International Journal of EXERCISE SCIENCE

Review Article

Bimanual Coordination in Individuals Post-stroke: Constraints, Rehabilitation Approaches and Measures: Systematic Review

YUTONG LIU[†1], ERYK PRZYSUCHA[‡1], TARYN KLARNER[‡1], CARLOS ZERPA[‡1], and MADARA KESHINI MARANSINGHE[‡2]

[1]School of Kinesiology, Lakehead University, ON, CANADA; 2Public Health and Health Systems, University of Waterloo, ON, CANADA

[†]Denotes graduate student author, [‡]Denotes professional author

ABSTRACT

International Journal of Exercise Science 17(3): 831-851, 2024. To couple or not to couple is a dilemma for the CNS when performing bimanual goal-directed actions. Numerous interacting individual and task-related constraints contribute to the issue of effective movement coordination, and their impact on the emerging actions must be inferred from valid methodologies. This is particularly important when examining coordination in individuals with stroke undergoing rehabilitation. The purpose of this review was to identify the different constraints that may impact inter-limb coupling, and the rehabilitation approaches implemented to enhance those actions. Also, the measures incorporated to examine the effects of rehabilitation methods were reviewed. A literature search was conducted using CINAHL, PubMed and PsycINFO. Following the PRISMA 2020 guidelines, 789 relevant studies were identified, with 20 articles fulfilling the established criteria. Results showed that the impact of sex, time after stroke, type of stroke, and age were not examined in any studies reviewed. In terms of task constraints, most did not examine bimanual coordination explicitly. Bimanual movement training was the most prevalent. Regarding the dependent variables, clinician-reported and performance based scales were frequently used, while only eight studies implemented kinematic analysis, and only three examined inter-limb organization. None made explicit inferences to the existing theories of inter-limb coordination. In conclusion, important individual and task constraints on inter-limb coordination were scarcely examined. Also, majority of the studies did not involve bimanual tasks, or any measures of inter-limb coupling, thus the inferences should be treated with caution. Conceptually, all studies were data driven.

KEY WORDS: Brain damage, upper-extremity, kinematics, inter-limb coordination, control

INTRODUCTION

Across the world, stroke has become the leading cause of death and the main cause of long-term adult disability and dysfunction. In North America, over 1 million of stroke survivors are living with long-term disability that requires assistance with the performance of daily activities. In Canada alone, more than 62,000 stroke cases are reported annually, and 700,000 people who are 20 years of age or older are living with the consequences of stroke. On average a stroke occurs every 30 minutes (4).

A stroke is an injury that results from lack of adequate blood supply to the brain, which is also known as a "brain attack", or a cerebrovascular infarction. An ischemic stroke is most prevalent as it occurs in 87% of all patients, and it results from obstruction of one or more vessel supplying blood to the brain. A hemorrhagic stroke occurs when a weakened blood vessel ruptures, whereas the transient ischemic attack is a brief episode of an ischemic stroke, with clinical symptoms lasting less than one hour, and without evidence of acute infarction. The incidence of stroke increases with age, with the number doubling for each decade after 55 years of age (4). Another factor that affects incidence of strokes is sex, where females have an overall higher lifetime risk of stroke than males because of longer life expectancy.

Motor deficits that are induced by stroke vary but often include partial loss of voluntary control over muscles on the contralateral side of the body from where the stroke occurred in the brain. This condition is often referred to as hemiparesis, which occurs in approximate 80-90% of all stroke survivors. Hemiparesis presents as reduced muscle strength, slower movement speed, and overall difficulties in coordinating and controlling multi-joint actions, including bimanual symmetrical and asymmetrical actions.

Due to the motor deficits resulting from stroke, regaining the capability to coordinate and control both arms has been emphasized. Many different clinical rehabilitation programs have been available, such as bilateral arm training, the use of end-effector robots and exoskeleton robots, as well constraint-induced movement training (CIMT). The effectiveness of these programs varies, and often the nature of the emerging inferences depends on the type of measures incorporated. In the existing literature these measures ranged from outcome focused clinical scales to more precise and accurate kinematic descriptors of the emerging movement patterns. In the context of motor control, the conceptual and methodological approaches implemented to examine issues of inter-limb coordination depended largely on the nature of the tasks being examined. In discrete bimanual actions, the concept of synergy or coordinative structure (24) has been primarily applied to tasks such as bimanual reaching in typically (21) and atypically functioning individuals including stroke patients (18). The status of spatial and temporal coupling between the arms can be examined via qualitative (angle-angle plots) and quantitative (correlational approach) measures derived from the behaviour of end effectors via forward kinematics or measures describing joint actions via inverse kinematics. In terms of rhythmical (continuous) actions the Haken-Kelso-Bunz (HKB) has been implemented in order to examine the elementary rules that underlie the organization of bimanual action (14). In this context, measures such as relative phase have been implemented to examine primarily the stability of temporal coupling between the effectors (22). Collectively, there have been numerous studies that provided an overview of the research focusing on the rehabilitation of bimanual coordination after stroke. However, many of them did not consider the degree to which different individual constraints impact the nature of inter-limb coordination explicitly. And, those that did, often implemented clinical measures exclusively.

Therefore, the first purpose of this project was to systematically review bimanual coordination interventions for stroke patients for the nature of individual and task constraints examined, and the respective interventions implemented. The second purpose was to review dependent variables used to derive inferences about the effectiveness of the respective treatments. The third purpose was to delineate if the rehabilitation studies reviewed were based on explicit conceptual frameworks.

METHODS

Protocol

To extract articles, electronic searches included Cumulative Index within Nursing and Allied Health Literature (CINAHL), PubMed, PsycINFO, and Web of Science databases were used. Google Scholar was used as a secondary search tool. A search string across all databases included the key text words “stroke”, “bimanual”, “coordination”, and “intervention”, along with their synonyms, such as “cerebrovascular accident”, “brain infarction”, “transient ischemic attack”, “brain hemorrhage”, “brain ischemia”, “interlimb”, “bilateral”, “coupled”, “rehabilitation”, “therapy”, “functional training”, “neurorehabilitation”, and “training”, to retrieve the appropriate articles.

Study Selection

The PICO selection criteria was used, which focused on the population of interest, type of intervention, nature of comparison and type of quantitative outcomes observed. It is a commonly used tool to identify components of systematic reviews in evidence-based medicine, and it is endorsed by the Cochrane Collaboration. Thus, the eligible studies for review included participants who were both adult males and females, over 19 years of age, and who have experienced either ischemic, hemorrhagic, or transient ischemic stroke. Regardless of the type of stroke experienced, the participants had to be involved in a bimanual rehabilitation program. The combination of bilateral movement training and supplementary assistive protocols such as auditory or rhythmic cues and active neuromuscular stimulation were accepted if the research met other inclusion criteria outlined previously. Studies involving randomized controlled trials (RCTs) were primarily considered, however pilot studies and cohort studies were also included if they met the inclusion criteria. Studies that were single-case reports without empirical data were excluded. All commentaries, systematic reviews, meta-analyses, studies that were not published in English, and those with non-human subjects were also excluded. To ensure accuracy and reproducibility in the review approach, a Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA) flowchart was used (31).

