

# A Smart Glove Digital System Promotes Restoration of Upper Limb Motor Function and Enhances Cortical Neuroplastic Changes in Subacute Stroke Patients: A Randomized Controlled Trial

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## Research article

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# Abstract

**Background:** The sensor-based soft smart glove device is able to achieve multiple degree of freedom and complex motions with soft components. The purpose of this study was to examine the effects of RAPAEEL® Smart Glove digital training system on functional restoration of upper extremity and cortical neuroplastic changes in subacute stroke patients while provided in combined with conventional occupational therapy (OT).

**Methods:** Fifty-two subacute stroke patients with upper extremity motor function deficit participated and 36 of them completed the interventional protocol (20 experimental group and 16 control group) . All participants were treated with conventional OT for 4 weeks, 5 times per week, 30 min per day. In addition, the experimental group received game-based digital hand motor training with the RAPAEEL® Smart Glove digital system for 4 weeks, 5 times per week, 30 min per day. The control group received additional OT for 30 min. The outcomes were assessed before intervention (T0), after 4 weeks of intervention (T1), and 4 weeks after cessation of intervention (T2) using Fugl-Meyer assessment (FMA) scale and Jebsen-Taylor hand function test (JTT). Oxygenated hemoglobin ( OxyHb ) levels over bilateral primary and secondary motor cortices during hand and wrist movement were measured using functional near infrared spectroscopy at T0 and T1.

**Results:** All groups demonstrated improved upper extremity motor function for FMA total score and all subscores of JTT at T1, however, only experimental group showed further improvement at T2 (  $p < 0.05$ ). Also, the experimental group had significantly greater improvements upper extremity score of FMA scale and all subscores of JTT at T1 and T2 (  $p < 0.05$ ). Concentration of OxyHb over the ipsilesional sensorimotor cortex during wrist and hand movement was more increased in the experimental group than control group at T1 (  $p < 0.05$ ).

**Conclusion:** This study demonstrated that training with the RAPAEEL® Smart Glove further improved upper extremity and hand motor function than conventional OT alone by enhancing ipsilesional motor cortical activity in subacute stroke patients.

## Background

Stroke is a leading cause of morbidity and the main cause of sensory-motor impairment worldwide. Several studies have reported that more than 65% of chronic patients have had motor and sensory problems in the hemiparetic upper extremity [1, 2]. Hand function is especially required for activities of daily living (ADL) such as manipulating objects, eating, holding utensils, turning a key in a lock,

handwriting, and computer and telephone use. Loss of hand function is a serious, common result of a cortical lesion from cerebrovascular attack [3]. Therefore, recovering hand function is of primary importance in neurorehabilitation of stroke survivors. Furthermore, timing must be considered when planning neurorehabilitation focused on neuroplasticity following a stroke [4]. Previous studies have demonstrated that earlier rehabilitation leads to greater neuroplasticity in cortical areas controlling hand function in the lesioned hemispheres [5, 6].

Conventional rehabilitation for hand function and neuroplasticity, such as constraint-induced movement therapy [7], high-intensity training, and repetitive task-oriented training [8], often have unsatisfactory results due to insufficient patient motivation. However, previous evidence suggests that intensive repeated training is likely necessary to modify neural organization and promote recovery of hand motor skills in stroke patients [9, 10]. To overcome these limitations, game-based virtual reality (VR) training is becoming a promising technology to promote motor recovery by providing high-intensity and repeated task-oriented rehabilitation with 3-dimensional game programs involving patient body movement [11-13]. More recently, robotic rehabilitation was posited to have a positive effect favoring attention; reducing effort to enhance motor control, specifically in the hand; boost motivation; boost adherence to treatment; and boost sensorimotor integration [14]. Consequently, robotic rehabilitation may complement standard rehabilitation for restoring hand function [15]. However, despite these advantages, a common problem with robotic devices is their high cost, large size, and rigid components. Most devices are designed for hospital use and are too complex for patients to use on their own at home. A sensor-based, soft, smart glove device can achieve multiple degrees of freedom and complex motions with soft components [16-18]. Peculiarly, a task-specific, interactive, game-based VR system combined with soft smart glove can be used for motor recovery in stroke patients [18]. We used the RAPAEL<sup>®</sup> Smart Glove digital system with game-based VR developed by Neofect (Yong-in, Republic of Korea) for task-oriented hand training with interactive motion recognition of the user's movement.

