the potential effects on motor recovery in individuals with CTS, as well as on the comparison of the effects. Our hypothesis is that the cross-education effects of therapeutic exercises performed with the unaffected hand are greater with the use of a mirror (MT) than training alone, given the additional participation of the mirror neuron network.

Therefore, this study aims to compare the effectiveness of MT versus therapeutic exercise for the unaffected hand, for improving strength, range of motion, muscle activity, pain and functionality in patients with CTS.

Methods

Study design

We conducted a randomized, parallel-group trial following the CONSORT guidelines.[24] Participants were randomly allocated to a mirror therapy group (MT) and an unaffected-hand therapeutic exercise group (TE) by a computer-generated random number list prepared by an external investigator; allocation was concealed. The statistician and the evaluator who performed the assessments were unaware of the group the patients had been assigned to. The study was approved by the Human Research Ethics Committee of the University of Valencia, Spain (num. 1681060) and registered at ClinicalTrials.gov (NCT05115396). All subjects were informed about the nature of this study, including all potential risks. Written informed consent was obtained prior to participation. All procedures took place in the laboratories of the University of Valencia, from September 2021 to June 2022.

Participants

The inclusion criteria were: (i) being over 18 years old, (ii) a medical diagnosis of CTS from qualified healthcare professionals who conducted nerve conduction studies, (iii) unilateral CTS, (iv) positive Phalen's or Tinel's tests,[25] and (v) symptoms such as paresthesia and pain in the median nerve region for at least 6 to 9 months.

Exclusion criteria were: (i) bilateral CTS, (ii) previous CTS surgery, (iii) diabetes, rheumatoid arthritis, or other CTS-related systemic diseases, (iv) clinical signs of cervical radiculopathy or polyneuropathy, (v) pregnancy, (vi) cognitive impairment, and (vii) having received any conservative treatment for CTS in the last month.

Procedure

An experienced physiotherapist recruited the participants, who were then randomly allocated to the MT or TE according to the statistician's instructions. Patients were assessed at baseline (T0), upon completion of the study (T1), and at one-month follow-up (T2). Demographic and clinical data were recorded at baseline. After an initial session to become familiarized with the protocol, participants underwent a six-week training intervention program, five days per week (two days performed at the laboratory and supervised by a physiotherapist, and three days at home without supervision), according to previous studies.[26,27]

Treatment procedures

Mirror therapy

The participants sat on a chair in front of a table with a square mirror in the sagittal plane between the arms. The unaffected hand was reflected laterally in the mirror, while the affected hand rested behind the mirror, aligned with the reflection thus making the mirrored healthy arm appear as the hidden affected arm. In addition, participants were asked to imagine that it was their own painful hand.[26] Participants then started a 20-minute exercise intervention, based on previous studies on mirror therapy and musculoskeletal hand pathologies.[26–28] The exercises included mobility exercises, tendon and median nerve gliding exercises,[29,30] strength exercises, and functional activities,[26–28] as specified in Table 1.

Therapeutic exercise for the unaffected hand

Participants from this group underwent the same exercise intervention as the former group, but they were asked to rest the affected hand under the table, out of sight (without using a mirror).

Assessment procedures and outcomes

Strength and wrist range of motion (ROM) were measured by a combined device that integrated a dynamometer (NedVEP/IBV, Valencia, Spain) and an inertial sensor unit (the InvenSense 9-Axis MEMS MotionTracking Device). This Inertial Measurement Unit (IMU) included the MEMS 3-axis accelerometer and gyroscope and a 3-axis magnetometer. Muscle activity was measured by a 3-channel superficial electromyography (BTS FreeEMG, Quincy, USA). Both devices were used simultaneously.

The patient was seated in a backless chair in front of a table but without leaning on it, feet flat on the ground. After shaving, if necessary, and then cleaning the skin with a 98º-alcohol swab,[31] six 1-cm^2-diameter electrodes were placed on the extensor carpi radialis (ECR), the flexor carpi radialis (FCR) and the abductor pollicis brevis (APB).[32] For the ECR on the lateral side of the forearm, one electrode was placed 10 mm from the lateral epicondyle and the other, 10 mm away; for the FCR on the medial side of the forearm, the first electrode, 1 cm from the medial epicondyle and the second, 1 cm away,[33]

Table 1
Exercise protocol in both intervention groups

Mobility exercises (10 repetitions each)	(1) Flexion - extension of the wrist (2) Ulnar- radial deviation (3) Supination – pronation (4) Closing - opening the hand (5) Flexion-extension of the fingers with the hand extended (6) Joining and separating the fingers with the hand extended (7) Touching the tips of each finger with the tip of the thumb
Tendon and median nerve gliding exercises (10 repetitions each)	Exercise 1. Tendon gliding exercises. (1) straight; (2) straight fist; (3) table top; (4) fist; (5) hook. Exercise 2. Nerve gliding exercises. (1) wrist in neutral, fingers and thumb in flexion; (2) wrist in neutral, fingers and thumb extended; (3) wrist and fingers extended, thumb in neutral; (4) wrist, fingers, and thumbs extended; (5) as in (4) with the forearm in supination; (6) as in (5) applying a gentle stretch to the thumb.
Strength exercises (8 repetitions each, 3 series)	(1) Squeezing a foam rubber ball (2) Separating the fingers against the resistance of a rubber band (3) Wrist extension with a weight of 1 kg (4) Wrist flexion with a weight of 1 kg
Functional activities (10 repetitions each)	(1) Lifting a cup (2) Picking up small objects (3) Stacking cubes (palmar grip) (4) Flipping cards

and two electrodes along the APB. Muscular electrical activity is measured for its relationship with strength development[34] and of this musculature in particular, for its contribution to activities of daily living. The NedVEP/IBV device was placed on the table, in front of the patient, at a distance that could be reached with a slight extension of the elbow.

