Original Article
Effect of rehabilitation therapy combined with neuromuscular electrical stimulation on cognitive dysfunction and activities of daily life in stroke patients

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Abstract: Objective: To determine the effects of rehabilitation therapy combined with neuromuscular electrical stimulation (NES) on cognitive dysfunction and ability to perform activities of daily living (ADLs) of stroke patients. Methods: The clinical data of 100 stroke patients treated in the Second Affiliated Hospital of Soochow University from February 2019 to August 2021 were retrospectively analyzed. According to the therapeutic regimen, the patients given rehabilitation therapy combined with NES were assigned to a study group (n=52) and those given rehabilitation therapy alone were assigned to a control group (n=48). The treatment efficacy in the two groups was evaluated, and the levels of plasma cortisol (Cor) and neuropeptide Y (NPY), neurological function, motor function, balance ability, swallowing function, cognitive function, negative emotions, and quality of life (QoL) after therapy were evaluated. The maximum amplitude of surface electromyography (sEMG) and swallowing time were compared between the two groups. Results: The study group yielded significantly better efficacy than the control group (P<0.05). Before therapy, there were no significant differences between the two groups in Cor and NPY levels, neurological function, motor function, balance ability, swallowing function, cognitive function, sEMG, swallowing time or negative emotions (P>0.05). After therapy, the above all indices all greatly improved, with more notso in the study group. In addition, after therapy, the study group had significantly better QoL indexes than the control group. Conclusion: Rehabilitation therapy combined with NES is effective in treating stroke. It can substantially ameliorate the cognitive dysfunction, prognosis and QoL in patients.

Keywords: Neuromuscular electrical stimulation, rehabilitation therapy, stroke, cognitive dysfunction, prognosis

Introduction

Stroke is a serious brain injury triggered by blocked blood circulation to the brain, with morbidity and mortality much higher than those of other brain injuries, which threatens quality of life (QoL) and health [1]. According to recent statistics, 116-219 out of 100,000 suffer stroke every year [2]. Stroke has become the primary cause of adult permanent disability, the second most frequently seen cause of dementia, and the third leading cause of mortality worldwide [3]. Moreover, according to statistics in recent years, the incidence of stroke in low-income countries has increased by 12% in the past 30 years, and stroke is increasingly common in a younger population [4]. Clinically, drug therapy and surgical therapy are available

for stroke, and timely and effective therapy should be given according to the lesion site in its acute stage to prevent serious complications [5].

The subsequent neurological dysfunction after stroke results in different degrees of disability and precludes self-care, causing a serious economic and mental burden to families [6]. Due to the long-term process of rehabilitation, the cognition, attitude, and behavior of stroke patients greatly impact their rehabilitation and directly affect their QoL [7]. Therefore, it is of profound significance to carry out early and comprehensive rehabilitation in stroke patients to improve their QoL and ability to perform activities of daily living (ADLs). Clinical rehabilitation training is usually used to help patients improve muscle

spasm and limb function, but the single intervention requires a long therapy cycle and may be limited by poor patient compliance [8]. Neuromuscular electrical stimulation (NES) therapy is a physical therapy to enhance muscle contraction, that has high application value in rehabilitation and physiotherapy of stroke patients [9]. According to previous research [10], NES can improve the swallowing and cognitive functions of stroke patients and improve their ability to perform ADLs. However, few related studies have explored whether NES combined with rehabilitation training has synergistic effect and can better promote patients' rehabilitation.

This study retrospectively analyzed the effects of NES combined with rehabilitation therapy on cognitive function, swallowing, and other related functions of patients with stroke to provide a reference for the selection of a clinical therapeutic regimen.

Methods and data

Clinical data

The clinical data of 100 stroke patients treated in the Second Affiliated Hospital of Soochow University from February 2019 to August 2021 were retrospectively analyzed. According to the therapeutic regimen, the patients given rehabilitation therapy combined with NES were assigned to a study group (n=52) and those given rehabilitation therapy alone were assigned to a control group (n=48). This study was performed with permission from the Medical Ethics Committee of the Second Affiliated Hospital of Soochow University (LLSH2019071).

