Do somatosensory deficits predict efficacy of neurorehabilitation using neuromuscular electrical stimulation for moderate to severe motor paralysis of the upper limb in chronic stroke?

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Abstract

Background: Various neurorehabilitation programs have been developed to promote recovery from motor impairment of upper extremities. However, the response of patients with chronic-phase stroke varies greatly. Prediction of the treatment response is important to provide appropriate and efficient rehabilitation. This study aimed to clarify whether clinical assessments, such as motor impairments and somatosensory deficits, before treatment could predict the treatment response in neurorehabilitation.

Methods: The data from patients who underwent neurorehabilitation using closedloop electromyography (EMG)-controlled neuromuscular electrical stimulation were retrospectively analyzed. A total of 66 patients with chronic-phase stroke with moderate to severe paralysis were included. The changes from baseline in the Fugl-Meyer Assessment– Upper Extremity (FMA-UE) and the Motor Activity Log-14 (MAL-14) of amount of use (AOU) and quality of movement (QOM) were used to assess treatment response, and multivariate logistic regression analysis was performed using the extracted candidate predictors, such as baseline clinical assessments, to identify predictors of FMA-UE and MAL-14 improvement. **Results:** FMA-UE and MAL-14 scores improved significantly after the intervention (FMA-UE p < 0.01, AOU p < 0.01, QOM p < 0.01). On multivariate logistic regression analysis, tactile sensory (p = 0.043) and hand function (p = 0.030) were both identified as significant predictors of FMA-UE improvement, tactile sensory (p=0.047) was a significant predictor of AOU improvement, and hand function (p=0.026) was a significant predictor of QOM improvement. The regression equations explained 71.2% of the variance in the improvement of FMA-UE, 69.7% of AOU, and 69.7% of QOM.

Conclusion: Both motor and tactile sensory impairments predict improvement in motor function, tactile sensory impairment predicts improvement in the amount of paralytic hand use, and motor impairment predicts improvement in the quality of paralytic hand use following neurorehabilitation treatment in patients with moderate to severe paralysis in chronic-phase stroke. These findings may help select the appropriate treatment for patients with more severe paralysis and to maximize the treatment effect.

Keywords: chronic stroke, motor function, motor recovery, neurorehabilitation, prediction model, somatosensory function

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Introduction

Motor impairment of the upper extremities is one of the major symptoms in patients with stroke. Motor impairment occurs in approximately 70% or more of patients,^{1,2} and various rehabilitation programs have been developed to promote recovery from motor impairment after stroke.³ In addition, with the recent development of neurorehabilitation, reports of interventions for residual motor paralysis in the chronic phase are increasing. However, the response to rehabilitation therapy of patients with chronic stroke varies greatly from patient to patient. Therefore, it is important to define an individualized rehabilitation treatment program according to the severity of stroke to provide appropriate and efficient rehabilitation. For this purpose, accurate prediction of the treatment response is necessary.

Somatosensory deficits, as well as motor impairments, are major symptoms in patients with stroke. Somatosensory deficits occur in more than 60% of patients⁴ and remain in about 40%of patients in the chronic phase.⁵ Along with motor impairments, somatosensory deficits affect motor functions and activities of daily living (ADLs), such as hand dexterity^{6,7} and grasping and manipulating objects.8-10 Although both motor and somatosensory functions are considered important predictors of motor function recovery in rehabilitation, many reports of patients with chronic stroke have focused only on motor function before intervention. In addition, reports using other clinical assessments, including of somatosensory deficits, are limited to mild to moderate paralysis.¹¹ Thus, whether somatosensory impairment has an impact on the recovery of motor function in neurorehabilitation of patients with chronic stroke who have more severe paralysis remains unclear.

In addition to recovery of motor function, increasing the AOU and improving the quality of movement (QOM) of the paralyzed hand are also major goals of neurorehabilitation.^{12,13} It has been reported that baseline motor and somatosensory functions can both be used as predictors of the AOU and improvement in the QOM of the paralyzed hand by neurorehabilitation in subacute stroke patients.¹⁴ A report on chronic stroke patients also showed that both motor and somatosensory functions have a significant impact on prediction.¹⁵ However, similar to the recovery of motor function, reports on the AOU and QOM of the paralyzed hand are limited to mild to moderate paralysis.

