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Facilitation of Sensory and Motor Recovery by Thermal Intervention for the Hemiplegic Upper Limb in Acute Stroke Patients

A Single-Blind Randomized Clinical Trial

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Background and Purpose—Thermal stimulation (TS) is commonly used in orthopedic rehabilitation, but the role of TS in the facilitation of sensorimotor recovery in hemiplegic patients remains unknown. This study addressed the issue of TS intervention in the facilitation of functional outcomes.

Methods—Forty-six stroke survivors were randomly assigned to standard rehabilitation treatment and standard treatment plus TS (30 minutes daily for 6 weeks). Twenty-nine patients completed the experiment. Six measures, including Brunnstrom stage, modified motor assessment scale, grasping strength, angles of wrist extension and flexion, sensation by monofilament, and muscle tone by modified Ashworth scale, were performed weekly to evaluate sensory and motor functional outcomes.

Results—The performance of Brunnstrom stage and wrist extension and sensation were improved significantly after TS intervention. Recovery rates of 6 measures after TS were significantly higher than those of the control, except for grasping. Similar muscle tones were found in both groups.

Conclusion—TS on the paretic hand significantly enhances the recovery of several aspects of sensory and motor functions in hemiplegic stroke patients. **(*Stroke*. 2005;36:2665-2669.)**

Key Words: clinical trials ■ rehabilitation ■ stroke

Stroke is the major disease that leads to an increase in the number of people with motor or sensory impairment or loss of function. Up to 85% of stroke patients show an initial deficit in the upper limb, and the recovery of the upper-limb function is often poor and only seen in less than half of the patients.[1,2] Early and repetitive stimulation of the arm has been demonstrated to create a clinically important long-lasting effect.[3–5] Consequently, therapists usually use facilitative techniques (eg, electromyographic biofeedback,[6] active neuromuscular stimulation for the wrist and fingers,[7,8] acupuncture-like electrical stimulation,[9] or sensorimotor stimulation of the arm[10]) in rehabilitative programs. Most previous studies emphasize motor outcome but pay little attention to the sensory part.[5–9] Somatosensory deficit in the upper extremity is found in most strokes and also has a negative impact on the functional improvement and even prolongs the period of rehabilitation and the length of hospital stay.[11,12] Poor functional recovery in stroke patients may be at least partially attributable to learned nonuse phenomenon and further leads to deterioration of motor function.[12,13] On the other hand, an active "driving"[14] or forced use[15,16] of the upper extremity has been proposed to be beneficial to rehabilitation. Accordingly, simultaneous activation of motor and sensory function during therapy may play a crucial role in rehabilitation.

Recently, numerous studies indicated that neuroplasticity and cortical reorganization are facilitated after sensory stimulation and repetitive motor practice in stroke patients.[17,18] Simultaneous activation of a large brain area is believed to enhance the neural plasticity. Activated brain areas by thermal stimulation (TS) are greater than those of tactile or mechanical stimulation, and it is almost identical to that of motor task.[19,20] Furthermore, thermal agent is not only a simple and convenient tool, but also an inexpensive modality than other training equipment in clinical rehabilitation. Although the thermal agent is commonly used in orthopedic rehabilitation,[21] to the best of our knowledge, there is no report evaluating the effect of TS intervention. In this study, we tested the hypothesis whether functional recovery could be facilitated in the shortest amount of time by additional TS in acute strokes.

Subjects and Methods

This is an observer-blinded randomized clinical trial comparing standard treatment with standard treatment plus TS. The research

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protocol was reviewed and approved by the ethics committee of the Tzu Chi University and Medical Center. All patients were informed about the entire experiment and signed their consent. Stroke patients were from the departments of rehabilitation medicine and neurology in Tzu Chi Buddhist General Hospital from October 2002 to November 2004, and they were randomly assigned to experimental (EXP) and control groups. Randomization was by computer-generated random numbers held in sealed envelopes by an individual not involved with the study. All patients had a CT or MRI brain scan. The stroke type was categorized into intracerebral hemorrhage or infarction. Brunnstrom stage of each patient was determined after interview. The main inclusion criteria included: (1) diagnosis of first-ever stroke <1 month, (2) no cardiac or orthopedic problem before stroke, (3) no cognition problem and able to follow directions indicated by therapist during experiment, and (4) motor deficit of the upper limb under Brunnstrom stage IV. Exclusion criteria were: (1) diabetic history or sensory impairment attributable to peripheral vascular disease or neuropathy, and (2) speech disorder or global aphasia.