The aim of this study was to examine the effects of RAPAEL<sup>®</sup> Smart Glove digital training combined with conventional occupational therapy (OT) compared with conventional OT alone on upper extremity function and cortical brain activation in sub-acute stroke patients.

## Methods

### Participants

This study included 51 participants with upper limb functional deficits caused by stroke, who presented at Samsung Medical Center of Seoul and Pusan National University Yangsan Hospital of Yangsan-si, Republic of Korea. All participants were eligible for inclusion if they met the following requirements: (1) age between 20 and 85 years, (2) > 3 weeks and < 3 months after stroke onset, (3) active range of motion (ROM) in the wrist > 10 degrees, and (4) unilateral upper limb deficit with a Fugl-Myer Assessment score > 22. Exclusion criteria were (1) history of preexisting neurological or psychiatric disorder, (2) multiple or bilateral stroke lesions, (3) Korean Mini-Mental State Exam (K-MMSE) score < 17, (4) aphasia, and (5)

pregnancy. Ethics approval was granted by the Pusan National University Yangsan Hospital Ethics Committee and written informed consent was obtained from all participants before the study. This study was retrospectively registered at ClinicalTrials.gov.

## Experimental design

A randomized controlled trial was performed to test the effectiveness of hand motor training with the RAPAEL<sup>®</sup> Smart Glove digital system and game-based VR in subacute stroke patients. Eligible participants were randomly placed in either the experimental group (hand motor training with the RAPAEL<sup>®</sup> Smart Glove digital system) or control group (conventional OT for the same amount of time as the experimental group) by a research administrator using a random number table after baseline assessment. All participants were assigned a code number.

## RAPAEL<sup>®</sup> Smart Glove digital system

The RAPAEL<sup>®</sup> Smart Glove digital system was designed to induce neuroplasticity for hand function and has two types of embedded sensors to collect information on individual motions in real-time. By applying a '*Learning Schedule Algorithm*' to game-like exercises, the RAPAEL<sup>®</sup> Smart Glove can create ADL-related tasks compatible with an individual's function level. The system provides information about a patient's current condition, exercise progress, and functional improvement by analyzing the active ROM.

## Intervention protocol

All participants were treated with 20 intervention sessions over 4 weeks: 5 times per week, 1 hour per day. The experimental group received game-based VR hand motor training with the RAPAEL<sup>®</sup> Smart Glove digital system for a total of 20 sessions at 5 sessions per week for 4 weeks. If participants missed any training during the intervention period, additional sessions were offered at another time during the week or during an optional additional week at the end of the intervention period. In each VR game, the participants were required to successfully perform tasks related to a specific intended movement to obtain a high score.

In the training protocol, the average time per session was 1 hour, divided into 30 min with the VR training program and 30 min of conventional OT. The intervention structure was customized to each participant's hand function level. As the session progressed, the training intensity gradually increased by changing the VR game level. The control group had 1-hour sessions of conventional OT alone without VR hand motor training.

## Outcome measures

We performed the following assessments before intervention (T0), immediately after the intervention (T1), and 4 weeks after the intervention (T2).

### Primary outcome: motor function

An occupational therapist performed upper extremity Fugl-Meyer assessment (UFMA) for motor impairment of the affected side and the Jebsen-Taylor hand function test (JTT) at T0, T1, and T2. Primary outcome was differences of these motor function scores between T1 and T0, T2 and T0. The UFMA consists of 33 items (3-point ordinal scale and range, 0–66), with higher scores indicating less impairment.[19] The JTT assesses hand function according to ADL with a series of 7 timed subtests, including writing, simulated page turning, picking up small objects, simulated feeding, stacking checkers, picking up large light objects, and picking up large heavy objects.[20] In original JTT, the subtest is considered missing if patient cannot complete the subtest within a certain amount of time.. In order to overcome this limitation of original JTT scoring system, we adopted the modified scoring system in this study as presented in the previous study. According to this modification, each subtest scored from 0 to 15 and the total score is the sum of each subtest scores ranged from 0 to 105) [21].