In order to perform the five tests, the patient should keep their back straight, shoulder adduction, 90º elbow flexion, neutral forearm pronosupination, and a neutral position of the wrist. Before each test, the NedVEP/IBV device was calibrated on the table. Then, the patient had to pick it up and hold it perpendicular to the ground for the start of the tests. The five tests included one specific strength assessment, three mobility assessments and one fatigue test which combined strength and mobility, using the following procedures (Fig. 1):

– The strength test evaluated the maximal handgrip contraction (Newton): participants had to hold a 5-second contraction, then relax for 5 seconds, and repeat the process 3 times. Maximum handgrip strength was recorded using the average of the three repetitions.
– The mobility test included: (1) wrist flexion-extension, (2) ulnar-radius deviation, (3) pronosupination, all starting with the described position. Participants had to perform 10 repetitions of all the movements with light self-determined speed ensuring the greatest possible ROM. This test registered the ROM (º). The average of the 10 repetitions of each movement was computed for subsequent analysis.
– The fatigue test consisted in performing maximum handgrip force for 30 seconds while performing wrist flexion and extension

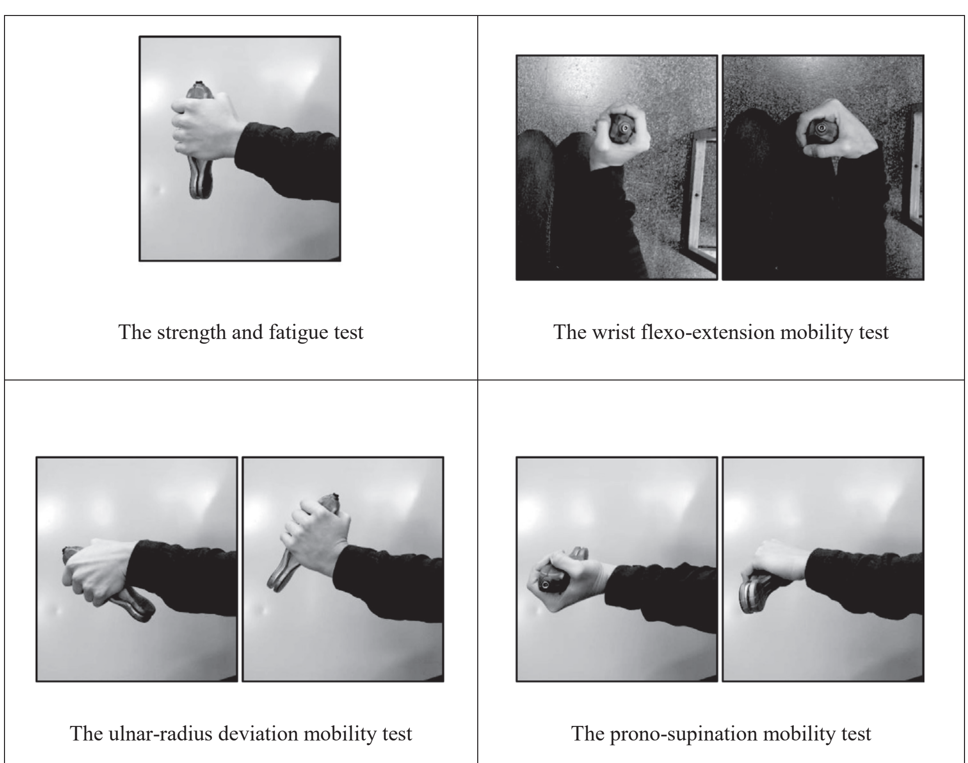

Fig. 1. Strength, fatigue and mobility tests with the NedVEP/IBV device.

movements to explore forearm muscle fatigue. The patient had to maintain maximum strength and maximum ROM.

Through this test, flexion-extension ROM (º) and fatigue index (%) were obtained. Fatigue represents the reduction in isometric strength in 30 seconds, calculated according to the method described by Meldrum et al.[35]

Muscle activation through electromyography (EMG) was registered for all the tests performed, specifically EMG activity (μV) of the FCR, ECR, and APB. The sampling frequency was programmed at 1024 Hz and the EMG signal was monitored using EMG Analyzer software (BTS FreeEMG, Quincy, USA). EMG data was filtered and analysed by Matlab (Massachusetts, USA). Raw signal was filtered through a fourth order "Butterworth" high-pass filter. A cut-off frequency of 10 Hz for the high-pass was used to reduce artefacts. The root mean square (RMS) values were calculated with a window of 200 ms. The peak value from the ten repetitions of each movement were used for the analysis. Maximum activation and the amplitude using the average of the ten peaks was obtained for all tests.

