Article

Not peer-reviewed version

Enhancing Upper Limb Functionality, Gross and Fine Motor Skills, Autonomy, and Quality of Life in Acute Stroke Patients: A Mirror Therapy, Cognitive Therapeutic Exercise, and Task-Oriented Training

Jessica Fernández-Solana , Rodrigo Vélez-Santamaría , Adrián Moreno-Villanueva , Sergio Álvarez-Pardo * , Jerónimo J. González-Bernal , Mirian Santamaría-Peláez , Josefa González-Santos

Posted Date: 1 February 2024

doi: 10.20944/preprints202402.0050.v1

Keywords: mirror therapy; cognitive therapeutic exercise; task-oriented training; upper limb; gross notor; fine motor; autonomy; quality of life; acute stroke

Article

Enhancing Upper Limb Functionality, Gross and Fine Motor Skills, Autonomy, and Quality of Life in Acute Stroke Patients: A Mirror Therapy, Cognitive Therapeutic Exercise, and Task-Oriented Training

Jessica Fernández-Solana [1], Rodrigo Vélez-Santamaría [1], Adrián Moreno-Villanueva [2,3], Sergio Álvarez-Pardo [2,*], Jerónimo J. González-Bernal [1], Mirian Santamaría-Peláez [1] and Josefa González-Santos [1]

[1] Department of Health Sciences, University of Burgos, 09001 Burgos, Spain ; jfsolana@ubu.es (J.F.-S.); mspelaez@ubu.es (M.S.-P.); jejavier@ubu.es (J.J.G.-B.); mjgonzalez@ubu.es (J.G.-S.)
[2] Faculty of Health Science, University Isabel I, Burgos, Spain; adrian.moreno@ui1.es (A.M.-V.)
[3] BIOVETMED & SPORTSCI Research group, Department of Physical activity and Sport, Faculty of Sport Sciences, University of Murcia, San Javier, Murcia.
* Correspondence: sergio.alvarez@ui1.es (S.A.-P)

Abstract: Mirror Therapy (MT) and Cognitive Therapeutic Exercise (CTE) are two neurorehabilitation techniques based on neuroplasticity and designed to enhance the functionality of the upper limb. Therefore, the aim is to assess the effectiveness of the combination of CTE and MT with task-oriented training (TOT) on fine and gross motor skills of the affected hand, as well as the functionality of the affected upper limb, autonomy, independence, and quality of life (QoL) in patients with acute stroke. This longitudinal and multicenter study involved a sample of 120 participants selected randomly and consecutively. Three groups were formed, including a control group (CG) and two treatment groups, one with MT and the other with CTE. The functionality of the upper limb, fine and gross motor skills, the quantity and quality of use of the affected upper limb, autonomy, and QoL were evaluated using various scales validated in the Spanish population at the baseline, after 20 treatment sessions, and at three months of follow-up. ANCOVA analysis was conducted, revealing statistically significant differences between assessments in the CG compared to the experimental groups (GEs), indicating a notable improvement in overall functionality, fine and gross motor skills, autonomy, and QoL in the latter. However, there were no significant differences between the GEs. Therefore, the application of either of these experimental combinations is crucial for the motor recovery, functionality, and improvement of the quality of life of individuals who have suffered a stroke.

Keywords: mirror therapy; cognitive therapeutic exercise; task-oriented training; upper limb; gross notor; fine motor; autonomy; quality of life; acute stroke

---

1. Introduction

Stroke is currently a major public health and quality of life (QoL) problem, and its incidence is increasing every day. In the last 3 decades the incidence has increased by 70%, its prevalence by 85% and consequently the mortality derived from a cardiovascular accident has increased in the last 30 years by 43% [1]. The vast majority of strokes are attributed to risk factors such as high systolic blood pressure, high body mass index, high fasting plasma glucose concentrations, environmental pollution and smoking. According to the World Stroke Organization (WSO), there are 12.2 million new strokes each year, which means that a stroke occurs every 3 seconds anywhere in the world. Since 1990, the number of people who have to live with the after-effects of a stroke has doubled to a staggering 101 million people. 1 out of every 4 inhabitants will have a stroke in their lifetime, that is why knowing how to treat the aftermath of the disease is essential to improve the QoL of people suffering from this disease [2].

These side effects largely involve the upper limbs, being a major cause of long-term disability [3]. These sequelae resulting from a stroke can be significant in terms of upper limb function loss. This loss not only affects mobility but also fine and gross motor skills, impacting the ability to perform activities of daily living (ADLs) such as dressing, feeding, or grooming. Fine motor skills, like the ability to grasp small objects, write, or perform other instrumental activities of daily living (IADLs), are compromised due to muscle weakness or lack of coordination. On the other hand, gross motor skills related to larger and more complex movements may also be limited, affecting the capacity to engage in various activities and task.

Another important sequelae that can be observed is "learned non-use", a common response after a stroke. In this case, the individual avoids using the affected upper limb due to motor difficulties or weakness. This behavior develops when the person overly relies on the unaffected limb to perform daily tasks, resulting in a lack of stimulation and use of the paralyzed limb. Additionally, autonomy is another characteristic that is also affected after a stroke. Those experiencing severe stroke sequelae may heavily depend on caregivers or therapists to carry out ADLs. This directly affects their independence, subsequently influencing their QoL, as limitations in upper limb function can hinder their participation in social, recreational, and work-related activities [4].

Rehabilitation after a stroke is essential to promote optimal recovery and improve patients' QoL. The importance lies in implementing a comprehensive approach with a complete strategy to address the various sequelae that arise after a stroke. Additionally, personalized treatment tailored to the unique needs and challenges of each individual is crucial.

To achieve this, the need for both pre- and post-treatment assessments to objectively measure the outcomes is emphasized. In this regard, various assessment tools for stroke patients provide data on upper limb function, fine and gross motor skills, such as the Action Research Arm Test (ARAT) or Box and Blocks Test (BBT), the use of the affected upper limb compared to its pre-stroke condition using the Motor Activity Log (MAL-30), the level of autonomy using the Functional Independence Measure-Functional Assessment Measure (FIM-FAM), and their QoL through the Stroke-Specific Quality of Life Scale (SS-QoL) [5–10].

In rehabilitation, evidence-based therapies play a crucial role as they are supported by studies and results confirming their effectiveness in improving functionality, restoring autonomy, and enhancing the QoL of these individuals. Examples of such therapies include Mirror Therapy (MT), Cognitive Therapeutic Exercise (CTE), and task-oriented training (TOT) [11].

MT is a rehabilitation technique employing visual illusions to enhance motor function in individuals who have experienced strokes or limb injuries. This therapy utilizes a mirror to create an illusion of normalcy in the affected limb [12]. The mirror reflects the unaffected limb while the affected one remains hidden behind it. By moving the healthy limb, its reflection creates the appearance of movement in the affected limb, tricking the brain into perceiving normal motion. MT focuses on repetitions of controlled and specific movements, stimulating neuroplasticity—the brain's ability to reorganize and adapt through experience and repeated practice. This therapy is believed to aid in restoring motor function, improving coordination, and reducing chronic pain associated with the affected limb [13–15].