Quality Assessment for Selected Studies

A quality assessment was carried out using the Downs and Black tool (12). This assessment tool was designed to examine the quality of study reporting, external validity, internal validity, as well as statistical power. The Downs & Black scale has been ranked in the top six quality assessment scales that are suitable for use in systematic reviews (12). Downs and Black score ranges were grouped into good (>19), fair (15-19), and poor (<15).

Quality Assessment for Review

A quality assessment tool for the current review was also included. The tool was the upgraded version of the “A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) scale (AMATAR-

2) (34). AMSTAR-2 was a 16-item assessment tool that evaluated systematic reviews of both randomized and non-randomized studies of healthcare interventions (34). The use of AMSTAR-2 ensures the methodological quality of the review.

RESULTS

Characteristics of Included Studies

The search yielded 789 titles/abstracts across the four databases. After the elimination of duplicates, 652 titles/abstracts remained for analysis. These abstracts were obtained and assessed based on the inclusion criteria. Among the 652 abstracts, 622 records were excluded.

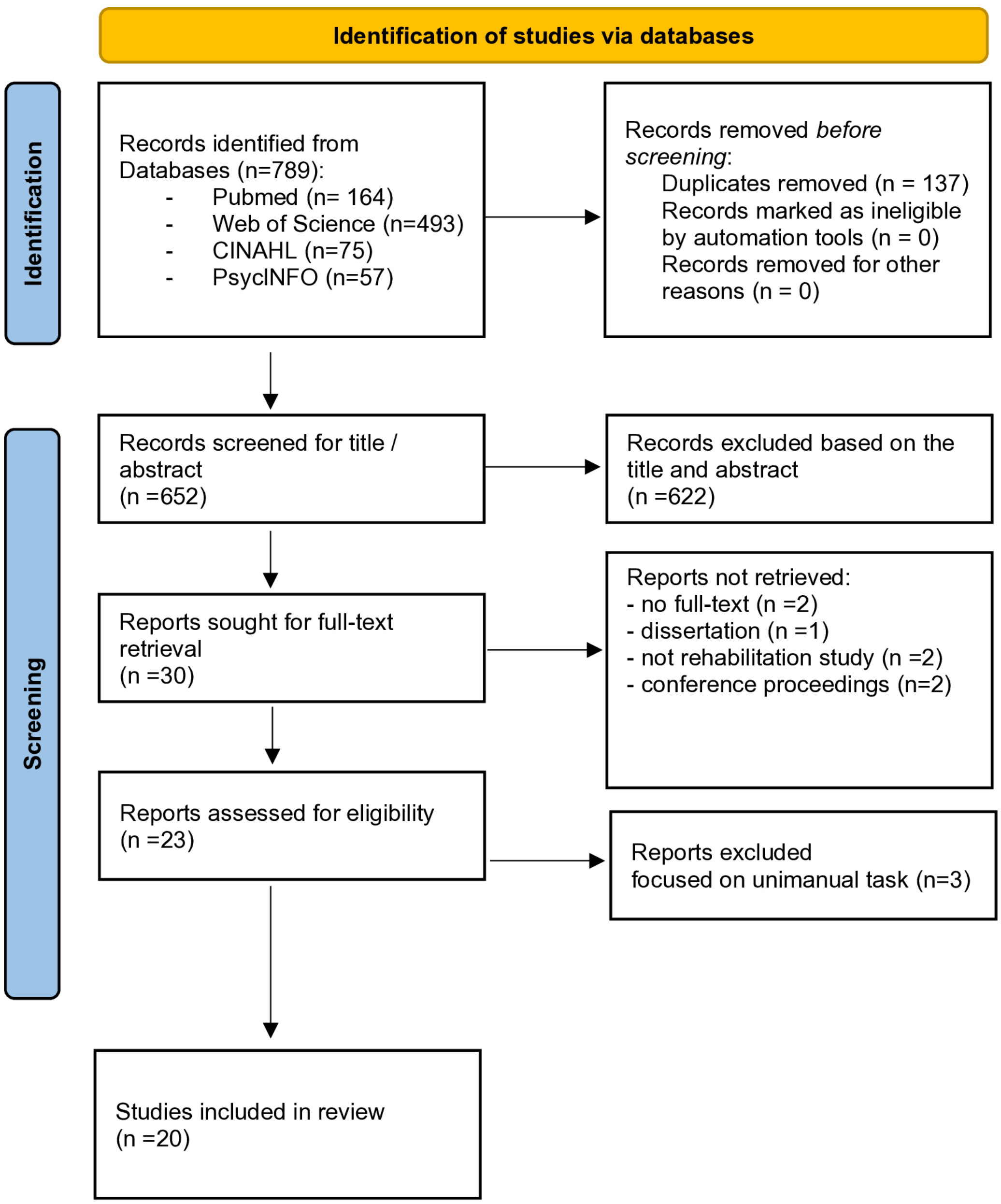

Figure 1. PRISMA flowchart for identification and inclusion of studies.

After the initial screening, 30 possibly relevant abstracts were retrieved for full-text screening. Two reviewers (Y.L.) and (T.K.) independently screened the full text of 30 articles and 10 additional studies were excluded. At the end of the screening, 20 eligible articles were included in this review. Collectively, fifteen randomized controlled trials (RCTs), four pilot studies and one cohort study were included, and all were published between 2000 and 2022.The screening and selection process is presented in a PRISMA flowchart (Figure 1).

Also, the overview of the included studies is presented in Table 1, whereas the author's assessment of risk for bias is presented in Table 2. Across the different categories, the primary concerns were detected in regards to allocation concealment, also there was higher risk of bias in blinding of participants and personnel, as well as in the blinding of outcome assessment.

Table 1. Characteristics of the studies selected in the review.

Authors/ Year	Purpose	Sample Description	Rehabilitation Approach	Primary Measures	Primary Results
Ambreen et al., (2021)	To compare the effects of Bilateral Arm Training (BAT) between left (LHS) and right hemispheric (RHS) stroke patients	N=19 Age: 53.6 yr 9F, 10M, Time post stroke >3 mos Stroke type: Ischemic	Bilateral arm training (BAT)	Fugl-Meyer Assessment for Upper Extremity (FMA-UE)	*FMA-UE:* LHS: Distal arm function did not improve. Overall performance score ($p < .008$), coordination ($p < .02$), and speed ($p < .01$) improved significantly. RHS: Distal arm function improved in the wrist ($p < .02$) and hand ($p < .007$) as did the overall score ($p < .02$).
Arya et al., (2019)	To develop an interlimb coupling rehabilitation protocol and examine its effect on motor recovery in stroke patients	EG N = 26 CG N = 24 Age =52.0yrs 10F, 40M Time post stroke >6 mos Stroke type: ischemic, hemorrhagic	Bilateral arm training (BAT) Conventional therapy (not specified)	Fugl-Meyer Assessment for Upper Extremity (FMA-UE) mRS: modified Rankin Scale	*FMA-UE:* EG improved in overall score ($p < .001$) *mRS:* No significant difference was found between groups. 15% of EG reached mRS-2 (slight disability)
Burgar et al., (2011)	To examine effectiveness of different doses of robot-assisted upper-limb therapy in acute stroke rehabilitation	Low-dose EG: N=19 High-dose EG: M=17 CG: N = 18 Age =63.1yr Gender: NA	Robot-assisted (RA) upper-limb therapy Conventional therapy (not specified)	Fugl-Meyer Assessment for Upper Extremity (FMA-UE) Wolf Motor Function Test	*FMA-UE:* No significant differences between the groups were evident. Moderate correlations between FMA-UE and the dose ($r = .34$, $p < .04$) and intensity ($r = .45$, $p < .005$) at post-intervention, as well as at follow-up ($r = .37$, $p < .04$). Intensity correlated