This study is part of a larger study in which the impact of this intervention protocol on variables such as pain, sensitivity and functionality were measured. In this manuscript, data related to pain and functionality will be presented as percentage of change after the intervention $\frac{(T2-T1)}{T1} \times 100$)and 1-month follow-up ($\frac{(T3-T1)}{T1} \times 100$). Pain was measured by a visual analogue scale (VAS) from "no pain" (0) to the "worst imaginable pain" (10).[36] In addition, functionality was measured with the Disabilities of the Arm, Shoulder, and Hand (DASH) Questionnaire.[37]

Sample size

Calculation of sample size was based on an α of 0.05, a statistical power of 0.8 and a Cohen's d of 0.3 for the main outcome, ROM, measured with the NedVEP/IBV device. Based on this calculation, we aimed to recruit 20 patients for each treatment group.

Statistical analysis

Data analysis was performed with the SPSS statistical program (v26). Inferential analyses were performed using a two-factor mixed multivariate analysis of variance (MANOVA) with a between-subject factor "treatment group" having two categories (i.e., MT group and TE group) and a within-subject factor "time measurements" having three categories (i.e., T0, T1, and T2). For post-hoc comparison between times, Bonferroni test was used. Normality and homoscedasticity were analysed by Shapiro-Wilk test and Levene's test, respectively. The α level was set ≤0.05. The effect size was determined using Cohen's d, categorized as follows: small (0.2–0.5), medium (0.5–0.8), or large (> 0.8).

Results

Participants

A total number of 58 participants were assessed for eligibility; 15 failed to meet the inclusion criteria and four declined to participate; thus, 39 participants (74.4% females and 25.6% males) were randomized and all of them completed the study (20 in the MT group and 19 in the TE group) (Fig. 2). The mean (SD) age of the sample was 54.2 (12.3) years. All the participants were diagnosed with unilateral CTS, and the mean time of evolution of the pathology was 9.6 (31.8) years. The affected hand was the right hand in 76.9% of the sample and the left hand in 23.1%. There were no significant differences between groups in participant characteristics, nor in the dependent variables of mobility, strength, and muscle activity at baseline ($p > 0.05$).

Effects of the interventions

A significant multivariate effect by "time measurements" was obtained $F(74,78) = 2.1$, $p = 0.001$, $\eta^2 = 0.7$. However, a non-significant multivariate effect of the interaction between "treatment group" and "time measurements" was reported ($p > 0.05$). The significant differences and effect size in the three assessments (i.e., T0, T1 and T2) for each intervention group and each variable are shown in the following tables.

Regarding wrist mobility (Table 2), there were no significant changes in flexion-extension, ulnar-radius deviation and pronosupination ROM and flexion-extension in the fatigue test, either after MT or after TE application (T0 compared to T1, $p > 0.05$; T0 compared to T2, $p > 0.05$). However, between-groups comparisons indicated that the MT significantly improved flexion-extension ROM compared to the TE group at T1 (mean difference (95% Interval Confidence, IC) = 17.5 (1.4–33.6), $p = 0.04$, d = 0.8); and at T2 (mean difference (95% IC) = 19.6 (3.8–35.4), $p = 0.02$, d = 0.8), as well as in flexion-extension in the fatigue test at T1 (mean difference (95% IC) = 17.7 (3.0–32.5), $p = 0.02$, d = 0.8); and at T2 (mean difference (95% IC) = 16.7 (2.8–30.7), $p = 0.02$, d = 0.8).

With regard to the strength test (handgrip) (Table 2), there was an improvement in the MT group after treatment (mean difference (95% IC) = 41.2 (16.2–66.1), $p = 0.001$, d = 0.7), although it was not maintained after one month ($p > 0.05$). In addition, no changes were reported in fatigue at T1 or T2 ($p > 0.05$). Similarly, the TE group failed to show significant improvements in maximal handgrip contraction or in fatigue at T1 and T2 ($p > 0.05$). No significant differences were found between groups in handgrip strength or fatigue ($p > 0.05$).

