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ORIGINAL REPORT

BILATERAL MOVEMENT-BASED COMPUTER GAMES IMPROVE SENSORIMOTOR FUNCTIONS IN SUBACUTE STROKE SURVIVORS: A RANDOMIZED CONTROLLED TRIAL

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Background: **Previous studies have reported that movement-based computer gaming is more effective than conventional intervention in enhancing upper limb rehabilitation.**

Objective: **To evaluate whether the use of bilateral movement-based computer games could augment the effects of conventional intervention in improving the upper limb motor function, grip strength and health-related quality of life of subacute stroke survivors.**

Methods: **A total of 93 subjects with subacute stroke were randomized into 2 groups receiving one of two 3.5-h interventions for 2 days per week over 8 weeks: *(i)* "bilateral movement-based computer games + conventional rehabilitation"; and *(ii)* "video-directed exercise + conventional rehabilitation" (control group).**

Results: **A total of 83 subjects completed the interventions and follow-up assessments. Compared with video-directed exercise + conventional rehabilitation, bilateral movement-based computer games + conventional rehabilitation produced greater improvements in upper limb motor impairment from mid-treatment to follow-up 1 month post-intervention, greater improvements in upper limb function from post-intervention to 1 month follow-up, and earlier improvements in grip strength (paretic) from mid-intervention to follow-up 1 month post-intervention. Subjects who received bilateral movement-based computer games + conventional rehabilitation also continued to improve in motor function from post-intervention to 1 month post-intervention.**

Conclusion: **Bilateral movement-based computer games may serve as an adjuvant therapy to conventional rehabilitation programmes for improving upper limb recovery among stroke survivors.**

Key words: stroke rehabilitation; subacute stroke survivors; upper limb function; computer gaming.

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LAY ABSTRACT

Upper limb sensorimotor impairment is a common and serious post-stroke sequel, affecting up to two-thirds of stroke survivors. Simultaneous bilateral training is a rehabilitative method that requires the use of both paretic and non-paretic sides completing identical tasks at the same time. Previous findings suggested that bilateral upper limb training was superior to unilateral upper limb training in improving upper limb motor impairment. Given that virtual reality-based therapy can be advantageous for engaging and encouraging participation in repetitive rehabilitative training tasks, this study aimed to investigate whether bilateral movement-based computer gaming (BMCG) using custom-made handlebars could better improve the upper limb motor function, grip strength and health-related quality of life of subacute stroke survivors than a conventional rehabilitation programme. After 16 sessions of bilateral BMCG, it was found that subacute stroke survivors had greater improvements in upper limb motor control, functional use of paretic upper limb and health-related quality of life than after a conventional rehabilitation programme. Thus, the combined use of computer gaming and bilateral movement-based training could be an adjunct therapy to conventional physiotherapy and occupational therapy in cognitively intact subacute stroke survivors.

Upper limb sensorimotor impairment is common after stroke, affecting up to two-thirds of all stroke survivors (1). Individuals with upper limb sensorimotor impairment have compromised hand and/or arm movements (2), which can lead to functional dependence and deteriorated quality of life. To promote independent living and recovery, effective stroke rehabilitation programmes should include repetitive and task-specific training for treating sensorimotor impairment and restoring motor function of the paretic upper limb.

Virtual reality-based therapy is an enjoyable method for keeping patients motivated (3) and encouraging the practice of functional tasks (4). In the virtual context, subjects practice motor movements responses to computer-generated sensory stimuli that closely simulate reality (5). Applying virtual reality-based therapy can encourage active participation in stroke rehabilitation (3) and repetitions of training tasks (6), and provide immediate feedback (7). Additional benefits have been demonstrated in various neuroplasticity studies and clinical trials. For example, a functional magnetic resonance imaging study (8), found that stroke survivors who received 4 weeks of movement-based computer gaming showed greater improvements than an inactive control group (n=5) in cortical reorganization of the primary sensorimotor cortex. In another clinical trial, 10 acute-stroke survivors who received 12 weeks of movement-based computer gaming and conventional therapy (i.e. standard occupational and physical rehabilitation) showed more significant improvements in the muscle strength and joint functions of their upper limbs, their paretic arm speed and their independence in activities of daily living compared with other acute stroke survivors (n=9) who received intense occupational therapy or interactive games using standard game consoles and conventional therapy over the same period (9).

Bilateral training is an effective rehabilitation-induced recovery training for upper limb motor impairment (10), based on the hypothesis that, in addition to injury-related reorganization, motor cortex functions can be altered by individual motor experience (10). To promote neural plasticity and regain movement control of the paretic side, simultaneous bilateral training requires that both paretic and non-paretic sides complete identical tasks at the same time. A recent systematic review and meta-analysis (11) demonstrated that bilateral upper limb training was superior to unilateral upper limb training in improving upper limb motor impairment, as measured by Fugl-Meyer Assessment of Upper Extremity (FMA-UE) (mean difference=2.21, 95% confidence interval (95% CI), 0.12–4.30, p=0.04).