Inclusion and exclusion criteria

Inclusion criteria: patients who met the diagnostic criteria of stroke [11] and had different degrees of dysphagia; patients with stable vital signs and clear consciousness; patients with detailed clinical data; patients tolerant to the therapy involved in this study; and those who signed an informed consent form.

Exclusion criteria: Patients with comorbid metastatic diseases, severe consciousness disorder, or other organic diseases such as coronary heart disease and renal failure, and those with cerebral apoplexy caused by non-vascular factors such as brain tumor or trauma according to examination.

Therapeutic regimen

Patients in both groups received the same basic therapy after admission, including control of blood pressure and blood glucose, and close monitoring of patients' vital signs. Patients in the control group were given routine rehabilitation training: (1) The affected limb joints of the patients were moved passively with an intensity from mild to strong, including shoulder girdle movement, so as not to cause pain to the patients. (2) The patients were assisted to turn over and practice on the affected side and the healthy side in bed alternatively. (3) The patients were instructed to do the stretching exercise of the dorsal extension of wrist joint and ankle joint. (4) The patients were required to take sitting exercise during non-therapy time. The bed head was lifted up by 30° for a sitting position, which was lasted for 30 min. With an increase of the patients' tolerance, the degree of bed angle should be gradually increased to 90°. (5) The patients were required to practice standing by the bed and then go up and down the stairs by themselves (1 time/d, 4 w in total).

In addition to the above routine rehabilitation therapy, the study group was treated with additional NES. Before therapy, the principle of therapy was introduced to the patients, and the issues such as how they would feel during therapy, the stimulation sites, therapy duration, electrode sizes, and placement positions were explained in detail. The intensity of therapy electrodes was determined according to the size of muscles to be stimulated. A ME294 four-channel neuromuscular electrical stimulator (manufacturer: Mettler Company, USA) was used for treatment, with settings as follows: power supply: 220-240 Vac; input current: 2.3 A; pulse frequency: 80 Hz; wave width: 300 ms. The electrode was placed above the hyoid bone and below the thyroid notch by an experienced doctor, and the stimulation lasted for 30 min (twice a day, 6 days a week, and 4 weeks in total).

Detection indexes

Before and after treatment, 5 mL fasting venous blood was acquired from each patient in the two groups by vacuum blood collection, and plasma Cor and NPY levels were detected by radioimmunoassay along with chemiluminescence immunoassay (Beijing North Institute of Biotechnology) under the kit instructions.

Outcome measures

Primary outcome measures: The efficacy in the two groups was evaluated by Mini-Mental State Examination (MMSE) [12]. The levels of plasma Cor and NPY before and after therapy were compared between the two groups. The changes In patients' QoL before and after therapy were assessed using the stroke-specific quality of life scale (SS-QOL) [13], which contains a total of 49 items with each item of 1-5 points. A higher score means better QoL.

Secondary outcome measures: The National Institutes of Health Stroke Scale (NIHSS) covering 15 items with a score ranging from 0-42 points was used to assess the neurological function of stroke patients [14]. A lower score indicates better neurological function. The Fugl-Meyer Assessment (FMA) was adopted to evaluate the motor function of patients [15], covering reflex activity, synergic movement of flexor muscles, and synergic movement of extensors. The assessment covers the upper limbs and lower limbs, with scores of 0-66 points for the upper limbs and 0-34 points for the lower limbs. A higher score suggests better motor function. The Berg balance scale was used to assess the balance function of stroke patients [16], which covered 14 items, such as standing (standing on both feet back and forth, standing on one leg, standing independently, standing with eyes closed), sitting down, stretching the upper arms forward, alternately stepping on the steps with both feet, and turning around, for a week. Each item is scored 0-56 points, and a higher score indicates a better balance ability. The Kubota water swallow test was adopted to evaluate the swallowing function [17]. The patient was instructed to sit up and drink 30 mL warm water, and their swallowing function was evaluated. Grade I: Drinking 30 mL water smoothly at a time without choking; Grade II: drinking 30 mL water in two times without choking; Grade III: Drinking 30 mL water at a time, but with choking; Grade IV: Drinking 30 mL water for more than 2 times, accompanied by choking; Grade V: It was difficult to drink 30 mL water because of frequent choking. The self-rating anxiety scale (SAS) and self-rating depression scale (SDS) were adopted to assess the negative emotional changes in the two groups [18]. A higher score indicates more serious anxiety or depression. The maximum amplitude of surface electromyography (sEMG) and swallowing time were collected by electromyography (HL-0817A).