CTE, also known as the Perfetti method, is a neurorehabilitation approach providing tailored and specific treatment for each patient. Its goal is to recover lost or altered movement due to central nervous system damage. It involves assigning the patient the task of solving a specific problem that can be addressed through fragmented movement of body segments, assisted by the therapist. This method aims to improve the specific motor deficits in the hemiplegic upper limb, working with patterns such as abnormal responses to stretching, abnormal radiation, motor mobility of basic schemes, and promoting the effectiveness and quality of muscle activation. Its focus lies in reactivating and strengthening the neural connections damaged by stroke [16–18].

On the other hand, TOT can be beneficial for these patients, representing an effective method to foster and develop motor skills and brain plasticity through the repetition of specific and practical tasks. This approach is based on carrying out adapted activities and tasks that simulate everyday actions. Professionals design personalized training programs, taking into account individual needs,

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 1 February 2024 doi:10.20944/preprints202402.0050.v1

motor deficits, and each patient's recovery goals. These programs focus on activities that replicate the actions required for the individual's daily routines. The effectiveness of TOT lies in its emphasis on functionality and the practical application of motor skills in real-life situations. Its purpose isn't just to restore motor function but also to enhance the patient's autonomy in daily activities, which can have a significant impact on their QoL [19–21].

Lastly, it's important to emphasize that in rehabilitation, prioritizing the optimization of treatment outcomes is essential. Therefore, combining various therapies or therapeutic approaches can help improve treatment effectiveness and expedite recovery. Recent research has demonstrated that the combination of these therapies activates central nervous system neuroplasticity more effectively than when applied separately, potentially enhancing motor function, autonomy level, and QoL of stroke patients [22–25]. Despite this, to date, no article has been published comparing which of these combined therapies, namely MT or CTE combined with TOT, is more effective in improving upper limb function after a stroke. Hence, this study aims to verify the effectiveness of combining these techniques on the overall motor function of the affected upper limb, fine and gross motor skills, use of the affected arm, and the QoL of stroke patients. The goal is to determine which of these combinations yields better results.

2. Materials and Methods

2.1. Study Design and Population

A multicenter and longitudinal study was conducted in collaboration with the University Hospital of Burgos (HUBU), the San Juan de Dios Hospital (Burgos), the Reina Sofía Hospital in Córdoba, and the University of Burgos (Spain). The study included 120 stroke patients.

The following criteria were established for the inclusion of participants in the study: (1) having a diagnosed residual hemiparesis due to an ischemic or hemorrhagic stroke, (2) having a level of mobility in the affected upper limb within stages II and IV of the Brunnstrom scale [26], (3) obtaining a score equal to or higher than 26 on the Montreal Cognitive Assessment (MoCA) [27,28], (4) being over 18 years old, and (5) signing the informed consent.

Exclusion criteria, based on diagnostic information provided by the neurologist's clinical evaluation, were as follows: (1) having a visual deficit or homonymous hemianopsia, (2) having Wernicke's or mixed aphasia, and (3) having hemineglect.

2.2. Procedure

The participants for this study were selected upon discharge from the Stroke Unit and the Neurology Service of both hospitals, using a consecutive selection method. To determine the required sample size, an adjusted formula for finite populations was applied, considering the known proportion of strokes in the population according to data from the National Institute of Statistics (INE) [29], with a 1% margin of error. This calculation indicated that the sample should consist of 81 stroke patients.

The study design was a randomized, controlled, and blinded clinical trial with three groups: one control group (CG) and two intervention groups (intervention 1 and intervention 2).

Participants were recruited by the rehabilitation doctor, who assessed whether they met the study's inclusion criteria. They were randomly assigned to groups through a masking process in a 1:1:1 ratio, centrally generated by an independent researcher using Epidat 4.2 (free-access software for epidemiological analysis that allows random assignment), before participant inclusion. Different researchers administered therapies in the experimental groups (GEs). The professionals responsible for implementing therapies in different centers were Occupational Therapists and Physiotherapists specialized and trained in the techniques used.

Participants were initially evaluated one month after the stroke, applying the inclusion and exclusion criteria. Data collection began after collaboration with participating centers.

During the intervention, which extended over 20 sessions for 5 days a week [30–32], the groups were divided so that participants in group EG1 received MT combined with TOT, while participants

 doi:10.20944/preprints202402.0050.v1

in group EG2 received CTE combined with TOT. Therapies were distributed in segments, dedicating 30 minutes to MT or CTE, and the remaining 30 minutes to TOT. Thus, all three groups followed their usual therapy as prescribed by the rehabilitation doctor. The GC received an additional 20 treatment sessions where MT and CTE were applied, respectively. Therapy was administered in the mentioned hospitals by occupational therapists or physiotherapists.

The research plan received approval from the IR Approval Committee of HUBU 2134/2019. Data collection was carried out in participating centers by designated personnel, and the data were anonymized before being shared with the research team, maintaining anonymity and confidentiality from that moment onward.

2.3. Instruments

Independent variables were collected covering sociodemographic data such as age and gender, as well as lifestyle habits like smoking and participation in physical activity. Additionally, general clinical variables were gathered, including the presence of hypertension (HTA), dyslipidemia, atrial fibrillation, a history of myocardial infarction, or diabetes mellitus (DM). Specific clinical variables post-stroke were also taken into account, such as the affected and dominant side, as well as the functionality of the upper limbs.

ARAT, a measure translated into Spanish and validated in the Spanish stroke population [6], was used. It describes the ability to use the upper limb in activities requiring grip, pressure, and gross movements for everyday tasks. These aspects are crucial for performing Activities of Daily Living (ADL). Inability to perform elements of the test is considered a valid indicator of upper limb limitation for activity [33].

The test consists of 19 items requiring manipulation and movement of objects, starting with the less affected upper limb. It is divided into 4 subscales (grasp, grip, pinch, and gross movement). Scores range on an ordinal scale from 0 to 3 for each upper limb separately, where 0 represents an inability to complete the test, and 3 indicates normal performance. Total possible scores range from 0 to 57 [34].

This scale is suitable for use in individuals who have experienced a stroke and is considered a valid and sensitive instrument for evaluating upper limb functional limitation in the early stages after a stroke (ACV). Therefore, it becomes a suitable measure for application in patients during the initial weeks following an acute stroke [34,35].

BBT. was also utilized, which is a simple measure used to assess gross motor skills in patients who have suffered a stroke. The test involves moving 150 wooden blocks in one minute from one compartment to another within a divided box, first using the unaffected upper limb and then the affected one. The score is determined by manually counting the number of blocks transported correctly in that time period [36,37].