Although increasing the motor experience of the paretic side is a potential way to promote neural plasticity, no previous study has investigated the effects of using customized computer games to improve recovery of the paretic upper limb. In the present study, therefore, it was hypothesized that the use of customized bilateral movement-based computer games (BMCG) could better engage people with stroke to practice functional training of both the paretic and non-paretic upper limbs simultaneously, and in turn, lead to better recovery of the paretic upper limb. Thus, this study was designed to test whether the combined use of BMCG and a conventional rehabilitation (CR) programme is more effective than the use of a CR programme in isolation in promoting the recovery of motor control, the functional use of the paretic upper limb in activities of daily living and health-related quality of life of the survivors of subacute stroke.

MATERIAL AND METHODS

The study began in August 2015 and all follow-up assessments were completed by August 2017. The study protocols were jointly approved by the clinical research ethics committees of the corresponding research hospital and research university (reference CRE-2012.343-T). The study was conducted in accordance with the principles of the Declaration of Helsinki for human experiments as well as the clinical practice standards of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (12). Written informed consent was obtained from all participants prior to the start of the study. Study data are available from the corresponding author on reasonable request.

The study involved a randomized, placebo-controlled, single-blinded clinical trial with a 1 month follow-up. Participants were subacute stroke survivors referred to the Geriatric Day Hospital at a regional public hospital within 1 week after discharged from the inpatient setting and were screened and enrolled by the physiotherapist-in-charge. The study was reported according to the Consolidated Standards of Reporting Trials Statement. Using the computer software G*Power version 3.1.0, an appropriate sample size was calculated based on the effect size from a pilot study with 10 subacute stroke survivors (d=0.64), with an α of 0.05 and a power of 0.80, in which the subjects received computer games combined with a CR programme for improving upper limb motor function. The required sample size was 80 (40 per group) for detecting a significant between-group difference. By further factoring an anticipated dropout rate of 10%, the calculated total sample size was 88.

Randomization of participants was performed by an offsite research assistant after informed written consent had been obtained. Using a random number table, the allocation of participants to 1 of 2 groups was stratified based on sex, age (45–70 vs 71–85 years) and type of stroke (ischaemic vs haemorrhagic). The subjects were notified of their allocated group by centralized phone calls, and reminded not to disclose this information to the assessor. The assessment and intervention were conducted in separate locations to further ensure that the assessors were blinded from the grouping of the subjects.

All participants were required to attend 4 assessments at the Geriatric Day Hospital at different intervals; these included assessments at: *(i)* baseline, *(ii)* mid-intervention (after 8 sessions of intervention), *(iii)* post-intervention (after 16 sessions of intervention), and *(iv)* follow-up (4 weeks after intervention). All assessments and data analyses were conducted by a full-time research assistant who was blinded from the

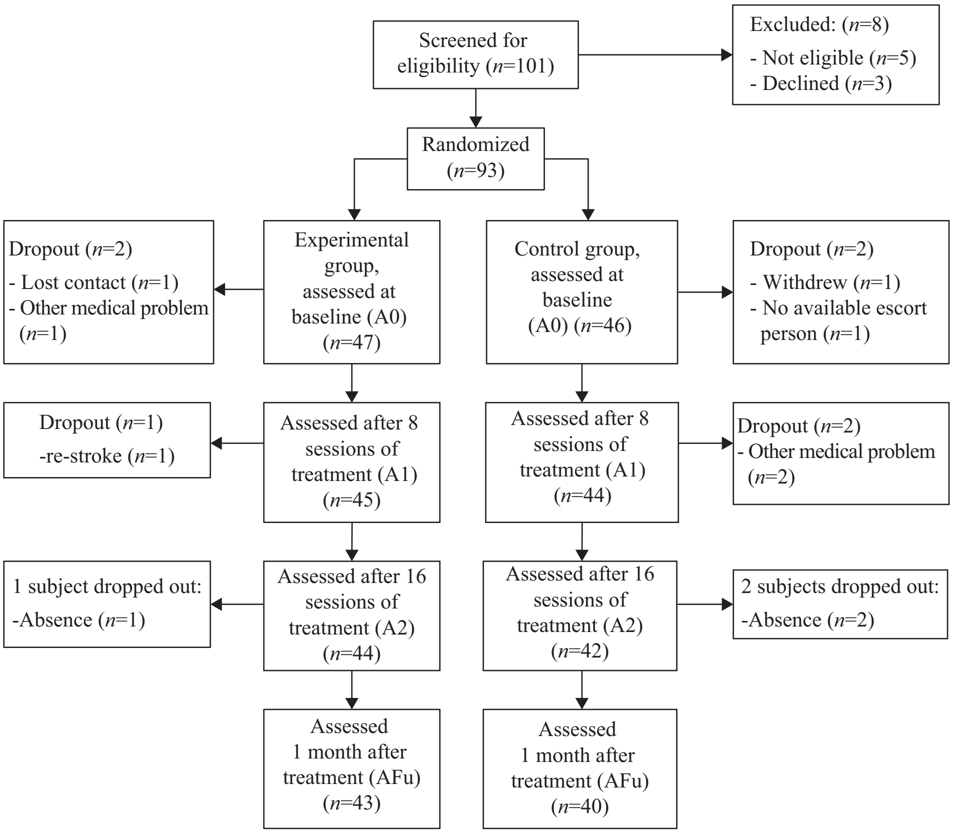

Fig. 1. Study flow.

allocation of groups and not involved in the intervention procedure.