		Time post stroke: 9-20 days Type of stroke: Ischemic stroke		(WMFT)	strongly with FMA after 6 months (r = .66, p < .001). *WMFT*: No significant differences between groups were evident.
Cauraugh & Kim, (2002)	To evaluate effectiveness of the bilateral coordination training, coupled with EMG stimulation on chronic stroke patients	Bimanual EMG: N = 10 Unimanual EMG: N = 10 Control: N =5 Age: =63.7yr 4 F, 21M Time post stroke >1 yr Stroke type: NA	Bilateral coordination training with EMG triggered stimulation.	Box and block test Reaction time test	*Box and block test:* Bimanual and Unimanual groups with EMG improved significantly vs control group (p < .04). *Reaction Time* Bimanual group improved in RT compared to two other groups (p < .001). Unimanual improved in RT compared to control group (p < .001).
Cauraugh et al., (2009)	To evaluate the effect of bilateral movement training (BAT) coupled with EMG stimulation, on chronic stroke patients	Bload N = 10 Bnoload N=10 BAT N =10. Age = 67.2 yr 10F, 19M Time post stroke >6 mos Stroke type: NA	Bilateral coordination training with EMG triggered stimulation	Box and block test Force production test Reaction time test	*Box and block test:* BAT groups with and without load improved (p < .05) *Force production:* BAT with and without load exhibited better muscle contraction (p < .04). *Reaction Time Test* BAT load group had faster RT than BAT no load group and control group (p < .004).
Chang et al., (2007)	To analyze the effect of conventional rehabilitation therapy, combined with bilateral force-induced isokinetic arm movement on stroke patients	N=20 Age = 57.1 yr 8F, 12F Time post stroke: >6 mos Stroke type: NA	Conventional training combined with robot-aided, bilateral force-induced isokinetic training	Fugl-Meyer Assessment for Upper Extremity (FMA-UE) Motor Assessment Scale (MAS) Kinematics (paretic arm only)	*FMA-UE* Significant improvement in FMA score (p < .001). *MAS*: No significant changes were noted. *Kinematics:* Improvements in movement time (p < .01), peak velocity (p < .03), and jerk score (p < .008) at post-test only.

Doost et al., (2021)	To compare the effect of robotic active-assisted training mode versus robotic active mode on bimanual motor skill learning	EG N= 23 CG: N=26 Age = 54.8 yr 30M, 19F Time post stroke >6 mos Stroke type: Ischemic; Hemorrhagic	Robot-assisted training (bilateral)	Speed-accuracy trade-off (SAT) Box and block test	*SAT* Both groups learned and retained bimanual cooperative tasks. *Box and block test:* No significant differences in the number of blocks transferred across both arms in stroke patients.
Gerardin et al., (2022)	To examine the effects of robotic arm training among chronic stroke patients and healthy individuals	EG M N =14, EG Mil N=10 CG N = 10, Age = 48.6 yr 17F, 17M Time post stroke >6 mos Stroke type: NA	Robotic-assisted training (bilateral)	Bimanual speed-accuracy trade-off (BiSAT) Fugl-Meyer Assessment for Upper Extremity	*BiSAT* Stroke patients with moderate ($p < .001$) and mild ($p < .01$) impairment improved. *FMA-UE* All three groups improved, but inter-group differences were not statistically significant
Jung et al., (2013)	To examine the effects of Bilateral arm training (BAT) on unilateral and bilateral reaching performance in individuals with stroke	N=15 Age =50.6 yr 4F, 11M Time post stroke >6 mos Stroke type: ischemic; hemorrhagic	Bilateral arm training (BAT)	Canadian Occupational Performance Measure (COPM) Motor Activity Log (MAL) Kinematics of paretic arm only	*COPM and MAL:* Significant improvement in amount and quality of the use of paretic arm. *Kinematics* Average velocity and peak velocity of the paretic arm showed significant improvement ($p < .05$) in bimanual and unimanual reaching.
Kale et al., (2019)	To compare the effect of constraint-induced movement therapy (CIMT) to bimanual arm task training (BAT) in stroke patients	CIMT: N= 15 BAT: N = 15 Age = 57.8 yr 20F; 10M Time post stroke: >3 mos Stroke Type: NA	Constraint-induced movement therapy (CIMT) Bimanual arm task training (BAT)	Action Research Arm Test (ARAT) Nine Hole Peg Test (NHPT)	*ARAT & NHPT* BAT and CIMT groups both showed significant differences between pre- and post test ($p < .001$), however the differences between the two programs were minimal.

Kim & Park, (2019)	To examine the effect of occupational-based bilateral arm training in the recovery of arm function in stroke patients	Sample: EG: N = 10 CG: N = 10 Age = 59.5 yr 12F, 8M Time post stroke >6 mos Type of stroke: ischemic & hemorrhagic	Occupational Bimanual arm task training (BAT) Task-based Bimanual arm task training (BAT)	Canadian Occupational Performance Measure (COPM) Stroke Impact Scale (SIS) Action Research Arm Test (ARAT)	*COPM:* Significant improvement in both performance (p < .01) and satisfaction (p < 0.001). *SIS:* Significant improvement in strength (p < .01) and ADL (p <.02) *ARAT:* Gross movement (p <.001) improved significantly; however, grasp, grip and pinch did not improve.
Liao et al., (2011)	To compare the effects of robot-assisted therapy on real-world arm activity and daily function in stroke patients	EG: N = 10 CG N =10 Age = 55.2 yr 7F, 13M Time post stroke >6 mos Stroke Type: NA	Robot-assisted therapy followed by performance of functional activities	Fugl-Meyer Assessment for Upper Extremity Functional Independence Measure (FIM) ABILHAND questionnaire	*FMA-UE* Significant improvements in EG group (p < .002) *ABILHAND* Significant improvement in EG group (p < .05). *FIM* No significant difference between groups (p = .80).
Lin et al., (2015)	To examine the effects of interlimb force coupling training on paretic arm in patients with chronic stroke	EG N =16 CG N = 17 Age = 55.1 yr 5F, 28M Time post stroke >6 mos Stroke type: ischemic; hemorrhagic	Bilateral isometric handgrip force training	Fugl-Meyer Assessment for Upper Extremity Wolf Motor Function Test (WMF) Motor Assessment Scale (MAS)	*FMA-UE* Significant improvement in EG vs CG (p < .001) *WMFT & MAS* Significant improvements in EG compared to CG (p <.001; p < .004), BI (p <. 037), respectively across the three measures
Pandian et al., (2015)	To evaluate the effects of motor training involving the less-affected side (MTLA) in stroke subjects	EG N =17 CG N=18 Age = 43.1 yr 16F, 19M Time post stroke >4 mos	Motor training and dose-matched conventional therapy	Brunnstrom Recovery Stage (BRS) Fugl-Meyer Assessment for Upper Extremity (FMA)	*BRS & FMA* Affected side showed significant improvement in both measures (p < .001)