MAL-30. The scale, constructed from a semi-structured interview, assesses the quantity and quality of the use of the affected upper limb in the performance of Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) in individuals who have suffered a stroke. It contains 30 items in each of the quantity and quality subscales. Scores are assigned independently for each of them, ranging from 0 (the affected arm is never used for the activity) to 5 (ability to use the affected arm for this activity at the same level as before the stroke).

The sum of all scores results in a total score obtained by averaging the items responded to (it is not necessary to respond to all items, only those for which the arm was used before the stroke). Therefore, a higher score on this scale indicates better movement quality and more normalized use of the affected upper limb in performing activities. The assessment is based on the patient's report and not on a direct evaluation of their motor function. Several studies support the robust psychometric properties of this instrument [38–42]; and it is a tool translated into Spanish and validated in the Spanish population that has suffered a stroke [5].

FIM-FAM. The Functional Independence Measure (FIM) is used to assess the level of autonomy in Activities of Daily Living (ADL). It is a global measure of disability consisting of 18 items and can be used independently or with an additional 12 items belonging to the FAM. It uses a scoring system ranging from 1 to 7, where 1 represents total dependence and 7 indicates total independence. The total possible score is 210, with a minimum score of 30 [43–45].

SS-QoL. This instrument is a specific questionnaire designed to assess the QoL in patients who have experienced a stroke. It distinguishes itself from other questionnaires by including items addressing vision, cognition, and communication. It is applicable even to patients with ischemic or hemorrhagic stroke and motor aphasia. The Spanish version has proven to be valid, reliable, and practical.

It consists of 38 items grouped into 8 areas (physical state, communication, cognition, emotions, feelings, Activities of Daily Living, common daily life activities, and socio-family functions), with two additional questions about sexual function and work activity. The rating scale ranges from 1 to 5, where 1 represents no difficulty in performing the tasks presented, and 5 indicates extreme difficulty. This instrument is the first developed in Spanish specifically to measure the QoL in patients who have suffered a stroke [46].

The following Table 1 shows the instruments or scales used for measurement in this study and the variables measured by each of them.

Table 1. Clinical variables of the sample.

Used scales	Variables measured
ARAT	Functionality, fine motor skills, and gross motor skills
BBT	Functionality, fine motor skills, and gross motor skills
MAL-30	Quantity and quality of use of the affected arm
FIM-FAM	Autonomy
SS-QoL	Quality of life

ARAT: Action Research Arm Test; BBT: Box and Blocks Test; MAL-30: Motor Activity Log; FIM-FAM: Functional Independence Measure-Functional Assessment Measure; SS-QoL: Stroke-Specific Quality of Life Scale.

2.4. Intervention

2.4.1. Mirror Therapy

In the course of MT treatment, the patient would be seated in a chair with forearms placed on a table, and a mirror would be positioned between both arms at a right angle to the torso. The affected limb was situated behind the mirror, outside the patient's field of vision, in a comfortable posture. Simultaneously, the healthy limb was arranged so that its reflection in the mirror was distortion-free, ensuring the removal of any objects or symbols exclusively visible to the healthy limb.

MT was executed through three distinct modes. Initially, in the first mode, the patient endeavored to replicate the movement of the healthy hand with the affected hand in a synchronized manner. Subsequently, in the second mode, the patient envisioned themselves performing the mirrored movement of the healthy hand with the affected hand. Finally, in the third mode, the therapist aided the patient's affected hand in mimicking the movement of the healthy hand. The exercises commenced with uncomplicated movements without objects in the initial sessions, progressed to movements involving objects in the intermediate sessions, and ultimately incorporated more intricate movements with objects in the concluding sessions. The progression was individually adapted based on the patient's recovery, commencing with initial mental imagery and advancing to therapist-assisted execution. All exercises were executed deliberately and repeated at least 15 times, with adjustments to complexity according to each patient's individual capacities and limitations.

2.4.2. Cognitive Therapeutic Exercise

CTE are organized into three tiers: primary, secondary, and tertiary levels. Initially, all patients participated in primary-level exercises to acquire proficiency in managing the stretching reaction, adjusting intensity, duration, and localization. Once this proficiency was attained, they advanced to secondary-level exercises. Later, tertiary-level exercises were introduced, wherein patients acquired the skill to modify movements based on perceptual hypotheses, having automated the control of abnormal secondary-grade motor behaviors.

At the primary level, the focus was on addressing excessive stretching reactions (spasticity) and diminished sensitivity, with the therapist executing movements alongside the patient. These exercises demanded the patient's constant active attention. Moving to the secondary level, efforts were directed towards managing the involuntary activation of muscle groups (abnormal irradiation). Here, the patient executed movements with minimal therapist assistance, incorporating various tactile, kinetic, weight, grip, and friction stimuli, combined with primary-level exercises. In the tertiary level, the emphasis was placed on controlling voluntary movements, involving their fragmentation, variability, and adaptation, with the ultimate goal of achieving complete automation of movements without any therapeutic assistance from the patient.

2.4.3. Task-Oriented Training

TOT was structured sequentially, adapting in each session to simulate everyday situations. Complex activities were broken down into simpler tasks to facilitate learning. Activities included the preparation and organization of food, handling clothing (both upper and lower), and personal care, covering actions such as brushing teeth, combing hair, or shaving, and even applying makeup. Brief rest periods were interspersed, and the difficulty of tasks increased gradually to enhance their execution.

2.5. Statistical Analysis

Descriptive analyses of the sample characteristics were conducted, presenting categorical variables in absolute frequencies and percentages, and continuous variables in means and standard deviations (SD). The normality of the dataset was assessed using the Kolmogorov-Smirnov test.

To analyze differences between groups concerning various assessments conducted during the intervention, an analysis of covariance (ANCOVA) was employed. In this analysis, the treatment group to which participants belonged was considered a fixed factor, while the differential scores of the evaluated variables (such as functionality, fine and gross motor skills, level of autonomy, and QoL were used as dependent variables, with the initial values of these same variables used as covariates.

To calculate the sample size, a formula adjusted for finite populations was used. This involved taking into account a known proportion of stroke cases in the population, relying on information from the National Institute of Statistics (INE) [29], and aiming for an estimated margin of error of 1%. Consequently, it was determined that the sample should include 81 stroke patients.

The statistical analysis was conducted using IBM SPSS Statistics version 28 (IBM Inc., Chicago, IL, USA). A significance level of $p < 0.05$ was considered indicative of statistical significance.

3. Results

The data were collected from 120 patients one month after suffering a stroke. The average age of these patients was 68.92 ± 11.79 years (range 41-96). The gender distribution was 58.3% for males (n=70) and 41.7% for females (n=50). Most participants were right-handed (95.8%; n=115). Additionally, an equal distribution was observed regarding the affected side, with 51.7% of participants experiencing impairment in the left upper limb (n=62) and 48.3% in the right (n=58). A similar distribution was found in relation to dominance, with 46.7% (n=56) of individuals showing a match between the affected upper limb and dominance, while 53.3% (n=64) did not match.

