

ORIGINAL ARTICLE

A Comparison of Bilateral and Unilateral Upper-Limb Task Training in Early Poststroke Rehabilitation: A Randomized Controlled Trial

Jacqui H. Morris, MSc, Frederike van Wijck, PhD, Sara Joice, PhD, Simon A. Ogston, PhD, Ingrid Cole, BSc, Ronald S. MacWalter, MD

ABSTRACT. Morris JH, van Wijck F, Joice S, Ogston SA, Cole I, MacWalter RS. A comparison of bilateral and unilateral upper-limb task training in early poststroke rehabilitation: a randomized controlled trial. *Arch Phys Med Rehabil* 2008;89:1237-45.

Objective: To compare the effects of bilateral task training with unilateral task training on upper-limb outcomes in early poststroke rehabilitation.

Design: A single-blinded randomized controlled trial, with outcome assessments at baseline, postintervention (6wk), and follow-up (18wk).

Setting: Inpatient acute and rehabilitation hospitals.

Participants: Patients were randomized to receive bilateral training (n=56) or unilateral training (n=50) at 2 to 4 weeks poststroke onset.

Intervention: Supervised bilateral or unilateral training for 20 minutes on weekdays over 6 weeks using a standardized program.

Main Outcome Measures: Upper-limb outcomes were assessed by Action Research Arm Test (ARAT), Rivermead Motor Assessment upper-limb scale, and Nine-Hole Peg Test (9HPT). Secondary measures included the Modified Barthel Index, Hospital Anxiety and Depression Scale, and Nottingham Health Profile. All assessment was conducted by a blinded assessor.

Results: No significant differences were found in short-term improvement (0–6wk) on any measure ($P>.05$). For overall improvement (0–18wk), the only significant between-group difference was a change in the 9HPT (95% confidence interval [CI], 0.0–0.1; $P=.05$) and ARAT pinch section (95% CI, 0.3–5.6; $P=.03$), which was lower for the bilateral training group. Baseline severity significantly influenced improvement in all upper-limb outcomes ($P<.05$), but this was irrespective of the treatment group.

Conclusions: Bilateral training was no more effective than unilateral training, and in terms of overall improvement in

dexterity, the bilateral training group improved significantly less. Intervention timing, task characteristics, dose, and intensity of training may have influenced the results and are therefore areas for future investigation.

Key Words: Cerebrovascular accident; Motor activity; Randomized controlled trial; Rehabilitation; Upper extremity.

© 2008 by the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation

ARM RECOVERY AFTER STROKE is typically poor, with 20% to 80% of patients showing incomplete recovery depending on the initial impairment.^{1,2} Upper-limb dysfunction in stroke is characterized by paresis, loss of manual dexterity, and movement abnormalities that may impact considerably on the performance of ADLs.³

Previous research⁴ has typically focused on motor learning approaches involving unilateral training of the hemiplegic arm. Recently, however, bilateral training, in which patients practice identical activities with both upper limbs simultaneously, has been proposed as a strategy to improve hemiplegic upper-limb control and function.⁵⁻⁹ Control of bilaterally identical synchronous movement appears to occur centrally through bilaterally distributed neural networks linked via the corpus callosum and involving cortical and subcortical areas.¹⁰ These networks indicate a common facilitatory drive to both motor cortices thought to lead to tight temporal and spatial coupling of limb movement observed during bilaterally identical synchronous voluntary movement.^{10,11} Beneficial effects of bilateral training in stroke are assumed to arise from this coupling effect in which the nonparetic limb provides a template for the paretic limb in terms of movement characteristics, facilitating restoration of movement.

Indeed, facilitatory effects observed during bilateral compared with unilateral paretic upper-limb movement in patients with chronic stroke have included increased velocity and smoothness of movement.^{12,13} Furthermore, several studies^{5-9,14} have indicated that therapeutic bilateral training programs may improve short-

From the Alliance for Self-Care Research (Morris, Joice), Community Health Sciences, (Ogston), and Department of Medicine and Therapeutics (MacWalter), University of Dundee, Dundee, UK; School of Health Sciences, Queen Margaret University, Edinburgh, UK (van Wijck); and Departments of Physiotherapy, Ninewells Hospital, Dundee, UK (Morris, Cole).

Presented in part to the UK Stroke Forum, December 7, 2006, Harrogate, UK, and the World Confederation of Physical Therapy Congress, June 4, 2007, Vancouver, BC, Canada.

Supported by the Chief Scientist Office, Scottish Executive Health Department (grant no. CHZ/4/80).

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

Reprint requests to Jacqui H. Morris, MSc, Clinical Research Fellow, Alliance for Self-Care Research, University of Dundee, 11 Airlie Pl, Dundee DD1 4HJ, UK, e-mail: j.y.morris@dundee.ac.uk.

0003-9993/08/8907-00557\$34.00/0
doi:10.1016/j.apmr.2007.11.039

List of Abbreviations

ADLs	activities of daily living
ANOVA	analysis of variance
ARAT	Action Research Arm Test
CI	confidence interval
HADS	Hospital Anxiety and Depression Scale
HRQOL	health-related quality of life
9HPT	Nine-Hole Peg Test
MBI	Modified Barthel Index
NHP	Nottingham Health Profile
RMA	Rivermead Motor Assessment
RCT	randomized controlled trial

and long-term unilateral performance of the hemiplegic arm in patients in the chronic poststroke period, suggesting a potential role for bilateral training in influencing poststroke upper-limb recovery of function. Two of those studies were small RCTs,^{8,14} whereas others involved case series^{5,6,9} or a single-group design⁷; thus, methodologic limitations mean that to date only limited evidence exists to support bilateral training as a rehabilitation strategy. Interventions have been diverse, involving functional tasks,^{5,6} simple prefunctional movements,^{7,9,14} and electromyographically triggered functional electric stimulation.⁸ As a result of this diversity, optimal intervention characteristics remain unclear, and only limited evidence exists to support bilateral training as a rehabilitation strategy.

Little is known about the effectiveness of bilateral training for upper-limb functional outcomes in more acute patients because studies published to date have mainly involved people in the chronic poststroke stage. During the early poststroke period, intensive upper-limb rehabilitation is known to influence short- and long-term outcomes⁴; therefore, the need to determine the effectiveness of bilateral training for patients in this stage is critical. Impairment severity also influences upper-limb recovery¹⁵; however, the effects of initial severity on responses to bilateral training during early rehabilitation are not known. Furthermore, upper-limb impairment influences poststroke quality of life as a significant predictor of low subjective well-being at 1 year¹⁶ and is associated with poststroke depression.¹⁷ However, the effects of bilateral training on these outcomes have not previously been examined.