When muscle activity was analysed (Table 3), the MT group showed no significant improvement in the electromyographic activity of any muscle group during wrist flexion-extension ($p > 0.05$). For pronosupination, a significant increase in the maximum ECR and FCR muscle activity (mean difference (95% IC) = 0.2 (0.1–0.3), $p = 0.03$, d = 0.7; and mean difference (95% IC) = 0.1 (0.02–0.1), $p = 0.001$, d = 1.0, respectively), and amplitude (mean difference (95% IC) = 146.4 (33.8–259.0), $p = 0.02$, d = 1.0; and mean difference (95% IC) = 50.0 (13.0–87.0), $p = 0.01$, d = 0.6, respectively) was found after treatment. Further, radial-ulnar deviation led to increased maximum FCR muscle activity after treatment (mean difference (95% IC) = 0.1 (0.02–0.1), $p = 0.02$, d = 0.7) and at follow-up (mean difference (95% IC) = 0.1 (0.01–0.1), $p = 0.04$, d = 1.0) and was accompanied by increased APB activity after treatment (mean difference (95% IC) = 0.1 (0.01–0.1), $p = 0.03$, d = 0.3). A similar pattern was found when measuring flexion-extension in the fatigue test with an increased ECR maximum muscle activity and amplitude (mean difference (95% IC) = 0.1 (0.01–0.1), $p = 0.03$, d = 0.7; and mean difference (95% IC) = 89.3 (19.9–158.6), $p = 0.01$, d = 0.8, respectively), whereas only amplitude remained improved at follow-up (mean difference (95% IC) = 128.4 (26.1–222-7), $p = 0.01$, d = 0.8, between T0 and T2). In addition, a significant increase of the FCR maximum muscle activity and amplitude (mean difference (95% IC) = 0.1 (0.01–0.2), $p = 0.02$, d = 0.7; and mean difference (95% IC) = 96.4 (11.7–181.2), $p = 0.02$, d = 0.7, respectively) was only noted at one month follow-up in flexion-extension of the fatigue test. During the strength test (handgrip), an increase in ECR and FCR maximum muscle activity was observed (mean difference (95% IC) = 0.1 (0.01–0.2), $p = 0.04$, d = 1.0; and mean difference (95% IC) = 0.1 (0.01–0.1), $p = 0.03$, d = 0.4, respectively) after treatment.

The TE group exhibited no significant changes in electromyographic activity in any of the wrist movements (i.e., flexion-extension, ulnar-radius deviation, pronosupination and flexion-extension in the fatigue test) and in the strength test (handgrip), either after treatment or at follow-up ($p > 0.05$).

When between groups differences were analysed, the MT showed higher electromyographic activity than the TE in FCR maximum muscle activity in pronosupination at T1 (mean difference (95%

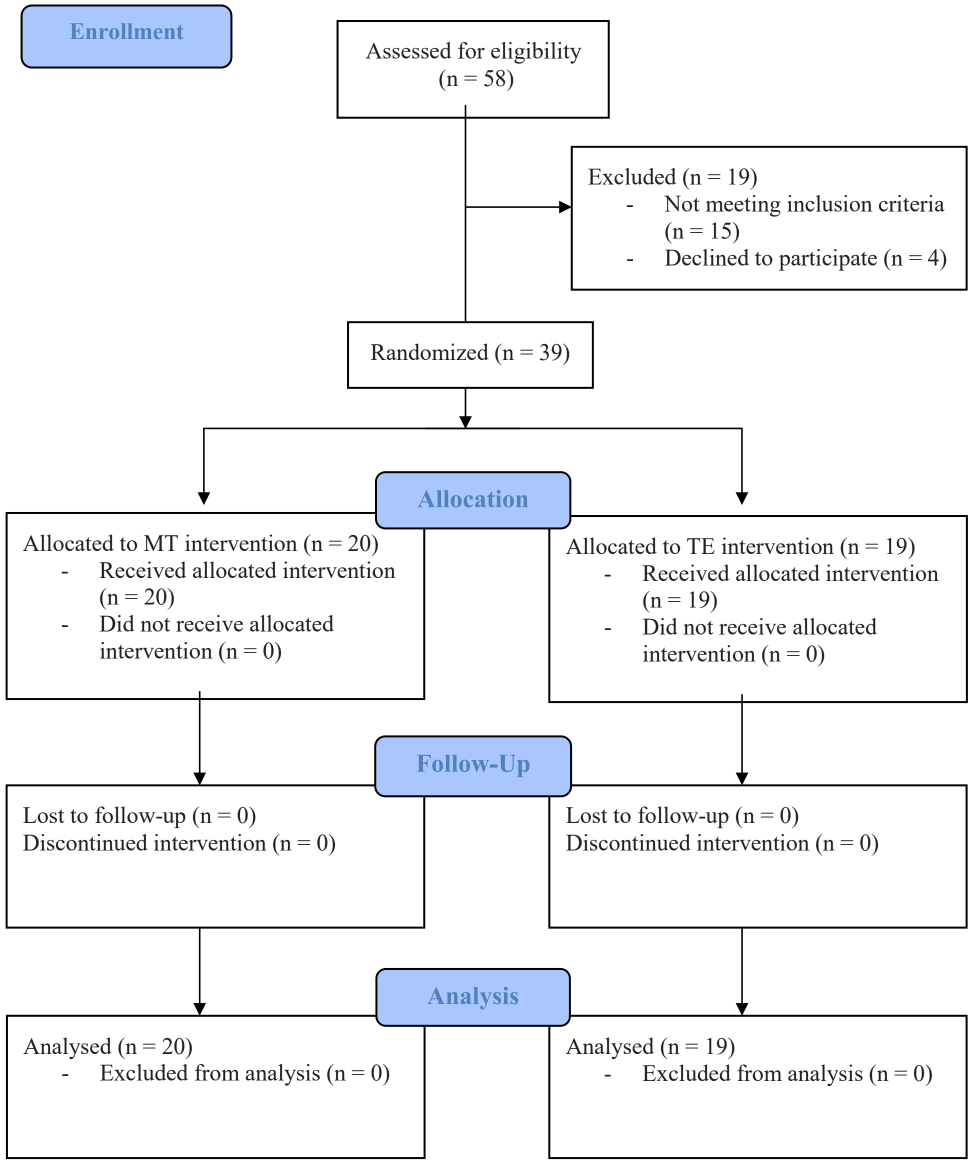

Fig. 2. CONSORT 2010 flow diagram of the study.