Regarding the diagnosed stroke type, the vast majority were cases of ischemic stroke (92.5%; n=111), while a smaller proportion corresponded to hemorrhagic strokes (6.7%; n=8). Table 2 provides some clinical variables of the sample.

Similarly, the distribution among the groups was 33.3% (n=40) for each, i.e., the CG, the MT group, and the CTE group.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 1 February 2024 doi:10.20944/preprints202402.0050.v1

Table 2 shows the differences found in the analysis between the treatment groups and the differential scores obtained between the first and second evaluation in the functionality of the affected upper limb, fine and gross motor skills, quantity and quality of use of the affected upper limb, autonomy, and QoL of stroke patients.

Statistically significant differences were obtained for all of them in functionality and gross and fine motor skills of the affected upper limb measured with ARAT ($F_{(2.116)}$= 13.513. p<0.001; η^2p= 0.189) and BBT ($F_{(2.116)}$= 10.741. p<0.001; η^2p= 0.156), the quantity and quality of use of the affected upper limb compared to the pre-stroke situation ($F_{(2.116)}$= 9.850. p<0.001; η^2p= 0.254 and $F_{(2.116)}$= 6.143. p=0.003; η^2p= 0.096), level of autonomy ($F_{(2.116)}$= 5.288. p=0.006; η^2p= 0.084), and QoL ($F_{(2.116)}$= 7.331. p<0.001; η^2p= 0.112).

Significant or highly significant differences are observed between the CG scores and the two GEs ps in all evaluated variables. However, no statistically significant differences are observed between the two GEs.

Table 2. ANCOVA analysis between the treatment group and the first-second evaluation.

Variables	Group	First evaluation mean (SD)	Second evaluation mean (SD)	Treatment group	Mean difference	SD	P	95% CI LI	95% CI LS	Observed power
Functionality, fine motor skills, and gross motor skills (ARAT)	CG	38.13 (22.129)	35.58 (24.552)	CTE	-10.537	2.738	<0.001**	-15.960	-5.114	0.998
				MT	-13.613	2.735	<0.001**	-19.029	-8.197	
	CTE	29.15 (20.482)	38.45 (19.833)	CG	10.537	2.738	<0.001**	5.114	15.960	
				MT	-3.076	2.694	0.256	-8.413	2.260	
	MT	29.50 (18.902)	41.83 (18.940)	CG	13.613	2.735	<0.001**	8.197	19.029	
				CTE	3.076	2.694	0.256	-2.260	8.413	
Functionality, fine motor skills, and gross motor skills (BBT)	CG	25.08 (24.091)	26.50 (24.496)	CTE	-5.473	2.050	0.009*	-9.533	-1.412	0.989
				MT	-9.380	2.030	<0.001**	-13.401	-5.359	
	CTE	16.80 (14.141)	23.93 (15.562)	CG	5.473	2.050	0.009*	1.412	9.533	
				MT	-3.907	2.021	0.056	-7.910	0.095	
	MT	19.80 (15.955)	30.75 (19.454)	CG	9.380	2.030	<0.001**	5.359	13.401	
				CTE	3.907	2.021	0.056	-0.095	7.910	
Quantity of use of the affected arm (MAL-30)	CG	2.39 (2.173)	2.51 (2.221)	CTE	-0.471	0.264	0.077	-0.995	0.052	0.930
				MT	-1.001	0.263	<0.001**	-1.523	-0.480	
	CTE	1.92 (1.955)	2.64 (1.479)	CG	0.471	0.264	0.077	-0.052	0.995	
				MT	-0.530	0.264	0.047*	-1.052	-0.008	
	MT	2.19 (2.012)	3.37 (1.845)	CG	1.001	0.263	<0.001**	0.480	1.523	
				CTE	0.530	0.264	0.047*	0.008	1.052	
Quality of use of the affected arm (MAL-30)	CG	2.33 (2.149)	2.52 (2.270)	CTE	-0.378	0.261	0.151	-0.895	0.140	0.882
				MT	-0.906	0.260	0.001**	-1.421	-0.391	
	CTE	1.75 (1.753)	2.46 (1.466)	CG	0.378	0.261	0.151	-0.140	0.895	
				MT	-0.529	0.260	0.044*	-1.043	-0.015	
	MT	1.99 (1.911)	3.16 (1.788)	CG	0.906	0.260	0.001**	0.391	1.421	
				CTE	0.529	0.260	0.044*	0.015	1.043	
Autonomy (FIM-FAM)	CG	135.60 (63.501)	141.00 (61.624)	CTE	-4.530	4.287	0.293	-13.020	3.960	0.827
				MT	-13.558	4.262	0.002*	-21.999	-5.118	
	CTE			CG	4.530	4.287	0.293	-3.960	13.020	

		156.70 (33.636)	167.88 (28.886)	MT	-9.028	4.215	0.034*	-17.377	-0.679	
	MT	152.73 (35.814)	169.65 (27.023)	CG	13.558	4.262	0.002*	5.118	21.999	
				CTE	9.028	4.215	0.034*	0.679	17.377	
QoL (SS-QoL)	CG	105.53 (37.989)	100.58 (37.043)	CTE	1.618	3.411	0.636	-5.138	8.375	0.993
				MT	11.957	3.386	0.001**	5.251	18.663	
	CTE	96.03 (26.105)	90.88 (28.987)	CG	-1.618	3.411	0.636	-8.375	5.138	
				MT	10.338	3.406	0.003*	3.593	17.084	
	MT	104.48 (30.573)	93.06 (31.292)	CG	-11.957	3.386	0.001**	-18.663	-5.251	
				CTE	-10.338	3.406	0.003*	-17.084	-3.593	

ARAT: Action Research Arm Test; BBT: Box and Blocks Test; MAL-30: Motor Activity Log; FIM-FAM: Functional Independence Measure-Functional Assessment Measure; SS-QoL: Stroke-Specific Quality of Life Scale; CG: Control Group; CTE: Cognitive Therapeutic Exercise; MT: Mirror Therapy. * $p<0.05$; ** $p<0.001$.

In Table 3, the differences found in the analysis between the treatment groups and the differential scores obtained between the first and third evaluation in the functionality of the upper limb, fine and gross motor skills, quantity and quality of use of the affected upper limb, autonomy, and QoL in stroke patients are observed.

Statistically significant differences were obtained for the functionality and gross and fine motor skills of the affected upper limb measured with ARAT ($F_{(2.116)}$= 8.138. $p<0.001$; η^2p= 0.123) and BBT ($F_{(2.116)}$= 11.987. $p<0.001$; η^2p= 0.171), the quantity and quality of use of the affected upper limb compared to the situation before the stroke ($F_{(2.116)}$= 7.978. $p<0.001$; η^2p= 0.121 and $F_{(2.116)}$= 8.958. $p<0.001$; η^2p= 0.134), and QoL ($F_{(2.116)}$= 10.244. $p<0.001$; η^2p= 0.150).