All participants received standard therapy from the existing ward rehabilitation team. The EXP group received 1 TS intervention session of 20- to 30-minute duration 5 times weekly, which was given by the same physical therapist. The control group had a visit of 15 to 20 minutes ≥3 times weekly from the intervention physiotherapist to discuss progress in rehabilitation. This contact could potentially offer benefit for the patients.

Intervention

Patients comfortably sat in a quiet room with their hands placed on a table. Temperatures of room and subjects' hands were noted before experiment. Thermal agent was made by general hot (≈75°C) or cold (<0°C) pack wrapped with 2 towels, which buffered the thermal conduction. The thermal agent was placed over the region of the hand and wrist. A thermal couple was placed in between the hand and thermal agent to measure the skin temperature. Changes of the skin temperature induced by thermal agents were nonlinear. In our pilot study (n=30), uncomfortable signs to heating and cooling agents occurred at 10.1±1.0 seconds (44.3±0.2°C) and 15.1±1.2 seconds (18.8±0.3°C), respectively. To avoid tissue damage, ceiling durations of heating and cooling stimulation on the paretic hand were limited by 15 seconds (48.8±0.3°C) and 30 seconds (14.0±0.2°C), respectively. During the development of uncomfortable sensation, patients were encouraged to actively move their paretic hands away from the stimuli or generated a reflex. Thus, the thermal agent could produce thermal sensation followed by voluntary/reflexive behavior.

During TS intervention, heating agent was first placed on the nonparetic hand, and the patient was asked to feel change of skin temperature. The patient learned to move the hand away from the heating agent when unpleasantness developed. In turn, the heating agent was put on the paretic hand 10 times and interleaved with a ≥30-second pause. Patients were encouraged to move the paretic hand away from heating agent if they felt uncomfortable or accepted 15-second stimulation. When skin temperature of the paretic hand dropped to baseline after 10-time heating stimulation, and an identical procedure was used for 30-second cooling agent. A session of TS, which contained 2 alternate cycles of heating and cooling stimulation, was performed once daily. The facilitative program contained 5 sessions per week and lasted for 6 weeks. Adverse effect was assessed during and after TS.

Assessments

The outcome measures were assessed weekly by the same physical and occupational therapists, who were blinded to the group of subjects. Motor function of the upper limb was measured with Brunnstrom stage. Functional activity of the upper and lower limb motor function was evaluated by modified motor assessment scale (MMAS). MMAS contains 8 items, and each item is graded on a 6-point scale. Reliability and validity of MMAS assessment has been documented.[22] To assess active range of movement of flexion and extension of the paretic wrist, goniometer was used. Angle of maximal wrist movement was taken for analysis (best of 5 measurements). Moreover, Jamar dynamometer (Sammons Preston) was used to evaluate grasping strength (best of 3 measurements). These tools have been well documented for their reliabilities.[23] Muscle tone of elbow and finger was evaluated by modified Ashworth scale,[24] which assesses global resistance to imposed movement (scale range 0 to 5; increased scores indicate increased resistance).

The Semmes–Weinstein monofilament (North Coast Medical Inc) was used to assess mechanical sensation. Sensation was graded on a 5-point scale according to the number of monofilament. Reliability of Semmes–Weistein assessment has been validated.[25] Under the consideration of sensation improvement, patients with deficit or absence of sensory function (EXP n=9; control n=10) were analyzed.

Statistics

Basic characteristics of the patients in the control and EXP groups were compared with Student *t* (continuous data), χ^2, or Fisher exact (nominal data) tests. Two-way repeated-measures ANOVAs were used to evaluate effects of group and time in 6 measures. Post hoc test was performed by Student-Newman–Keuls test. Change rate of each measure was assessed with Student *t* or Mann–Whitney *U* (non-normality data) tests. Statistical significance was assumed for $P<0.05$.