The purpose of this study was first to compare effects of bilateral simultaneous upper-limb task training to conventional unilateral upper-limb task training on recovery in acute stroke in terms of upper-limb motor performance and activity and independence in ADLs, HRQOL, and mood. Second, we wanted to determine whether responses in relation to upper-limb recovery were related to the severity of the initial impairment.

METHODS

Design

This was an RCT with blinded assessment at baseline, post-intervention assessment at 6 weeks, and follow-up assessment at 18 weeks. Participants were recruited from a cohort of stroke patients sequentially admitted to Ninewells Hospital, Dundee, Scotland, a large teaching hospital with acute rehabilitation facilities. Assessment and intervention were conducted there, in associated rehabilitation hospitals, or in participants' homes depending on their rehabilitation status. The Tayside Committee on Medical Research Ethics provided ethics approval.

Participants

Participants were identified from medical records by the lead researcher (JHM) and were screened between 2 and 4 weeks after stroke onset. Inclusion criteria were as follows: acute unilateral stroke confirmed by a computed tomography scan; persistent upper-limb motor impairment, defined by scores of less than 6 on each of the upper-limb sections of the Motor Assessment Scale¹⁸; ability to participate in 30-minute physiotherapy sessions; and ability to sit unsupported for 1 minute. Exclusion criteria were severe neglect, aphasia or cognitive impairment that would limit participation, previous stroke resulting in residual disability, premorbid arm impairment, hemiplegic shoulder pain, or inability to provide informed consent.

Primary Outcome Measure

Action Research Arm Test. The ARAT is a frequently used, validated, and reliable measure of upper-limb func-

tion^{19,20} with 4 subsections: grip, grasp, pinch, and gross. Its maximum summed score is 57, indicating best performance. Published guidelines were used.²⁰ ARAT performances were videotaped and used to assess inter- and intrarater reliability. Single-measure intraclass correlation coefficients were all greater than .95 ($P < .001$), which could be classified as high.²¹

Secondary Outcome Measures

Rivermead Motor Assessment. The RMA upper-limb section was selected as a more impairment-oriented measure of upper-limb performance than the ARAT. Scores range from 0 to 15, with higher scores representing better performance.^{22,23}

Nine-Hole Peg Test. The 9HPT assesses fine manual dexterity at upper ranges of ability.^{2,24} Scores were calculated as pegs per second.

Modified Barthel Index. The MBI assesses independence in ADLs.²⁵ Scores range from 0 to 100, and higher scores indicate greater independence in ADLs.

Nottingham Health Profile. The NHP, part 1,²⁶ assesses HRQOL across 6 domains: energy, pain, emotion, sleep, social isolation, and physical mobility. Weighted scores range from 0 to 600, with lower scores indicating better HRQOL.

Hospital Anxiety and Depression Scale. The HADS assesses mood.²⁷ The total score ranged between 0 and 42, with subscales of anxiety and depression ranging from 0 to 21. Higher scores indicate greater depression and/or anxiety.

Randomization and Blinding

Participants were randomly assigned to receive bilateral or unilateral training by using concealed web-based randomization, designed by the study statistician (SAO), 2 to 4 weeks after stroke onset and after provision of written informed consent and baseline assessment. Stratifying factors included the side of hemiplegia, stroke classification as determined by the Oxford Community Stroke Project classification,²⁸ and baseline upper-limb activity measured by the ARAT.¹⁹ Two therapists (an occupational therapist and physiotherapist) trained to use the measures, blinded to treatment allocation and otherwise uninvolved in the trial, collected baseline, postintervention, and follow-up data by using standardized protocols. Participants were instructed not to indicate their group allocation to assessors.

Intervention

Bilateral group. Participants allocated to bilateral training practiced identical tasks with each arm simultaneously. Training lasted 20 minutes a session 5 weekdays a week over 6 weeks in addition to usual therapy. Participants performed as many trials as possible in each session to a maximum of 30 trials of each task, a total of 120 trials per session. The duration and intensity of training reflected other bilateral training studies⁵⁻⁷ and was pragmatic, given the acute stage of recovery and ongoing usual therapy. Also reflecting the pragmatic nature of the study, participants discharged home before the end of the intervention period continued training at home twice a week through supervised visits of 30 minutes in duration from the same therapists, in line with the usual discharge and follow-up procedures.

Equipment and task protocols were standardized and portable. The program incorporated 4 core tasks typically found difficult by stroke patients; 3 had been used previously in bilateral training studies.^{5,6} Participants were asked (1) to move a doweling peg 2cm in diameter by 4cm in height from tabletop to attach to the underside of a shelf placed at eye level; (2) to move a 7-cm³ block from the table onto a shelf at shoulder

height; (3) to grasp an empty glass, take to the mouth, and return to starting position; and (4) to point to targets raised 30cm from the table and positioned at midline, 40cm to the right, and 40cm to the left of midline.

The fourth task was included because pointing is an important upper-limb function involving proximal and distal control, for which task constraints could be progressed by using targets of varying size.

Participants were assigned to a core protocol if they were able to complete the 4 core tasks at the first training session or to a modified protocol when the core tasks could not be completed. The modified protocol involved tabletop activities incorporating components of the core tasks, including reaching, forearm pronation and supination, wrist extension, and grasp. Training sessions were organized to enhance skill acquisition and retention through block practice in the cognitive stage of learning progressing to random practice in the associative stage of learning.²⁹ Progressive, standardized graded variations of the core and modified tasks, with specific motor or functional goals and incorporating a range of everyday objects of differing shapes and sizes, were piloted and developed to provide a variation of reaching distances, accuracy, dexterity, and strength requirements. The aim was to encourage active participation matched to the degree of the impairment. Participants allocated to the modified protocol who had very little or no active movement were facilitated in their attempts to achieve goals with assistance from the therapists who withdrew physical assistance as soon as the participant showed active involvement. Goals for these participants, within the modified protocol, involved simple wrist and hand movement and reaching to points marked on the tabletop. Progression for all participants occurred when a participant was successful in 75% of the randomly scheduled trials. To facilitate self-evaluation of performance and maintain participant engagement, knowledge of results was provided after 5 trials using systematic feedback from therapists on goal achievement and movement pattern.³⁰

Two senior stroke rehabilitation physiotherapists each with 15 years of experience conducted the intervention.