However, no statistically significant differences were observed in the functionality and fine and gross motor skills of the right affected upper limb measured with the BBT ($F_{(2.116)}$= 1.674. p=0.197; η^2p= 0.058), nor for autonomy ($F_{(2.116)}$= 2.088. p=0.129; η^2p= 0.035).

Similar to Table 2, significant or highly significant differences are observed between the scores of the CG and the two GEs in all the aforementioned significant variables, but not between the two GEs.

Table 3. Analysis of Covariance (ANCOVA) between the treatment group and the first-third evaluation.

Variables	Group	First evaluation mean (SD)	Third evaluation mean (SD)	Treatment group	Mean difference	SD	P	95% CI LI	95% CI LS	Observed power
Functionality, fine motor skills, and gross motor skills (ARAT)	CG	38.13 (22.129)	36.75 (24.330)	CTE	-10.067	2.827	<0.001**	-15.667	-4.467	0.994
				MT	-13.315	2.824	<0.001**	-18.908	-7.722	
	CTE	29.15 (20.482)	39.08 (21.007)	CG	10.067	2.827	<0.001**	4.467	15.667	
				MT	-3.248	2.782	0.245	-8.759	2.263	
	MT	29.50 (18.902)	42.63 (19.228)	CG	13.315	2.824	<0.001**	7.722	18.908	
				CTE	3.248	2.782	0.245	-2.263	8.759	
Functionality, fine motor skills, and gross motor skills (BBT)	CG	25.08 (24.091)	29.08 (24.986)	CTE	-12.165	3.144	<0.001**	-18.393	-5.938	0.955
				MT	-9.199	3.113	0.004*	-15.365	-3.033	
	CTE	16.80 (14.141)	34.30 (16.857)	CG	12.165	3.144	<0.001**	5.938	18.393	
				MT	2.966	3.099	0.341	-3.172	9.104	

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 1 February 2024 doi:10.20944/preprints202402.0050.v1

	MT	19.80	33.865	CG	9.199	3.113	0.004*	3.033	15.365	
		(15.955)	(19.705)	CTE	-2.966	3.099	0.341	-9.104	3.172	
Quantity of use of the affected arm (MAL-30)	CG	2.39	2.73	CTE	-0.690	0.267	0.011*	-1.219	-0.160	0.951
		(2.173)	82.327)	MT	-1.047	0.266	<0.001**	-1.575	-0.520	
	CTE	1.92	3.08	CG	0.690	0.267	0.011*	0.160	1.219	
		(1.955)	(1.605)	MT	-0.358	0.267	0.182	-0.886	0.170	
	MT	2.19	3.64	CG	1.047	0.266	0.000	0.520	1.575	
		(2.012)	(1.637)	CTE	0.358	0.267	0.182	-0.170	0.886	
Quality of use of the affected arm (MAL-30)	CG	2.33	2.61	CTE	-0.698	0.259	0.008	-1.211	-0.185	0.970
		(2.149)	(2.274)	MT	-1.076	0.258	<0.001	-1.586	-0.566	
	CTE	1.75	2.87	CG	0.698	0.259	0.008	0.185	1.211	
		(1.753)	(1.612)	MT	-0.378	0.257	0.144	-0.887	0.132	
	MT	1.99	3.43	CG	1.076	0.258	<0.001	0.566	1.586	
		(1.911)	(1.606)	CTE	0.378	0.257	0.144	-0.132	0.887	
Autonomy (FIM-FAM)	CG	135.60	152.55	CTE	-1.522	3.683	0.680	-8.817	5.773	0.422
		(63.501)	(55.492)	MT	5.510	3.662	0.135	-1.742	12.763	
	CTE	156.70	176.13	CG	1.522	3.683	0.680	-5.773	8.817	
		(33.636)	(26.296)	MT	7.032	3.622	0.055	-0.142	14.206	
	MT	152.73	172.45	CG	-5.510	3.662	0.135	-12.763	1.742	
		(35.814)	(26.345)	CTE	-7.032	3.622	0.055	-14.206	0.142	
QoL (SS-QoL)	CG	105.53	85.18	CTE	-20.768	5.173	<0.001	-31.014	-10.523	0.985
		(37.989)	(37.332)	MT	-19.570	5.135	<0.001	-29.739	-9.400	
	CTE	96.03	82.98	CG	20.768	5.173	<0.001	10.523	31.014	
		(26.105)	(27.945)	MT	1.199	5.165	0.817	-9.030	11.428	
	MT	104.48	84.00	CG	19.570	5.135	<0.001	9.400	29.739	
		(30.573)	(27.133)	CTE	-1.199	5.165	0.817	-11.428	9.030	

ARAT: Action Research Arm Test; BBT: Box and Blocks Test; MAL-30: Motor Activity Log; FIM-FAM: Functional Independence Measure-Functional Assessment Measure; SS-QoL: Stroke-Specific Quality of Life Scale; CG: Control Group; CTE: Cognitive Therapeutic Exercise; MT: Mirror Therapy. * $p<0.05$; ** $p<0.001$.

4. Discussion

The aim of this study was to assess the effectiveness of combined MT and CTE with TOT in patients with acute stroke regarding the functionality of the affected upper limb, fine and gross motor skills, the quantity and quality of the affected limb's use, autonomy, and QoL.

Our results demonstrate a significant improvement in scores after the application of complementary treatment, between the first and second assessment, following 20 sessions of MT or CTE combined with TOT in the GEs compared to the CG, which received only standard therapy. In addition to the differences found between scores obtained in the first and second assessments, statistically significant differences are also observed between the GEs and the CG in the differential scores between the first and third assessments. This indicates that the GEs showed a superior improvement in all analyzed variables, without significant differences between them. Statistically significant improvements are also evident in our results when considering long-term scores. Comparing scores between the first assessment and the third, i.e., 3 months after the second assessment or the intervention's completion, statistically significant differences can be observed for the measured variables. In addition to finding significant improvement, it appears that the improvements achieved are maintained in the long term.

 doi:10.20944/preprints202402.0050.v1

Statistically significant differences are observed for the functionality and fine and gross motor skills of the affected upper limb, measured with the ARAT and BBT scales ($p<0.001$), the quantity of use of the affected upper limb compared to the pre-stroke situation ($p<0.001$), and QoL ($p<0.001$). Other studies employing the same assessment instruments also suggest that MT intervention is beneficial for improving the motor functionality of the right upper limb, with MT being more effective than other therapies [47–49]. This may be attributed to the visual stimulation provided to the hemiplegic upper limb through the reflection of the normal side, which, in turn, stimulates the cerebral cortex and spinal area, replacing the lost proprioceptive sense. Additionally, it activates mirror neurons when observing, imagining, or attempting to execute movements [50].

