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Effects of visual terminal feedback on hand dexterity in relation to visuospatial ability in subacute stroke: a preliminary study

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Hand dexterity impairments in patients with stroke reduce activities of daily living (ADL) and quality of life. Visuospatial ability is associated with motor learning, but this has not previously been reported in patients with subacute stroke. We aimed to investigate whether visual terminal feedback (FB) affected motor learning of hand dexterity and the relationship among visuospatial ability. Overall, 17 subacute stroke patients (age: 66.1 ± 13.8 years) with mild upper limb motor impairment were included. The experimental task was the grasping force control task. The visuospatial task was the Rey–Osterrieth Complex Figure Test (ROCFT). The experimental protocol was conducted in 2 consecutive days: day 1 consisted of a pre-test (PRE), practice, and short-term retention test (SRT), and day 2 consisted of a long-term retention test (LRT) and the ROCFT. Grasping errors were significantly decreased in the SRT and LRT than in the PRE. Furthermore, ROCFT scores (copy and recall) and LRT grasping errors were moderately negatively correlated (ρ = -0.51 and − 0.53). In conclusion, visuospatial ability is an important factor associated with motor learning in subacute stroke patients. Future studies should use visual terminal FB, and training programs for visuospatial ability should be considered in stroke rehabilitation.

Keywords Augmented feedback, Grasping force adjustment ability, Motor learning, Stroke, Task-specific training, Visuospatial ability

Abbreviations

ARAT	Action Research Arm Test
EHI	Edinburgh Handedness Inventory
FB	feedback
FMUE	Fugl–Meyer assessment for the upper extremity
KP	knowledge of performance
KR	knowledge of results
MR	mental rotation
MoCA	Montreal Cognitive Assessment
RMSE	root mean square error
ROCFT	Rey–Osterrieth Complex Figure Test

The incidence of stroke is increasing worldwide, and stroke adversely affects many patients[1]. Approximately 85% of stroke survivors experience motor paralysis of the upper extremities, and 50% still have residual motor deficits more than 6 months after onset[2]. Particularly, patients have difficulty improving movements that require hand dexterity, such as manipulating objects and grasping. Such reduced hand activity results in reduced activities of daily living (ADLs) and quality of life[3]. Pennati et al.[4]investigated changes in the sensorimotor function and

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precision grasping ability of the upper extremities and hands over a 6-month period post-stroke and found that precision grasping remained impaired even in patients with improved sensorimotor function. Patients with stroke have impaired hand coordination of the paralyzed upper extremity when performing actions such as grasping objects and using tools. This can lead them to avoid using the paralyzed upper extremity and to compensate by using the non-paralyzed upper extremity, causing learned non-use of the paralyzed upper extremity[5]. Therefore, training using coordinated movements of the paralyzed hand is important for improving hand dexterity in patients with stroke.

Task-specific training is a common strategy for improving hand coordination in patients with stroke[6]. It is used to improve motor skills in tasks based on real-life environmental conditions. In a systematic review of task-oriented training components for upper extremity and hand motor skills in patients with stroke, Timmermans et al.[6]reported that feedback (FB) on performance has a strong therapeutic effect. FB facilitates motor learning and can be classified into two main categories: intrinsic and extrinsic. Intrinsic FB represents sensory information that individuals obtain from their own movement, whereas extrinsic FB represents information provided externally as instructions about movement results, such as knowledge of results (KR) and knowledge of performance (KP)[7]. Extrinsic FB includes various FB strategies, such as the timing and frequency of FB provision.

Previous randomized controlled trials have focused on upper-limb and hand motor function in patients with subacute stroke and have compared the improvement of motor function in conditions with and without task-oriented training. However, the details of FB strategies, such as frequency and timing of FB, are unknown[8–10]. In a previous study focusing on the effects of FB on upper-limb motor learning and hand coordination, 37 patients with chronic stroke were classified into three different FB conditions (KR, KR + KP, and no KR), and their performance on a finger-reaching task using the paralyzed upper limb was compared. The KR and KR + KP groups showed greater improvement than the no KR group with respect to movement accuracy and movement time reduction at post-test (after 2 weeks) and retention test (after 1 month)[11].

Furthermore, a previous study comparing performance in a finger-reaching task among 28 patients with chronic stroke in two different FB conditions (KR and KR + KP groups) showed that only the KR + KP group had improved motor patterns[12]. However, negative effects of extrinsic FB in patients with chronic stroke have also been reported. A study of the effects of FB and no-FB conditions on motor learning in an upper-limb tracking task in patients with chronic stroke showed that motor learning was inhibited in the FB condition[13,14]. In summary, there is no consistent consensus on FB strategies to enhance motor learning of the upper extremities and hand coordination in patients with subacute and chronic stroke.