### Secondary outcome: cortical activation changes in the motor cortical regions

To investigate cortical activation by changes of oxygenated hemoglobin (OxyHb), we used the NIRScout® system (NIRx Medical Technology, Berlin, Germany), which is a multi-modal, compatible, functional near-infrared spectroscopy system (fNIRS) platform. This system has many optodes consisting of 16 sources and 16 detectors, which cover the sensorimotor cortex (SMC), premotor cortex (PMC), and supplementary motor area (SMA) using 45 channels of interest. The NIRScout® uses two different wavelengths (760 nm and 850 nm) with a sampling rate of 3.91 Hz. The optodes were positioned according to the international 10/20 system, and the channel distance (i.e., distance between the source and detector) was 3.0 cm.

Changes in OxyHb concentration over the ipsilesional primary motor cortex is the secondary outcome which was analyzed by the NIRS-SPM (Near Infrared Spectroscopy-Statistical Parametric Mapping) [22] software package in MATLAB (The Mathworks, USA). To investigate cortical activity in the affected side of the brain, left brain lesions were flipped from left to right in the data preprocessing stage so all included lesions were set on the right. We used a modified Beer-Lambert law to calculate OxyHb level following change in cortical concentration [23]. The international 10/20 system was used to position optodes with the cranial vertex (Cz) located beneath the 1st source. The nasion, left ear, right ear, and

inion were identified in each subject. A stand-alone application was used for spatial registration of the 49 functional channels on the Montreal Neurological Institute brain.

Gaussian smoothing with a 2s full width at half maximum (FWHM) was applied to correct noise from the fNIRS system. A wavelet discrete cosine transform (DCT)-based detrending algorithm was used to correct signal distortion due to breathing or movement, and a general linear model (GLM) analysis with a canonical hemodynamic response curve was then performed to model the hypothesized OxyHb response under the experimental conditions [22]. To investigate changes in cortical activation during wrist and hand movements, we selected 5 regions of interest (ROIs) defined by Brodmann area (BA) or anatomical markers: primary SMC (BA 1, 2, 3, and 4), PMC (BA 6), SMA (anterior boundary: vertical line to the anterior commissure, posterior boundary: anterior margin of primary SMC, medial boundary: midline between the right and left hemispheres, lateral boundary: 15 mm lateral to the midline between the right and left hemispheres).

## Statistical Analysis

All statistical analyses were performed with SPSS version 22.0 (IBM, Armonk, N.Y., USA), and the significance level was set at 0.05. The Shapiro-Wilk test was used to confirm that all outcome variables were normally distributed. The independent t-test for continuous parameters, Mann-Whitney U test for ordinal parameters, and  $\chi^2$  test for categorical parameters were used to compare baseline characteristics between groups. For measures of dependent parameters, a repeated-measures ANOVA was used to compare UFMA and JTT scores among time points (T0, T1, and T2).

For changes in OxyHb concentration, statistical parametric mapping (SPM) t-statistic maps were computed for group analyses and were considered significant at an uncorrected threshold of  $p < 0.05$ . Means, SDs, and 95% CIs were provided to depict the change within each group during the study and the training effect.

## Results

Thirty-six participants completed the 20-session intervention program and assessments at T1 and T2. One participant from the experimental group and 5 from the control group did not complete the intervention program. Fig. 1 provides a CONSORT flow diagram of participant recruitment and retention through this study. General characteristics of the 36 participants are shown in Table 1. No significant differences in general characteristics or dependent variables were observed between groups.