		Stroke type: ischemic; hemorrhagic			
Van Delden et al., (2015)	To examine the degree of interlimb coupling as a result of bilateral versus unilateral training and control treatment	mCMT N=22 mBATRAC N=19 CG = 19 Age = 59.8 yr 19F, 41M Time post stroke > 10 w Stroke type: NA	Unilateral training: modified (mCIMT) Bilateral training (mBATRA) & dose-matched control group	Kinematics (Paretic arm only) Movement harmonicity	*Kinematics* No significant differences from pre to post intervention & post to follow-up. *Movement harmonicity* mBATRAC group had greater movement harmonicity with the paretic arm than control group and also had larger amplitudes with the paretic arm than mCIMT group ($p < .004$).
Whitall et al., (2000)	To examine the effects of bilateral arm training with rhythmic auditory cueing (BATRAC) hemiparetic arm actions of stroke patients	N=14 Age = 63.8 yr 8F, 8M Time post stroke >1 yr Stroke type: NA	Bilateral arm training with rhythmic auditory cueing (BATRAC)	FMA-UE, WMFT Isometric strength ROM paretic arm	*FMA-UE; WMFT;* Significant changes across the measures ($p < .0004$; $p < .02$) respectively. *Isomeric strength* Improvement in elbow ($p < .05$) and wrist flexion ($p < .02$) *ROM* Improvement in shoulder extension ($p < .004$) & wrist flexion ($p < .03$)
Whitall et al., (2011)	To examine the effect of bilateral arm training with rhythmic auditory cueing (BARTAC) versus dose-matched therapeutic exercises (DMTE) on upper-limb interlimb function in stroke patients	EG N = 42 CG N =50 Age = 58.7 yr 42F, 50M Time post stroke >6 mos Stroke type: NA	Bilateral arm training with rhythmic auditory cueing (BARTAC) Dose-matched therapeutic exercises (DMTE)	FMA-UE Isokinetic strength of elbow action ROM of joints of the paretic arm	*FMA-UE* Significant changes in BATRAC group ($p < .03$) *Isokinetic Strength* Elbow extension strength increased in BATRAC ($p < .05$), but not DMTE. DMTE improved strength of shoulder and wrist extension and elbow flexion in paretic arm ($p < .05$) *ROM* No significant changes across the joints & training types
Wu et al., (2011)	To examine the effect of Constrained Induced Movement Therapy (CIMT), and	CIMT N = 22 BAT N = 22 CG N = 22 Age = 53.1 yr 17F, 49M	Constrained Induced Movement Therapy (CIMT)	Kinematics Wolf Motor Function Test (WMFT)	*Kinematics* CIMT and BAT groups had smoother reaching trajectories in unilateral ($p < .03$) and bilateral tasks ($p < .03$) than the control group. *WMFT & MAL*

	Bilateral Arm Training (BAT) on upper limb functioning in stroke patients	Time post stroke >6 mos Stroke type: NA	Bilateral Arm Training (BAT)	Motor Activity Log (MAL)	CIMT group had improved WMFT score ($p < .04$) and higher functional ability scores ($p < .02$) CIMT group also had higher gains in MAL-($p < .005$) than BAT and control groups.
Wu et al., (2007)	To examine the effect of Constrained Induced Movement Therapy (CIMT), and traditional therapy on upper limb functioning in stroke patients	EG N = 15 CG N =15 Age =54.0 yr 13F, 17M Time post stroke 1-3 yr Stroke type: NA	Modified Induced Movement Therapy (CIMT) Traditional therapy (not specified)	Kinematics (paretic arm) Motor Activity Log (MAL) Functional Independence Measure (FIM)	*Kinematics* Significant changes in MT ($p < .01$), total displacement ($p < .01$) and time to peak velocity ($p < .009$) *FIM/MAL* In bimanual task CIMT group showed greater gains in FIM ($p < .004$) and MAL-AOU ($p < .0001$) and MAL-QOM ($p < .01$)

Table 2. Author's risk of bias assessment for the respective studies

Domains	Random sequence generation	Allocation concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Ambreen et al., 2021	×	×	×	×	✓	✓
Arya et al., 2020	✓	✓	✓	✓	✓	✓
Burgar et al., 2011	✓	×	×	✓	✓	✓
Cauraugh & Kim, 2002	✓	×	×	×	?	✓
Cauraugh et al., 2009	✓	×	×	✓	?	✓
Chang et al., 2007	×	×	×	×	✓	✓
Doost et al., 2021	✓	×	✓	×	✓	✓
Gerardin et al., 2022	✓	×	×	×	✓	✓
Jung et al., 2013	×	×	×	×	✓	✓
Kale et al., 2019	✓	×	×	✓	✓	✓
Kim & Park, 2019	✓	✓	✓	×	✓	✓
Liao et al., 2012	✓	×	×	✓	✓	✓
Lin et al., 2015	✓	✓	✓	✓	✓	✓
Pandian et al., 2015	✓	✓	✓	✓	✓	✓
Van Delden et al., 2015	✓	✓	✓	×	✓	✓
Waller et al., 2008	✓	×	×	✓	✓	✓
Whitall et al., 2000	×	×	×	×	?	✓
Whitall et al., 2011	✓	×	✓	✓	✓	✓
Wu et al., 2007	✓	?	✓	×	✓	✓
Wu et al., 2011	✓	?	✓	✓	?	✓

Methodological Considerations

In terms of sample characteristics, the mean age ranged from M = 43.1 years old (32), to M = 67.2 years old (7). All the studies involved heterogeneous samples comprised of both males and females. The size of the sample ranged from 14 participants (36) to 111 participants (37).

However, only three studies included more than 50 participants (6), (37), (39). Only seven studies incorporated a power-analysis calculation (7), (23), (25), (27), (36), (39), (40).

In regards to the stroke type, participants with ischemic stroke were exclusively included in three studies (1), (6), (29), while six studies recruited participants with hemorrhagic and ischemic stroke(2), (11), (16), (23), (27), (32). The remaining 11 studies did not identify the type of stroke that the participants were diagnosed with (7), (8), (9), (13), (17), (25), (36), (37), (38), (39), (40). Also, the majority of the studies included participants who were in at chronic stage of stroke (<6 months post-stroke). One study included participants at the sub-acute stage of recovery, in which the mean time after stroke was 9.4 weeks (36). Three studies included both subacute and chronic stages of stroke participants (1), (17), (32).

The review identified three main types of interventions. Bimanual movement training was implemented in 14 studies (1), (2), (7), (8), (16), (17), (23), (27), (29), (32), (36), (37), (38), (40), bimanual robot-assisted training was used in five studies (6), (9), (11), (13), (25), and constraint-induced movement training was implemented in four studies (17), (36), (39), (40). Also, in the 14 studies that examined bimanual movement training, six studies combined supplementary protocols, including a bimanual training and an EMG-triggered neuromuscular stimulation approach (7), (8) and a bilateral arm training with rhythmic auditory cueing approach (29), (36), (37), (38).