Visuospatial ability has recently attracted attention as a factor that enhances motor learning[15–18]. Visuospatial ability is an important component that includes various cognitive functions that aid the encoding of visual images[19]and are involved in integrating the location of oneself with objects and tools. The superior and inferior parietal lobes have been shown to be responsible for this function in brain regions[20]. Visuospatial ability has been assessed using neuropsychological assessment tools such as the Montreal Cognitive Assessment (MoCA), Mental Rotation (MR), and the Rey–Osterrieth Complex Figure Test (ROCFT)[21]. The ROCFT specializes in the assessment of visuospatial functions, including visuospatial construction and visuospatial memory, compared to other neuropsychological assessments. The measurement time is approximately 5–10 min, so therapists can conveniently use it in clinical settings[22]. Particularly, the ROCFT result has been found to be an important predictor of motor learning capacity in older individuals[15,18]. Furthermore, VanGilder et al.[16] validated a predictive model of motor learning in patients with chronic stroke and showed that the ROCFT scores were a factor in constructing a well-fitting model.

However, the relationship between visuospatial ability and motor learning in patients with subacute stroke (< 6 months) remains unclear. The patients in the study by VanGilder et al. were in the chronic phase (mean time since onset: 3.8 years) and were younger (mean age: 58.4 years) than the cohort in the present study. The sample size was also small ($n = 7$). Validating the relationship between visuospatial ability and motor learning can confirm that visuospatial ability is an important component of hand coordination rehabilitation in patients with stroke during the recovery phase. Thus, as a preliminary study, we aimed to clarify FB strategies that enhanced the motor learning of hand coordination and to determine the relationship between visuospatial ability and motor learning in patients with subacute stroke. We hypothesized that the use of visual terminal FB in patients with stroke would improve the ability to adjust the grasping force, even in patients with motor impairments. We also hypothesized that the relationship between visuospatial ability and motor learning in patients with stroke would be positive, with higher visuospatial ability correlating with higher motor learning ability.

Results

Participant characteristics

A total of 19 patients with subacute stroke were included from July 2021 and August 2022. However, one patient was discharged before motor function evaluation, and one patient withdrew during the experiment. Consequently, 17 patients (8 males/9 females) with a mean age of 66.1 ± 13.8 years completed the trial. Figure 1 shows the participant recruitment process. Table 1 presents the participant characteristics. The participants had mild motor deficits in the upper extremities of the paralyzed side. There were six participants with right hemiplegia and 11 participants with left hemiplegia.

Change in ability to adjust grasping force

Figure 2 shows the root mean square error (RMSE) values for the test and practice blocks. According to the Shapiro–Wilk test, the pre-test (PRE, $p = 0.022$), short-term retention test (SRT, $p = 0.002$), long-term retention test (LRT, $p = 0.045$), Block 3 ($p = 0.021$), Block 4 ($p = 0.033$), and Block 5 ($p = 0.013$) data were not normally distributed, whereas data from Blocks 1 ($p = 0.271$) and 2 ($p = 0.338$) were normally distributed. The results of the Friedman test showed a significant main effect ($F = 23.65$, $df = 2$, $p < 0.001$). In addition, the post hoc