Participants

After an initial screening, a total of 93 subjects aged between 45 and 85 years were recruited for the study (Fig. 1). The subjects met the following criteria: *(i)* they had a single stroke 1 week to 6 months before the study, as confirmed by magnetic resonance imaging or computed tomography; *(ii)* they scored $\geq$7 out of 10 on the Chinese version of the Abbreviated Mental Test; *(iii)* they could hold a game controller with their paretic hand; and *(iv)* they were able to follow verbal instructions for performing exercises. Exclusion criteria were: any individual who was involved in a drug study or another clinical trial, who used a cardiac pacemaker or who had receptive dysphasia or any additional medical condition that would hinder proper assessment and treatment. All eligible participants were randomized into 1 of 2 groups: *(i)* an experimental group that received a combination of BMCG and a CR programme, and *(ii)* a control group that received video-directed exercise (VDE) and the CR programme.

Intervention

All participants attended 16 sessions of their assigned treatments (in 2 sessions per week for 8 weeks, and at 3.5 h per session) at a geriatric day hospital. In each session, the subjects in both study groups first received 3 h of the CR programme, which was identical for both groups and consisted of physiotherapy and occupational therapy sessions (Appendix I); this was followed by 30 min of their assigned intervention (i.e. BMCG or VDE).

The subjects in the BMCG + CR group received 30 min of bilateral movement-based computer game intervention following the CR programme. During the BMCG sessions, the subjects played 3 different computer games (for 10 min each, and 30 min in total) using a customized game controller. The game controller had a custom-made handlebar (Fig. 2) at one end for the paretic hand; the other end was for the non-paretic hand. The subjects were required to move their paretic and non-paretic arms bilaterally in a nearly symmetrical and self-assistive pattern to complete the computer games (Fig. 3); doing so required directional control, strategy, timing, strength and endurance. Details of the computer games are summarized in Appendix II.

Following the CR programme, the subjects in the control (VDE+CR) group continued to perform a video-directed exercise for 30 min, while being monitored by a patient care assistant. In the VDE, the subjects were instructed to perform upper limb movement exercises that they had previously learned from attending training sessions at the geriatric day hospital

Fig. 2. Custom controller attached on the custom-made handlebars (AbleX, Auckland, New Zealand) with one end for the paretic hand and the other end for non-paretic hand.

(Fig. 3). The VDE served as a "care-as-usual" control that provided treatment hours.

Measures

Primary outcome. The Fugl-Meyer Assessment of the Upper Extremity (FMA-UE) was used for evaluating upper limb impairment. The FMA-UE has demonstrated excellent test–retest reliability (r=0.965) among individuals with chronic stroke (13).

Secondary outcomes. The Action Research Arm Test (ARAT) was used to evaluate upper limb function. It has demonstrated excellent intra-rater (r=0.996–0.997) and excellent inter-rater reliability (intraclass correlation coefficient (ICC)=0.995) for individuals with chronic stroke (14).

The grip strength (GS) of each subject's hands (i.e. including both the paretic and non-paretic sides) was measured using a digital handgrip dynamometer (Jamar Dynamometer, Sammons Preston Rolyan, Bolingbrook, Illionis, USA). GS was first assessed for the hand on the non-paretic side, then for the hand on the paretic side, with a 1-min interval in between. GS was measured by having the subject hold the handgrip dynamometer with their arm up to a 90° angle and squeezing the grip measurement.

The Chinese version of the Short-Form Health Survey (SF-36-C) was used to assess health-related quality of life. It has demonstrated good internal consistency (Cronbach's alpha: 0.85–0.87) in samples of healthy adults (15).

Data analysis

Baseline characteristics were summarized as descriptive statistics and analysed by group. The Kolmogorov–Smirnov test was used to test for normality of the data. For the baseline characteristics, continuous variables, including age, body mass index (BMI), number of stroke and post-stroke days, were compared using Student's *t*-test for normally distributed data and Mann Whitney *U* test for non-normally distributed data, respectively. Categorical data, including sex, types of stroke, areas of stroke, hemiplegic side, education level, working prior stroke and placement, were compared using χ^2 test. Linear mixed-effects models (LMM) were used to evaluate the effects of the 2 different interventions on both arms of every subject over the 3 time-points, while adjusting for potential confounding variables, such as socio-demographic characteristics and baseline values of variables of interest. Maintenance effects were analysed by comparing the results of the assessments at post-intervention and follow-up using the same mixed-effects modelling approach. As non-normally distributed data and random dropout data were accommodated by the LMM automatically, other statistical measures for accounting for non-normal data distribution and non-compliance and missing outcomes (e.g. intention-to-treat analysis) were not required.