Control group. Participants in the unilateral training group followed the same program as the bilateral training group but used the paretic upper limb only. The intervention and control sessions occurred away from normal therapy areas so that regular therapists were unaware of group allocation.

Procedure

Participants fulfilling the inclusion and exclusion criteria were provided with study information by the lead researcher (JHM). After this, written informed consent was obtained from those wishing to take part in the study, baseline assessments were conducted, and participants were given an identification number. To randomize participants to bilateral or unilateral training, the lead investigator (JHM) entered participant identification number and stratification factors into the randomization program and then informed the therapists of group allocation.

Power Calculations

Power calculations were based on the suggestion that a difference of 10% of maximum ARAT score, 6 points, represents a minimal clinically significant difference.³¹ Fifty-three participants in each group were required for 80% power to detect this difference on the ARAT at P equal to or less than .05.

Statistical Analysis

Data were analyzed using SPSS.^a Change scores were created by subtraction of baseline from outcome scores at 6 and 18

weeks. Groups were examined for baseline differences and differences in change between baseline and 6 weeks (0–6) and baseline and 18 weeks (0–18) by using chi-square for categorical data, independent samples t tests, and Kruskal-Wallis tests as appropriate.

Additionally, 3 severity subgroups were created according to baseline ARAT and 9HPT scores. The main and interaction effects of subgroup and treatment group were examined by using factorial ANOVA. Change scores between 0 and 6 weeks and between 0 and 18 weeks on the ARAT, RMA, and 9HPT were dependent variables. Subgroup and treatment group allocation were entered as fixed factors, and baseline scores on each measure were entered as covariates.

RESULTS

Data Screening

No deviations from random allocation occurred. Baseline data were complete for all participants. The MBI and NHP baseline scores were skewed and therefore were transformed to approximate normality using square root. The 9HPT baseline score remained skewed after inverse and logarithmic transformation; therefore, nonparametric tests were used for baseline group comparison. Change scores were all normally distributed.

Participants

Between October 2002 and June 2005, 1239 patients were screened for inclusion. One hundred six patients (61 men, 45 women) met criteria and agreed to participate. Ninety-seven (91.5%) participants completed the intervention and postintervention test at 6 weeks. Five participants from the bilateral training group and 4 from the unilateral training group dropped out before 6 weeks for reasons indicated in figure 1. Eighty-five (80%) patients completed follow-up at 18 weeks (see fig 1), with 5 in the bilateral training and 7 in the unilateral training group lost to follow-up. Using t tests and, where appropriate, nonparametric equivalents, no significant differences at baseline in terms of characteristics or baseline scores existed between participants completing the intervention and those who did not ($P>.05$). Reasons for loss to follow-up are provided in figure 1. There were also no significant differences in terms of baseline characteristics or scores on baseline measures between participants who were lost to follow-up and those who were not. Therefore, analysis was conducted using the complete 6-week dataset ($n=97$) and the complete 18-week dataset ($n=85$). Blinding was preserved in all cases.

Group Characteristics

No statistically significant differences were found at baseline between the bilateral and unilateral training groups (table 1); however, the hospital length of stay was significantly longer for the bilateral training group ($P=.03$) (see table 1), as was the number of intervention sessions ($P=.04$). These differences occurred because 19 (34%) of 56 participants in the bilateral training group compared with 27 (54%) of 50 in the unilateral training group went home during the intervention period. The total number of training trials across the sessions was 1093 ± 711 for the unilateral training group and 1066 ± 413 for the bilateral training

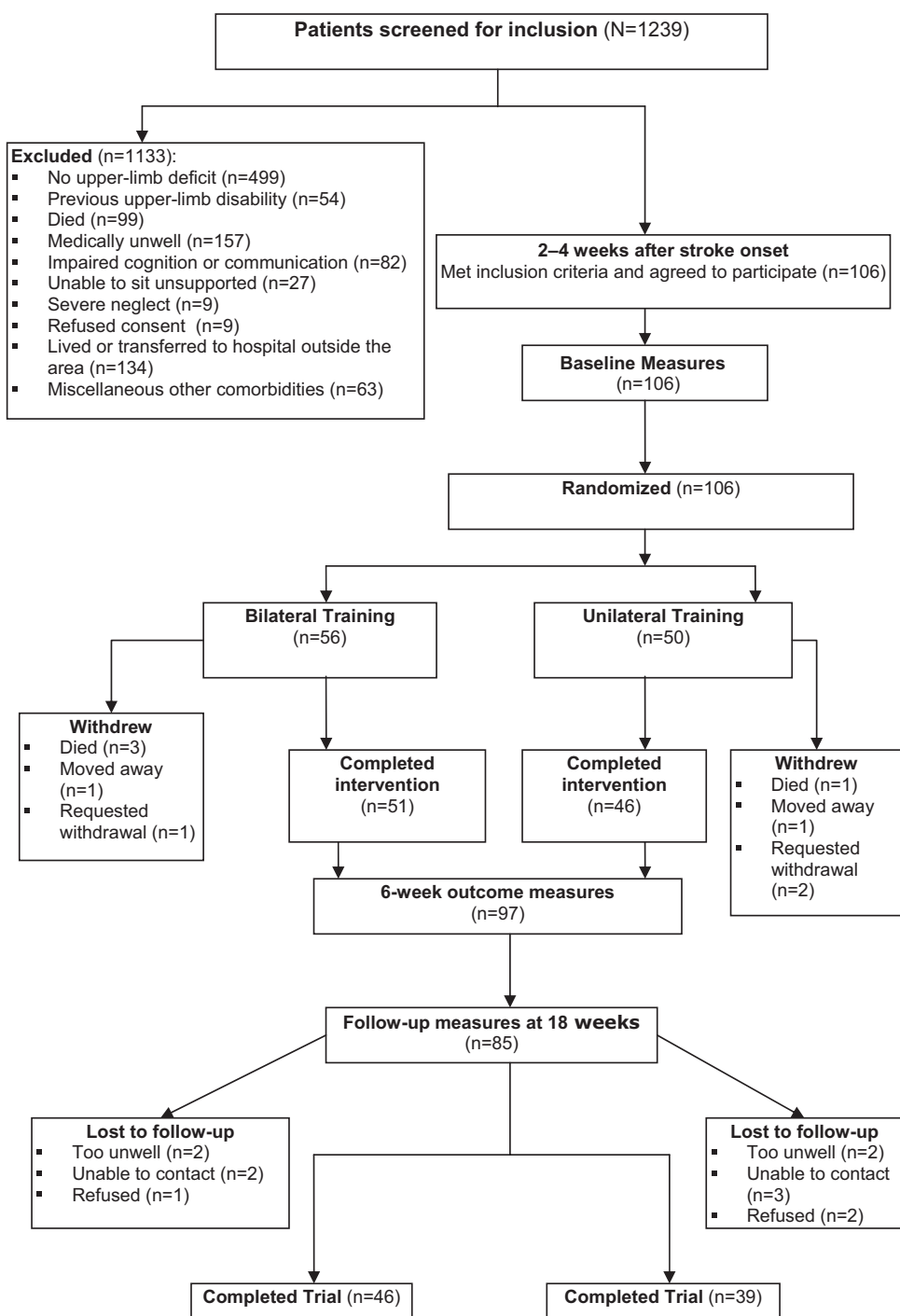


Fig 1. Progress of participants through the trial.