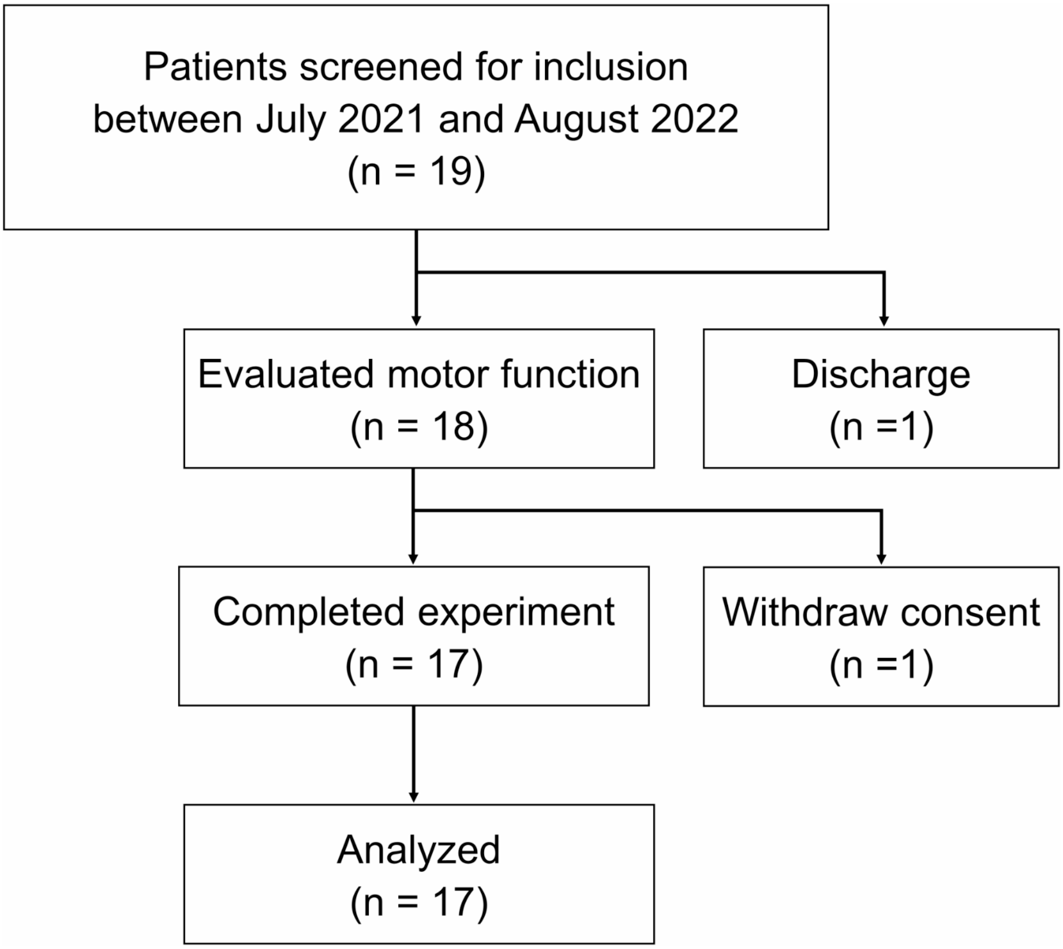

Fig. 1. Progress of the participants through the experiment. Two participants have dropped out of the study, and 17 participants are included in the final analysis.

	Sex	Age (years)	Days	EHI	Stroke type	Affected hemisphere	FMUE (0–66)	ARAT (0–57)
1	F	72	69	10	Infarction	Left	56	56
2	M	57	125	78.9	Infarction	Right	57	57
3	F	76	151	100	Hemorrhage	Left	56	55
4	M	46	69	60	Infarction	Left	66	57
5	M	71	60	90	Hemorrhage	Left	66	57
6	M	61	111	90	Infarction	Right	54	56
7	M	72	55	100	Infarction	Left	54	53
8	F	83	56	80	Hemorrhage	Left	48	57
9	F	77	144	100	Hemorrhage	Left	65	57
10	F	75	44	90	Infarction	Left	64	57
11	M	42	30	100	Hemorrhage	Left	57	52
12	F	49	39	50	Hemorrhage	Left	63	57
13	M	85	47	100	Infarction	Left	66	56
14	F	67	41	100	Hemorrhage	Left	51	57
15	M	46	54	100	Infarction	Right	64	57
16	F	81	49	100	Infarction	Right	62	57
17	F	64	34	100	Infarction	Left	65	57

Table 1. Participant characteristics. *Days* days since onset stroke, *EHI* Edinburgh Handedness Inventory, *FMA* Fugl–Meyer Assessment for upper extremity, *ARAT* Action Research Arm Test.

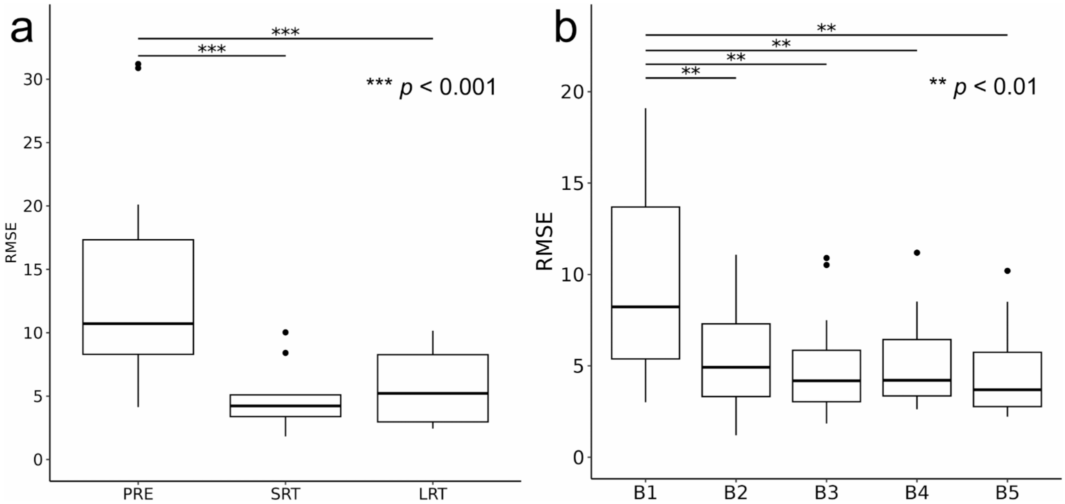

Fig. 2. Change in ability to adjust grasping force. (**a**) Results of grasping errors. The center line shows the median value. Whiskers indicate values below 1.5 times the interquartile range (IQR) above the first quartile and up to 1.5 times the IQR above the third quartile; data beyond this are shown as outliers, indicated by black points. Abbreviations: PRE, pre-test; SRT, short-term retention test; LRT, long-term retention test. (**b**) Results of grasping errors in each practice block. Abbreviations: B1–B5, Block 1–5.