Furthermore, QoL in the GEs is higher than in the CG. These results align with other studies indicating that applying MT and CTE treatment improves QoL [48], or even that any form of intervention, regardless of the therapy, significantly enhances QoL [19,51]. It is noteworthy that low functionality of the affected upper limb is the primary predictor of low QoL [52]. Statistically significant differences were also observed for the variables of quality of use of the affected upper limb compared to the pre-stroke situation ($p=0.003$) and the level of autonomy ($p=0.006$). These results are also supported by previous research, where a physical exercise intervention program improved motor capacity and functionality, in addition to enhancing levels of self-confidence, motivation, and subjective perception of effort towards performing daily life tasks that involved active participation and muscle group engagement [47–50]

Similarly, statistically significant differences are observed between the two GEs and the CG, showing a superior improvement in both GEs compared to the CG. However, no statistically significant differences were found between the two GEs where TOT was combined with MT and CTE. Therefore, it seems that engaging in physical activity with the aim of recovering mobility and functionality of the affected limb, regardless of its nature, is better than implementing a more austere program based on the non-application of physical exercise to avoid functional discomfort and patient discomfort, as advanced by the majority of the scientific literature on this topic [50–52].

As seen, there are significant differences in the quantity and quality of the use of the affected upper limb compared to the pre-stroke situation. This is supported by other studies indicating that after a stroke, many patients continue to use their affected upper limb in ADL in addition to its use in therapy, achieving normal performance [53]. However, it is worth noting that, to the best of the authors' knowledge, there is no study to date that has considered whether the affected limb coincides with the patient's dominant limb. Applying logic based on findings from investigations in other scientific fields, such as those analyzing the effects of the same training load on muscle performance in the dominant and non-dominant limb, it could be that patients whose affected limb coincides with their dominant limb obtain greater functional benefits and motor competence than those where the affected and dominant limbs do not coincide. Alternatively, training on the non-affected limb may stimulate gains or prevent losses in neuromotor recruitment on the affected limb [54–58]. However, future research should develop and confirm this research hypothesis.

The study presents certain limitations, such as the small sample size, which hinders the extrapolation of results. It would be beneficial to expand the sample to improve representativity. Additionally, slightly adjusting the inclusion and exclusion criteria could facilitate participant selection, as recruitment was hindered by the difficulty in finding patients who met all the proposed criteria. Furthermore, the study's initiation before the pandemic made recruitment challenging over an extended period, and many recruited patients experienced the pre-COVID period or interrupted treatments due to infection, which could have influenced the results in some way. Similarly, the clinical context in which the study was conducted may limit the extrapolation of results to other contexts.

Some future lines of research that could be pursued include long-term follow-up of patients to better understand how initial improvement translates into longer-term outcomes. Combined interventions with other therapeutic methods could be implemented and compared to observe improvements or effectiveness. The study could include additional emotional variables that may influence the relationship between motor skills, functional outcomes, autonomy, or QoL, such as cognitive ability, emotional status, or social participation.

5. Conclusions

In conclusion, our results have demonstrated the effectiveness of combining MT and CTE techniques simultaneously with TOT to improve functionality of the affected upper limb, fine and gross motor skills, the quantity and quality of use of the affected upper limb compared to the pre-stroke situation, autonomy, and QoL.

Furthermore, a significant improvement was observed for all variables following the completion of treatment and sometime thereafter, suggesting that the majority of the achieved improvements persist beyond the treatment period.

However, it can also be concluded that both techniques yield positive results for the improvement of the variables used in the study. Both MT and CTE have shown significant results for all variables, with no significant differences between the GEs. Therefore, both MT and CTE, along with their combination with TOT, are suitable choices for addressing functionality, fine and gross motor skills, the use of the upper limb, autonomy, and QoL in the acute and subacute phases of patients who have suffered a stroke.

Author Contributions: The following statements should be used "Conceptualization. J.F.-S. and M.S.-P.; methodology. J.J.G.-B. and J.G.-S.; software. J.F.-S. and M.S.-P.; validation. J.F.-S. and M.S.-P.; formal analysis. S.A.-P. and A.M.-V.; investigation. J.F.-S., J.G.-S. and R.V.-S.; resources. S.A.-P. and R.V.-S.; data curation. J.F.-S.; writing—original draft preparation. S.A.-P., A.M.-V. and R.V.-S.; writing—review and editing. S.A.-P., A.M.-V. and R.V.-S.; visualization. J.F.-S. and J.J.G.-B.; supervision. M.S.-P. and J.G.-S.; project administration. J.J.G.-B. and J.G.-S. All authors have read and agreed to the published version of the manuscript."

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the University Hospital of Burgos (HUBU 2134/2019, 25 June 2019).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Owolabi MO, Thrift AG, Mahal A, Ishida M, Martins S, Johnson WD, et al. Primary stroke prevention worldwide: translating evidence into action. The Lancet Public health. 2022;7(1):e74–85.
2. Feigin VL, Brainin M, Norrving B, Martins S, Sacco RL, Hacke W, et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. International journal of stroke : official journal of the International Stroke Society. 2022;17(1):18–29.
3. Poltawski L, Allison R, Briscoe S, Freeman J, Kilbride C, Neal D, et al. Assessing the impact of upper limb disability following stroke: a qualitative enquiry using internet-based personal accounts of stroke survivors. Disability and rehabilitation. 2016;38(10):945–51.
4. Sivan M, O'Connor RJ, Makower S, Levesley M, Bhakta B. Systematic review of outcome measures used in the evaluation of robot-assisted upper limb exercise in stroke. Journal of rehabilitation medicine. 2011;43(3):181–9.
5. Santamaría-Peláez M, Pardo-Hernández R, González-Bernal JJ, Soto-Cámara R, González-Santos J, Fernández-Solana J. Reliability and Validity of the Motor Activity Log (MAL-30) Scale for Post-Stroke Patients in a Spanish Sample. International journal of environmental research and public health. 2022;19(22).
6. Fernández-Solana J, Pardo-Hernández R, González-Bernal JJ, Sánchez-González E, González-Santos J, Soto-Cámara R, et al. Psychometric Properties of the Action Research Arm Test (ARAT) Scale in Post-Stroke Patients-Spanish Population. International journal of environmental research and public health. 2022;19(22).
7. Fernández-Concepción O, Ramírez-Pérez E, Álvarez MA, Buergo-Zuáznabar MA. Validation of the stroke-specific quality of life scale (ECVI-38). Revista de Neurologia. 2008;46(3):147–52.
8. Colomer C, Llorens R, Sánchez C, Ugart P, Moliner B, Navarro MD, et al. Reliability and validity of the Spanish adaptation of the Functional Independence Measure + Functional Assessment Measure. European journal of physical and rehabilitation medicine. 2023;59(4):452–7.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 1 February 2024 doi:10.20944/preprints202402.0050.v1