Task Constraints

The methodologies of 12 studies did not include measures of bimanual coordination explicitly, before or after the intervention (1), (2), (7), (8), (9), (17), (23), (25), (27), (32), (36), (37). Five studies did however implement discrete tasks (6) Among those, bimanual symmetrical reaching was implemented in three studies (6), (16) where the participants were asked to move two arms simultaneously in the forward direction from the side of the table to a target. An asymmetrical bimanual task, which involved opening a drawer with the affected arm and retrieving an object with the unaffected arm, was used in the other two studies (39), (40). In addition, three studies implemented bimanual continuous tasks (11), (13), (36). In the first, participants needed to rotate two handles of robotic devices by circular mirror bilateral movements in order to lift a tray on the screen (11). In the second, i participants were asked to control a cursor on the screen via two robotic handles, in which each hand moved in a single axis via either right-left or front-back motions (13). And in the third, bimanual rhythmic wrist flexions and extensions in an in-phase and anti-phase pattern were incorporated (36).

Dependent Measures

Clinical Scales

In terms of the dependent measures used, nine studies implemented clinical scales as the only outcome measure of interest (2),(7),(8),(17),(23),(25), (27), (32), (39) whereas the remaining studies implemented clinical scales as well as kinematic analysis. Among the studies which used clinically-derived outcomes measures, 20 scales were identified. The overall motor function in upper extremity was examined in seven scales, which can be further subdivided as clinician-reported and performance-based measures. The most frequently used clinician-reported scale was the Fugl-Meyer Assessment-Upper Limb (1),(2),(6),(9),(13),(25),(26), (29), (32), (36),(37), and Wolf Motor Function Test (1),(6),(27),(29),(36),(37),(39). The remaining measures such as Ashworth scale (6), (9), Brunnstrom Recovery Stages (32), the Action Research Arm Test (17), (23), and Motor Assessment Scale (27) were used less frequently. Gross motor function was investigated via performance-based scales including the Box and Block Test (7), (8), (11), (13), and two clinician-reported measures included Manual Muscle Testing (32) and Minnesota Manual Dexterity Test (32). In regards to fine motor function, the Nine Hole Peg Test specifically measured finger dexterity and was used in one study (17). In addition, the Purdue Pegboard Test, which evaluated gross motor function of the arms, hands and fingers as well as fine fingertip dexterity according to the performance of a pin-placing test, was used in one study (26).

Kinematic Analysis
Out of the 20 studies examined, eight implemented kinematic analysis (9),(16),(29), (36),(37),(38),(39),(40). However, only two studies evaluated the nature of movement coordination between the arms via product (29) and process (36) measures. In the present review none of the studies examined implemented angle-angle plots in order to infer the qualitative nature of bimanual coupling. From the quantitative standpoint, only one study calculated the cross-correlation coefficient as the measure of the strength of temporal coupling between two arms (36).

The remaining studies examined the nature of movement control of the paretic arm only in either unimanual tasks (9),(16),(36),(37),(38),(39) or bimanual tasks (1),(38),(39). In the spatial domain, the nature of control was investigated in 5 out of 20 studies (16),(29),(36),(37),(38). Of those five, two studies examined movement straightness of the paretic arm in terms of end-effector space and trajectory (16), (29),whereas the total displacement of the paretic hand was examined in only one study (38). In terms of joint space analysis, two studies measured the range of motion of the shoulder, elbow, wrist, and thumb on the paretic side of the body only (36),(37). The temporal control of the paretic arm was measured in 5 out of 20 studies (9),(16),(29),(39),(40). This included measures in end effector space of temporal control that was inferred from movement time (9),(29),(39),(40), peak velocity (9),(16),(29), the percentage of time to peak velocity (9),(39),(40) mean velocity (16) and peak acceleration (29). Movement smoothness, representing the discontinuity and segmentation of the movements, was evaluated in two studies by the jerk score (9) and the number of movement units (29),(39). None of the studies examined the issues of temporal control in joint space.

Conceptual Considerations
None of the studies reviewed were deductive in nature as they did not implement or design the intervention or measures to test any explicit motor control theories or models. One study explicitly framed its training protocol within the dynamic system approach (8). However, the methodology of this study was not aligned with the dynamic system approach since the order parameter (relative phase) and interlimb coupling were not examined. Thus, this study was not classified as theory-driven research. In addition, some studies implicitly referred to motor control concepts such as interlimb coupling (7), (16), (27),(3),(36),(40) coordinative structures (8),

(32),(37),(38) and Fitts' law as applied to bimanual discrete actions (29). However, the methodological considerations and results of these studies were not explicitly discussed in the context of the related theory. The rest of the studies were data-driven research, in which the authors did not explicitly or implicitly mention any related theoretical frameworks or concepts of motor control (1), (6),(9),(16),(17), (23), (25),(40).

DISCUSSION

From a systematic review of the literature, twenty studies were extracted and used to make inferences on constraints, rehabilitation approaches and measures of bimanual coordination in individuals' post-stroke. Collectively, important individual and task constraints on inter-limb coordination were scarcely examined as independent variables. Although the majority of studies included did use bilateral arm training as the most prevalent rehabilitation approach, most studies did not involve bimanual tasks, or any measures of inter-limb coupling as outcome measures limiting the validity of the emerging inferences as related to bimanual actions. Despite the richness of theories and models in the field of inter-limb movement organization, all studies were data-driven research.

Individual and Task Constraints

In terms of the age of the participants, sexes, and stages post stroke, these factors were not considered as independent variables in the designs of the reviewed studies. This is an important issue as often the age of the participants spanned more than 20 years, on average. Considering that the prevalence of stroke is rising among younger adults, the effect of different rehabilitation approaches may be age specific. In a similar context, sex of the participants was also not included in the designs as an independent variable. Stroke could have a greater impact on females than males since females have poorer functional recovery and lower quality of life after stroke. In regards to the stage of post-stroke recovery, 15 studies recruited individuals who were characterized as chronic, while three studies included patients who were classified as both chronic and sub-acute, or in acute and sub-acute stroke stage. From the motor functioning standpoint, the perceptual-motor status of chronic stroke patients is relatively stable. On the other hand, when an individual is considered to be in the acute or subacute stage of recovery, the motor performance may be more variable. Hatem and colleagues (15) reported that a greater time since stroke onset was associated with more bimanual coordination impairments, thus suggesting that the nature of gains resulting from a rehabilitation may also vary by time since stroke. The noted heterogeneous nature of the samples is an important issue to consider in regard to the internal validity of the emerging inferences. Given the different trajectories of recovery, the implemented approaches may have different effects on participants resulting in potential false positive and false negative inferences. The potential presence of such person-by-treatment interaction, and its consequences need to be considered. Thus, making inferences about the effectiveness of the approach based on aggregated data, without consideration of the effect at the individual level of analysis, warrants caution. An alternative research approach, broadly classified as small-N designs, involves serial observations of single persons or small groups before, during, and after an intervention period. This may represent a foundation for evidence-based rehabilitation at the level of the individual patient which would enable researchers to provide clinicians with practical information for making decisions to improve the care of a specific patient.