This study aimed to determine the effects of clinical assessments of motor impairments and somatosensory deficits on the prediction of treatment response, such as recovery of motor impairments (increases in the amount of use and in the QOM of the paralyzed hand) in rehabilitation of patients with moderate to severe paralysis in chronicphase stroke. We hypothesized that both pretreatment motor and somatosensory functions would be useful predictors of recovery of motor impairments (increased amount of use and improved QOM of the paralyzed hand).

Methods

Study design

This study was a retrospective review of data from patients who underwent hybrid assistive neuromuscular dynamic stimulation (HANDS) therapy for chronic upper limb motor paralysis at Keio University Hospital from May 2017 to November 2020. The inclusion criteria¹⁶ for HANDS therapy were (1) age above 18 years; (2) more than 6 months after the onset of the stroke; (3) surface EMG of the extensor digitorum communis or extensor pollicis longus can be detected; and (4) capable of raising the upper limb of the paretic side to the height of the nipple. The exclusion criteria¹⁶ were (1) severe cognitive impairment; (2) the presence of unilateral spatial neglect or severe aphasia; (3) severe pain in the paralytic upper extremity; (4) contracture of the hand joint or metacarpophalangeal (MP) joint (hand joint dorsiflexion <0° or MP joint extension $<-10^{\circ}$; (5) major psychiatric complications; (6) use of a pacemaker or other implanted stimulation device; and (7) no injection of botulinum toxin in the 3 months before and during hospitalization. Sixty-six patients with chronic-phase hemiplegic stroke with moderate to severe paralysis [total Fugl-Mever Assessment (FMA) score ≤ 45 points]³ were included in the study. For participants who were hospitalized several times during the study period, the assessment performed at the first hospitalization was used, and data from the second and subsequent admissions were excluded. This study was approved by the Institutional Ethical Review Board (20190144). A summary of the study was published on the hospital's public website, and participants were guaranteed the right to have their data excluded from the study.

Interventions (HANDS therapy)¹⁶

HANDS therapy facilitates the use of the paretic upper limb for daily living movements by using EMG-controlled neuromuscular closed-loop electrical stimulation (NMES) and a wrist-hand splint. The closed-loop EMG-controlled NMES was developed by Muraoka¹⁷ and is commercially available as MURO stimulation (Pacific Supply, Osaka, Japan). The non-paretic upper limb is not restrained, so it is possible to perform bilateral movements in daily living movements, which can improve the recovery of motor function and increase the amount of use of the paretic upper limb. All patients were hospitalized, and the intervention period was 21 days. Occupational therapy, such as stretching and upper limb function training, was given for 90 min, 5 days a week.

Outcome measures and potential predictors

A baseline clinical evaluation was performed on the admission day. The following examinations were performed: FMA for motor function; Motor Activity Log-14 (MAL-14) for amount and quality of limb use; Modified Ashworth Scale (MAS) for spasticity; Semmes-Weinstein Monofilament Examination (SWME) for tactile sensation; and the Thumb Localizing Test (TLT) for proprioception. In addition to these clinical measures, age, sex, time since onset, and dominant hand paralysis were independent predictors. The primary outcome was the change from baseline to the end of HANDS therapy in FMA and MAL-14.

Fugl-Meyer Assessment. The FMA is a measure of function in patients with stroke.¹⁸ The Upper Extremity Subscale is a 33-item, total 66-point rating scale ranging from 0 to 2 points, which evaluates upper extremity movement, reflexes, and coordination. The higher the score, the milder the motor dysfunction. This assessment measure has good reliability and validity in patients with stroke.^{19,20} The clinically meaningful minimal change (MCID) has been reported to be 4.25–7.25 points according to previous studies.²¹ In this study, the sum of A and D of the FMA subscale was classified as the FMA proximal score, and the sum of B and C was classified as the FMA distal score and used for the analysis.²²

Motor Activity Log-14. The MAL-14 is a self-report scale to assess the amount and quality of use of the affected upper limb in daily life in patients with stroke.^{23,24} The AOU and QOM are

scored on a scale of 0 to 5 for each of the 14 items, and the mean value is calculated by the number of items evaluated. The higher the score, the higher the amount and quality of use of the affected upper limb. It is an evaluation index with good reliability and validity in patients with stroke,^{25–27} and the MCID in patients with chronic-phase stroke is 10% of the scale, that is, 0.5 points.²⁸