9. Furuta H, Mizuno K, Unai K, Ebata H, Yamauchi K, Watanabe M. Functional Independence Measure Subtypes among Inpatients with Subacute Stroke: Classification via Latent Class Analysis. Progress in rehabilitation medicine. 2022;7(0):n/a.
10. Hsieh HC, Liao RD, Yang TH, Leong CP, Tso HH, Wu JY, et al. The clinical effect of Kinesio taping and modified constraint-induced movement therapy on upper extremity function and spasticity in patients with stroke: a randomized controlled pilot study. European journal of physical and rehabilitation medicine. 2021;57(4):511–9.
11. Heart & Stroke Foundation. Canadian Partnership for Stroke Recovery. Clinician's Handbook ꟾ EBRSR - Evidence-Based Review of Stroke Rehabilitation [Internet]. [cited 2023 Nov 30]. Available from: https://www.ebrsr.com/clinician-handbook
12. Muñoz-Gómez E, Inglés M, Aguilar-Rodríguez M, Sempere-Rubio N, Mollà-Casanova S, Serra-Añó P. Effects of mirror therapy on spasticity and sensory impairment after stroke: Systematic review and meta-analysis. PM & R : the journal of injury, function, and rehabilitation. 2023;15(11).
13. Nogueira NG de HM, Parma JO, Leão SES de A, Sales I de S, Macedo LC, Galvão ACDR, et al. Mirror therapy in upper limb motor recovery and activities of daily living, and its neural correlates in stroke individuals: A systematic review and meta-analysis. Brain research bulletin. 2021;177:217–38.
14. Kundi MK, Spence NJ. Efficacy of mirror therapy on lower limb motor recovery, balance and gait in subacute and chronic stroke: A systematic review. Physiotherapy research international : the journal for researchers and clinicians in physical therapy. 2023;28(2).
15. Seyyah M, Topuz S. The effect of mirror therapy on joint movement, pain and functionality in acute upper limb burns. Burns : journal of the International Society for Burn Injuries. 2023;49(6):1432–8.
16. Diaz Castro WM, Rodriguez Lopez YC. Método Perfetti como Estrategia Terapéutica en la Rehabilitación de Pacientes con Enfermedad Cerebrovascular: Revisión Bibliográfica. Movimiento Científico, ISSN-e 2011-7191, Vol 13, No 1, 2019, págs 65-70. 2019;13(1):65–70.
17. Serrat M, Sanabria-Mazo JP, Almirall M, Musté M, Feliu-Soler A, Méndez-Ulrich JL, et al. Effectiveness of a Multicomponent Treatment Based on Pain Neuroscience Education, Therapeutic Exercise, Cognitive Behavioral Therapy, and Mindfulness in Patients With Fibromyalgia (FIBROWALK Study): A Randomized Controlled Trial. Physical Therapy. 2021;101(12):1–12.
18. Parra Horta MA. Evidencia del aprendizaje motor en el ejercicio terapéutico cognoscitivo: artículo de revisión. fisioGlía: revista de divulgación en Fisioterapia, ISSN-e 2340-6151, Vol 5, No 3, 2018, págs 53-56. 2018;5(3):53–6.
19. Alsubiheen AM, Choi W, Yu W, Lee H. The Effect of Task-Oriented Activities Training on Upper-Limb Function, Daily Activities, and Quality of Life in Chronic Stroke Patients: A Randomized Controlled Trial. International journal of environmental research and public health. 2022;19(21).
20. Almhdawi KA, Mathiowetz VG, White M, delMas RC. Efficacy of Occupational Therapy Task-oriented Approach in Upper Extremity Post-stroke Rehabilitation. 2016;23(4):444–56.
21. Preissner K. Use of the Occupational Therapy Task-Oriented Approach to optimize the motor performance of a client with cognitive limitations. The American journal of occupational therapy : official publication of the American Occupational Therapy Association. 2010;64(5):727–34.
22. Cano-de-la-Cuerda R, Molero-Sánchez A, Carratalá-Tejada M, Alguacil-Diego IM, Molina-Rueda F, Miangolarra-Page JC, et al. Theories and control models and motor learning: clinical applications in neuro-rehabilitation. Neurologia (Barcelona, Spain). 2015;30(1):32–41.
23. Michaelsen SM, Dannenbaum R, Levin MF. Task-specific training with trunk restraint on arm recovery in stroke: randomized control trial. Stroke. 2006;37(1):186–92.
24. Bayón-Calatayud M, Gil-Agudo A, Benavente-Valdepeñas AM, Drozdowskyj-Palacios O, Sanchez-Martín G, Del Alamo-Rodriguez MJ. Eficacia de nuevas terapias en la neurorrehabilitación del miembro superior en pacientes con ictus. Rehabilitación. 2014;48(4):232–40.
25. Bai Z, Zhang J, Zhang Z, Shu T, Niu W. Comparison Between Movement-Based and Task-Based Mirror Therapies on Improving Upper Limb Functions in Patients With Stroke: A Pilot Randomized Controlled Trial. Frontiers in Neurology. 2019;10:288.
26. Waghavkar SN, Ganvir SS. Effectiveness of Mirror Therapy to Improve Hand Functions in Acute and Subacute Stroke Patients. International Journal of Neurorehabilitation. 2015;02(04).
27. Gomez-Moreno SM, Cuadrado ML, Cruz-Orduña I, Martínez-Acebes EM, Gordo-Mañas R, Fernández-Pérez C, et al. Validation of the Spanish-language version of the Montreal Cognitive Assessment as a screening test for cognitive impairment in multiple sclerosis. Neurologia (Barcelona, Spain). 2021;
28. Ramírez-Moreno JM, Bartolomé Alberca S, Muñoz Vega P, Guerrero Barona EJ. Screening for cognitive impairment with the Montreal Cognitive Assessment in Spanish patients with minor stroke or transient ischaemic attack. Neurologia (Barcelona, Spain). 2019;37(1):38–44.
29. Instituto Nacional de Estadística (INE). Problemas o enfermedades crónicas o de larga evolución en los últimos 12 meses según sexo, país de nacimiento y grupo de edad. Población de 15 y más años. [Internet].