Evaluation of clinical efficacy

The Mini-mental State Examination (MMSE) was adopted for efficacy evaluation as follows: Basically cured: The MMSE score decreased by more than 90% after therapy; markedly effective: the MMSE score decreased by 46%-90% after therapy; effective: the MMSE score decreased by 18%-45% after therapy; ineffective: the MMSE score decreased by less than 18% after therapy [5]. Total effective therapy rate = [(basically cured cases + markedly effective cases + effective cases)/the total number of patients × 100%.

Statistical analyses

SPSS20.0 was used for data analysis, and GraphPad Prism 8 software was used for visualization of the data. Counted data (rate) were analyzed by the chi-square test, and measured data (mean ± standard deviation) were analyzed using the t test. The inter-group comparison and intra-group comparison were carried out using the independent-samples T test and paired t test, respectively. Logistic regression was used to analyze the risk factors of adverse outcomes. Receiver operating characteristic (ROC) curves were drawn to analyze the value of risk factors in predicting the efficacy in patients. A P value less than 0.05 was regarded as a significant difference.

Results

Comparison of baseline data

According to comparison of clinical data, the control group and the study group were similar in age, gender, body mass index (BMI), course of disease, past medical history, smoking, and alcohol consuming history (P>0.05, **Table 1**).

Clinical efficacy on patients

According to the comparison of clinical efficacy between the two groups, the study group showed significantly higher overall clinical efficacy than the control group, and also a significantly higher total effective rate than the control group (**Table 2**, all P<0.05).

Table 1. Baseline data

Items	Control group (n=48)	Study group (n=52)	P value
Age (years)			0.984
≥60	37	40	
<60	11	12	
Gender			0.413
Male	27	25	
Female	21	27	
Course of disease			0.462
≥9 weeks	27	33	
<9 weeks	21	19	
BMI (kg/m^2)			0.078
≥23	21	14	
<23	27	38	
Past medical history			
Hypertension	25	30	0.573
Diabetes mellitus	20	20	0.743
Smoking history			0.531
Yes	27	26	
No	21	26	
Alcoholism history			0.665
Yes	12	15	
No	36	37	
Stroke type			0.847
Bleeding	24	25	
Infarct	24	27	

Note: BMI, Body mass index.

Table 2. Evaluation of efficacy in patients

Group	Cured	Markedly effective	Effective	Ineffective	Total effective rate
Control group (n=48)	5	12	19	12	36 (75.00)
Study group (n=52)	15	22	10	5	47 (90.38)
X^2/Z value		-3.543			4.187
P-value		<0.001			0.040

Comparison of serum Cor and NPY levels

The changes in serum Cor and NPY levels in the two groups before and after therapy were detected. The results showed that the serum Cor and NPY levels in both groups decreased significantly after therapy, with significantly lower levels in the study group than the control group (**Figure 1**, all P<0.05).

Comparison of QoL and negative emotions

The SS-QoL, SAS, and SDS scores were evaluated to determine the patients' QoL and nega-

tive emotions. According to the results, after therapy, the SS-QoL scores of the two groups increased significantly, while the SAS and SDS scores decreased significantly (all P<0.05). Furthermore, the study group exhibited significantly higher SS-QoL scores and significantly lower SAS and SDS scores than the control group after treatment (**Table 3**, all P<0.05).