Modified Ashworth Scale. The MAS is the most widely used clinical rating scale to measure muscle spasticity. The examiner assesses resistance to extension, or spasticity, by rapidly extending the patient's limb through the range of motion. Spasticity is scored on a six-point scale of 0, 1, 1+, 2, 3, and 4, depending on the extent and intensity. The higher the score, the stronger the spasticity. It is an evaluation index with excellent reliability and validity in patients with stroke.²⁹ Based on previous studies, the above scoring was replaced by numerical values of 0–6, respectively, and the worst value (worstMAS) of the MAS in the flexors of the elbow, wrist, and proximal interphalangeal (PIP) joints was used for analysis in this study.³⁰

Semmes-Weinstein Monofilament Examination. The SWME is a semi-quantitative evaluation method for tactile sensation.^{31,32} It is widely used in various diseases such as diabetes mellitus and compression neuropathy, and it is reliable and validated in stroke.³³ The threshold of tactile sensation is measured using a total of 20 filaments with a target force of 0.008–300g. With the patient's eyes closed, the examiner presses the filament onto the area to be examined for tactile sensation until it bends 90°. Beginning with the thinnest filament, the smallest threshold is used as the test result. Based on a previous study,¹⁵ the value of target force (grams) taken as the natural logarithm (LnSWME) was used for analysis in this study.

Thumb Localizing Test. The TLT is a measure to assess the proprioception of the affected upper limb in patients with stroke.³⁴ The patient's affected upper limb is moved by the examiner to four different compartments in space (proximal and distal to chest level, proximal and distal to abdominal level). The patient pinches the affected side's thumb with the healthy upper limb while keeping the eyes closed. It is scored on a fourpoint scale from 0 to 3, based on the distance the affected thumb is missed in the pinching motion. The farther the distance of the missed pinch, the higher the score. In other words, the higher the

Table 1. Baseline clinical characteristics.

Measure	Baseline value	Range
Age (years)	51.9 ± 15.4	18–79
Sex (male/female)	45/21	-
Time from onset (days)	1239 ± 932	201-4011
Dominant hand paralysis (yes/no)	33/33	-
Total FMA arm score (0–66)	28.2±8.3	11–45
FMA proximal score (0–42)	21.1 ± 5.2	10-23
FMA distal score (0–24)	7.1 ± 5.2	1–20
WorstMAS score (0–5)	2.30 ± 0.70	1–3
SWME natural logarithm data (–4.83 to 5.70)	-0.78 ± 3.34	-4.83 to 5.70
WorstTLT score (0–3)	1.59 ± 1.05	0–3
Total AOU of MAL-14 (0.00–5.00)	0.58 ± 0.42	0.00-1.79
Total QOM of MAL-14 (0.00–5.00)	0.50 ± 0.33	0.00-1.23

AOU, amount of use; FMA, Fugl-Meyer Assessment; MAL-14, Motor Activity Log-14; MAS, Modified Ashworth Scale; QOM, quality of movement; SWME, Semmes-Weinstein Monofilament Examination; TLT, Thumb Localizing Test.

Table 2. Treatment effects on outcome measures.

Outcome	Mean \pm SD	t value	p value
FMA Baseline	28.21 ± 8.28	11.43	< 0.01
FMA Posttreatment	33.05 ± 9.47		
AOU Baseline	0.58 ± 0.42	7.72	<0.01
AOU Posttreatment	0.96 ± 0.53		
QOM Baseline	0.50 ± 0.33	9.09	< 0.01
QOM Posttreatment	0.85 ± 0.45		

AOU, amount of use; FMA: Fugl-Meyer Assessment; QOM, quality of movement.

score, the stronger the proprioceptive deficit. This test has good reliability and validity in stroke.^{33,35} In this study, the worst value (worstTLT) of the four compartments was used for analysis.

Statistical analysis

A paired t test was used to evaluate the effect of neurorehabilitation treatment on FMA and MAL-14 scores. Univariate logistic regression

analysis was used to extract candidate predictors with a p < 0.1. Multivariate logistic regression analysis was then performed using the extracted candidate predictors to identify predictors of achieving MCID for the FMA and MAL-14 scores. In this study, following previous studies, the MCIDs for FMA and MAL-14 were set at 6 and 0.5 points, respectively. The group of patients who improved more than the MCID was set to 1, and the group of patients who did not improve was set to 0. Value of p < 0.05 was considered significant, and the predictive equations and odds ratios of significant predictors were identified for analysis. Multicollinearity among the predictors was examined using the variance inflation factor (VIF), and a VIF value >10 was considered to indicate multicollinearity. Statistical analysis was performed using SPSS 26.