Table 2
Effects of the interventions on ROM, fatigue and strength in the two groups

	MT group (n = 20)			TE group (n = 19)		
	T0	T1	T2	T0	T1	T2
ROM						
Wrist flexion-extension (º)	148.1 (21.7)	160.4 (23.9)	162.6 (20.5)	139.8 (17.7)	142.8 (25.7)	142.9 (27.8)
Ulnar-radius deviation (º)	108.7 (23.5)	117.7 (20.3)	117.2 (26.1)	110.4 (21.8)	116.0 (17.1)	112.8 (22.3)
Pronosupination (º)	178.7 (23.0)	184.0 (17.0)	188.1 (18.8)	179.2 (18.8)	183.7 (16.9)	186.0 (24.3)
Flexion-extension in the fatigue test (º)	124.0 (24.5)	128.8 (25.3)	127.3 (23.6)	115.6 (20.4)	111.1 (19.6)	110.6 (19.1)
Strength and fatigue						
Handgrip (*N*)	143.8 (63.1)	185.0 (54.8)*	167.6 (68.1)	146.2 (82.1)	167.5 (65.7)	158.6 (66.9)
Fatigue (%)	68.3 (8.2)	70.2 (7.1)	68.2 (5.9)	69.7 (10.6)	68.3 (5.4)	70.7 (7.6)

MT = mirror therapy; TE = therapeutic exercise group; N = Newtons; T0 = baseline; T1 = post-intervention; T2 = 1-month follow-up; ROM = range of motion.
Data are expressed as mean (SD).
* Significant differences compared to baseline ($p \le 0.05$).

Table 3
Effects of the interventions on muscle activity in the two groups

	MT group (n = 20)			**TE group** (n = 19)		
	T0	**T1**	**T2**	**T0**	**T1**	**T2**
MAXIMAL MUSCLE ACTIVITY						
APB						
Wrist flexion-extension	0.2 (0.2)	0.2 (0.2)	0.2 (0.1)	0.2 (0.2)	0.2 (0.2)	0.2 (0.1)
Ulnar-radius deviation	0.2 (0.2)	0.2 (0.2)*	0.2 (0.1)	0.3 (0.2)	0.3 (0.2)	0.3 (0.1)
Pronosupination	0.3 (0.2)	0.3 (0.2)	0.3 (0.1)	0.2 (0.1)	0.2 (0.1)	0.2 (0.1)
Flexion-extension in the fatigue test	0.3 (0.2)	0.3 (0.2)	0.3 (0.1)	0.2 (0.1)	0.2 (0.1)	0.2 (0.1)
Handgrip	0.3 (0.2)	0.3 (0.2)	0.3 (0.12)	0.2 (0.1)	0.3 (0.2)	0.2 (0.1)
ECR						
Wrist flexion-extension	0.2 (0.1)	0.3 (0.1)	0.3 (0.1)	0.3 (0.2)	0.3 (0.2)	0.3 (0.2)
Ulnar-radius deviation	0.3 (0.2)	0.3 (0.2)	0.3 (0.2)	0.3 (0.2)	0.4 (0.1)	0.4 (0.2)
Pronosupination	0.3 (0.2)	0.4 (0.1)*	0.4 (0.2)	0.3 (0.2)	0.4 (0.2)	0.4 (0.2)
Flexion-extension in the fatigue test	0.3 (0.2)	0.4 (0.1)*	0.4 (0.2)	0.3 (0.2)	0.4 (0.2)	0.4 (0.2)
Handgrip	0.2 (0.1)	0.3 (0.1)*	0.2 (0.1)	0.2 (0.2)	0.2 (0.1)	0.3 (0.3)
FCR						
Wrist flexion-extension	0.1 (0.1)	0.2 (0.2)	0.2 (0.1)	0.1 (0.1)	0.2 (0.2)	0.2 (0.1)
Ulnar-radius deviation	0.1 (0.1)	0.2 (0.2)*	0.2 (0.1)*	0.2 (0.1)	0.3 (0.1)	0.3 (0.2)
Pronosupination	0.2 (0.1)	0.3 (0.1)*	0.3 (0.2)*	0.2 (0.1)	0.3 (0.2)	0.3 (0.2)
Flexion-extension in the fatigue test	0.2 (0.1)	0.3 (0.1)	0.3 (0.2)*	0.2 (0.1)	0.3 (0.2)	0.3 (0.2)
Handgrip	0.3 (0.2)	0.3 (0.2)*	0.3 (0.2)	0.3 (0.2)	0.3 (0.2)	0.3 (0.2)
AMPLITUDE						
APB						
Wrist flexion-extension	207.8 (208.9)	204.6 (163.3)	235.2 (212.0)	245.0 (247.6)	191.0 (131.9)	178.1 (191.2)
Ulnar-radius deviation	120.7 (111.6)	164.8 (128.3)*	132.3 (117.0)	105.3 (86.2)	112.8 (89.9)	100.1 (94.4)
Pronosupination	186.9 (156.8)	203.6 (144.0)	216.2 (148.7)	193.9 (142.7)	190.1 (120.6)	195.8 (164.1)
Flexion-extension in the fatigue test	276.4 (250.2)	287.9 (195.3)	288.5 (146.9)	271.2 (247.6)	219.9 (112.2)	201.5 (116.8)
Handgrip	1410.6 (816.1)	1327.7 (738.6)	1337.1 (798.5)	803.0 (514.0)	1164.1 (819.0)	1073.0 (591.8)
ECR						
Wrist flexion-extension	158.9 (97.4)	229.1 (98.5)	215.4 (117.0)*	222.6 (155.0)	206.0 (120.8)	218.9 (140.1)
Ulnar-radius deviation	144.9 (81.1)	188.2 (101.6)	143.0 (54.7)*	148.0 (77.0)	175.3 (95.8)	121.6 (54.3)
Pronosupination	107.7 (50.7)	254.1 (250.2)*	180.9 (155.1)*	125.9 (107.9)	115.5 (84.3)	144.7 (117.8)
Flexion-extension in the fatigue test	276.4 (118.4)	365.7 (95.2)*	400.8 (214.7)*	326.9 (188.3)	315.2 (109.2)	345.1 (187.2)
Handgrip	1017.7 (529.8)	1210.5 (482.9)	1051.3 (676.5)	829.2 (584.0)	921.3 (445.7)	1098.2 (609.9)
FCR						
Wrist flexion-extension	90.0 (63.2)	137.9 (92.0)	140.7 (87.6)*	115.8 (76.5)	134.6 (105.7)	130.2 (102.5)
Ulnar-radius deviation	64.0 (38.8)	105.3 (61.9)*	95.3 (64.7)*	86.8 (63.1)	87.1 (53.6)	85.1 (60.4)
Pronosupination	71.3 (54.6)	121.3 (102.9)*	158.7 (145.0)*	64.1 (40.7)	74.1 (64.6)	87.9 (59.4)
Flexion-extension in the fatigue test	213.7 (149.6)	262.9 (111.8)	310.1 (130.3)*	231.6 (141.4)	264.5 (158.1)	251.6 (175.1)
Handgrip	1087.0 (665.3)	1256.7 (561.4)	1247.7 (697.0)	937.1 (545.8)	1210.8 (585.2)	1240.9 (728.5)