To examine whether the intervention effects will be different in those with different levels of upper limb impairment and different post-stroke duration, we

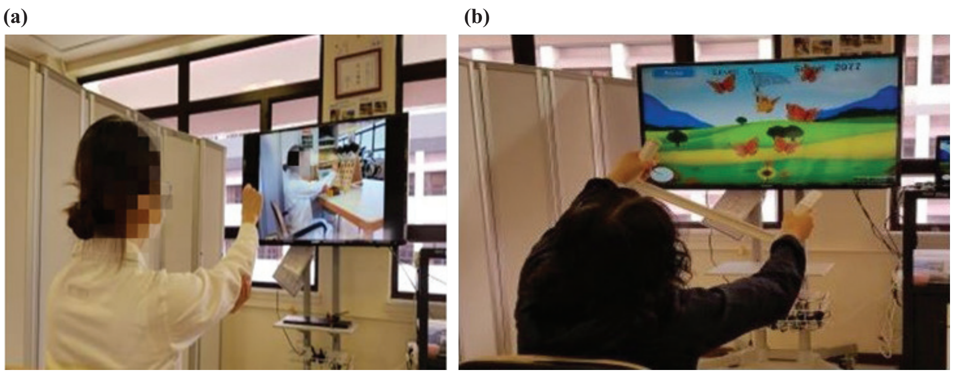

Fig. 3. Screenshots of the study. (a) Control group subjects performing video-directed exercise while being monitored by a patient care assistant. (b) Intervention group subject performing movement-based computer games using the customized game controller.

categorized 2 subgroups based on each subject's *(i)* upper limb capacity (a "moderate to severe" impairment indicated by a baseline FMA-UE score of 0–39 vs a "minimal to mild" impairment indicated by a baseline FMA-UE score of 40–66), and *(ii)* post-stroke time (more than 8 weeks vs 8 weeks or less). We used an analysis of covariance (ANCOVA) with intention-to-treat analysis to investigate the differences between groups in significant Group × Time interactions and/or time effects at mid-intervention, post-intervention and at 1 month post-intervention.

The level of statistical significance was set at p-value ≤ 0.05. All analyses were conducted in SPSS 23.0 (IBM, Armonk, NY, USA). All p-values were corrected using Bonferroni's correction to maintain an overall type I error of 5%.

RESULTS

The 2 study groups did not differ significantly in baseline characteristics (Table I). Owing to reasons not related to the study (e.g. recurrent stroke events), 4 (8.5%) and 6 (13%) participants dropped out of the BMCG+CR and VDE+CR groups, respectively. No adverse events occurred during any of the intervention and assessment sessions.

Table I. Characteristics of participants ($n=93$)

Characteristics	BMCG + CR ($n=47$)	VDE + CR ($n=46$)	U or χ^2 (p-value)
Age (years, mean ± SD)*	65.1±10.02	66.0±9.0	1031 (0.70)
Sex, n (%)**			0.11 (0.74)
Men	27 (57.4)	28 (60.9)	
Women	20 (42.6)	18 (39.1)	
BMI*	22.1 ± 2.5	22.4 ± 2.7	1024.50 (0.66)
Types of stroke, n (%)**			–0.48 (0.64)
Infarct	38 (80.9)	38 (82.6)	
Haemorrhage	9 (19.1)	8 (17.4)	
Number of stroke*	1.1 ± 0.4	1.2 ± 0.5	1053.00 (0.70)
Post-stroke duration,			
Post-stroke days (mean±SD)*	57.55 ± 24.66	63.43 ± 39.59	1031.00 (0.39)
≤ 8 weeks, n (%)**	29 (61.7)	25 (54.35)	0.52 (0.47)
> 8weeks, n (%)**	18 (38.3)	21 (45.65)	6.25 (0.18)
Areas of stroke, n (%)**			
Cerebral	42 (89.4)	38 (82.6)	
Cerebellar	2 (4.3)	0 (0)	
Mid brain/pons	3 (6.4)	7 (15.2)	
Other	0 (0)	1 (2.2)	
Hemiplegic side, n (%)**			0.87 (0.35)
Right	21 (44.7)	25 (54.3)	
Left	26 (55.3)	21 (45.7)	
Education level, n (%)**			4.26 (0.24)
Primary	16 (34.0)	21 (45.7)	
Secondary	20 (42.6)	17 (37.0)	
Tertiary	4 (8.5)	6 (13.0)	
Illiterate	7 (14.9)	2 (4.3)	
Working prior to stroke, n (%)**			1.05 (0.31)
Yes	18 (38.3)	13 (28.3)	
No	29 (61.7)	33 (71.7)	
Placement, n (%)**			1.45 (0.23)
Home	42 (89.4)	37 (80.4)	
OAH	5 (10.6)	9 (19.6)	

BMI: body mass index; OAH: old age home.
p-value: *Mann-Whitney U test, **χ^2 test.