Results

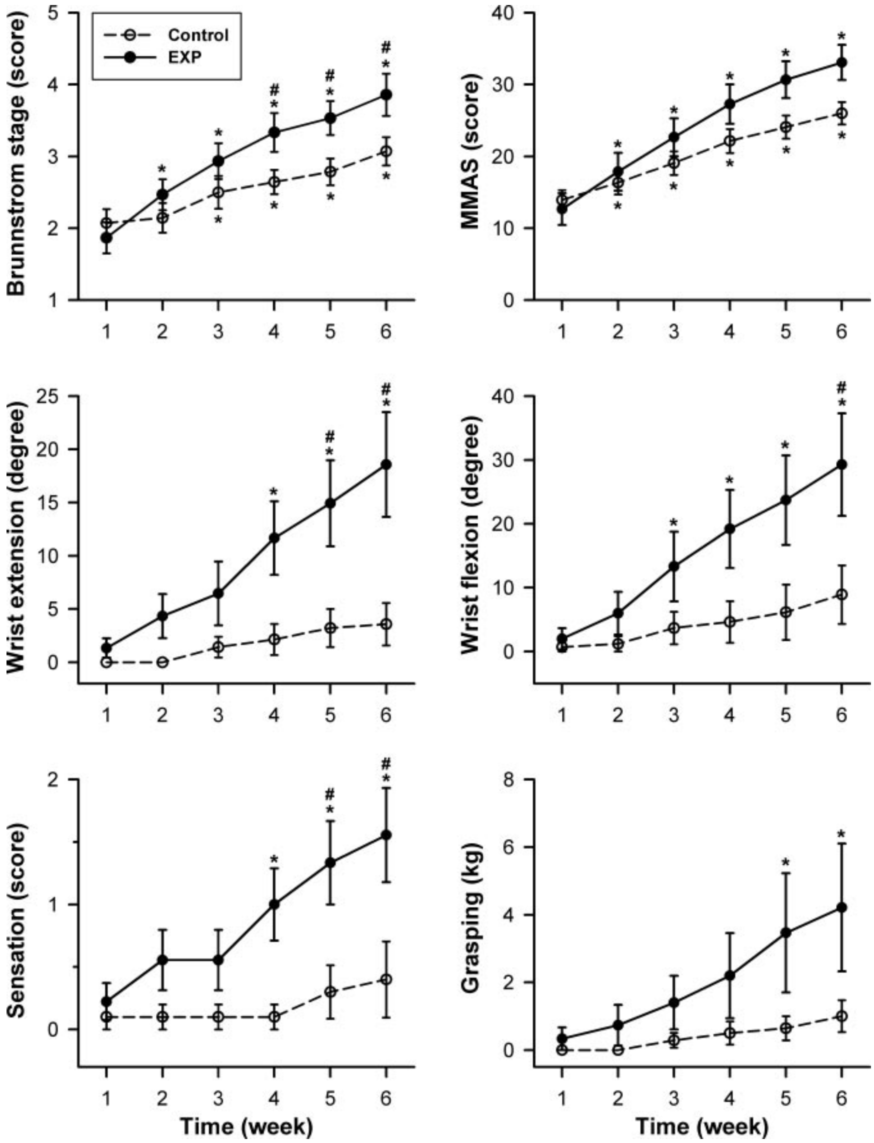
Forty-six patients with a presumed diagnosis of stroke met the criteria initially enrolled in the study. They were assigned randomly to EXP and control groups. Twenty-nine subjects completed the treatment protocol (EXP n=15; control n=14). Seventeen patients did not finish the experiment because of discharge from hospital, pulmonary infection, transfer to home-care settings, or searching alternative Chinese medicine therapy. No physical damage or adverse effect was reported after 6-week TS. Basic characteristics of patients are shown in Table 1. No significant difference was found in demographic data and baseline values of all measures. A well randomization existed in this study.

The Figure shows changes of 6 functional measures of both groups. The results of the group comparison are summarized in Table 2. All measures displayed significant difference (group×time in Table 2). Moreover, patients showed progressively significant improvement (time in Table 2). Sensory/motor recovery of the EXP group, including Brunnstrom stage, wrist extension, and sensation, was significantly greater than those of

TABLE 1. Basic Characteristics of the Control and EXP Groups

Variable	EXP	Control	*P* Value
Age (y)	58.5 (12.9)	59.6 (12.0)	0.90 (*t*)
Gender (male/female)	6/9	10/4	0.14 (F)
Stroke onset to treatment (d)	14.3 (6.8)	12.4 (6.6)	0.47 (*t*)
Type of stroke (I/H)	9/6	8/6	0.82 (χ)
Side of paresis (R/L)	5/10	6/8	0.88 (F)
Brunnstrom stage (score)	1.87 (0.83)	2.07 (0.73)	0.51 (M)
MMAS (score)	12.67 (8.62)	13.93 (5.15)	0.64 (*t*)
Grasping (kg)	0.33 (1.29)	0.00 (0.00)	0.77 (M)
Wrist flexion (°)	2.00 (6.49)	0.71 (2.67)	0.79 (M)
Wrist extension (°)	1.33 (3.52)	0.00 (0.00)	0.55 (M)
Sensation (score)	0.22 (0.44)	0.10 (0.32)	0.68 (M)
Muscle tone (score)	0.27 (0.46)	0.50 (0.52)	0.29 (M)

Results are mean (SD) unless otherwise stated. I indicates infarction; H, hemorrage; R, right; L, left. Statistics: *t*, Student *t* test; F, Fisher exact test; χ, χ^2 test; M, Mann–Whitney *U* test.