Primary outcome

The UFMA and JTT scores before and after intervention are presented in Table 2 and Fig. 2. UFMA total score improved significantly in both groups after the intervention. In addition, UFMA total score had a significant group  $\times$  time interaction such that the experimental group had more improvement ( $p < 0.05$ ). In particular, the wrist and hand items of the UFMA clearly improved. The JTT total score to assess hand function in ADL improved significantly in both groups. In addition, the JTT total score had a significant group  $\times$  time interaction such that the experimental group demonstrated more improvement ( $p < 0.05$ ). More interestingly, for each individual JTT component (simulated page turning, picking up small objects, simulated feeding, stacking checkers, picking up large light objects, and picking up large heavy objects) except for the writing, the experimental group had significantly greater improvement than the control group ( $p < 0.05$ ).

### Secondary outcome

Statistical parametric mapping  $t$  image revealed  $t$ -statistic maps for OxyHb concentration during wrist and hand movement. During wrist and hand movement after the intervention, OxyHb values increased significantly in the right SMC (affected hemisphere) (uncorrected,  $p < 0.01$ ) in the experimental group only (see Fig. 3). On the other hand, OxyHb values increased significantly in the left SMC only during wrist movement and in the left SMC and bilateral PMCs during hand movement in the control group.

In the time-course of hemodynamic responses, OxyHb values increased significantly in the right SMC (independent  $t$ -test,  $*p < 0.05$ ) during wrist movement (see Fig. 3). Also, OxyHb values tended to increase in the right SMC ( $*p = 0.086$ ) during hand movement.

## Discussion

The current study was conducted to examine the effect of neurorehabilitation with the RAPAE<sup>®</sup> Smart Glove digital system on upper extremity motor function and cortical brain activation in sub-acute stroke patients. The findings from this study suggest that convergent VR training with the RAPAE<sup>®</sup> Smart Glove digital system and conventional OT has some key benefits in terms of neurorehabilitation quality compared with matched conventional OT. Game-based VR training with the RAPAE<sup>®</sup> Smart Glove digital system was more effective than conventional therapy alone in restoring upper extremity motor function and ADLs in sub-acute stroke patients. Our results showed that the game contents were closely related to ADLs, so it showed a positive effect not only on simple motor recovery, but also ADL recovery as assessed by JTT. More importantly, the recovered upper extremity motor function and ADLs were maintained for 4 weeks after the intervention.

Cortical changes result from changes in behavioral patterns, which is important in neurorehabilitation.[24] Especially, intensive neurorehabilitation training in sub-acute stroke can induce changes in cortical sensorimotor maps and maximize improvements in motor function.[25] Sensory information is crucial in motor learning and post-stroke recovery, and retained sensory function is considered a positive

prognostic indicator of motor function outcome.[26] Motor relearning is defined as reacquiring motor skills after central nervous system injury and is facilitated by repetitive active movement.[27] Sensory stimulation training to restore motor function has been performed with various VR-based biofeedback and haptic devices.[28-31] VR systems combined with haptic devices have been reported to improve sensory stimulation and biofeedback more than VR systems alone, resulting in greater SMC activity and motor learning.[32] The results of this study demonstrate that combining game-based VR training and the RAPAEL<sup>®</sup> Smart Glove digital system as a haptic device increased SMC activation and improved upper extremity motor function.

In rehabilitation, patient motivation is important in achieving a positive clinical outcome.[33] None of the participants in this study who completed 20 training sessions with the RAPAEL<sup>®</sup> Smart Glove digital system experienced adverse events. This result indicates that game-based VR training with the RAPAEL<sup>®</sup> Smart Glove digital system does not pose a risk to patients while increasing their motivation. In addition, participant attitudes regarding the game-based training were mostly positive. The findings of the current study demonstrated a beneficial effect of game-based VR training with the RAPAEL<sup>®</sup> Smart Glove digital system on upper extremity motor function and increased SMC activation in the sub-acute stage of stroke. However, this study had several limitations. The statistical power was low because of the small number of participants. Therefore, these results cannot be generalized to all sub-acute stroke patients. The small number of fNIRS analyses was due to data loss and contributed to the low statistical power. Additionally, long-term follow-up was not included. We suggest that further research examines the long-term effects of game-based VR training with the RAPAEL<sup>®</sup> Smart Glove digital system. Furthermore, future research should examine the possibility of home rehabilitation using the game-based VR training with the RAPAEL<sup>®</sup> Smart Glove digital system.