MT = mirror therapy; TE = therapeutic exercise group; T0 = baseline; T1 = post-intervention; T2 = 1-month follow-up; APB = abductor pollicis brevis; ECR = extensor carpi radialis; FCR = flexor carpi radialis.
Data are expressed as mean (SD).
* Significant differences compared to baseline ($p \leq 0.05$).

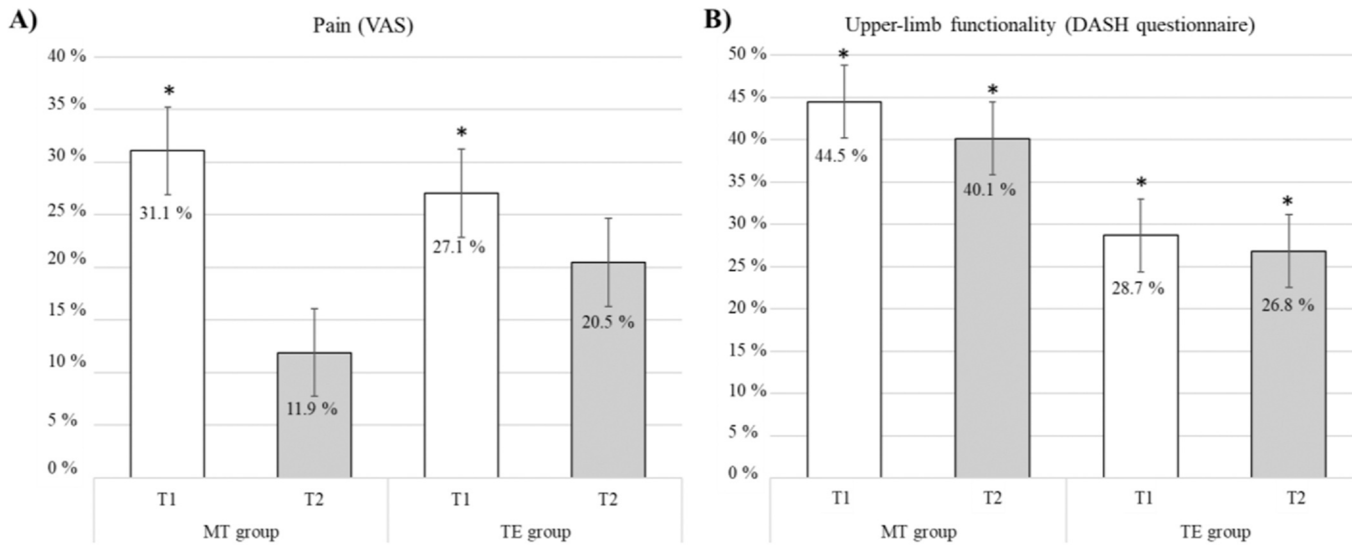

Fig. 3. (**A**) Percentage of change in pain measured with the Visual Analog Scale (VAS). (**B**) Percentage of change in limitation of functionality measured by the Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH) questionnaire. T1: post-intervention; T2: 1-month follow-up. * Significant differences compared to baseline ($p \leq 0.05$).