group, which was not significantly different between the groups ($P=.34$); therefore, we can be fairly certain that the dose of therapy was similar for participants in each group. Additionally, there were no significant differences at baseline in terms of any characteristics or outcome measures between participants in the bilateral training group and those in the unilateral training group who were discharged during this period ($P>.05$). At baseline, 39 (69%) patients of 56 in the bilateral training group and 28 (56%) of 50 in the unilateral training group were allocated to the modified task

protocol (see table 1), a difference that was not significant ($P=.15$). During the study, 12 patients in the bilateral training group and 13 in the unilateral training group progressed to one or more of the core tasks so that by the end of the study, of the participants who completed the intervention, 27 (52%) of 51 in the bilateral training group and 15 (33%) of 46 in the unilateral training group had undertaken the modified task protocol, again a difference that was not significantly different ($P=.06$). The mean number of sessions before progression occurred was 15.1 ± 6.0 in the bilateral

Table 1: Baseline Characteristics and Outcome Scores

Characteristic	Bilateral Training (n=56)	Unilateral Training (n=50)
Male/Female (n)	34/22	27/23
Age (y)	67.9±13.1	67.8±9.9
Side of deficit (left/right)	27/29	27/23
Ischemic/hemorrhagic stroke	3/53	6/44
Handedness (left/right)	27/29	25/25
Dominant hand affected (yes/no)	49/7	43/7
Nottingham Sensory Assessment upper limb (max, 84)	71.3±14.5	65.2±19.2
Motor Assessment Scale, median (range) (max, 18)	2.0 (0.0–14.0)	5.5 (0.0–12.0)
Oxfordshire Community Stroke Project classification		
Total anterior circulation	3	2
Partial anterior circulation	31	28
Lacunar	21	18
Posterior circulation	1	2
Days to intervention	22.6±5.6	23.2±5.7
Intervention sessions	21.3±5.3	19.0±5.5*
Core task allocation/modified task allocation	17/39	22/28
Hospital stay, median (range)	80 (3–259)	47 (9–284)*
Upper-limb measures, baseline scores		
ARAT total (max, 57)	13.4±15.3	18.5±17.2
Grasp (max, 18)	4.9±6.0	6.7±6.5
Grip (max, 12)	2.7±3.3	4.0±4.0
Pinch (max, 18)	2.2±3.9	3.1±5.4
Gross (max, 9)	3.6±3.2	4.6±3.1
RMA (max, 15)	3.4±3.3	4.3±3.1
9HPT, pegs/s (median, IQR)	0.00 (0.00–0.02)	0.00 (0.00–0.05)
Other measures, baseline scores		
MBI (0–100)	58.5±25.3	65.7±23.5
NHP (0–600)	180±121	174±118
HADS mood: anxiety (0–21)	6.6±4.8	5.9±3.3
HADS mood: depression (0–21)	6.2±3.2	6.6±3.7

NOTE. Values are mean ± SD unless otherwise stated.
* $P \leq .05$.

training group and 14.1 ± 5.4 in the unilateral training group, a difference that was not significant ($P = .68$). Review of the usual therapy records indicated that bilateral training was used by regular therapists in only 1 case.

Change in Upper-Limb Outcomes and ADLs

Both groups improved during the intervention period (table 2); however, no significant differences were found between groups in the mean change between baseline and 6 weeks on the total ARAT score ($P = .68$), ARAT subsections grasp ($P = .43$), grip ($P = .53$), pinch ($P = .41$), and gross ($P = .77$) or in the change in the RMA ($P = .06$), 9HPT ($P = .51$) (see table 2), and the MBI, the measure of ADL independence ($P = .27$) (table 3). For the 85 participants who completed the follow-up assessment at 18 weeks, the difference between groups in the mean change between baseline and 18 weeks on the pinch subsection of the ARAT (95% CI, 0.3–5.6; $P = .03$) and on the 9HPT (95% CI, 0.0–0.1; $P = .05$) reached significance, indicating poorer recovery for the bilateral training group (fig 2). No significant

differences were found in the mean change in the total ARAT score ($P = .16$), ARAT grasp ($P = .45$), grip ($P = .21$), or gross ($P = .52$) or on the RMA ($P = .41$) (see table 2) or MBI ($P = .13$) (see table 3) over this period.

Change in HRQOL and Mood

There were no significant differences between bilateral and unilateral training groups between baseline and 6 weeks in change in quality of life (NHP) ($P = .25$), in HADS anxiety ($P = .19$), and HADS depression ($P = .42$) (see table 3). Similarly, no significant differences were found in change between baseline and 18 weeks on the NHP ($P = .34$), HADS anxiety ($P = .43$), and HADS depression ($P = .42$) (see table 3).

The Effects of the Severity of the Impairment on Upper-Limb Outcomes

We were interested in the effects of baseline severity on outcomes; therefore, 3 severity subgroups were created from ARAT and 9HPT baseline scores. Participants in subgroup 1 scored 0 to 3 on the ARAT ($n = 38$), had little or no upper-limb movement, and had no manual dexterity as evidenced by an inability to place any pegs in the 9HPT; participants in subgroup 2 scored between 4 and 28 on the ARAT ($n = 42$) and showed some upper-limb motor control but no fine manual dexterity as evidenced by the inability to place any pegs. Participants in subgroup 3, scoring between 29 and 56 on the ARAT ($n = 26$), could with 4 exceptions place some or all pegs, indicating good manual dexterity.