## Conclusions

The results of this study demonstrate important benefits of game-based VR training with the RAPAEL<sup>®</sup> Smart Glove digital system combined with conventional OT. We recommend game-based VR training with RAPAEL<sup>®</sup> Smart Glove digital system to improve upper extremity motor function and cerebral cortex activation in sub-acute stroke patients.

## Abbreviations

OT: occupational therapy; FMA: Fugl-Meyer assessment; JTT: Jebsen-Taylor hand function test; OxyHb: Oxygenated hemoglobin; ADL: activities of daily living; VR: virtual reality; ROM: range of motion; K-MMSE: Korean Mini-Mental State Exam; UFMA: upper extremity Fugl-Meyer assessment; fNIRS: functional near-infrared spectroscopy system; SMC: sensorimotor cortex; PMC: premotor cortex; SMA: supplementary motor area; FWHM: full width at half maximum; DCT: discrete cosine transform; GLM: general linear model; ROIs: regions of interest; BA: Brodmann area; SPM: statistical parametric mapping.

# Declarations

## Funding

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## Ethics approval and consent to participate

Ethics approval was granted by the Pusan National University Yangsan Hospital Ethics Committee (Reference No. PNUYH-03-2015-002) and written informed consent was obtained from all participants before the study. This study was retrospectively registered at ClinicalTrials.gov (NCT02431390).

## Authors' contributions

YHK and HJL contributed to experimental design, experimental progress, data analysis and drafting the manuscript. AL, HGK and HYS contributed to setting up the experiment and collecting data. WHC, SHK and HJL contributed to experimental design, data analysis and data interpretation. Also, YHK and YIS contributed to setting up the experiment and revising the manuscript. YHK gave conceptual advice and edited the manuscript. Finally, RAPAEL<sup>®</sup> Smart Glove digital system developed by Neofect was provided for this study. All authors read and approved the final manuscript.

## Availability of data and materials

The data that support the findings of this study are available from the corresponding author on reasonable request.

## Consent to publish

Not applicable.

## Acknowledgements

Not applicable.

## Competing interests

The authors declare that there are no conflicts of interest, financial or otherwise, related to the submitted manuscript or any associated with this research.

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## Tables

**Table 1.** Baseline Characteristics of Participants

Characteristic	Experimental Group (n = 20)	Control Group (n = 16)
Sex (male / female)	10 / 10	7 / 9
Age (yrs)	57 (12.8)	63.7 (8.6)
Stroke onset duration (days)	24.7 (16.3)	34 (25.5)
Etiology		
Ischemic / Hemorrhagic	11/9	13/3
Side of stroke		
Right / left	13/7	9/7
MAS grade (0 / 1 / 1+)		
Elbow (Flexion/Extension)	0/2/1	0/1/1
K-MMSE (score)	25 (3.97)	25.31 (3.57)

Values are expressed as mean (SD).