Comparison of motor function and balance abilities

After therapy, the Berg and FMA scores of the two groups increased significantly (P<0.05), with significantly higher Berg and FMA scores in the study group than those in the control group (**Table 4**, P<0.05), indicating the study group acquired better motor function and balance ability.

Comparison of neurological function and swallowing function

The swallowing function and neurological function of patients after therapy were evaluated by the Kubota water swallow test and NIHSS. According to the results, the NIHSS scores of patients decreased significantly after therapy (P<0.05), with a more significant decrease in the study group than that in the control group (**Table 5**, P<0.05). In addition, the study group showed a significantly lower grade of Kubota water swallow test than the control group (**Table 6**, P<0.05).

Comparison of sEMG and swallowing time

The changes of sEMG and swallowing time were compared between the two groups. Results showed that the sEMG of the patients after treatment was significantly higher than that
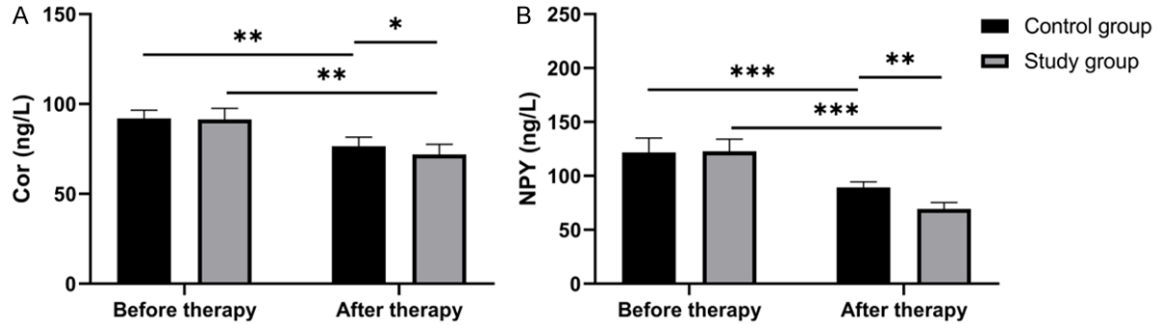
Figure 1. Changes in Cor and NPY before and after therapy. A. Changes in Cor level before therapy and after therapy. B. Changes in NPY level before therapy and after therapy. Note: *P<0.05, **P<0.05, ***P<0.001, Cor, Cortisol; NPY, Neuropeptide Y.

Table 3. Changes of QoL and negative emotions before and after therapy

Group	SS-QOL score		SAS score		SDS score	
	Before therapy	After therapy	Before therapy	After therapy	Before therapy	After therapy
Control group (n=48)	118.87±16.05	166.14±23.38*	56.13±4.48	38.42±4.44*	55.67±5.52	36.73±4.54*
Study group (n=52)	118.54±15.23	180.41±24.63*	56.48±5.34	31.73±6.33*	56.46±4.45	30.87±4.22*
T value	0.103	2.944	0.359	6.066	0.428	6.697
P-value	0.918	0.004	0.720	<0.001	0.795	<0.001

Note: *P<0.05 vs. before therapy, SS-QOL, Stroke-specific quality of life scale; SAS, Self-rating anxiety scale; SDS, self-rating depression scale.

Table 4. Changes in motor function and balance ability before and after therapy

Group	Berg score		FMA score	
	Before therapy	After therapy	Before therapy	After therapy
Control group (n=48)	19.85±3.27	24.29±4.22*	57.25±6.68	71.79±4.14*
Study group (n=52)	19.50±2.77	29.65±4.17*	59.17±5.92	77.52±4.01*
T value	0.586	6.384	1.525	7.027
P-value	0.559	<0.001	0.130	<0.001

Note: *P<0.05 vs. before therapy, FMA, Fugl-meyer assessment.