Using the factorial ANOVA, from baseline to 6 weeks, no significant interaction effect between the ARAT subgroup and group allocation was found for change in the upper-limb variables ($P > .05$) (table 4). However, there were 3 significant main effects in which baseline severity predicted recovery on the ARAT ($P < .01$), RMA ($P = .02$), and 9HPT ($P < .01$) (see table 4). From baseline to 18 weeks, no significant interaction effect between the ARAT subgroup and group allocation was found for change on the upper-limb variables ($P > .05$) (see table 4). Again, 3 significant main effects existed in which baseline severity on the ARAT predicted recovery over this period on the ARAT ($P = .01$), RMA ($P = .04$), and 9HPT ($P < .01$).

DISCUSSION

This study compared the effects of bilateral and unilateral upper-limb task training on upper-limb outcomes, ADLs, HRQOL, and mood during early poststroke rehabilitation. It also examined whether responses to upper-limb training were related to the severity of the initial impairment. To our knowledge, this is the largest RCT to date to investigate bilateral upper-limb training in participants with acute stroke. Although both groups improved, we found no beneficial effects of bilateral over unilateral training in terms of upper-limb recovery over 6 weeks of intervention or at the 18-week follow-up, regardless of the initial severity. In fact, recovery of dexterity, measured by the ARAT pinch subscale and 9HPT between baseline and 18 weeks, was significantly poorer for participants receiving bilateral training. Furthermore, there were no beneficial effects of bilateral training over unilateral training in terms of performance in ADLs, HRQOL, or mood.

Although direct comparisons with other bilateral training studies are difficult because of diverse methodologies and outcomes, our findings do not support previous studies in which participants with predominantly chronic stroke exhibited improved motor and functional outcomes with bilateral training.⁵⁻⁹ Our findings may differ from those studies for 2 possible

Table 2: Change Scores on ARAT Total, Grasp, Grip, and Gross Subsections and RMA (upper-limb section) for Bilateral and Unilateral Training Groups

Upper-Limb Measures 6-Week Scores and Change 0 to 6 Weeks	Bilateral Training (n=51)	Unilateral Training (n=46)	<i>P</i> (95% CI for difference in mean change between groups)	Upper-Limb Measures 18-Week Scores and Change 0 to 18 Weeks	Bilateral Training (n=46)	Unilateral Training (n=39)	<i>P</i> (95% CI for difference in mean change between groups)
ARAT total (max, 57)	27.9±19.5	34.3±19.8		ARAT total (max, 57)	29.0±21.9	37.6±21.2	
Change	14.3±13.2	15.4±12.6	0.68 (-4.1 to 6.3)	Change	14.3±13.2	18.6±13.6	0.16 (-1.7 to 1.3)
Grasp (max, 18)	9.5±6.6	11.6±6.8		Grasp (max, 18)	9.8±7.5	12.2±7.0	
Change	4.2±4.4	4.9±5.1	0.43 (-1.2 to 2.7)	Change	4.3±5.3	5.1±4.8	0.45 (-1.4 to 3.0)
Grip (max, 12)	6.0±4.3	7.6±4.3		Grip (max, 12)	5.9±4.7	8.2±4.6	
Change	3.2±2.9	3.6±3.3	0.53 (-0.9 to 1.7)	Change	3.0±3.3	3.8±3.0	0.21 (-0.5 to 2.2)
Gross (max, 9)	5.3±3.2	6.3±3.1		Gross (max, 9)	5.6±3.5	6.2±3.4	
Change	1.7±2.4	1.8±1.8	0.77 (-0.7 to 1.0)	Change	1.8±2.6	1.5±1.6	0.52 (-1.3 to 0.6)
RMA (max, 15)	5.5±3.5	7.1±3.8		RMA (max, 15)	6.0±4.1	7.3±4.0	
Change	1.9±2.3	2.8±2.7	0.06 (-0.1 to 2.0)	Change	2.3±3.1	2.8±3.0	0.41 (-0.8 to 1.9)

NOTE. Values are mean ± SD.

reasons: the nature of the intervention tasks and the timing of the intervention.

In our study, participants were trained in complex multijoint functionally relevant tasks, whereas other bilateral training studies have involved protocols using simple repetitive movements with electric stimulation⁸ or auditory cueing.^{7,14} Such augmentation of bilateral movement may provide more effective upper-limb coupling and consequent facilitation of the paretic arm than was possible with the free movements practiced in our study, suggesting that the effects of bilateral training may be influenced by task constraints. Furthermore, visualizing and processing information from the nonparetic limb, while simultaneously attempting to perform new, progressively changing, relatively complex precise motor goals with both arms may have provided a dual-task challenge greater than in other studies. Evidence suggests that stroke participants find tasks requiring divided attention difficult,³² and aimed movements of the hemiplegic arm require greater attentional resources than aimed movements in healthy subjects.³³ Anecdotally, participants receiving bilateral training in our study reported difficulty in attending to both limbs during practice, suggesting that attentional demands and task complexity may have influenced outcomes.

Intervention timing may also have influenced outcomes. We found no effects of bilateral training with acute stroke participants, whereas studies showing positive effects were conducted mainly with participants with chronic stroke.^{7,8,14} Stroke appears to alter normal transcallosal inhibition, resulting in increased intact hemisphere excitability during hemiparetic arm movement that may be inhibitory in nature, thus suppressing output from the damaged hemisphere.³⁴ Depending on the lesion site and size, this overactivation appears transient, and more normal contralateral activation patterns resume over time.³⁵ Identical motor commands generated in each hemisphere during bilateral movement may modulate transcallosal inhibition, balancing stroke-related interhemispheric overactivity and facilitating output from the damaged hemisphere as well as from normally inhibited ipsilateral pathways of the undamaged hemisphere to augment movement of the paretic arm.^{9,36} The extensive disruption of normal transcallosal inhibition soon after stroke may, however, render bilateral training less effective than in chronic stages when interhemispheric interactions have resumed a more normal balance; therefore, the effects of bilateral training may be time dependent. Therefore, future studies should investigate cortical activation patterns during bilateral training in the early poststroke period.

We found no significant between-group differences in the change in dexterity between baseline and 6 weeks; however, participants receiving unilateral training showed significantly better longer-term improvement in dexterity, suggesting that this group showed accelerated dexterity gains in the posttreatment phase. Given that training specificity is thought to be critical to training effect,⁴ bilateral practice of dexterity tasks in which both arms perform identical movement may be somewhat artificial and probably insufficiently related to everyday life dexterity requirements to provide a training effect. Tasks involving fine finger control are most commonly performed unilaterally or with hands performing bimanually different but coordinated tasks (eg, when tying shoelaces or typing). A mismatch between practice mode and performance requirements for dexterity tasks in everyday life may thus have led to the lower transfer of training effects to recovery of long-term dexterity in the bilateral training group.