Temporal changes of 6 measures (mean±SEM) in the control and EXP groups. *$P<0.05$ vs first week; #$P<0.05$ vs control group by Student-Newman–Keuls test.

the control group (group in Table 2). Recovery curves of 6 measures for both groups appeared to deviate 4 weeks after TS (Figure). Moreover, recovery rates of the EXP group were remarkably higher than those of the control group 4 and 6 weeks after treatment in all measures, particularly for Brunnstrom stage, MMAS, wrist extension, and sensation (Table 3).

Previous studies have indicated that spasticity is increased by noxious heat stimulation and alleviated by cold agent.[21] In this study, muscle tone and its gain did not show significant difference (Table 4).

Discussion

To the best of our knowledge, this is the first study to evaluate the effect of TS intervention on rehabilitation of acute strokes. This study was a well-randomized single-blind clinical trial. TS significantly increased the outcomes of Brunnstrom stage, wrist extension, and sensation. Moreover, TS significantly enhanced recovery rates of all outcomes except grasping. Although the sample size is small, TS effect was significant. Moreover, muscle tone was not altered by TS.

One of the key difficulties in studying the clinic effects of TS is in devising an appropriate control group. In this study, TS consisted of 2 major components (thermal sensation and active motor response). When TS is being administrated, it is clearly not feasible to blind the patients to their treatment allocation. Alternatively, it may be worthwhile considering the use of an inactive dummy or placebo stimulator in the control group, for example, placing a room-temperature water pack of comparable weight covered with towels on the hands of the control group. The choice of the control group intervention also will depend on whether the study is pragmatic or exploratory. In a pragmatic study, it is appropriate to establish the effects of adding TS to standard treatment. This will then give valuable information about the likely clinical impact of the intervention, although it may be more difficult to determine the mechanism of any effect.

In this study, there was a considerable dropout rate (≈37%), resulting in the small sample size. Although the baselines of all measurements in both groups are not statistically significant, the small sample size places the study at risk for a type II error. The small sample size and the high dropout rate after

TABLE 2. Results of 2-Way Repeated-Measures ANOVA of All Measures

Variable	df	F	P Value
Brunnstrom stage			
Group	1	6.26	0.018
Time	5	65.30	0.0001
Group×time	5	8.13	0.0001
MMAS			
Group	1	1.64	0.21
Time	5	220.76	0.0001
Group×time	5	13.80	0.0001
Grasping			
Group	1	2.08	0.16
Time	5	7.30	0.0001
Group×time	5	2.60	0.028
Wrist flexion			
Group	1	3.82	0.061
Time	5	15.32	0.0001
Group×time	5	4.81	0.0004
Wrist extension			
Group	1	4.73	0.038
Time	5	19.69	0.0001
Group×time	5	5.18	0.0002
Sensation			
Group	1	5.71	0.028
Time	5	14.96	0.0001
Group×time	5	5.87	0.0001

randomization further limit the generalization of the results to the broader stroke population. An intention-to-treat analysis should be used to further minimize the effect of dropout.

Brunnstrom stage, wrist extension, and sensation exhibited significant difference after TS intervention. Same phenomena also appeared in their change rates (Table 3). The data confirm that these measures reliably reflect functional ability of the upper limb. Moreover, we found that the wrist flexion was not as sensitive as the wrist extension. The result may arise from different emphases of synergy pattern. First, TS elicited volitional movement, and the movement chiefly highlighted on activation of extensor muscle. Second, flexor synergy of upper limb is dominant after stroke and may affect the improvement of upper limb motor function.[6] Although the difference on wrist flexion was not significant, change rates of wrist flexion and extension were significantly facilitated by TS. Accordingly, TS plays an important role in the sensory/motor recovery of the upper limb.