Table 5. Comparison of NIHSS scores

Group	NIHSS score	
	Before therapy	After therapy
Control group (n=48)	18.44±1.89	12.13±1.30
Study group (n=52)	18.37±2.47	8.29±1.26
T value	0.163	15.000
P-value	0.870	<0.001

Note: MMSE, Mini-mental state examination.

before treatment, and the swallowing time of the patients after treatment was significantly shorter than that before treatment. Further comparison showed that after treatment, the sEMG was significantly higher while the swallowing time was significantly shorter in the study group than the control group (**Table 7**).

Analysis of risk factors influencing efficacy

The two groups were grouped again according to the clinical efficacy after therapy. Among them, 83 patients were assigned to the effective group and 17 patients were assigned to the ineffective group. A univariate analysis revealed significant differences between the two groups in the disease course, therapeutic regimen, Cor, and NPY levels (all P<0.05, **Table 7**), which were then assigned (**Table 8**) and included in the multivariate logistics regression analysis. The results showed that the course of disease, therapeutic regimen, and NPY were independent risk factors affecting the cognitive function of patients (P<0.05, **Table 9**). According to ROC curve-based analysis, only the course of disease and NPY could be used as

Table 6. Comparison of swallowing function

Group	Grade I	Grade II	Grade III	Grade IV	Grade V
Control group (n=48)	14	12	11	8	3
Study group (n=52)	25	18	4	5	0
X^2/Z value			-2.766		
P-value			0.006		

Table 7. Comparison of sEMG and swallowing time before and after treatment

Group	sEMG (μV)		swallowing time (s)	
	Before therapy	After therapy	Before therapy	After therapy
Control group (n=48)	326.79±36.59	565.04±28.10	1.71±0.29	1.44±0.22
Study group (n=52)	317.30±32.44	753.21±45.53	1.69±0.28	1.13±0.16
T value	1.375	24.630	0.300	8.198
P-value	0.172	<0.001	0.764	<0.001

Note: sEMG, Surface electromyography.

outcome measures to predict the recovery of cognitive function after therapy (**Figure 2** and **Tables 10**, **11**).

Discussion

Stroke seriously threatens human health, with fast onset and high disability and mortality rates [19]. After stroke, patients' motor cortex and cognitive function are both damaged, seriously compromising their QoL [20]. According to the survey, approximate 50%-70% of patients suffer cognitive dysfunction after stroke, and most of them are clinically given rehabilitation training related to motor function, but rarely related to cognitive dysfunction. This seriously hinders the recovery of their neurological function [21].

At the current stage, rehabilitation training is the main method to treat stroke hemiplegia clinically, which can promote the reorganization of motor cortex function in undamaged areas and restore the motor function of patients [22]. Rehabilitation training can also improve the metabolism of the body and the blood circulation and prevent muscular atrophy. However, rehabilitation training alone is unable to satisfactorily improve the patients' balance ability and neurological function [23, 24]. Neuromuscular electrical stimulation (NES) is a therapeutic method that stimulates nerves or muscles with low frequency pulse current to cause muscle contraction, so as to improve muscle function or treat neuromuscular diseases [25,

26]. In the study by Zhang et al. [27], early acupuncture combined with rehabilitation therapy alleviated the cognitive dysfunction of stroke patients. In this study, rehabilitation training combined with NES was applied to treat the cognitive dysfunction of stroke patients. The results showed that the clinical efficacy was significantly improved through the combined therapy, and the total effective rate was significantly increased. This shows that combined therapy can alleviate the cognitive dysfunction of patients. Cortisol (Cor) is a glucocorticoid secreted by adrenal gland, which is the terminal secretion product of hypothalamus-pituitary-adrenal (HPA) axis. Stimulation of the body by the outside factors can promote its secretion to improve the body's physiological and behavioral response [28]. NPY is mainly distributed in the sympathetic nervous system, which can regulate the proliferation function of neuron precursor cells and has a potential protective effect on brain [29]. Increased Cor and NPY levels indicate the damage of patients' cognitive function. In this study, the levels of Cor and NPY in both groups decreased significantly after therapy, with significantly lower levels in the study group than those in the control group, indicating that NES can improve the blood flow in the brain, promote the absorption of hematoma, and relieve the neurological impairment and stress response.