Furthermore, anatomically, distal upper-limb muscles involved in dexterity show predominantly contralateral corticospinal control, and contributions of ipsilateral and bilateral control mechanisms to dexterity performance are limited.³⁷ Ipsilateral pathways from the undamaged hemisphere thought to become accessible for hemiparetic arm motor control during bilateral training⁹ are therefore unlikely to be involved in dexterity, which may explain poorer dexterity recovery of the bilateral training group. However, results must be interpreted carefully because many participants could not perform the dexterity tests (38% at 6wk, 26% at 18wk) because of poor finger control, reflecting floor effects of the tests.

Independence in ADLs improved for both groups but did not differ between groups during the study, despite greater unilateral training group recovery in dexterity. The MBI is probably too insensitive to detect dexterity changes, and participants may also have compensated with the unaffected upper limb to achieve independence in ADLs, a recognized phenomenon.²⁰

The change in HRQOL and mood did not differ between groups despite greater unilateral training group recovery in dexterity, suggesting that change in dexterity was not sufficiently clinically significant to influence these outcomes. Although upper-limb outcomes are known to influence HRQOL and well-being a year poststroke,¹⁶ they may have little impact on HRQOL and mood in acute stroke when ambulation may be a greater concern to the patient.²⁵

Table 3: Change Scores on the MBI, NHP, and HADS for Bilateral and Unilateral Training Groups

Measure 6-Week Scores and Change 0 to 6 Weeks	Bilateral Training (n=51)	Unilateral Training (n=46)	P (95% CI for difference in mean change)	Measure 18-Week Scores and Change 0 to 18 Weeks	Bilateral Training (n=46)	Unilateral Training (n=39)	P (95% CI for difference in mean change)
MBI (0-100)	83.0±16.2	85.1±19.2		MBI (0-100)	86±16.9	86.3±18.4	
Change	23.4±17.0	19.6±17.1	0.27 (-10.7 to 3.1)	Change	24.9±23.5	18.1±15.7	0.13 (-15.6 to 2.0)
NHP (0-600)	126.0±101.0	104.0±85.0		NHP (0-600)	122.0±110.0	92.0±92.0	
Change	-50.8±99.0	-73.7±95.3	0.25 (-62.3 to 16.3)	Change	-54.5±15.0	-77.5±105.1	0.34 (-70.8 to 4.7)
HADS anxiety (0-21)	5.2±4.1	5.7±3.9		HADS anxiety (0-21)	5.6±4.5	4.6±3.6	
Change	-1.4±3.5	-0.4±3.5	0.19 (-0.5 to 2.3)	Change	-1.1±3.6	-0.5±3.1	0.43 (-0.9 to 2.1)
HADS depression (0-21)	5.8±3.3	5.7±3.5		HADS depression (0-21)	5.4±3.5	4.5±3.2	
Change	-0.3±3.2	-0.8±2.9	0.42 (-1.8 to 0.7)	Change	-0.9±3.8	-1.4±2.1	0.42 (-1.9 to 0.8)

NOTE. Values are mean ± SD.

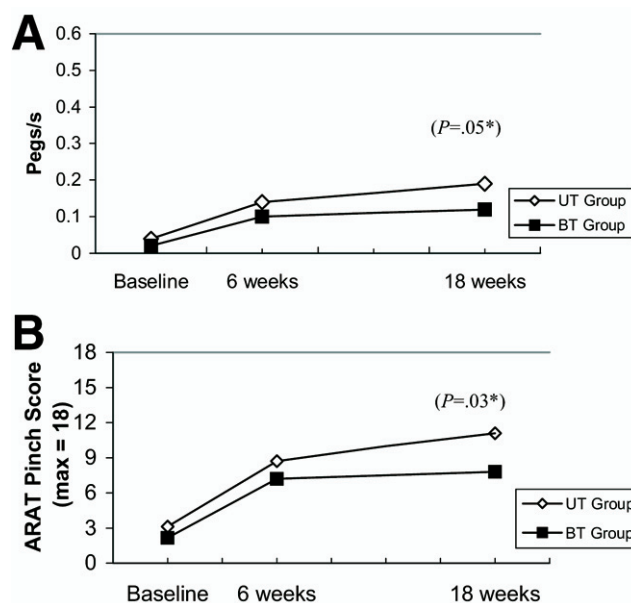


Fig 2. Change in dexterity in (A) 9HPT and (B) ARAT pinch between baseline, 6 weeks, and 18 weeks for bilateral (BT) and unilateral training (UT) groups. *Significant at *P* ≤ .05.

Study Limitations

In terms of study limitations, participants presented with various sites, types of lesion, and severity of motor deficits, leading to high variability in upper-limb scores that may have masked significant results. To account for influences of severity on responses to training, we created severity subgroups. Results suggest no benefits for bilateral over unilateral training for the subgroups, but baseline severity did influence recovery, supporting previous evidence.³⁸ Participant numbers in each subgroup may have been too small to detect significant differences in relation to the effects of training group allocation.

The bilateral training group showed lower baseline scores on all physical measures, which may have contributed to the findings. Although not statistically different, the difference in total ARAT scores was probably clinically significant.³¹ Patients were allocated to modified or core tasks depending on their performance at the first training session. Each protocol involved standardized tasks and progression and either unilateral or bilateral practice. The main difference between protocols was that in the modified protocol, when participants could not achieve a task, physical assistance was provided by the therapist until the patient was able to perform the task independently, thus adding additional variables that may have influenced results to the otherwise carefully standardized therapeutic program. The difference between groups in the proportion of participants allocated to or completing the core and modified protocols did not reach statistical significance, and there was no significant difference in the number of sessions taken to progress to the core protocol on one or more tasks. Nonetheless, a greater proportion of patients in the bilateral training group received modified training throughout, probably reflecting the baseline clinical characteristics of that group.