In addition to the individual constraints, the nature of the emerging behavior is affected by the characteristics of the tasks being performed. In the context of bimanual coordination research, the primary factors to consider are the desired degree of symmetry, as well whether the task is of discrete or rhythmical nature. In symmetrical actions tight interlimb coupling, in both the spatial and temporal domains, is an indication of effective coordination. On the other hand, in asymmetrical actions the coupling strength between two arms varies depending on the degree of asymmetry required to perform the task effectively. In this case, often other outcome measures such as time to completion, or the functional outcome of the activity may serve as the primary indices of effectiveness. In the current review three studies implemented bimanual symmetrical task where the participants were required to reach forward with two arms simultaneously (7), (29). However, among those only one study examined the nature of symmetry between the arms (29). The results showed that following the intervention, the symmetry between the hands improved as both the affected and unaffected hands exhibited mirror-liked straight trajectories. In motor control, this type of spatial superimposition is referred as "enslaving". Aside from the subjective "eyeballing" of the emerging paths, researchers have also used straightness of endpoint trajectory variable confirming the qualitative inferences as the paths of both wrists were in fact spatially coupled. In two studies, bimanual asymmetrical tasks were implemented where the participants needed to open the drawer with the affected arm and retrieve an object with the unaffected arm (39),(40). Compared to symmetrical reaching, this asymmetrical task requires the ability to decouple two arms since the affected arm needs to reach and pull the drawer, while the unaffected arm is reaching, grasping, and transporting an object. In these studies, only performance of the paretic arm was examined. The results revealed that the velocity as well as percentage of time to peak velocity, and peak velocity were enhanced after training (39), (40). However, given that the nature of the emerging (dec)coupling was not measured, this study provided insight into the nature of movement control of the paretic arm, rather than coordination between both arms.

In terms of continuous tasks, one study examined interlimb coupling in bimanual actions (6). Individuals with stroke were assigned to three experimental groups, including BATRAC, CIMT, and dose-matched control treatment, and all subjects were required to perform rhythmic wrist extensions and flexions. Cross-correlations were calculated for both the in-phase and anti-phase modes, before and after the interventions. As expected, results showed that interlimb coupling was significantly stronger during the in-phase mode than during the anti-phase mode across all measurements (39). This is consistent with the predictions of the HKB model (20).

From the neurological standpoint the nature of the tasks involved in the training as well as in the baseline and retention / transfer tests is an important one. When considering highly skilled bimanual tasks, an enormous degree of cooperativity on a kinematic and kinetic level between the hands, can be observed. As each limb is however controlled separately in opposing hemispheres of the CNS, the exchange of information between the hemispheres is necessary in order to warrant this cooperative behaviour. Various electrophysiological, lesion and imaging studies have shown that the execution of bimanual movements involves a complicated interaction between a variety of motor areas within the cortex, including the supplementary motor area, the primary and premotor cortex, the sensory cortices, the cingulate motor area and the cerebellum. For example, Ullen et al. (35) showed that brain activation differs during in- and anti-phase movements, as well as the polyrhythmic tapping patterns of the index fingers. The right anterior cerebellum and the CMA seem to be more active during symmetrical in-phase actions, whereas the SMA is active during the anti-phase movements. Collectively, it is evident that neurologically the planning and execution of bimanual tasks is highly dependent on the nature of the tasks examined. Thus, the presence of methodological differences across the studies warrants caution when making broad inferences about the nature of the emerging actions and their underlying neurol mechanisms in the context of inter-limb organization.

Bimanual Training and Approaches to Rehabilitation

Despite the existence of various rehabilitation approaches only less than 15% of stroke survivors regained full recovery of the upper limbs (33). In the case of bimanual actions, the importance of coordination between the two arms for self care, home, work, and leisure activities is self-evident. The control of the arms is interactive and coordinated, involving a varying degree of coupling or symmetry between them. At the neural level, it has been shown that bilateral movement control entails specific processes that are not shared with unilateral movements. Hence, practicing bimanual movements is expected to evoke the bilateral neural networks, which presumably are absent in unilateral arm movement. Thus, from clinical standpoint it appears that unilateral training, of the affected arm alone, does not transfer to the performance of bilateral tasks. However, it should be pointed out that other researchers hypothesized that unilateral training may be just as beneficial (10).

The current review revealed that majority of the studies did in fact address bimanual coordination explicitly. The bilateral arm training was most prevalent. This approach is based on the premise that movement of the non-paretic upper limb supports movement of the paretic upper limb when performed simultaneously. Thus, the participants are trained to perform a "default mode" of bimanual coupling with either symmetric (e.g., arms moving together in the same direction) or asymmetric (e.g., one arm pushes away while the other is pulling towards) patterns to stimulate informational exchanges between both hemispheres, and then to improve the motor function of the paretic arm (30). Another type of bimanual training that was used, although not as frequently as the previously discussed approach, was training involving external devices. In the context of bimanual rehabilitation, a functional brain imaging study on robot-assisted task-oriented bimanual training (RBMT) reported that, compared with unilateral hand movement, robot-assisted bilateral hand movement induced greater excitatory responses in the motor cortex (28) suggesting the clinical effectiveness of RBMT. In recent research, Keeling and colleagues (19) showed that the use of the bimanual robotic tasks for rehabilitation in subacute stroke is also feasible and suggested that the use of robotic devices added to standard of care therapy could augment recovery. This is due to the fact that robotic devices offer the possibility of providing intensive task-specific training while regulating different task parameters in order to make the constraints more or less complex given the individual capabilities of the patient. Also, from the measurement standpoint they allow to quantify the nature of the emerging outcomes such as mean and maximum end-effector velocity or spatial trajectory (2). This represents an important advantage over other approaches which use predominantly clinical scales which focus on movement outcome alone, rather than the process unfolding during the trajectory formation.

The third most frequently implemented approach was constraint-induced movement training (CIMT), which is considered as specialized task-oriented training approach. CIMT focuses mainly on the control of one limb rather than the coordination between them. The implicit assumption of CIMT, for improving bimanual coordination function, is that as soon as the basic aspects of unimanual control are relearned, they can be more easily integrated into more complex bimanual movement patterns (15). It has been suggested that motor recovery after CIMT may occur due to the exploitation of the existing less active motor pathways. The activation of the undamaged hemisphere contra-lateral to the lesion(s) can counteract adverse brain functions and enhance neuroplastic modifications relating to motor recovery (1). Although the use of this technique is currently considered the gold-standard intervention for treating the paretic upper limb (5), (38). it is effectiveness in enhancing bimanual coordination still remains equivocal.

Dependent Measures

Adequate reliability and validity are essential for any behavioural scales in order to render clinically relevant inferences. In relation to the clinical tools incorporated to assess the nature of upper limb coordination, the key issue is that of sensitivity and responsiveness of the scores to change in behaviour. An instrument that measures what it is supposed to measure is expected to be responsive to a clinical intervention and should detect real change whether the change is induced experimentally or naturally. Thus, sensitivity to change is an important dimension of test construct validity. An important limitation of the existing scales here is the fact that the construct of "coordination", and more specifically "inter-limb coordination" is not assessed. In fact, more often than not the construct of coordination was only implicitly operationalized. The process of "coordination" regardless of the level of organization or measurement is intimately related to the nature of the relationship between components being coupled, in time and/or space. In the current review none of the scales identified examined explicitly this process. As a result the measures used, by default can not be sensitive to the changes in the construct of interest, if they fail to measure the key concept within the domain of the construct.