UAS: Modified Ashworth Scale, K-MMSE: Korean version of Mini-Mental State Exam

**Table 2.** Upper extremity Fugl-Meyer assessment in the Experimental and Control Groups

Variable	Experimental group (n = 20)			Control group (n = 16)			p-value
	T0	T1	T2	T0	T1	T2	
Total	41.3 (8.90)	54.8 (8.27)**	58.7 (7.53) <sup>†,‡</sup>	37.13 (12.84)	45.13(10.44)**	49.3 (10.98) <sup>†,‡</sup>	0.027
Upper extremity	27 (4.95)	32.2 (3.73)**	33.85 (3.54) <sup>†,‡</sup>	26.25 (6.10)	30.38 (3.85)**	31.19 (4.31) <sup>‡</sup>	0.148
Wrist	4.7 (2.41)	8.05 (2.48)**	8.25 (2.45) <sup>‡</sup>	3.31 (2.98)	4.69 (2.63)**	6.44 (2.87) <sup>†,‡</sup>	0.010
Hand	6.1 (3.34)	10.75 (3.09)**	11.85 (2.48) <sup>†,‡</sup>	5.56 (3.85)	7.69(3.75)**	8.81 (3.54) <sup>†,‡</sup>	0.019
Coordination / Speed	2.4 (1.14)	3.8 (1.51)**	4.35 (1.42) <sup>†,‡</sup>	1.69 (1.85)	2.38 (1.78)	2.88 (1.45) <sup>†,‡</sup>	0.052

Values are presented as mean (SD). \*  $p < 0.05$  and \*\*  $p < 0.01$  for within-group comparisons (T1-T0), <sup>†</sup>  $p < 0.05$  (T2-T1) and <sup>‡</sup>  $p < 0.05$  (T2-T0) for within-group comparisons.