In line with other upper-limb studies in stroke,⁴ change scores were the variable of interest in the study because they account for heterogeneity within the sample at baseline. The use of change scores for subgroup analysis may be a less than optimal approach because it eliminates the variable of time as

Table 4: Change Scores and Main and Interaction Effects for Severity Subgroups

	Subgroup	Bilateral Training		Unilateral Training		ANOVA				
		n	Change	n	Change	Source of Variance	df	F	P	
Change 0 to 6 weeks										
ARAT (max, 57)	1	12	10.7±15.3	23	8.4±12.0	Main effects: treatment group	1,89	0.04	.85	
	2	22	20.1±11.2	17	20.4±13.1	subgroup	2,89	7.94	.00*	
	3	12	13.5±8.3	11	13.4±8.3	Treatment group by subgroup	2,89	0.13	.87	
RMA (max, 15)	1	12	2.0±2.8	23	1.7±3.0	Main effects: treatment group	1,89	2.48	.12	
	2	22	1.9±1.8	17	3.6±2.6	subgroup	2,89	4.12	.02*	
	3	12	1.4±1.9	11	2.6±2.4	Treatment group by subgroup	2,89	1.30	.28	
9HPT (pegs/s)	1	12	0.01±0.04	23	0.01±0.01	Main effects: treatment group	1,89	0.10	.75	
	2	22	0.08±0.12	17	0.11±0.12	subgroup	2,89	18.16	.00*	
	3	12	0.19±0.19	11	0.17±0.11	Treatment group by subgroup	2,89	0.84	.43	
Change 0 to 18 weeks										
ARAT (max, 57)	1	10	11.0±17.2	20	10.9±15.1	Main effects: treatment group	1,78	0.68	.41	
	2	18	17.8±13.7	15	24.9±13.4	subgroup	2,78	5.41	.01*	
	3	11	15.7±5.5	11	15.3±7.0	Treatment group by subgroup	2,78	0.74	.48	
RMA (max, 15)	1	10	2.3±3.9	20	2.5±3.9	Main effects: treatment group	1,78	0.38	.54	
	2	18	2.1±2.6	15	3.4±2.8	subgroup	2,78	3.27	.04*	
	3	11	2.6±1.6	11	2.3±2.4	Treatment group by subgroup	2,78	0.47	.63	
9HPT (pegs/s)	1	10	0.02±0.06	20	0.04±0.06	Main effects: treatment group	1,78	2.48	.12	
	2	18	0.09±0.13	15	0.15±0.15	subgroup	2,78	17.91	.00*	
	3	11	0.21±0.12	11	0.24±0.15	Treatment group by subgroup	2,78	0.48	.62	

NOTE. Values are mean ± SD. Subgroup 1 is patients scoring 0 to 3 on the ARAT at baseline. Subgroup 2 is patients scoring 4 to 28 on the ARAT at baseline. Subgroup 3 is patients scoring 29 to 57 on the ARAT at baseline.

*Significant at $P \leq .05$.

a factor in the analysis. We elected to conduct subgroup analysis in this way to provide consistency with the main analysis, which addressed change. We can be fairly certain that results of the ANOVA using change scores was robust given that we additionally conducted the same analysis of subgroups on outcome scores at 6 and 18 weeks and found the same pattern of results, which we have not presented here.

Of the patients who completed the intervention, there were no deviations from randomized allocation leading to change of group; therefore, intention-to-treat analysis for protocol violation was not required. We had no follow-up data for participants who did not complete the intervention; therefore, their data were classified as missing. Missing data caused by dropouts and losses to follow-up may therefore have influenced our findings. Given that we found no baseline differences between those who did not complete the study and the rest of the sample and we can explain dropout and loss to follow-up (see fig 1), we can be fairly certain that there were no particular characteristics that predisposed patients to dropout or not to complete the follow-up tests. We therefore elected to present an analysis of the complete cases only. To ensure that this was a robust representation of the findings, we performed analysis using 3 different methods of imputation for the missing data. After testing that the missing data were randomly distributed, analysis of datasets with substitution of the unilateral and bilateral training group mean values for the missing data on each measure in each of those groups, carry forward of the last known value, and expectation maximization using SPSS to generate missing values³⁹ were all conducted. None of these methods produced findings that were different from the results in which no method of imputation was used and provides us with a reasonable degree of certainty that results from the complete data were not biased by the missing cases.

Measurements were conducted at 2 endpoints using functional measures selected for clinical relevance but were relatively crude. Other studies, performed by using kinematic analysis, have shown

immediate improvements in the quality and timing of upper-limb movement during bilateral conditions in chronic stroke¹² and in some cases during subsequent unilateral performance.^{5,6,8} Immediate and subtle effects of bilateral training on movement parameters may have therefore been missed in our study.

Although the training dose was in line with other bilateral training studies,^{5,7} compared with some recent studies of other upper-limb intervention,⁴⁰ the dose of therapy in this study was low. Given the additional attentional demands faced by the bilateral training group, the therapy dose may have been insufficient to provide an effect of bilateral training.

Future work should examine optimal timing, dose and training characteristics for bilateral training, and its effects on patients at different stages of recovery using sensitive measures of impairment and function. Relationships between tasks practiced, test tasks, and functional outcomes also need further investigation, along with the effects of lesion location and the severity of impairment.

CONCLUSIONS

This study suggests that 20 minutes a day of bilateral training of functionally related tasks is no more effective than unilateral training for upper-limb recovery in acute stroke patients, regardless of the initial severity of the impairment. Furthermore, for recovery of dexterity, bilateral training actually appears less beneficial. Independence in ADLs, HRQOL, and mood were not influenced by bilateral training. Several other studies have found benefits of bilateral training; therefore, this approach cannot be rejected altogether as an upper-limb intervention in stroke on the basis of our study findings. The study does suggest that training characteristics, such as the nature of the tasks trained and the strength of interlimb coupling required for effects, may influence outcomes; therefore, future work should examine the optimal timing, dose, and

training tasks that might optimize the already known facilitatory effects of interlimb coupling.

Acknowledgments: We thank the research physiotherapists and occupational therapist who executed the treatment and assessment protocols and physiotherapists in hospitals across Dundee and Angus for their assistance throughout the trial.