Effects of BMCG + CR vs VDE + CR on upper limb rehabilitation

Primary outcome: upper limb motor impairment. LMM analysis revealed a significant Group × Time interaction effect (mean difference: 1.63; $p=0.001$) (Fig. 4a and Table II). The subjects in the BMCG + CR group demonstrated greater improvements in FMA-UE scores from mid-intervention to 1 month follow-up than the subjects in the VDE + CR group (Appendix III). In comparison with their FMA-UE scores at baseline, both groups demonstrated significant improvements from mid-intervention to 1 month post-intervention (Appendix IV).

Secondary outcomes: upper limb motor function, grip strength and health-related quality of life. Significant Group × Time interaction effects were revealed for the ARAT scores (mean difference: 2.04; $p=0.001$) (Fig. 4b and Table II). The BMCG + CR group showed better improvements in ARAT scores than did the VDE + CR group from post-intervention to 1 month follow-up (Appendix III). In comparison with their ARAT scores at baseline, both groups showed significant improvements from mid-intervention to 1 month post-intervention (Appendix IV). The BMCG + CR group showed relatively early improvements in their GS on the paretic side (in comparison with that at baseline) from mid-intervention to 1 month post-intervention. The VDE + CR group showed similar improvements in GS on the paretic side, but at a later stage (at 1 month post-intervention).

Significant time differences between groups were observed for the improvements in GS of the non-paretic side (mean difference: 0.54, $p=0.003$), as well as in the Physical Component Summary (PCS) scores (mean difference 1.29, $p<0.001$) and the Mental Component Summary (MCS) scores (mean difference 2.24, $p<0.001$) of the SF-36-C (Fig. 4d–f and Table II). The BMCG + CR group demonstrated improvements in GS of the non-paretic side (in comparison with that at baseline) at a relatively early stage; that is, starting from mid-intervention to 1 month follow-up (Appendix IV). The VDE + CR group showed similar improvements in GS on the non-paretic side, but at a later stage (at 1 month post-intervention). In the PCS scores of the SF-36-C, both groups demonstrated improvements (in comparison with their scores at baseline) from mid-intervention to 1 month follow-up (Appendix IV). However, the BMCG + CR group demonstrated significant improvements in the MCS scores of the SF-36-C at an earlier stage (from mid-intervention to 1 month follow-up) than the VDE + CR group (at 1 month post-intervention).