Product Measures

The use of kinematic analysis, which is a standard methodological approach in motor behavior research provides an insight into the nature of trajectory formation of the end effector (forward kinematics) as well as the changes occurring at the joint level (inverse kinematics). Despite this, less than half of the studies implemented kinematic analysis as the primary measure of interest. In order to examine spatial control, linear displacement or distance of the end-effector can be quantified, as well as the angular displacement of the individual's joints. Among the reviewed studies, five investigated the issue of spatial control. The analysis of trajectory confirmed improvements in the hand trajectory of the paretic arm in a bimanual reaching task (e.g., (29)), whereas the other analyses failed to confirm such effects which was examined in the unimanual domain (e.g., (16)). Kinematic changes in the temporal domain represent another important aspect of motor performance in the context of manual self-paced tasks such as reaching and grasping. The relevant measures can be derived from velocity profiles, such as peak velocity, time to peak velocity, and peak acceleration. In this review, five studies investigated the issue of temporal controll via measures of velocity and movement smoothness such as jerk scores and the number of movement units. Across all the intervention programs implemented, significant improvements were found in the smoothness measures of the paretic arm after rehabilitation. These findings were robust as they emerged across stroke participants who were involved in different rehabilitation programs (e.g., BAT, BATRAC, and CIMT) and performed different tasks (e.g., bimanual symmetrical and asymmetrical reaching). Thus, it appears where the impact of intervention on spatial control requires further research, the existing studies although still limited in terms of the number, showed positive impact of the respective interventions on temporal control.

Process Measures

Kinematic process measures allow making inferences about the nature of the spatial and temporal coupling between the arms via qualitative (angle-angle plots) and quantitative (correlations) methodological approaches. Regarding correlations, the nature of the emerging coupling can be inferred from the degree of the coefficients with smaller values implying decoupling, whereas larger values indicating a larger degree of synchrony, in time and space. Among the studies reviewed only one implemented this approach. Van Delden and colleagues (36) examined interlimb coupling in bimanual continuous actions where the individuals with stroke were assigned to three experimental groups, including BATRAC, CIMT, and dose-matched control treatment. The participants were asked to perform rhythmic wrist extensions and flexions, and cross-correlations were calculated for both the in-phase and anti-phase modes, before and after the interventions. The results showed that interlimb coupling was significantly stronger during the in-phase mode as compared to anti-phase mode across all measurements, which is consistent with the predictions of the HKB model (20). When the respective pre and post comparisons were examined, improvements in in-phase coupling were evident in the control group and bimanual arm training group. However, the magnitude of coupling in the anti-phase mode did not change in any groups. In terms of the qualitative measures of coordination, such as angle-angle plots, none of the studies reviewed implemented this approach. Collectively, these findings indicate that although implicitly the studies reviewed here aimed at examining the nature of the emerging coordination tendencies, the methodologies implemented failed to address the issue of coordination explicitly. Thus, the conclusions emerging from these studies, regarding the impact of different interventions on the nature of the emerging coordination have to be treated with caution, as they may lead to false positive or negative inferences.

Theoretical Approaches to the Design of Bimanual Rehabilitation after Stroke

In the field of motor control, theories are essential as they afford researchers to postulate the mechanisms underlying emerging behavior. Also, theoretical models allow for delineation of the constraints under which motor behavior changes, as well as they allow predictions of the relationship between different constraints and emerging motor behavior (e.g., reaching and grasping). In rehabilitation research, theory can provide a framework to understand the relationship between intervention inputs, how the intervention is designed and implemented, and the corresponding outcomes. Based on the current review, none of the studies were classified as theory driven as they were not explicitly linked to any explicit conceptual frameworks. One study designed the training protocol in the context of the dynamic system approach, but the methodologies and results were not explicitly discussed within the implications of the HKB model and dynamic systems approach (8). In addition, the degree and stability of interlimb coupling was not examined and control parameters were not manipulated to make inferences about the stability or flexibility of the emerging temporal adaptations. Several studies included well known motor control constructs as related to study of coordination or control, such as bimanual coupling (2),(7), (27),(32),(36),(40), coordinative structures (8),(32),(37),(38) and Fitts' law in bimanual discrete actions (29). However, these concepts were only referred to as a justification for implementing bimanual arm training, and the corresponding conceptual and methodological assumptions were not implemented or tested. Thus, despite the existence of a plethora of theatrical frameworks regarding formation and adaptations in inter-limb coordination all the studies in the current review were data driven. This trend reflects a more global tendency in clinical research to disregard the conceptual frameworks that underly the emerging actions, rather than simple description of the phenomena. The fact that data driven research still represents the primary impetus in this clinical field undermines the validity of the inferences.

In terms of the present work, a few limitations were also identified. The overall quality of the current review was deemed as moderate. This was inferred from AMSTAR-2 scale which indicated that there was more than one weakness, however there were no critical flaws, and the content provided an accurate summary of the results in the included studies. In terms of the inclusion / exclusion criteria, an important limitation was the fact that the search was only conducted on English-language articles, thus it is plausible that studies published in other languages were omitted. Also, the literature search generated a relatively small number of studies compared to other systematic reviews in this domain. Finally, from the motor control standpoint, the review only focused on behavioral description of movement via kinematics. Thus, other types of measures and respective methodologies, such as kinetics and EMG analysis were not considered. These approaches provide meaningful insights into the underlying mechanisms of the emerging coordination and control processes at intra- and inter-limb level of organization.

Stroke can result in significant and chronic functional deficits of upper-extremity function, especially bimanual coordination, warranting rehabilitation. The review of 20 studies that met the criteria revealed that although interventions are geared towards bimanual symmetrical or asymmetrical actions, tasks involving bimanual coordination, measured with kinematic analysis as outcomes measures, are lacking. Given the richness of theories and models in the field of inter-limb movement organization, rehabilitation methodologies should be framed and measured with a theory-driven approach.

REFERENCES

1. Ambreen H, Tariq H, Amjad I. Effects of bilateral arm training on upper extremity function in right and left hemispheric stroke. J Pak Med Assoc 1–9, 2020.

2. Arya KN, Pandian S, Sharma A, Kumar V, Kashyap VK. Interlimb coupling in poststroke rehabilitation: a pilot randomized controlled trial. Top Stroke Rehabil 27(4): 272–289, 2020.

3. Balasubramanian S, Colombo R, Sterpi I, Sanguineti V, Burdet E. Robotic assessment of upper limb motor function after stroke. Am J Phys Med Rehabil 91(11): S255–S269, 2012.

4. American Stroke Association. Retrieved from: https://www.heart.org/en/health-topics/consumer-healthcare/what-is-cardiovascular-disease, 2022.

5. Boehme AK, Esenwa C, Elkind MSV. Stroke risk factors, Genetics, and Prevention. Circ Res 120 (3): 472–495, 2017.

6. Burgar CG, Lum PS, Scremin AME., Garber SL, Van der Loos HFM, Kenney D, Shor P. Robot-assisted upper-limb therapy in acute rehabilitation setting following stroke: Department of Veterans Affairs multisite clinical trial. J Rehabil Res Dev 48(4): 445, 2011.