test revealed significant differences between the PRE and SRT ($p < 0.001$) and between the PRE and LRT (all $p < 0.001$) (Fig. 2a). Meanwhile, there were no significant differences between the SRT and LRT ($p = 0.330$). The practice block also showed a significant main effect ($F = 26.682$, $df = 4$, $p < 0.001$) (Fig. 2b). Post hoc tests showed significant differences between Block 1 and all other blocks (Block 1 vs. Block 2: $p = 0.003$, Block 1 vs. Block 3: $p = 0.002$, Block 1 vs. Block 4: $p = 0.005$, Block 1 vs. Block 5: $p = 0.003$).

Relationship of test performance with motor function and visuospatial ability

Figure 3 shows the correlations among test performance, motor function (Fugl–Meyer Assessment for the Upper Extremity [FMUE] and Action Research Arm Test [ARAT]), and visuospatial ability (copy score, organization score, and 3-min delayed-recall score). Spearman's rank correlation coefficients revealed a moderately negative correlation of performance in the LRT with the copy score ($p = 0.038$, $\rho = -0.51$) and the 3-min delayed-recall score ($p = 0.028$, $\rho = -0.53$). No significant correlations were found between test performance and motor function parameters as well as between pre-test and SRT performance and visuospatial ability.

Discussion

The relationship between visuospatial ability and motor learning in patients with subacute stroke (<6 months) remains unclear. This study showed that visual terminal FB enhanced motor learning of the ability to adjust grasping force in patients with subacute stroke. Furthermore, although motor function was not associated with motor learning ability of adjusting the grasping force, visuospatial ability was associated with this ability. There was better improvement in the ability to adjust the grasping force in the SRT and LRT than in the PRE. These results support the appropriateness of an FB strategy.

FB timing can be classified into concurrent FB (FB given during the trial) and terminal FB (FB given after the trial is completed)[23]. In visual FB, concurrent FB better improved performance during practice than did terminal FB. However, visual concurrent FB has been shown to make learners dependent on extrinsic FB, thus overlooking intrinsic FB (i.e., proprioception) and inhibiting motor learning[23]. Our result was similar to those of previous studies on older individuals and patients with stroke[24,25]. In contrast, visual terminal FB has been shown to enhance motor learning in movement tasks with a simple task complexity by facilitating visuomotor transformations, thus improving the preplanning of movements in the next trial[26]. Furthermore, with respect to FB frequency, previous research has shown that granting FB in all practice trials (i.e., 100% FB) inhibits motor learning[27]. However, a meta-analysis showed no differences in motor learning according to FB frequency[28]. The participants in this study were older and had mild upper-extremity motor impairments, based on age and FMUE results[29]. Rehabilitation in older patients with stroke provides functional improvement; however, this improvement decreases with increasing age[30]. The current study, which included older patients with subacute stroke and mild motor impairments, suggested that FB strategies are effective in enhancing motor learning.

The results of this study also showed a moderate positive correlation between visuospatial ability and performance in adjusting grasping force, but there was no correlation between motor function and performance in adjusting grasping force. These results suggest that visuospatial ability is a more important factor in motor learning than motor function or pre-test task performance in patients with subacute stroke. Other methods have been used to assess visuospatial ability, such as the MoCA and MR. However, the ROCFT can evaluate visuospatial construction and memory in visuospatial ability[21]. Visuospatial construction is used to understand the presented visual FB rapidly. Participants need to recognize the grasping error within the short presentation