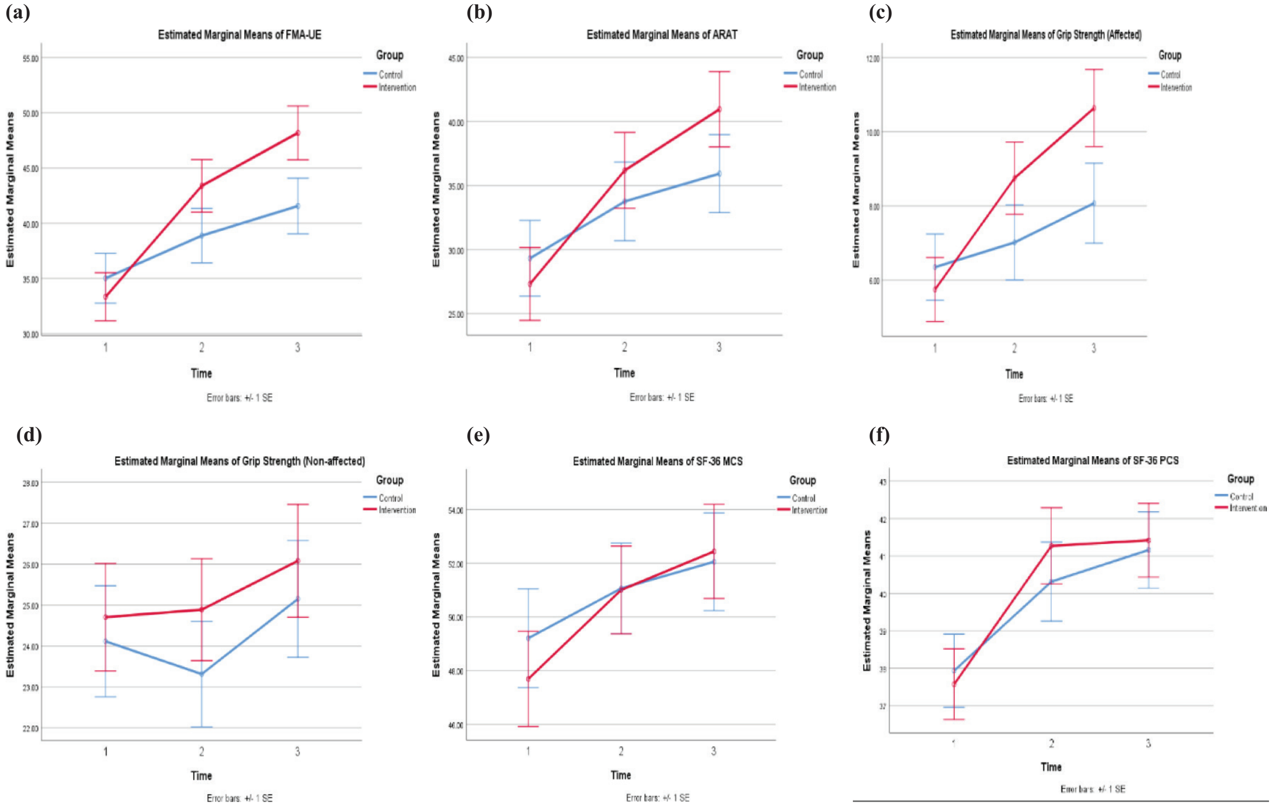

Fig. 4. Effects after 1 and 2 months. (a) Fugl-Meyer Assessment of Upper Extremity. (b) Action Research Arm Test. (c) Grip strength (paretic side). (d) Grip strength (non-paretic side). (e) MCS: Mental Component Summary. (f) PCS: Physical Component Summary.

Maintenance effects of the BMCG + CR and VDE + CR

The BMCG + CR group continued to show improvements in their FMA-UE and ARAT scores during post-intervention to 1 month post-intervention. The VDE + CR group continued to show improvements in their ARAT scores during post-intervention to 1 month post-intervention. Neither group showed significant reductions in maintenance effects for any other variables of interest (Appendix IV).

Subgroup analysis of the minimal to mild upper limb impairment and moderate to severe upper limb impairment groups

After controlling for the effects of baseline values, subjects with moderate to severe impairment who received BMCG + CR training showed better improvements than those who received VDE + CR intervention in FMA-UE scores ($F_{1,\,49}=12.20-18.87$, $p<0.001$), ARAT scores ($F_{1,\,49}=9.69-11.25$, $p=0.002-0.003$) and GS (paretic) scores ($F_{1,\,49}=6.98-8.00$, $p=0.007$–0.011) from mid-intervention to 1 month post-intervention. Subjects with minimal to mild impairment who received BMCG + CR intervention showed better improvements than those who received VDE + CR training in FMA-UE scores ($F_{1,\,38}=8.21-9.77$, $p=0.006$) at mid-intervention. They also showed better improvements in GS (paretic) scores ($F_{1,\,38}=11.10$, $p=0.002$) at mid-intervention (Appendix Va).

Subgroup analysis of the less acute (more than 8 weeks) stroke and more acute (less than 8 weeks) stroke groups

After controlling for the effects of baseline values, subjects with less acute stroke (more than 8 weeks after stroke) who received BMCG + CR intervention showed better improvements than subjects who received VDE + CR intervention in FMA-UE scores ($F_{1,\,36}=16.68-25.74$, $p<0.001$) from mid-intervention to 1 month post-intervention (Appendix Vb). Subjects with more acute stroke (8 weeks or less after stroke) who received BMCG + CR intervention showed better improvements in FMA-UE scores ($F_{1,\,51}=12.41-14.98$, $p<0.001$) at 1 month post-intervention, as well as better improvements in GS (paretic) scores ($F_{1,\,51}=8.26$, $p=0.020-0.040$) at post-intervention.

DISCUSSION

This study tested the hypothesis that BMCG training could augment the effects of a CR programme for upper limb rehabilitation among survivors of subacute stroke.

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Table II. Linear mixed-effects models of the effects of variables of interests