[cited 2023 Nov 30]. Available from: https://www.ine.es/jaxi/Datos.htm?path=/t15/p420/a2014/p01/l0/&file=02009.px
30. Luo Z, Zhou Y, He H, Lin S, Zhu R, Liu Z, et al. Synergistic Effect of Combined Mirror Therapy on Upper Extremity in Patients With Stroke: A Systematic Review and Meta-Analysis. Frontiers in neurology. 2020;11.
31. Saavedra-García A, Moral-Munoz JA, Lucena-Anton D. Mirror therapy simultaneously combined with electrical stimulation for upper limb motor function recovery after stroke: a systematic review and meta-analysis of randomized controlled trials. Clinical rehabilitation. 2021;35(1):39–50.
32. Pérez-Cruzado D, Merchán-Baeza JA, González-Sánchez M, Cuesta-Vargas AI. Systematic review of mirror therapy compared with conventional rehabilitation in upper extremity function in stroke survivors. Australian occupational therapy journal. 2017;64(2):91–112.
33. Kwakkel G, Lannin NA, Borschmann K, English C, Ali M, Churilov L, et al. Standardized measurement of sensorimotor recovery in stroke trials: Consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable. International journal of stroke : official journal of the International Stroke Society. 2017;12(5):451–61.
34. Pike S, Lannin NA, Wales K, Cusick A. A systematic review of the psychometric properties of the Action Research Arm Test in neurorehabilitation. Australian occupational therapy journal. 2018;65(5):449–71.
35. Lang CE, Wagner JM, Dromerick AW, Edwards DF. Measurement of upper-extremity function early after stroke: properties of the action research arm test. Archives of physical medicine and rehabilitation. 2006;87(12):1605–10.
36. Hsieh YW, Lin YH, Zhu JD, Wu CY, Lin YP, Chen CC. Treatment Effects of Upper Limb Action Observation Therapy and Mirror Therapy on Rehabilitation Outcomes after Subacute Stroke: A Pilot Study. Behavioural neurology. 2020;
37. Chen CL, Chen CY, Chen HC, Wu CY, Lin KC, Hsieh YW, et al. Responsiveness and minimal clinically important difference of Modified Ashworth Scale in patients with stroke. European journal of physical and rehabilitation medicine. 2019;55(6):754–60.
38. Arlette Doussoulin S, Saiz JL, Blanton S. Propiedades psicométricas de una versión en castellano de la escala Motor Activity Log-30 en pacientes con extremidad superior parética por accidente cerebro vascular. Revista chilena de neuro-psiquiatría. 2013;51(3):201–10.
39. Sada A, Abdullahi A, Hassan AB. Hausa translation, cross-cultural adaptation, and assessment of psychometric properties of the motor activity log. Disability and rehabilitation. 2021;43(16):2375–81.
40. Amaral Saliba V, Penaforte Chaves Júnior I, Coelho de Morais Faria C, Teixeira-Salmela L. Propiedad psicométricas da Motor Activity Log: uma revisão sistemática da literatura. Fisioter. 2008;21(3):59–67.
41. Taub E, Mcculloch K, Uswatte G, Morris DM, Bowman M, Crago J, et al. UAB Training for CI Therapy Motor Activity Log (MAL) Manual. 2011;
42. Van Der Lee JH, Beckerman H, Knol DL, De Vet HCW, Bouter LM. Clinimetric properties of the motor activity log for the assessment of arm use in hemiparetic patients. Stroke. 2004;35(6):1410–4.
43. Law J, Fielding B, Jackson D, Turner-Stokes L. The UK FIM+FAM Extended Activities of Daily Living module: evaluation of scoring accuracy and reliability The UK FIMþFAM Extended Activities of Daily Living module: evaluation of scoring accuracy and reliability. Disability and Rehabilitation. 2008;1–6.
44. Turner-Stokes L, Siegert RJ. A comprehensive psychometric evaluation of the UK FIM + FAM. Disability and rehabilitation. 2013;35(22):1885–95.
45. Nayar M, Vanderstay R, Siegert RJ, Turner-Stokes L. The UK Functional Assessment Measure (UK FIM+FAM): Psychometric Evaluation in Patients Undergoing Specialist Rehabilitation following a Stroke from the National UK Clinical Dataset. PLOS ONE. 2016;11(1):e0147288.
46. Ramírez E, Alvarez MA. Validation of the stroke-specific quality of life scale (ECVI-38). Revista de Neurología. 2008;46:147–52.
47. Carayol M, Ninot G, Senesse P, Bleuse JP, Gourgou S, Sancho-Garnier H, et al. Short- and long-term impact of adapted physical activity and diet counseling during adjuvant breast cancer therapy: the 'APAD1' randomized controlled trial. BMC cancer. 2019;19(1).
48. Damsbo AG, Mortensen JK, Kraglund KL, Johnsen SP, Andersen G, Blauenfeldt RA. Prestroke Physical Activity and Poststroke Cognitive Performance. Cerebrovascular diseases (Basel, Switzerland). 2020;49(6):632–8.
49. Koevoets EW, Schagen SB, de Ruiter MB, Geerlings MI, Witlox L, van der Wall E, et al. Effect of physical exercise on cognitive function after chemotherapy in patients with breast cancer: a randomized controlled trial (PAM study). Breast cancer research : BCR. 2022;24(1).
50. Van Vulpen JK, Peeters PHM, Velthuis MJ, Van Der Wall E, May AM. Effects of physical exercise during adjuvant breast cancer treatment on physical and psychosocial dimensions of cancer-related fatigue: A meta-analysis. Maturitas. 2016;85:104–11.

51. Oberlin LE, Waiwood AM, Cumming TB, Marsland AL, Bernhardt J, Erickson KI. Effects of Physical Activity on Poststroke Cognitive Function: A Meta-Analysis of Randomized Controlled Trials. Stroke. 2017;48(11):3093–100.
52. Ren X, Wang X, Sun J, Hui Z, Lei S, Wang C, et al. Effects of physical exercise on cognitive function of breast cancer survivors receiving chemotherapy: A systematic review of randomized controlled trials. The Breast : Official Journal of the European Society of Mastology. 2022;63:113.
53. Lundquist CB, Nguyen BT, Hvidt TB, Stabel HH, Christensen JR, Brunner I. Changes in Upper Limb Capacity and Performance in the Early and Late Subacute Phase After Stroke. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2022;31(8).
54. Adamson M, MacQuaide N, Helgerud J, Hoff J, Kemi OJ. Unilateral arm strength training improves contralateral peak force and rate of force development. European journal of applied physiology. 2008;103(5):553–9.
55. Carroll TJ, Herbert RD, Munn J, Lee M, Gandevia SC. Contralateral effects of unilateral strength training: evidence and possible mechanisms. Journal of applied physiology (Bethesda, Md : 1985). 2006;101(5):1514–22.
56. McGregor KM, Crosson B, Mammino K, Omar J, García PS, Nocera JR. Influences of 12-Week Physical Activity Interventions on TMS Measures of Cortical Network Inhibition and Upper Extremity Motor Performance in Older Adults-A Feasibility Study. Frontiers in aging neuroscience. 2018;9(JAN).
57. Goodwill AM, Pearce AJ, Kidgell DJ. Corticomotor plasticity following unilateral strength training. Muscle & nerve. 2012;46(3):384–93.
58. Lee M, Gandevia SC, Carroll TJ. Unilateral strength training increases voluntary activation of the opposite untrained limb. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology. 2009;120(4):802–8.