7. Cauraugh JH, Coombes SA, Lodha N, Naik SK, Summers J. J. Upper extremity improvements in chronic stroke: Coupled bilateral load training. Restor Neurol Neurosci 27(1): 17–25, 2009.

8. Cauraugh JH, Kim S. Two coupled motor recovery protocols are better than one. Stroke, 33(6): 1589–1594, 2002.

9. Chang J-J, Tung W-L, Wu W-L, Huang M-H, Su F-C. Effects of robot-aided bilateral force-induced isokinetic arm training combined with conventional rehabilitation on arm motor function in patients with chronic stroke. Arch Phys Med Rehabil 88(10): 1332–1338, 2007.

10. Chiu YH, Chen KC. Bilateral vs unilateral arm training for patients with stroke. Arch Phys Med Rehabil 102(11): 2270–2271, 2021.

11. Doost MY, Herman B, Denis A, Sapin J, Galinski D, Riga A, Laloux P, Bihin B, Vandermeeren Y. Bimanual motor skill learning and robotic assistance for chronic hemiparetic stroke: a randomized controlled trial. Neural Regen Res 16(8): 1566–1573, 2021.

12. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 52(6): 377–384, 1998.

13. Gerardin E, Bontemps D, Babuin NT, Herman B, Denis A,Bihin B, Regnier M, Leeuwerck M, Deltombe T, Riga A, Vandermeeren Y. "Bimanual motor skill learning with robotics in chronic stroke: comparison between minimally impaired and moderately impaired patients, and healthy individuals. J Neuroeng Rehabil 19(1): 28, 2022.

14Haken H, Kelso JAS, Bunz HA. Theoretical model of phase transitions in human hand movements. Biol Cybern 51(5): 347–356, 1985.

15. Hatem SM, Saussez G, Faille MD, Prist V, Zhang X, Dispa D, Bleyenheuft Y. Rehabilitation of motor function after stroke: A multiple systematic review focused on techniques to stimulate upper extremity recovery. Frontiers in Human Neuroscience 13(10): 442, 2016.

16. Jung N-H, Kim K-M, Oh J-S, Chang M. The effects of bilateral arm training on reaching performance and activities of daily living of stroke patients. J Phys Ther Sci 25(4), 449–452, 2013.

17. Kale AA, Kekatpure V, Mahendrakar N. Effect of constraint induced movement therapy versus bimanual task training for improvement of motor hand function in stroke patients. Indian J Physiother Occup Ther 13(1): 23, 2019.

18. Kantak S, McGrath R, Zahedi N. Goal conceptualization and symmetry of arm movements affect bimanual coordination in individuals after stroke. Neurosci Lett 626: 86–93, 2016.

19. Keeling AB, Piitz M, Semrau JA,Hill MD, Scott SH, Dukelow SP. Robot enhanced stroke therapy optimizes rehabilitation (RESTORE): a pilot study. J Neuroeng Rehabil 18(1): 10, 2021.

20. Kelso JAS. Phase transitions and critical behavior in human bimanual coordination. Am J Physiol Regul Integr Comp Physiol 246(6): R1000–R1004, 1984.

21. Kelso JAS, Putnam CA, Goodman D. On the space-Time structure of human interlimb co-ordination. Q J Exp Psychol A 35(2): 347–375, 1983.

22. Kelso JAS, Schöner G. Self-organization of coordinative movement patterns. Hum Mov Sci 7(1): 27–46, 1988.

23. Kim SH, Park JH. The effect of occupation-based bilateral upper extremity training in a medical setting for stroke patients: A single-blinded, pilot randomized controlled trial. J Stroke Cerebrovasc Dis 28(12): 104335, 2019.

24. Kugler PN, Kelso JAS, Turvey MT. 1 On the concept of coordinative structures as dissipative structures: I. Theoretical Lines of Convergence. Adv Psychol 1: 3–47, 1980.

25. Liao W, Wu C, Hsieh Y, Lin K, Chang W. Effects of robot-assisted upper limb rehabilitation on daily function and real-world arm activity in patients with chronic stroke: a randomized controlled trial. Clin Rehabil 26(2): 111–120, 2012.

26. Lin K, Chen Y, Chen C, Wu C, Chang Y. The effects of bilateral arm training on motor control and functional performance in chronic stroke: A randomized controlled study. Neurorehabil Neural Repair 24(1): 42–51, 2010.

27. Lin C-H, Chou L-W, Luo H-J, Tsai P-Y, Lieu F-K, Chiang S-L, Sung W-H. Effects of computer-aided interlimb force coupling training on paretic hand and arm motor control following chronic stroke: A randomized controlled trial. PLoS One 10(7): e0131048, 2015.

28. Ma D, Li X, Xu Q, Yang F, Feng Y, Wang W, Huang J-J, Pei Y-C, Pan Y. Robot-assisted bimanual training improves hand function in patients with subacute stroke: A randomized controlled pilot study. Front Neurol 13: 884261, 2022.

29. McCombe Waller S, Liu W, Whitall J. Temporal and spatial control following bilateral versus unilateral training. Hum Mov Sci 27(5): 749–758, 2008.

30. Mudie MH, Matyas TA. Can simultaneous bilateral movement involve the undamaged hemisphere in reconstruction of neural networks damaged by stroke? Disabil Rehabil 22(1–2): 23–37, 2000.

31. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffman TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hrobjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Int J Surg 88: 105906, 2021.

32. Pandian S, Arya KN, Kumar D. Effect of motor training involving the less-affected side (MTLA) in post-stroke subjects: a pilot randomized controlled trial. Top Stroke Rehabil 22(5): 357–367, 2015.

33. Sainburg R, Good D, Przybyla A. Bilateral synergy: A framework for post-stroke rehabilitation. J Neurol Transl Neurosci 1(3), 2013.

34. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry D. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ j4008, 2017.

35. Ullén F, Forssberg H, Ehrsson HH. Neural networks for the coordination of the hands in time. J Neurophysiol 89(2): 1126–1135, 2003.

36. Van Delden A, Lex EQ, Beek PJ, Roerdink M, Kwakkel G, Peper C, Lieke E. Unilateral and bilateral upper-limb training interventions after stroke have similar effects on bimanual coupling strength. Neurorehabil Neural Repair 29(3): 255–267, 2015.

37. Whitall J, Waller SM, Silver KHC, Macko RF. Repetitive bilateral arm training with rhythmic auditory cueing improves motor function in chronic hemiparetic stroke. Stroke 31(10): 2390–2395, 2000.

38. Whitall J, Waller SC, Sorkin JD, Forrester LW, Macko RF, Hanley DF, Goldberg AP, Luft A. Bilateral and unilateral arm training improve motor function through differing neuroplastic mechanisms. Neurorehabil Neural Repair 25(2): 118–129, 2011.

39. Wu C, Chen C, Tang SF, Lin K, Huang Y. Kinematic and clinical analyses of upper-extremity movements after constraint-induced movement therapy in patients with stroke: A randomized controlled trial. Arch Phys Med Rehabil 88(8): 964–970, 2007.

40. Wu C, Chuang L, Lin K, Chen H, Tsay P. Randomized trial of distributed constraint-induced therapy versus bilateral arm training for the rehabilitation of upper-limb motor control and function after stroke. Neurorehabil Neural Repair 25(2): 130–139, 2011.