	Group	Baseline (mean ± SD)	4 weeks (midway through treatment) (mean ± SD)	8 weeks (end of treatment) (mean ± SD)	12 weeks (1 month follow-up) (mean ± SD)	Time effect [Mean difference (95% CI), *p*-value]	Group effect [Mean difference (95% CI), *p*-value]	Interaction effect [Mean difference (95% CI), *p*-value]
Primary outcome								
FMA-UE (0–66, higher better)	BMCG + CR	32.43 (12.77)	42.93 (14.02)	48.18 (13.05)	50.70 (13.39)	4.19 (3.52, 4.86), 0.000	9.19 (2.06, 16.32), 0.012	1.63 (0.67, 2.59), 0.001
	VDE + CR	34.15 (16.30)	37.93 (17.80)	41.56 (18.87)	43.68 (18.88)			
Secondary outcomes								
ARAT (0–57, higher better)	BMCG + CR	26.0 (17.74)	35.44 (17.92)	40.95 (17.04)	43.23 (17.04)	4.43 (3.61, 5.24), 0.000	8.93 (0.65, 17.21), 0.035	2.04 (0.87, 3.21), 0.001
	VDE + CR	27.41 (20.35)	32.64 (21.90)	35.93 (21.82)	37.53 (21.84)			
GS, paretic	BMCG + CR	5.49 (5.38)	8.65 (6.75)	10.64 (7.40)	11.13 (7.83)	1.72 (1.29, 2.16), 0.000	3.36 (0.04, 6.75), 0.052	0.78 (0.16, 1.40), 0.015
	VDE + CR	5.90 (5.81)	6.88 (5.92)	8.07 (6.31)	9.12 (6.66)			
GS, non-paretic	BMCG + CR	24.47 (7.59)	24.95 (7.47)	26.08 (8.84)	26.04 (8.92)	0.54 (0.20, 090), 0.003	−2.13 (− −6.08, 1.82), 0.286	0.24 (−0.27, 0.75), 0.344
	VDE + CR	23.58 (9.50)	23.24 (8.85)	25.15 (9.45)	24.74 (9.31)			
PCS (0–100, higher better)	BMCG + CR	37.76 (6.36)	41.41 (6.43)	41.42 (7.01)	42.40 (6.94)	1.29 (0.71, 1.86), <0.001	0.52 (2.86, 3.91), 0.759	0.03 (−0.80, 0.87), 0.93
	VDE + CR	37.96 (6.25)	39.93 (7.00)	41.16 (5.97)	42.20 (6.71)			
MCS (0–100, higher better)	BMCG + CR	47.14 (11.95)	50.92 (11.38)	52.44 (12.15)	54.99 (9.78)	2.24 (1.28, 3.20), <0.001	−2.25 (−7.43, 2.93), 0.390	0.73 (−0.65, 2.11), 0.294
	VDE + CR	48.36 (11.56)	50.58 (10.07)	52.05 (11.07)	53.71 (10.76)			

FMA-UE: Fugl-Meyer Assessment of Upper Extremity; ARAT: Action Research Arm Test; GS: Grip Strength; PCS: Physical Component Summary; MCS: Mental Component Summary; BMCG + CR: bilateral movement-based computer game and conventional rehabilitation programme; VDE + CR: video-directed exercise and conventional rehabilitation programme.

The findings suggested that BMCG using a customized game controller might aid the upper limb rehabilitation of people with subacute stroke.

These findings are consistent with those of previous studies, which showed that the combined use of virtual reality-based therapies and CR programmes could alleviate upper limb motor impairment (16, 17) and improve upper limb motor function (16). The BMCG + CR group demonstrated improvements (mean differences) of 15.75 points, 14.95 points, 5.15 kg, 1.61 kg, 3.66 points and 5.3 points over the baseline values of the FMA-UE and ARAT scores, GS (paretic and non-paretic) scores and the PCS and MCS scores of the SF-36, respectively. These improvements reached the minimally clinically important difference (MCID) values for subacute stroke survivors in the scores of the FMA-UE (9–10 points) (18), ARAT (12–17 points) (19) and GS (paretic) (5.0–6.5 kg) (20). The benefits of the BMCG + CR intervention for health-related quality of life were evidenced by the 9.69% and 11.24% improvements from the baseline values of the PCS and MCS scores, respectively.

As expected, our bilateral movement intervention successfully induced improvements in motor impairment and motor function; its combined use with virtual reality-based training could thus augment these effects of treatment. According to the "experience-related reorganization" hypothesis (10), bilateral movements could cause coupling effects between the paretic and non-paretic sides, and through the interhemispheric connections, reactivate the lesioned hemisphere (21); they could also generate identical motor commands in both cerebral hemispheres (22). Consequently, movement of the paretic upper limb could excite the normally inhibited intact hemisphere, resulting in the suppression of output from the lesioned hemisphere (23). In turn, this would modulate transcallosal inhibition and optimize stroke-related inter-hemispheric hyperactivity (24). This experience-related reorganization could enhance the output from both the lesioned cerebral hemisphere and the inhibited ipsilateral pathways of the intact cerebral hemisphere (23) that facilitate movement of the paretic side. Thus, the augmenting effects of computer gaming observed in this study could have been produced because the computer gaming interface created sensory stimulations that engaged and encouraged the study participants to practice their training tasks eagerly, repetitively and bilaterally. This intensive repetition of training of the upper limbs probably brought about cortical reorganization that contributed to functional recovery, as reflected in the treatment effects of BMCG in this study (25, 26).