Neurogenic dysphagia is also a common complication of stroke, which is tied to the neurological impairment of stroke patients. Long-

Table 8. Multivariate analysis

Items	Effective group (n=83)	Ineffective group (n=17)	*P* value
Age (years)			0.490
≥60 (n=77)	65	12	
<60 (n=23)	18	5	
Gender			0.654
Male (n=52)	44	8	
Female (n=48)	39	9	
Course of disease			0.009
≥9 weeks (n=60)	45	15	
<9 weeks (n=40)	38	2	
BMI (kg/m^2)			0.557
≥23 (n=35)	28	7	
<23 (n=65)	55	10	
Hypertension			0.851
Yes (n=55)	46	9	
No (n=45)	37	8	
Diabetes mellitus			0.514
Yes (n=40)	32	8	
No (n=60)	51	9	
Smoking history			0.597
Yes (n=53)	43	10	
No (n=47)	40	7	
Alcoholism history			0.723
Yes (n=27)	23	4	
No (n=73)	60	13	
Stroke type			0.373
Hemorrhage (n=49)	39	10	
Infarction (n=51)	44	7	
Therapeutic regimen			0.040
Control group (n=48)	36	12	
Study group (n=52)	47	5	
Cor (ng/L)	91.09±5.30	94.61±5.21	0.014
NPY (ng/L)	121.06±12.39	128.88±8.56	0.015

Note: Cor, cortisol; NPY, Neuropeptide Y.

Table 9. Assignment of efficacy

Items	Assignment
Course of disease	9 weeks =1, <9 weeks =0
Therapeutic regimen	Control group =1, study group =0
Cor (ng/L)	Data belonging to continuous variables were analysed their raw data
NPY (ng/L)	Data belonging to continuous variables were analysed their raw data
Efficacy	Cured, markedly effective, effective =0, ineffective =1

Note: Cor, Cortisol; NPY, neuropeptide Y.

term difficulty in eating is likely to give rise to fluid and electrolyte imbalance and nutrient deficiency, which is not conducive to the recovery of neurological function and will cause great psychological pressure to patients and compromise their QoL [30, 31]. Therefore, we also observed the swallowing function, motor function, balance ability, negative emotions and
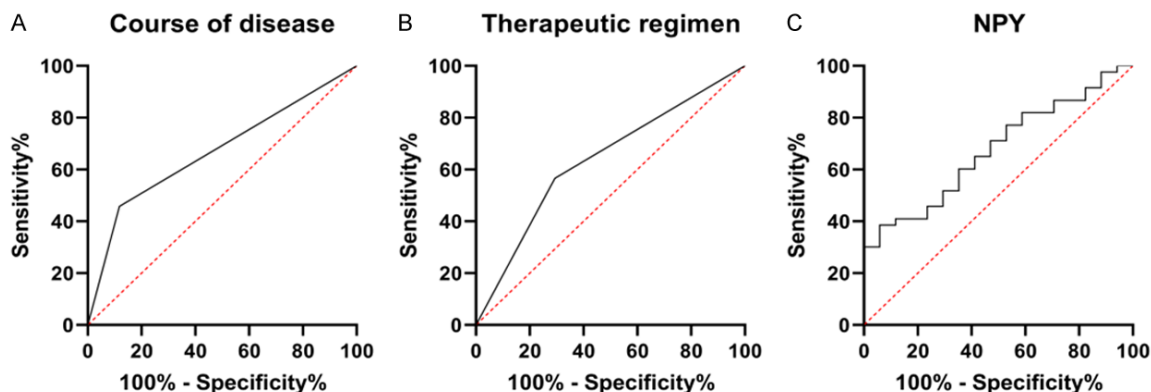
Figure 2. ROC curves of course of disease, therapeutic regimen, and NPY in predicting the curative effect in patients. A. ROC curve of course of disease in predicting the curative effect on patients. B. ROC curve of therapeutic regimen in predicting the curative effect on patients. C. ROC curve of NPY in predicting the curative effect on patients. Note: ROC, Receiver operating characteristic curve; NPY, Neuropeptide Y.