IC) = 0.1 (0.01–0.2), $p = 0.02$, d = 0.9) and at T2 (mean difference (95% IC) = 0.1 (0.01–0.2), $p = 0.04$, d = 0.7); and in ECR muscle activity amplitude in pronosupination at T1 (mean difference (95% IC) = 138.6 (16.2–261.1), $p = 0.03$, d = 0.8).

As shown in Figure 3A, MT and TE groups significantly reduced pain intensity (mean difference (95% IC) = 2.7 (1.0–4.3), $p = 0.002$, d = 1.1; and mean difference (95% IC) = 1.8 (0.2–3.5), $p = 0.02$, d = 0.7, respectively) at T1. However, no significant differences were observed at T2 ($p > 0.05$). Additionally, there was a significant improvement on upper-limb functionality through the DASH questionnaire at T1 in the MT group (mean difference (95% IC) = 13.5 (6.0–21.0), $p < 0.001$, d = 0.8) and in the TE group (mean difference (95% IC) = 10.2 (2.5–17.9), $p = 0.01$, d = 0.5). The improvements were maintained at T2 (mean difference (95% IC) = 13.8 (4.4–23.1), $p = 0.002$, d = 0.8; and mean difference (95% IC) = 10.8 (1.1–20.4), $p = 0.02$, d = 0.4, respectively) (Fig. 3B). When conducting between-groups comparisons, no significant differences in pain intensity and upper-limb functionality were observed at either T1 or T2 ($p > 0.05$).

Discussion

This is the first study to assess the effectiveness of cross-education with and without mirror therapy in people with CTS. The findings disclose that MT improved wrist flexion-extension ROM and handgrip strength, whereas training the unaffected limb without the mirror achieved no such improvements. In addition, MT significantly improved maximum muscle activity and amplitude for several important CTS-related muscles, contrary to the results obtained for the TE intervention. Specifically, the electromyographic activity for the maximum muscle activity and amplitude of ECR and FCR improved in pronosupination and handgrip after MT. However, neither protocol achieved significant changes in ROM when ulnar-radius deviation and pronosupination were tested. Further, no significant results were obtained for fatigue.

Changes in the mobility of the untrained limb could be associated with neural inhibition or psychophysiological factors, for example, changes in stretch tolerance, rather than changes in the passive properties of the soft tissues of the joint.[38] Particularly, when the effect of our protocol on wrist mobility was analysed, we found that ROM did not achieve significant levels following MT. However, only MT achieved an effect on flexion-extension ROM beyond 10º.[39] Generally flexion-extension is the most affected gesture in people with CTS, since flexing and extending the wrist increases the pressure on the patient's carpal canal three times more than in a neutral wrist position.[40] In addition, median nerve displacement in these patients is primarily affected in wrist flexion movements compared to healthy people.[41] Therefore, many patients avoid performing these wrist movements for fear of triggering the symptoms. In this regard, MT has been shown to be effective in increasing ROM in people with fear-avoidance,[42] which may explain the results obtained for flexion-extension, and not for the other wrist movements. In addition, these results are consistent with those found in the literature. The study by Başkaya et al.[43] reported that the MT group significantly improved shoulder flexion and abduction ROM compared to a group that received TE for the unaffected limb in people with adhesive capsulitis. Similarly, wrist and hand movement also improved after MT combined with conventional rehabilitation in patients with orthopedic hand injuries.[27] However, larger effects on wrist flexion-extension (28.7%) and pronation supination (10.0%) after strength training on the non-fractured arm during the sling immobilization period were observed by Magnus et al.[44] The possible explanation for these discrepancies could be that ROM is more limited in people who have suffered a fracture involving immobilization than in those with CTS. Thus, starting from lower ROM values would have yielded greater effects.

Some CTS patients show decreased grip strength.[3] Consequently, measurements of hand muscle strength have been devised for clinical decision-making and outcome evaluation.[45,46] This holds significance as maintaining optimal grip strength in cases requiring surgery predicts higher postoperative satisfaction.[47] In this regard, the MT group reported a significant 22.25% increase in grip strength after the intervention, whereas the TE group's maximum strength increased by 12.71% compared to baseline, not reaching a level of significance. Contralateral strength transfer may be due to the bilateral activation of the left and right primary motor cortex (M1).[48,49] In addition, MT, which combines the cross-education phenomenon with the activation of the mirror neuron system,[50] may have greater benefits on strength than the isolated application of non-MT training of the unaffected limb,[51,52] since mirror-based movement visualization leads to an additional facilitation of M1 beyond that produced by ipsilateral hand movement alone.[23] In fact, studies that apply only TE on the unaffected hand obtained minor changes. For example, in the study by Barss et al.[53], a significant increase of 7.8% in the untrained hand strength was observed from session 12 onwards; likewise, the study by Boyes et al.[54] reported that the untrained arm increased strength by 8.4–9.0% after 4 weeks of intervention. Moreover, Coombs et al.[55] revealed a 15% improvement in wrist extensor voluntary dynamic strength in the untrained limb. This may be explained by the fact that these studies were carried out on healthy people, thus the benefits were more modest. In addition, the type of exercise as well as its dosage can condition strength gains.[56] In this regard, we combined mobility, functional and strength-resistance exercises, while the above studies applied a single series of maximum strength training (between 90%–100% of the maximal isometric contraction). Additionally, loss of muscle strength may start to become noticeable after a few weeks of not exercising. This may explain why the effects on strength diminished at the one-month follow-up, as patients were instructed not to exercise at home or receive other treatments during this time. Even so, it can be observed that the strength values were still higher than the baseline. Thus, in clinical practice, it would be desirable to explain to the patient the importance of continuing the strengthening treatment at home in order to maintain the improvements gained in strength over time.