Results

All patients completed the treatment intervention. Table 1 shows the baseline clinical characteristics of the included patients. There were no missing data for any of the outcomes in the 66 included patients. Comparisons of the mean values before and after intervention showed significant changes in FMA, MAL-14 AOU, and MAL-14 QOM (FMA p < 0.01, AOU p < 0.01, QOM p < 0.01), and all outcomes improved after the intervention (Table 2).

Predictors of improving hand function

On univariate logistic analysis of the FMA model, LnSWME (p=0.033) and the FMA distal score (p=0.022) were identified as candidate predictors (Table 3). On multivariate logistic regression analysis using these factors, LnSWME (p=0.043, $\beta=-0.193$) and the FMA distal score (p=0.030, $\beta=0.117$) were both identified as significant predictors (Table 4). The VIF values of these predictors were all less than 10; thus, no multicollinearity was found in the model. The Hosmer–Lemeshow test for goodness of fit of the model showed p=0.583, and Nagelkerke R^2 was 0.200. The final logistic regression equation was as follows:

Logit $p(FMAgain \ge 6) = -1.510 - 0.193 \times$ (LnSWME) + 0.117 × (FMA distal score).

This regression equation explained 71.2% of the variance in the improvement of upper limb function with treatment intervention.

Table 3. Univariate logistic regression analysis.

Measure	β	p	Odds ratio	95% confidence interval
FMA				
Age	0.018	0.308	1.018	0.983-1.054
Sex	0.405	0.455	1.500	0.518-4.345
Time from onset	0.000	0.710	1.000	0.999-1.000
Dominant hand paralysis	-0.262	0.609	0.769	0.281-2.103
FMA proximal score	0.017	0.736	1.017	0.923-1.120
FMA distal score	0.120	0.022*	1.128	1.018-1.250
WorstMAS	-0.441	0.223	0.643	0.312-1.328
LnSWME	-0.197	0.033*	0.821	0.686-0.984
WorstTLT	-0.308	0.208	0.728	0.444-1.193
AOU	-0.445	0.486	0.641	0.183-2.241
QOM	0.313	0.691	1.367	0.292-6.401
AOU				
Age	0.005	0.743	1.005	0.973-1.039
Sex	-0.080	0.883	0.923	0.319-2.674
Time from onset	0.000	0.611	1.000	0.999-1.000
Dominant hand paralysis	-0.254	0.615	0.776	0.288-2.087
FMA proximal score	0.025	0.606	1.025	0.932-1.128
FMA distal score	0.094	0.064*	1.098	0.995-1.213
WorstMAS	0.016	0.965	1.016	0.499-2.067
LnSWME	-0.183	0.037*	0.832	0.701-0.989
WorstTLT	-0.318	0.199	0.727	0.447-1.183
AOU	-0.024	0.968	0.976	0.299-3.187
QOM	0.199	0.798	1.220	0.267-5.586
QOM				
Age	0.002	0.916	1.002	0.968-1.037
Sex	-0.121	0.834	0.886	0.284-2.763
Time from onset	0.000	0.503	1.000	1.000-1.001
Dominant hand paralysis	-0.580	0.287	0.560	0.193-1.627
FMA proximal score	0.082	0.125	1.085	0.978-1.204

(Continued)

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Table 3.	(Continued)
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Measure	β	p	Odds ratio	95% confidence interval
FMA distal score	0.118	0.026*	1.125	1.014-1.247
WorstMAS	-0.009	0.981	0.991	0.466-2.107
LnSWME	-0.115	0.197	0.892	0.749-1.061
WorstTLT	0.078	0.762	1.081	0.654-1.787
AOU	0.312	0.620	1.366	0.399-4.677
QOM	0.371	0.652	1.449	0.289-7.255

AOU, amount of use; FMA, Fugl-Meyer Assessment; MAL-14, Motor Activity Log-14; MAS, Modified Ashworth Scale; QOM, quality of movement; SWME, Semmes-Weinstein Monofilament Examination; TLT, Thumb Localizing Test. *p < 0.10.