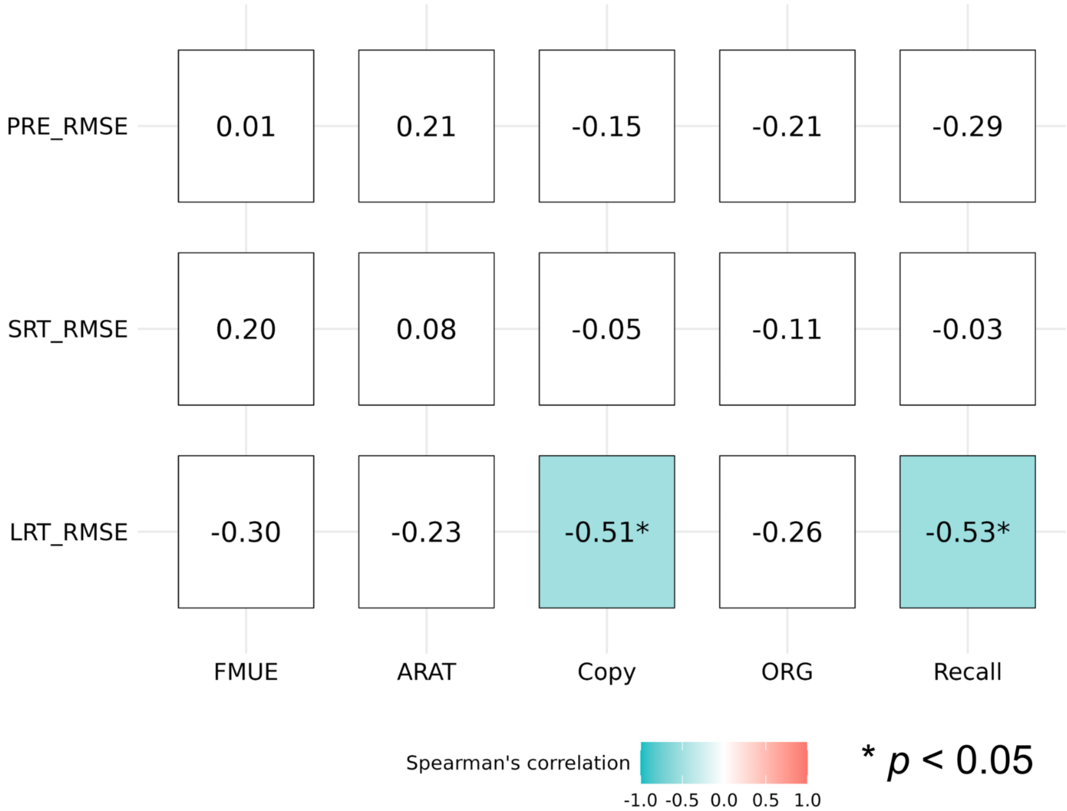

Fig. 3. Correlation of test performance with motor function and visuospatial function. Values in tiles indicate Spearman rank correlation coefficients. Combinations showing significant correlations are color coded, with Spearman's rank correlation coefficients close to 1 shown in red and those close to −1 shown in blue. Combinations that do not show significant correlations are shown in white. Abbreviations: PRE, pre-test; SRT, short-term retention test; LRT, long-term retention test; FMUE, Fugl–Meyer assessment for upper extremity; ARAT, Action research arm test; Copy, copy score; ORG, organization score; Recall, 3-min delayed-recall score.

time (10 s) of the FB after the trial ends. This suggests that visuospatial construction contributes to rapid visual FB screen recognition. Visuospatial memory might have contributed to the correct encoding of the presented visual FB, and the retention and recall of important information for motor planning for the next trial. Both visuospatial construction and memory involve the superior and inferior parietal lobe regions, which translate visual information into limb movements[31,32]. Furthermore, visuospatial training suggests improving visuospatial function by enhancing the activity of the prefrontal cortex and the functional connectivity of the frontoparietal circuit[33,34]. Therefore, visuospatial training for patients with subacute stroke should be considered for rehabilitation.

However, few studies have focused on the relationship between visuospatial ability and motor learning in patients with stroke, with only one study including a small number of patients with chronic stroke (n=7)[16]. Compared with previous studies on motor learning in patients with stroke, this study included a larger number of patients in the recovery phase (n = 17), increasing the reliability of the results.

This study had some limitations. First, no control conditions, such as a control group or concurrent FB group, were included. Furthermore, FB was not used in the test phase to establish an experimental schedule that reflects a rehabilitation setting, and data were collected under a single condition using terminal FB alongside an assessment of motor function and visuospatial function. Future research should examine the disease's effect on visuospatial function and hand dexterity by using healthy individuals of the same age and sex. Moreover, setting FB conditions other than visual terminal FB would make this study more meaningful. Second, patients with stroke or severe motor impairments and non-subacute stroke were excluded. Based on the inclusion and exclusion criteria, only patients with subacute stroke who could manipulate the grasping device were included. Patients with stroke accompanied by severe motor impairments had difficulty using the grasping device independently. Rehabilitation programs using virtual reality (VR) have introduced new possibilities[35]. VR training has proven effective in improving motor function, yet has not assessed visuospatial function. VR relies heavily on visuospatial function, so it is important to clearly evaluate this function and understand the training mechanism. In future research, examining the effectiveness of rehabilitation programs addressing visuospatial function in patients with severe stroke is key to fostering better recovery in patients. Therefore, our findings should be cautiously considered for different attributes, such as motor function (severe or moderate) and stage (acute or chronic). Future studies should examine FB strategies that enhance motor learning in patients with stroke in different movement tasks, with assessment of visuospatial ability, and visuospatial ability training methods that enhance motor learning.

Conclusions

Task-specific training using visual FB is effective for patients and indicates that visuospatial ability, rather than motor function, is related to motor learning. Thus, training programs for visuospatial ability should be considered in stroke rehabilitation.