In terms of muscle activity, no changes were reported after TE on the unaffected hand in any of the movements evaluated. This is in accordance with previous studies. Barss et al.[53] aimed to characterize the time course of changes in strength during unilateral handgrip training in healthy participants using two different dosages (i.e., 3 times per week for 6 weeks or daily training for 18 consecutive days). They observed that, in both cases, despite the increase in strength in the FCR and ECR muscles, there were no changes in muscle activity. Similarly, Boyes et al.[54] assessed the cross-education effects of a handgrip training program also using two different dosages (i.e., 2 × 6 repetitions 10 times per week or 5 × 8 repetitions 3 times per week). Thus, despite finding a significant improvement in strength, alterations in neurological mechanisms were not detected via EMG activity in FCR and ECR muscles. This may be due to the fact that, although cross-education effect favors the recruitment strategy in the untrained limb, the smaller neuromuscular changes may not be detectable via surface EMG.[45] Additionally, the neural adaptations in the cross-education training are mainly due to supraspinal mechanisms which need other specific measurement methods, such as transcranial magnetic stimulation, to be registered.[15,16,18]

However, when muscle activity was analysed in the MT group, there was an increase in peak muscle activation of the ECR and FCR muscles, especially in pronosupination movement and handgrip during the strength test. This may be explained in that the adaptations in the neuromuscular system achieved with the cross-education effect may be enhanced by adding the mirror neuron system-based stimulation through the reflection of the unaffected hand in the mirror.[50] This is consistent with the study by Gámez-Santiago et al.,[57] who after six weeks of MT (5 sessions per week) observed a significant improvement in mean EMG activity relative to handgrip strength in the ECR and FCR muscles in older patients with post-stroke hemiplegia. However, no significant muscle activity changes were found during flexion-extension. It should be noted that wrist extensors are highly active when exerting combined grip and wrist forces, whereas the wrist flexors are highly dependent on the task performed.[58] This could explain why a test with simple flexion-extension movements failed to reflect changes in ECR and FCR muscle activation. In addition, also when wrist ulnar-radius deviation movement was analysed, no significant changes were observed. This may be due to the surface electrodes not being specifically placed on the muscles involved in the movement (i.e., flexor carpi radialis, flexor carpi ulnaris)[59] and therefore the activity was not accurately measured. However, the scarce number of studies evaluating the effects of MT on muscle activity during simple wrist movements prevents any comparison between results.

The clinical implication of this finding is that people with unilateral CTS who may have difficulty in exercising with the affected hand because of pain during or after exercise, may experience benefits in mobility, handgrip strength, pain and functionality by training the contralateral upper limb through MT.

Study limitations

This study has some limitations. It was conducted with people with unilateral CTS, thus its results cannot be extrapolated to people with bilateral CTS or who have undergone CTS surgery. Additionally, our findings may be influenced by the heterogeneity associated to the severity of nerve conduction impairment of the participants, as it was not taken into account as a covariate. Further, it was carried out in a particular setting, thus the results are not entirely generalizable. Future investigations should consider longer follow-up periods to assess sustained outcomes and better account for the natural variability of CTS symptoms. Moreover, potential future studies may evaluate different dosages to ascertain if a treatment with fewer sessions is equally effective, as fewer clinical appointments may be more feasible for many clinics. Finally, the application of surface electrodes on the forearm muscles may not allow potential changes on the cortico-spinal pathway derived from mirror neuron stimulation to be assessed properly.

Conclusions

Without waiving the aforementioned limitations, MT seems to be a good strategy to improve wrist flexion-extension ROM, handgrip strength, and ECR and FCR muscle activity compared to a TE protocol performed with the unaffected hand in people with unilateral CTS. However, no significant improvements in ulnar-radius deviation and pronosupination ROM, APB muscle activity and fatigue were reported after the MT intervention. Additionally, it is an effective method to improve hand functionality.

Institutional ethical approval

The study protocol was approved by the Human Research Ethics Committee of the University of Valencia (Spain).

Source of funding

This work was partially supported by Grants from the Spanish Government (PID2021-125694OB-I00; co-financed by EU FEDER funds), Generalitat Valenciana, Conselleria d′Innovació, Universitats, Ciència i Societat (CIAICO/2021/215); and from Universitat de València (INV19-01-13-07).

This study has been registered at ClinicalTrials.gov (NCT05115396).

Declaration of Competing Interest

The authors declare that there is no conflict of interest.

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