## Figures

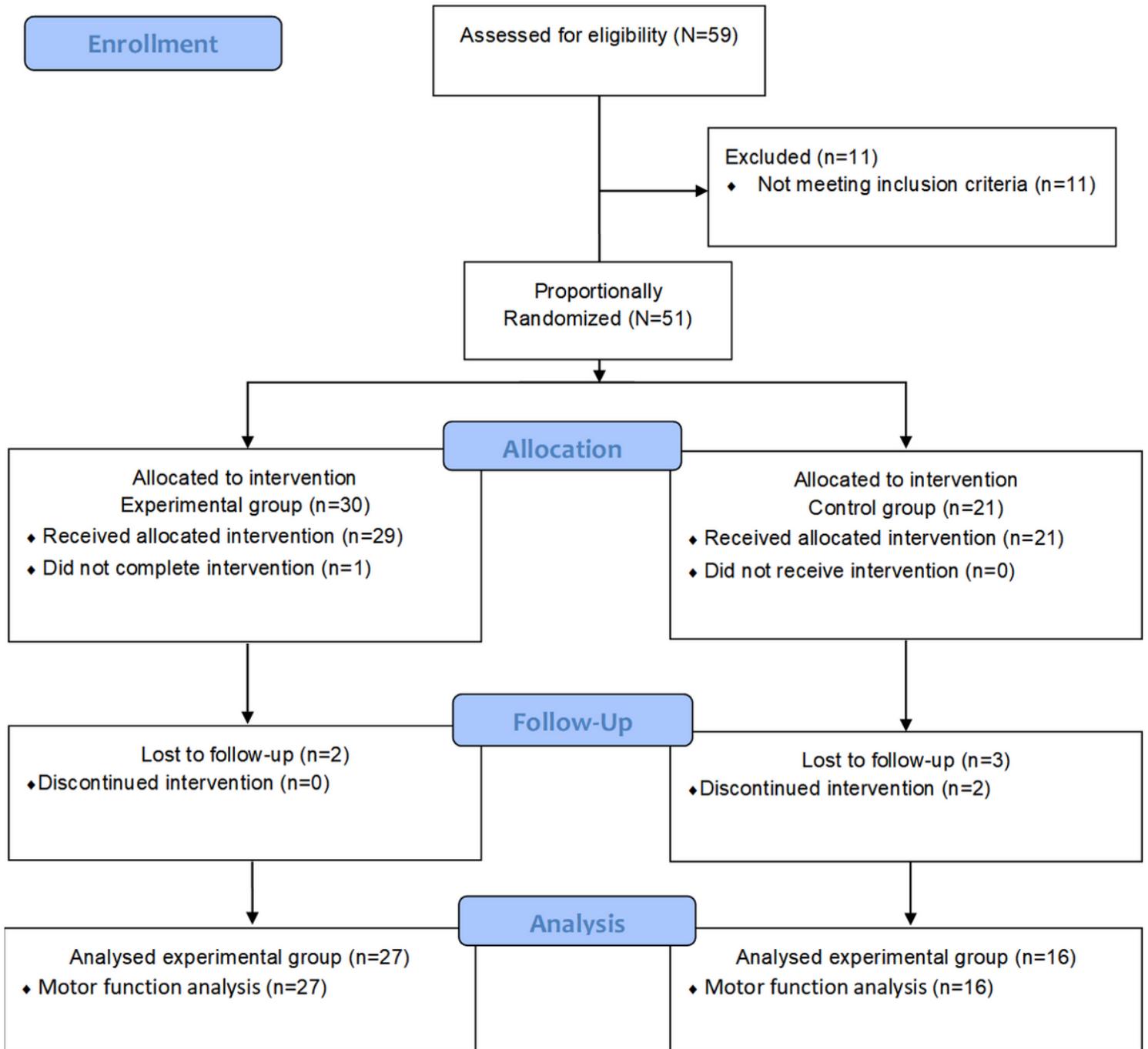


Figure 1

CONSORT flow diagram of this study.