Several previous studies of virtual reality-based training for stroke survivors focused mainly on survivors with "mild to moderate" disability (4, 27, 28). This study considered stroke survivors with "moderate-to-severe" and "minimal-to-mild" motor impairments separately (29, 30). The current study's BMCG+CR intervention could induce better improvements in the FMA-UE, ARAT and GS (paretic) scores than the control (VDE+CR) intervention in the moderate-to-severe group. Potentially, the bilateral training that involved the customized game controller facilitated exercise of the paretic limb with support and assistance from the non-paretic limb, in a bilateral and coordinated pattern of normal upper limb movement. Without the computer gaming environment and customized game controller to engage the subjects, those with moderate-to-severe impairment would probably less often simultaneously exercise both their paretic and non-paretic sides. In comparison, subjects with minimal-to-mild impairment could continue to benefit from the CR training, as their need for self-assistance from the paretic side was potentially minimal. This would explain why no significant difference was observed in motor impairment, motor function and GS (paretic) between subjects with minimal-to-mild impairment who received either the BMCG+CR or VDE+CR intervention.

Most previous studies investigated the effects of bilateral movement training and virtual reality-based stroke rehabilitation on individuals who were than 6 months post-stroke (31). To expand the understanding of such rehabilitations for individuals with different post-stroke times, the current study considered subjects with less acute stroke (8 weeks or more after stroke) and more acute stroke (less than 8 weeks after stroke). The findings suggested that the BMCG + CR intervention could induce better improvements in the FMA-UE and GS (paretic) scores than the control (VDE + CR) intervention in both the less acute and more acute subgroups, as well as additional improvements in the ARAT scores in the more acute subgroup. As recovery of upper limb control and function is well known to occur within the first 3–6 months after a stroke, the benefits of the current study BMCG + CR intervention in improving upper limb function of the paretic side were more obvious in survivors of a more acute stroke than those of a less acute stroke.

In contrast to the recent findings of Rodriguez-Hernandez (32), the current study BMCG+CR intervention was not superior to conventional training in improving the health-related quality of life of survivors of a subacute stroke. One possible explanation is that different aspects of quality of life were assessed in the current study from those assessed by Rodriguez-Hernandez (32). Here, we summarized health-related quality of life in 2 summary components (i.e. the PCS and the MCS). In comparison, Rodriguez-Hernandez (32) used the EuroQoL-5 dimensions instrument (EQ-5D-5L) and EuroQoL visual analogue scale (EQ-VAS), in which health-related quality of life was assessed based on 5 domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and overall health status. Nonetheless, as observed by Rodriguez-Hernandez (32) as well as in the current study, both the BMCG+CR intervention and conventional intervention were effective in improving quality of life when subjects' post-training scores were compared against their scores at baseline.

This study has several strengths. First, it used a custom-made game controller, which could detect 3-dimensional movements of the paretic hands, instead of a commercial game controller, which may not have been user-friendly for stroke survivors. Secondly, the treatment dosages of both the intervention and control programmes were high (up to 420 min per week for 8 weeks).

This study had several limitations. First, the study subjects could not be blinded to the interventions that they received. Secondly, the recruited subjects might have posed a threat to the external validity of the study. The majority of the recruited subjects had only experienced their first stroke, aged around 65 years, cognitively intact, in subacute stage, and more than half of those in the BMCG+CR group had moderate to severe upper limb impairment. Thus, the generalizability to those with chronic stroke, younger age, cognitively impaired, and with only mild upper limb impairment was limited. Thirdly, our participants were not blinded to the intervention, which might have exaggerated the estimated intervention effects. Fourthly, there were multiple outcome variables in the present study; thus, the risk of false-positive results was increased. Although Bonferroni corrections were performed to protect from an overall type I error in the multiple comparisons of secondary outcomes (p-value $0.05/4=0.0125$), it might increase the risk of type II errors. Fifthly, the current study did not assess the level of fatigue that could be associated with upper limb motor function in stroke survivors. Nonetheless, we measured the associated health outcomes of fatigue by evaluating the level of grip strength and health-related quality of life. Finally, the results of the current statistical analyses should be interpreted with caution. In the current study, the observed parameters were non-normally distributed at post-intervention, which violated the assumptions of parametric test. In addition, we adopted mean and standard deviation (SD) to describe the central tendency and variability of the FMA and ARAT observations. It is debatable that we could not assume that the responses on the ordinal scale were equal and the data were normally distributed. However, the LMM was robust enough to analyse the data with non-normal distribution (33). Thus, we used the LMM to deal with the non-normally distributed data in the current study.

CONCLUSION

This study provides empirical evidence for the efficacy of an 8-week, 16-session BMCG+CR intervention is more effective than the use of CR intervention alone in improving the recovery of upper limb motor control and the functional use of the paretic upper limb in activities of daily living of a cohort of subacute stroke survivors after approximately 50 days of inpatient hospital stay. Training involving movement-based computer gaming can augment the treatment effects of routine conventional physiotherapy and occupational therapy in cognitively intact subacute stroke survivors.

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Author contributions

Conceptualization: SSLL, SSMN and JW; methodology: SSLL and SSMN; formal analysis and investigation: SSLL, TWL and CWKL; writing – original draft preparation: SSLL and TWL; writing – review and editing: SSMN, CWKL and JW; resources: SSLL, SSMN and CWKL; supervision: SSMN and JW.

Conflicts of interest

The authors have no conflicts of interest to declare.

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