Methods

Ethics

This study was approved by the Ethics Committee of the Ibaraki Prefectural University of Health Sciences (approval number: 995) and was registered in the UMIN clinical trial (UMIN000049991). The experimental design was conducted in accordance with the principles of the Declaration of Helsinki. All participants provided written informed consent after adequate explanation of the conditions of participation in the study.

Participants

This study was conducted at Ibaraki Prefectural University Hospital, which had a convalescent rehabilitation ward[36]. All patients were diagnosed with stroke by their previous physician and transferred to Ibaraki Prefectural University Hospital for rehabilitation, where physical therapy, occupational therapy, and speech therapy were initiated. Patients admitted to the hospital between July 2021 and August 2022 were consecutively screened. The sample size was based on the study by Riga et al.[37], who set up an experimental design similar to this study, as there were no previous studies using the same experimental design. The inclusion and exclusion criteria for the current study were set according to those described by Tabu et al.[38]. The inclusion criteria were as follows: (1) ability to understand verbal instructions; (2) absence of any disease that interfered with task performance, such as hand pain; (3) mild motor paralysis in the paralyzed upper limb and fingers (Brunnstrom recovery stage 4 or higher); (4) ability to extend the wrist joint on the paralyzed side by 20° or more voluntarily; (5) ability to extend the proximal interphalangeal joints and metacarpophalangeal joints of the first to third fingers voluntarily by at least 10° on the paralyzed side; and (6) ability to sit independently. The exclusion criteria were as follows: (1) previous experience with a similar task, (2) orthopedic or neurological disease of the hand that interfered with daily life on the non-paralyzed side, (3) cognitive impairment (Mini Mental State Examination score < 21), (4) visual impairment (hemianopsia, diplopia, and reduced visual acuity) that prevented them from seeing the monitor, and (5) deemed unsuitable for study participation by the attending investigator.

Equipment

The grasping force was quantitatively measured using a device from iWakka (Nagoya Institute of Technology, Japan). This device consisted of a monitor, grasping device, control box, and Windows PC (Microsoft, Redmond, WA) with the iWakka Viewer application installed. The grasping device had a height of 80 mm, a diameter of 65 mm, and a weight of 0.112 kg. The force of grasping could be visualized by measuring the strain of the plate spring produced when the grasping device was opened and closed with a strain gauge, and a maximum grasping force of 0.5 kg could be measured (Fig. 4a). In previous studies, this device was used to evaluate and practice the ability to adjust the grasping force in healthy young and older adults and patients with stroke[39–42]. The

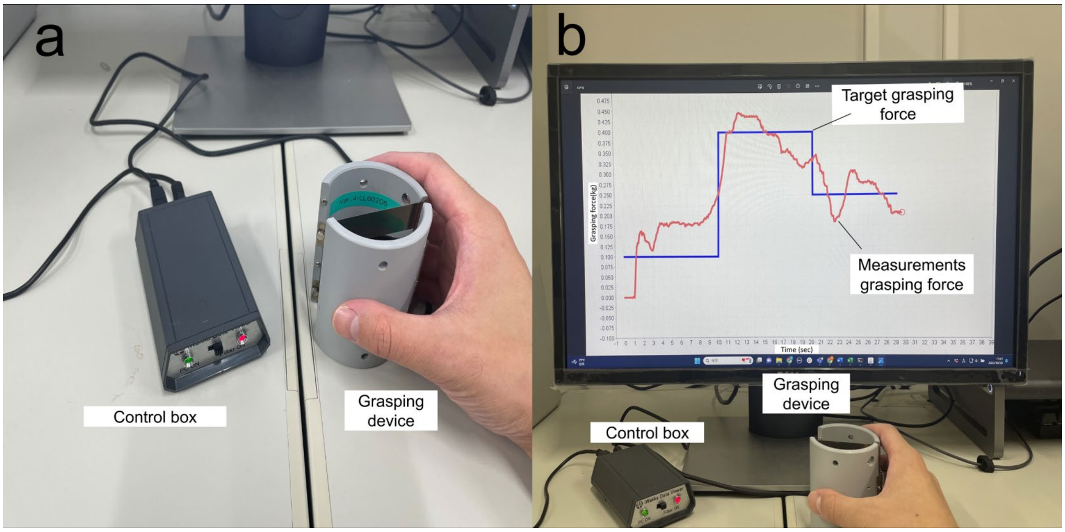

Fig. 4. Experimental equipment and experimental environments. (**a**) Grasping device (right) and control box (left). We can quantitatively assess the participant's grasping force in the range of 0–0.5 kg. (**b**) Feedback during the experimental task. Participants receive feedback on how accurately they adjusted the measured grasping force (red line) relative to the target grasping force (blue line).

sampling frequency was 10 Hz, and the spring constant of the plate spring was 4.82×10^2 N/m. The measurement environment was based on the report of Yamamoto et al.[41]. Particularly, the participants placed the device on a table with an aluminum plate to reduce the effects of friction and performed the task while seated in a chair. The participants and could check the difference between the target grasping force and the measured grasping force (grasping error) reflected on the monitor as visual FB and were expected to improve their task performance by adjusting their movement for the next trial (Fig. 4b).