Table 10. Logistic regression analysis of measurements

Items	β	SE	Wals	P value	OR value	95% C.I. Of EXP (B)	
						Lower limit	Upper limit
Course of disease	1.926	0.811	5.640	0.018	6.859	1.400	33.604
Therapeutic regimen	1.266	0.630	4.044	0.044	3.547	1.033	12.186
Cor	0.051	0.163	0.098	0.754	1.052	0.764	1.449
NPY	0.075	0.032	5.715	0.017	1.078	1.014	1.147

Note: Cor, Cortisol; NPY, Neuropeptide Y.

Table 11. ROC values of measured data

Items	Area under the curve	95% CI	P value	Specificity	Sensitivity	Youden index
Course of disease	0.670	0.543~0.796	0.027	88.24%	45.78%	34.01%
Therapeutic regimen	0.636	0.494~0.777	0.078	70.59%	56.63%	27.21%
NPY	0.675	0.551~0.799	0.023	94.11%	38.55%	32.67%

Note: NPY, Neuropeptide Y.

QoL of the two groups. In the present study, after therapy, compared to the control group, the swallowing function, sEMG, swallowing time, motor function, and balance ability of the study group were all significantly improved, and the negative emotions and the quality of life were also significantly ameliorated. In the study by Byeon et al. [32], the patients' swallowing function was improved after treatment with the Mendelsohn maneuver combined with neuromuscular electrical stimulation, and their quality of life was improved. In the study by Zeng et al. [27], through treatment of NES, the patients' anxiety and depression were alleviated. These results were all consistent with our findings. We believe that the NES therapy can stimulate muscles using low frequency current, which can promote passive muscle contraction, then stre-

ngthen muscle strength, reduce muscle spasm, and help expand the range of limb activities, thus helping complete various rehabilitation training and enhancing the effect of rehabilitation training. In addition, rehabilitation training can transmit the motor sensation and muscle contraction signal pulse to the brain through limb sensory stimulation, stimulate the reorganization of brain function, activate the closed nerve pathway, and reduce the damage of neurological function, so as to improve the motor function of patients' limbs, and improve the ability to perform ADLs and alleviate the patients' negative emotions.

Finally, logistic regression analysis was carried out in this study. The results showed that treatment, course of disease, and NPY were inde-

pendent risk factors affecting the efficacy in patients. According to a previous study [33], the course of disease was closely related to the rehabilitation of patients, and a longer course of disease was associate with inferior rehabilitation efficacy in patients, which is consistent with our results. Moreover, another study has shown that an increase in NPY indicates that the nervous system of the body is overexcited, leading to cerebral vasoconstriction, which is not conducive to the recovery of patients [34]. Combination treatment is a protective factor affecting the curative effect, which shows that rehabilitation therapy combined with NES can better alleviate the cognitive dysfunction of stroke patients. In addition, further analysis shows that the course of disease and NPY have predictive value for the efficacy of patients and are expected to become measures of outcome.

Through analysis, this study has determined that rehabilitation therapy combined with NES can effectively alleviate the cognitive dysfunction of stroke patients and enhance their QoL and interaction ability. However, it still has some limitations. Due to the short time span, the study population is limited. Secondly, due to the retrospective nature, there might be some bias in the results. Therefore, we hope to carry out more clinical research in the future to solidify our conclusions.

In sum, rehabilitation therapy combined with NES is effective in treating stroke. It can substantially improve cognitive dysfunction, prognosis and QoL of patients.

Disclosure of conflict of interest

None.

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