—●— Experimental group    - -○- - Control group

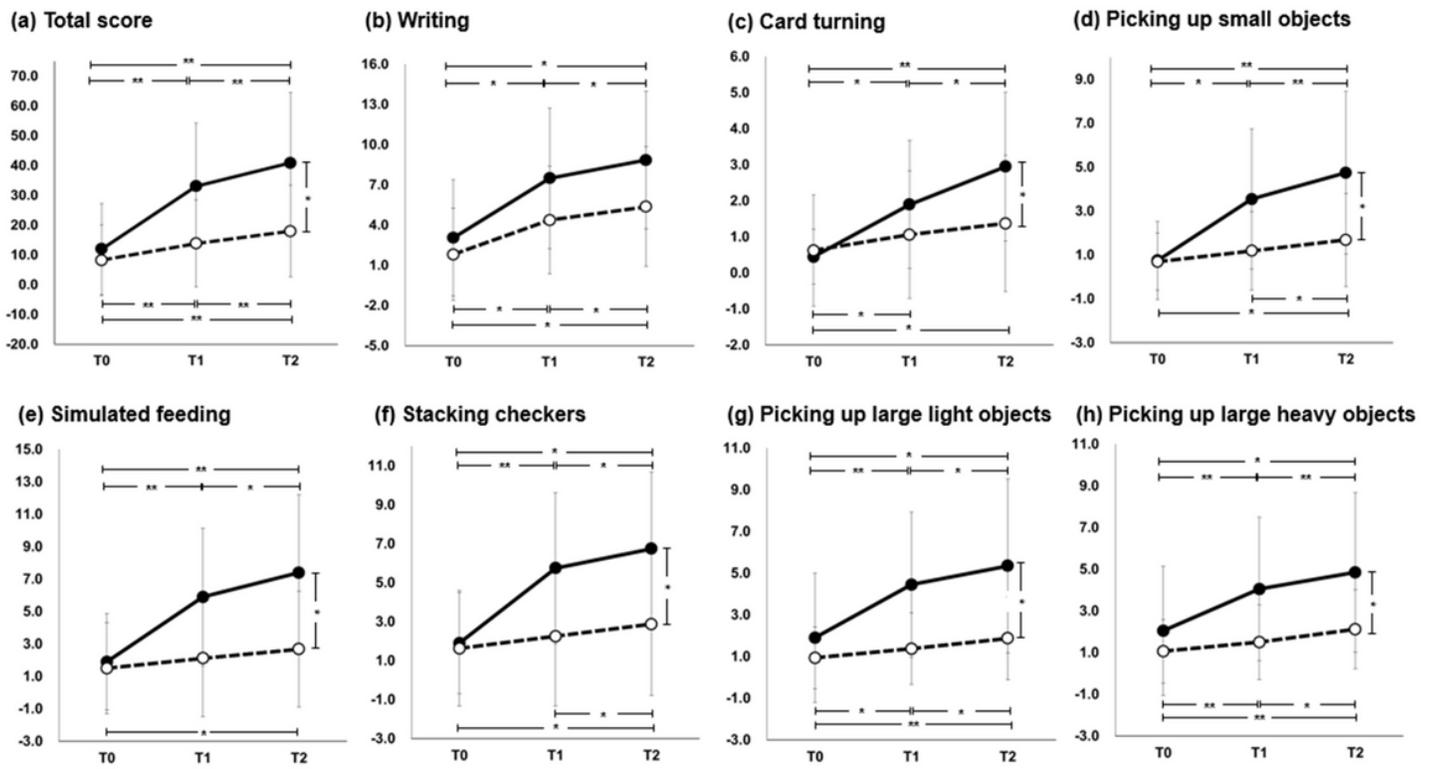


Figure 2

Group analysis of Jebsen-Taylor hand function test in experimental and control group. \*p < 0.05, \*\*p < 0.01.

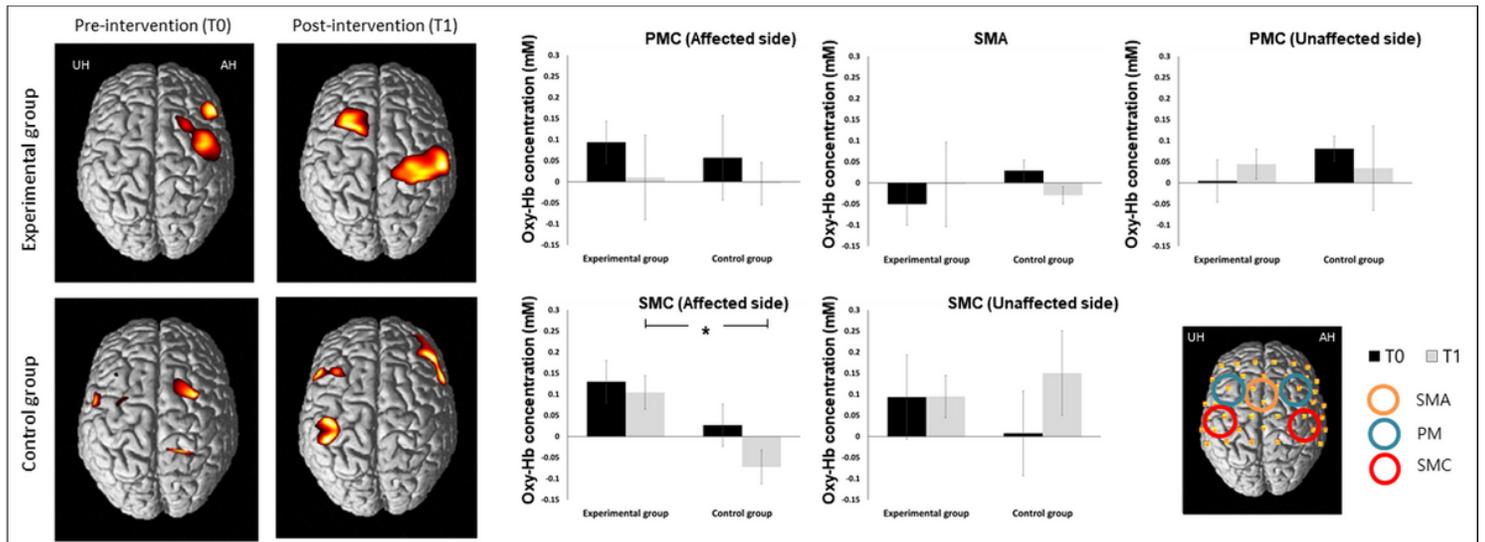


Figure 3

The results of group analysis of OxyHb in experimental and control group. Group-average activation map of OxyHb during wrist flexion/extension using NIRS-SPM (uncorrected, p < 0.01) OxyHb: oxygenated hemoglobin, SMC: sensorimotor cortex; PMC: premotor cortex; SMA: supplementary motor area