Experimental design

This study was conducted over 2 consecutive days. The participants completed the Edinburgh Handedness Test (EHI), PRE, practice, and SRT on day (1) The LRT and visuospatial ability assessment were completed on day (2) The EHI was used to assess handedness. After EHI, the participants performed a familiarization task in which they grasped the grasping device for 10 s at a force of 0.1 kg, without viewing the monitor, for five trials. The experimental task, including familiarization, was performed using the paralyzed upper limb. The results were not provided to the participants. The experimental task started after the completion of five trials of the familiarization task.

Experimental task

Figure 5 shows the experimental tasks performed in this study. The task trial consisted of adjusting the grasping force for 30 s, 10 s for each waveform, in the order of 0.1, 0.4, and 0.25 kg target grasping force. The participants performed the task without viewing the monitor during the task trials. The trial results were provided to the participants after trial completion. FB was provided by presenting the trial results on the monitor for 10 s. A metronome (6 bpm) was used to signal the change in the target grasping force. This allowed the participants to change their adjusted grasping force in accordance with the timing of the change in the target grasping force. Specifically, the purpose of this task was to learn coordinated hand movements by trying to bring the measured grasping force as close to the target grasping force as possible, based on the tactile and motor sensations that occur when grasping devices.

The test phase (PRE, SRT, and LRT) consisted of 3 trials, each without FB, and the practice phase consisted of 15 trials (5 practice blocks × 3 trials per block) with FB. The interval between trials was 10 s. For the practice trials, the next trial started 15 s after the end of the feedback period, and the interval between practice blocks was 1 min. The PRE was conducted to assess the pre-practice conditions. The SRT and LRT were conducted to assess the immediate and long-term effects of practice, respectively. The SRT was conducted 5 min after the completion of the last trial (15th trial) of the fifth practice block, and the LRT was conducted 24 h after the SRT was completed (Fig. 6).

The ROCFT is a neuropsychological assessment of visuospatial ability (visuospatial construction and memory) that consists of copy and recall trials[43]. In this study, a copy trial and a 3-min delayed-recall trial were implemented. Previous studies have shown that information is forgotten by 2–3 min after the end of the copy trial[44]and that performance does not differ between a 3-min and a 30-min delayed-recall trial in various age groups (18–74 years)[45]. Therefore, a recall trial was performed 3 min after the end of the copy trial. During the copy task, the order of descriptions was recorded using a video camera. To prevent participants from noticing

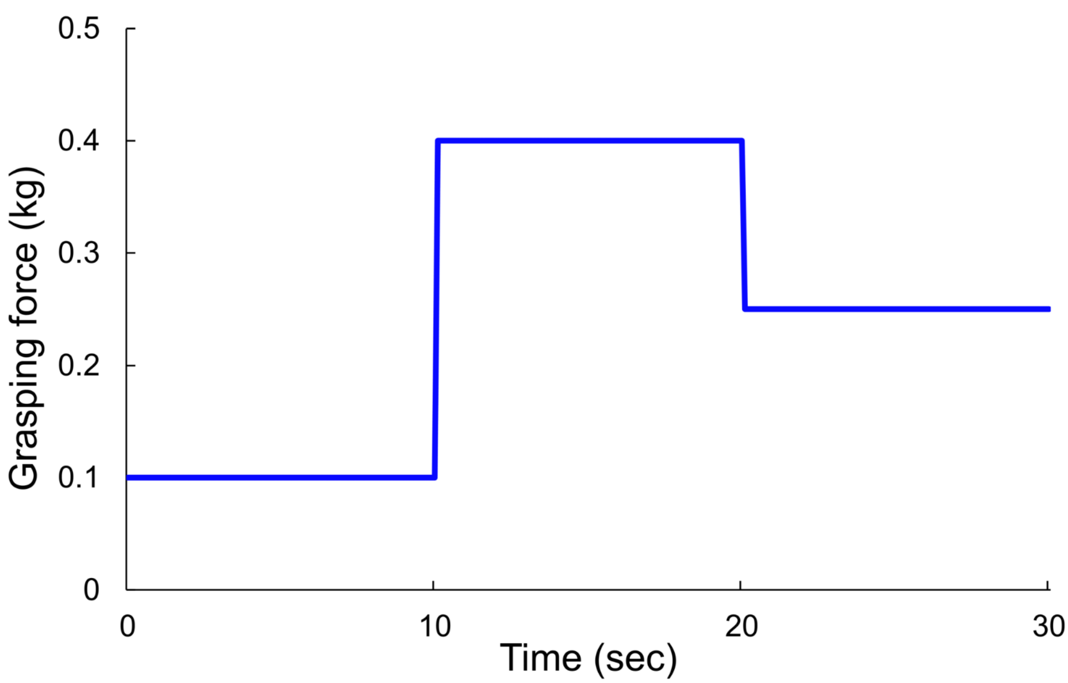

Fig. 5. Experimental task. The target grasping force is shown in blue solid line.