References

- Nakayama H, Jorgenson HS, Raaschou HO, Olsen TS. Recovery of upper extremity function in stroke patients: the Copenhagen stroke study. *Arch Phys Med Rehabil* 1994;75:394-8.
- Parker VM, Wade DT, Langton Hewer R. Loss of arm function after stroke: measurement, frequency, and recovery. *Int Rehabil Med* 1986;8:69-73.
- Sveen U, Bautz-Holter E, Sødving KM, Wyller TB, Laake K. Association between impairments, self-care ability and social activities 1 year after stroke. *Disabil Rehabil* 1999;21:372-7.
- Winstein CJ, Rose DK, Tan SM, Lewthwaite R, Chui HC, Azen SP. A randomized controlled comparison of upper-extremity rehabilitation strategies in acute stroke: a pilot study of immediate and long-term outcomes. *Arch Phys Med Rehabil* 2004;85:620-8.
- Mudie MH, Matyas TA. Upper extremity retraining following stroke: effects of bilateral practice. *J Neurol Rehabil* 1996;10:167-84.
- Mudie MH, Matyas TA. Can simultaneous bilateral movement involve the undamaged hemisphere in reconstruction of neural networks damaged by stroke? *Disabil Rehabil* 2000;22:23-37.
- Whitall J, McCombe Waller S, Silver KH, Macko RF. Repetitive bilateral arm training with rhythmic auditory cueing improves motor function in chronic hemiparetic stroke [published erratum in: *Stroke* 2007;38:e22]. *Stroke* 2000;10:2390-5.
- Cauraugh JH, Kim S. Two coupled motor recovery protocols are better than one: electromyogram-triggered neuromuscular stimulation and bilateral movements. *Stroke* 2002;33:1589-94.
- Stinear JW, Byblow WD. Rhythmic bilateral movement training modulates corticomotor excitability and enhances upper limb motricity poststroke: a pilot study. *J Clin Neurophysiol* 2004;21:124-31.
- Swinnen SP. Intermanual coordination: from behavioural principles to neural-network interactions. *Nat Rev Neurosci* 2002;3:348-59.
- Kelso JA, Southard DL, Goodman D. On the nature of human interlimb coordination. *Science* 1979;203:1029-31.
- Cunningham CL, Stoykov ME, Walter CB. Bilateral facilitation of motor control in chronic hemiplegia. *Acta Psychol (Amst)* 2002;110:321-37.
- Harris-Love ML, McCombe Waller S, Whitall J. Exploiting interlimb coupling to improve paretic arm reaching performance in people with chronic stroke. *Arch Phys Med Rehabil* 2005;86:2131-7.
- Luft AR, McCombe Waller S, Whitall J, et al. Repetitive bilateral arm training and motor cortex activation in chronic stroke: a randomized controlled trial [published erratum in: *JAMA* 2004;292:2470]. *JAMA* 2004;292:1853-61.
- Parry RH, Lincoln NB, Vass CD. Effect of severity of arm impairment on response to additional physiotherapy early after stroke. *Clin Rehabil* 1999;13:187-98.
- Wyller TB, Holmen J, Laake P, Laake K. Correlates of subjective well-being in stroke patients. *Stroke* 1998;29:363-7.
- Penta M, Tesio L, Arnould C, Zancan A, Thonnard J. The ABILHAND questionnaire as a measure of manual ability in chronic stroke patients: Rasch-based validation and relationship to upper limb impairment. *Stroke* 2001;32:1627-34.
- Carr JH, Shepherd RB, Nordholm L, Lynne D. Investigation of a new motor assessment scale for stroke patients. *Phys Ther* 1985;65:175-80.
- Lyle RC. A performance test for assessment of upper limb function in physical rehabilitation treatment and research. *Int J Rehabil Res* 1981;4:483-92.
- Platz T, Pinkowski C, van Wijck F, Kim IH, di Bella P, Johnson G. Reliability and validity of arm function assessment with standardized guidelines for the Fugl-Meyer Test, Action Research Arm Test and Box and Block Test: a multicentre study. *Clin Rehabil* 2005;19:404-11.
- Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull* 1979;86:420-8.
- Lincoln N, Leadbitter D. Assessment of motor function in stroke patients. *Physiotherapy* 1979;65:48-51.
- Adams SA, Ashburn A, Pickering RM, Taylor D. The scalability of the Rivermead Motor Assessment in acute stroke patients. *Clin Rehabil* 1997;11:42-51.
- Heller A, Wade DT, Wood VA, Sunderland A, Hewer RL, Ward E. Arm function after stroke: measurement and recovery over the first three months. *J Neurol Neurosurg Psychiatry* 1987;50:714-9.
- Shah S, Vanclay F, Cooper B. Improving the sensitivity of the Barthel Index for stroke rehabilitation. *J Clin Epidemiol* 1989;42:703-9.
- Hunt SM, McEwen J. The development of a subjective health indicator. *Sociol Health Illn* 1980;2:231-46.
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361-70.
- Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet* 1991;337:1521-6.
- Hanlon RE. Motor learning following unilateral stroke. *Arch Phys Med Rehabil* 1996;77:811-5.
- Winstein C. Motor learning considerations in stroke rehabilitation. In: Duncan P, Badke M, editors. *Stroke rehabilitation: the recovery of motor control*. Chicago: Year Book Medical; 1987. p 109-34.
- Van der Lee JH, Wagenaar RC, Lankhorst GJ, Vogelaar TW, Devillé WL, Bouter LM. Forced use of the upper extremity in chronic stroke patients: results from a single-blind randomized clinical trial. *Stroke* 1999;30:2369-75.
- McDowd JM, Filion DL, Pohl PS, Richards LG, Stiers W. Attentional abilities and functional outcomes following stroke. *J Gerontol B Psychol Sci Soc Sci* 2003;58:P45-53.
- Platz T, Bock S, Prass K. Reduced skilfulness of arm motor behaviour among motor stroke patients with good clinical recovery: does it indicate reduced automaticity? Can it be improved by unilateral or bilateral training? A kinematic motion analysis study. *Neuropsychologia* 2001;39:687-98.
- Liepert J, Bauder H, Wolfgang HR, Miltner WH, Taub E, Weiller C. Treatment-induced cortical reorganization after stroke in humans. *Stroke* 2000;31:1210-6.
- Feydy A, Carlier R, Roby-Brami A, et al. Longitudinal study of motor recovery after stroke: recruitment and focusing of brain activation. *Stroke* 2002;33:1610-7.
- Cauraugh JH, Summers JJ. Neural plasticity and bilateral movements: a rehabilitation approach for chronic stroke. *Prog Neurobiol* 2005;75:309-20.
- Tanji J, Okano K, Sato KC. Neuronal activity in cortical motor areas related to ipsilateral, contralateral, and bilateral digit movements of the monkey. *J Neurophysiol* 1988;60:325-43.
- Feys H, Weerdt W, Nuyens G, van de Winckel A, Selz B, Kiekens C. Predicting motor recovery of the upper limb after stroke rehabilitation: value of a clinical examination. *Physiother Res Int* 2000;5:1-18.
- Tabachnick BG, Fidell LS. *Using multivariate statistics*. 4th ed. Boston: Allyn & Bacon; 2001.
- Taub E, Uswatte G, King DK, Morris D, Crago JE, Chatterjee A. A placebo-controlled trial of constraint-induced movement therapy for upper extremity after stroke. *Stroke* 2006;37:1045-9.

Supplier

- Version 11; SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.