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lable 4.	Multivariate	logistic	rearession	analysis
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Measure	β	p	Odds ratio	95% confidence interval
FMA				
LnSWME	-0.193	0.043*	0.825	0.684-0.994
FMA distal score	0.117	0.030*	1.125	1.011-1.251
Constant	-1.510	0.002*	0.221	
Hosmer-Lemeshow P		0.583		
Nagelkerke R ²		0.200		
AOU				
LnSWME	-0.178	0.047*	0.837	0.702-0.997
FMA distal score	0.090	0.052	1.094	0.988-1.211
Constant	-1.145	0.015*	0.318	
Hosmer-Lemeshow p		0.303		
Nagelkerke R ²		0.156		
QOM				
FMA distal score	0.118	0.026*	1.125	1.014-1.247
Constant	-1.729	0.001*	0.177	
Hosmer-Lemeshow p		0.748		
Nagelkerke R ²		0.108		

AOU, amount of use; FMA, Fugl-Meyer Assessment; QOM, quality of movement; SWME, Semmes-Weinstein Monofilament Examination. *p < 0.05.

Predictors of increasing daily use

On univariate logistic regression analysis in the MAL-14 AOU model, LnSWME (p = 0.037) and the FMA distal score (p=0.064) were identified as candidate predictors (Table 3). On multivariate logistic regression analysis using these factors, LnSWME was identified as a significant predictor with p = 0.047 ($\beta = -0.178$), whereas the FMA distal score was not significant (Table 4). On the univariate logistic regression analysis in the OOM model, the FMA distal score ($p = 0.026, \beta = 0.118$) was identified as the only predictor (Tables 3 and 4). The VIF values of the predictors were all less than 10 in the AOU model, and no multicollinearity was observed in the model. The goodness of fit of the model was Hosmer-Lemeshow p=0.303 and Nagelkerke $R^2=0.156$ for AOU and Hosmer-Lemeshow p = 0.748 and Nagelkerke $R^2 = 0.108$ for QOM.

The final logistic regression equations were as follows:

Logit $p(\text{AOUgain} \ge 0.5) = -1.145 - 0.178 \times (\text{LnSWME}),$

Logit $p(\text{QOMgain} \ge 0.5) = -1.729 + 0.118 \times$ (FMA distal score).

These regression equations explained 69.7% of the variance in MAL-14 AOU and 69.7% of the variance in MAL-14 QOM.

Discussion

This is the first report to show the effects of various clinical assessments, including of somatosensory deficits, on the therapeutic effects of neurorehabilitation in patients with chronic stroke who have more severe upper limb paralysis. The results suggested that the baseline motor and tactile sensory function status predicted the recovery of motor function, the baseline tactile sensory function status predicted the improvement of the amount of use of the paralyzed hand, and the baseline motor function status predicted the improvement of the amount of the QOM of the paralyzed hand.

Both baseline motor and tactile sensory functions were identified as predictors of improvement over MCID in the FMA. For improvement of the FMA, it has been reported that baseline motor function predicts motor function recovery following various interventions, such as constraint-induced movement therapy (CIMT), repetitive transcranial magnetic stimulation (rTMS), transcranial direct current (rTMS), transcranial direct current stimulation (tDCS), and robot therapy (RT).^{36–41} This study using NMES also suggested that baseline motor function predicted motor function recovery, as in these previous studies.

In addition to this result, this study suggests that tactile sensory functional status is a predictor of motor function recovery as well. In a previous report of the relationship between somatosensory functional status and motor function recovery, Ingemanson and colleagues¹¹ reported that somatosensory functional status predicted motor function recovery in RT in 30 patients with mild motor paralysis (around 46 points on the FMA). This result suggests that somatosensory input plays an important role in the central nervous system in regulating motor learning and motor neuron activity. In addition, George and colleagues'42 study on CIMT in patients who met the motor criteria (mild/moderate motor impairment) used in the EXCITE study43 reported that somatosensory function, as well as baseline motor function, is an influential factor for motor recovery in rehabilitation interventions. The present results using the NMES intervention and including patients with more severe motor paralysis than in previous studies were also consistent with these previous studies.