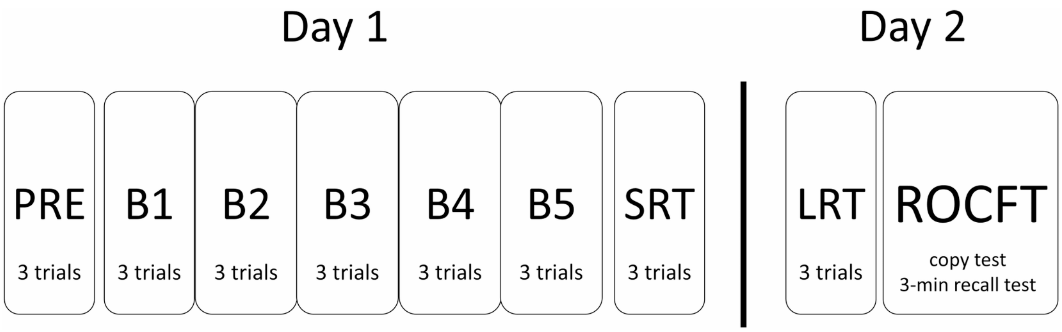

Fig. 6. Experimental schedule. The participants perform the pre-test (PRE), practice test, and short-term retention test (SRT) on day 1 and the long-term retention test (LRT) and Rey–Osterrieth Complex Figure Test (ROCFT) on day 2. One block consists of three trials, with one block for each of the three tests (PRE, SRT, and LRT) and five blocks (B1 to B5) for the practice test. SRT is conducted 5 min after completion of the last trial of the practice test, and LRT is conducted 24 h after the SRT.

the replay task, a 10-item personality test[46] was conducted between the copy and recall trials after completion of the copy trial. This prevented participants from noticing the presence of a recall trial.

Measurement outcome

The FMUE and ARAT were used to evaluate motor function. In a systematic review of the outcome measures of upper extremity function in patients with stroke, the FMUE was the most commonly used upper extremity function assessment tool, while the ARAT was a measure commonly used in combination with FMUE[47]. Motor function assessment was performed within 1 week prior to the start of the study. The RMSE was calculated from the absolute values of the target grasping force and the measured grasping force per unit time. A smaller RMSE thus indicated a greater ability to adjust the grasping force. We used the central 5-s interval of each target grasping force (e.g., for a 0–10-s interval, the interval from 2.5 to 7.5 s was used) as the analysis interval to exclude any deviation in grasping timing that occurred when the target grasping force switched.

Measurements of visuospatial ability included copy, organization, and 3-min delayed-recall scores on the ROCFT. The copy score indicated whether the participants were able to understand the form and relative position of each unit of the figure and copy it accurately. Meanwhile, the 3-min delayed-recall score indicated whether encoding of the copied figure, retention of the encoding memory, and recall of the retained memory were performed accurately. The scoring method for the copy and 3-min delayed-recall scores was based on the method of Loring et al.[48] and used a 36-point scale. The organization score indicated the organizational strategy for how the figure was segmented and described when it was depicted. The scoring method for the organization score was based on the method of Chervinsky et al.[49] and used a 36-point scale. Higher scores for each item indicated higher visuospatial ability.

Statistical analysis

First, the Shapiro–Wilk test was conducted to examine the normality of the RMSEs. Then, based on the results of the Shapiro–Wilk test, Friedman tests were conducted with the RMSE as the dependent variable and the tests (PRE, SRT, and LRT) and practice block (blocks 1–5) as factors to clarify the effects of practice and motor learning on the ability to adjust the grasping force. When significant differences were found in the Friedman test, the Wilcoxon signed-rank sum test with Holm's correction was implemented. Next, Spearman's rank correlation coefficients were calculated for performance on each test and motor function (FMUE, ARAT) and visuospatial ability (ROCFT) to clarify the relationship of performance on each test with motor function and visuospatial ability (copy score, organization score, and 3-min delayed-recall score). All analyses were performed using R software (version 4.3.1; R Core Team, Vienna, Austria). A p value of < 0.05 was considered statistically significant.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request (j.yabuki@mejiro.ac.jp).

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Study Design: JY, TK, RY, KY, WN, and KA. Data collection: JY. Data analysis: JY. Data interpretation: JY, TK, RY, KY, WN, and KA. Manuscript writing: JY. Manuscript review: JY, TK, RY, KY, WN, and KA. All authors have read and approved the final version of the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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