It is known that somatosensory input is closely related to motor learning and motor coordination.44 In the study of RT by Ingemanson and colleagues,¹¹ proprioceptive sensation was involved in motor recovery, and in the study of CIMT by George and colleagues,⁴² proprioceptive and tactile sensations were both involved in motor recovery. However, in this study, tactile sensation had a greater effect on the recovery of motor function than proprioceptive sensation. The reason for this difference in somatosensory modalities may be that, in RT, proprioceptive sensation is associated with passive joint movements caused by robotic movements, and in CIMT, both proprioceptive and tactile sensations act as the main intrinsic feedback for the use of the affected limb. In contrast, in this study, the patients had difficulty in voluntary joint movement due to more severe motor dysfunction, and transcutaneous electrical stimulation using NMES was performed, thus suggesting that the tactile sensation may have been the main intrinsic feedback. However, it

remains to be seen which of the somatosensory modalities will have a greater impact on the recovery of motor function.

With respect to the improvement over MCID in MAL-14, tactile sensation was identified as a predictor in the AOU and motor function was identified as a predictor in the OOM. Regarding the prediction of improvement in the AOU, baseline motor functions such as FMA distal score, ARAT (Action Research Arm Test), WMFT (Wolf Motor Function Test), and BBT (Box and Block Test) have been reported to be useful predictors in previous studies that did not include somatosensory assessment in interventions such as CIMT, 37,45 RT, and mirror therapy.^{40,46} On the contrary, a previous study by Rafiei and colleagues¹⁵ on CIMT in patients with mild to moderate paralysis in chronic stroke reported that although they did not analyze direct explanatory factors for improvement in AOU, tactile sensation is the most powerful predictor for daily use. This study suggests that tactile sensation is a better predictor of improvement in AOU than motor function in patients with moderate to severe paralysis. It has been reported that the presence of somatosensory impairment is likely to indicate a behavioral phenomenon of avoiding the use of the affected upper limb called 'learned nonuse'.47 In neurorehabilitation interventions aimed at increasing the amount of use of the affected limb in patients with severe paralysis, as with mild to moderate paralysis, assessing and accurately understanding the somatosensory deficits may contribute to appropriate and efficient interventions.

On the contrary, regarding the prediction of OOM improvement, in a previous report on CIMT in patients with subacute stroke whose AOU scores were greater than 2.5 points by Park and colleagues,14 motor function measures such as WMFT and FMA were identified as predictors for patients, but somatosensory function was not. A previous report by Rafiei and colleagues¹⁵ on CIMT in patients with chronic stroke whose QOM was around 1.2-1.6 points also reported that WMFT had a significant impact as a predictor. In addition, even in reports that do not include somatosensory assessment, many have reported that motor function measures such as ARAT, FMA distal score, WMFT, and BBT are useful.^{37,40,45,46} The present results are generally consistent with these reports and suggest that baseline motor function may be a better predictor

of QOM even in patients with more severe motor paralysis. In this study, FMA was used as a rating scale for motor function, but many studies of predicting improvement in AOU and QOM have also used different assessment scales, such as ARAT, WMFT, and BBT, as candidate predictors. It will be necessary to continue to examine which of these rating scales or combinations of rating scales are better predictors.

Limitations

The study has two limitations. First, this was a single-center study of the effects of a specific intervention; thus, it cannot be generalized to the entire population of patients eligible for neuro-rehabilitation for chronic stroke. Since this was limited to interventions using NMES, further research is needed to determine whether the results of this study can be generalized to other treatments, such as CI therapy and robotic interventions. Second, all logistic regression equations in this study had a low accuracy rate of about 70%, and the Nagelkerke R^2 value, which is the fit of the model, was also low, at about 0.1–0.2. Thus, it is necessary to identify predictors that can explain the variance better.

Conclusion

The results of this study suggest that the levels of motor and tactile sensory impairment predict the improvement in motor function, the level of tactile sensory impairment predicts the improvement in the amount of paralytic hand use, and the level of motor impairment predicts the improvement in the quality of paralytic hand movement as the effects of neurorehabilitation treatment in patients with moderate to severe motor paralysis in chronic-phase stroke. To maximize the therapeutic effect of neurorehabilitation, it is important to define an individualized rehabilitation treatment program according to the severity of each patient. The findings of this study may help select appropriate treatment for patients with more severe paralysis and to maximize the treatment effect. Factors such as higher brain function, frequency of paralytic hand use during occupational training time, and maintaining motivation to continue training also appear to be important for therapeutic intervention. Therefore, it is necessary to select more comprehensive candidate predictors that include these factors in future studies.

Conflict of interest statement

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