The difference on MMAS was not significant. This finding is not surprising because the MMAS is an overall index of functional recovery, including upper and lower limb. For functional activity, the patient may compensate with the nonhemiplegic side. It confirms that the MMAS is an insensitive measure for assessing the effect of an intervention on the recovery of the upper limb. Instead, change rate of MMAS revealed significant difference (Table 3). Change rate of functional outcome is associated with subsequent development of rehabilitation. Thus,

TABLE 3. Recovery Rates at Fourth and Sixth Week in All Measures

Variable	EXP	Control	P Value
Brunnstrom stage/week			
Week 4	0.49 (0.25)	0.19 (0.17)	0.004 (M)
Week 6	0.39 (0.17)	0.20 (0.11)	0.005 (M)
MMAS/week			
Week 4	4.87 (1.45)	2.74 (1.23)	0.001 (*t*)
Week 6	3.99 (0.86)	2.41 (0.79)	0.001 (*t*)
Grasping/week			
Week 4	0.62 (1.23)	0.17 (0.42)	0.25 (M)
Week 6	0.77 (1.18)	0.20 (0.35)	0.19 (M)
Wrist flexion/week			
Week 4	5.73 (6.78)	1.31 (3.34)	0.04 (M)
Week 6	5.43 (5.42)	1.64 (2.98)	0.07 (M)
Wrist extension/week			
Week 4	3.44 (3.58)	0.71 (1.82)	0.02 (M)
Week 6	3.43 (3.14)	0.71 (1.49)	0.01 (M)
Sensation/week			
Week 4	0.26 (0.22)	0.00 (0.00)	0.01 (M)
Week 6	0.27 (0.17)	0.06 (0.14)	0.02 (M)

M indicates Mann–Whitney *U* test.

change rate of MMAS may be more sensitive than MMAS itself for the study of intervention.

Grasping and its change rate revealed no significant difference. The difference on muscle tone also was not significant. Indeed, grasping is related to muscle strength.[7,8] Grasping primarily arises from activation of fingers. Although TS elicited volitional/reflexive behavior of the hand and wrist, it differed strikingly from fine motor training. Consequently, the improvement of finger muscle control was not remarkable.

According to statistical results (Table 2), the significant improvement by TS was shown in the sensory/motor function of the upper limb (eg, Brunnstrom stage). Moderate effect was seen in the measures of functional activity (ie, MMAS and grasping). Indeed, occurrence of the obvious deviation of functional recovery curve lagged behind that of motor recovery (Figure). Thus, the instant improvement within a short period is particularly sensitive in the sensory/motor function.

Several mechanisms of neuronal plasticity have been proposed in an attempt to explain motor recovery in brain damage patients.[17,18] However, it is impossible to identify the neuronal processes underlying the improved outcome from this type of study. It seemed more appropriate to find an explanation based on hypothesized therapeutic elements such as motor and sensory stimulation and reduction of spasticity. TS did not affect muscle

TABLE 4. Muscle Tones Before and After 6-Week TS and Their Changes (Gains)

Muscle Tone	EXP	Control	P Value
Before	0.27 (0.46)	0.50 (0.52)	0.29 (M)
After	0.67 (0.98)	1.21 (1.05)	0.15 (M)
Gain	0.40 (0.63)	0.71 (0.73)	0.26 (M)

M indicates Mann–Whitney *U* test.

tone as measured with Ashworth scale, but it significantly increased sensory and motor outcomes. Thus, muscle spasticity may not be a major cause for the improvement of functional outcome.

TS contained 2 major components: thermal sensation and volitional/reflexive motor activity. The heating/cooling stimulation can simultaneously activate multiple specific/nonspecific neural pathways, resulting in recruiting activities of several brain areas.[14,26] Recently, functional imaging studies demonstrated that the heating/cooling stimulation activates a large brain area, which is almost identical to that of motor task.[19,20] The simultaneous activation of many brain areas may be helpful for facilitating the sensorimotor interaction then accomplishing the desired rewiring of the brain. Moreover, sensory recovery is advantageous to avoid learned nonuse, resulting in reinforcement of motor learning.[11,12] On the other hand, we observed that the volitional/reflexive motor activity induced by TS expressed a potential impact on acute stroke patients at the beginning. This psychological driving component may play an important role in the rehabilitative progress. Moreover, the volitional/reflexive motor activity can trigger the attention on the paretic hand and prompt the patient to use the paretic hand. Forced-used strategy could reverse the effect of learned nonuse.[15,16] Accordingly, motor activity provoked by TS has a definite contribution on the functional recovery.

Numerous kinds of facilitative techniques have been proposed and estimated to reduce functional impairment and disability of stroke patients.[3–10] Those treatments are more complicated and expensive than TS used in this study. In addition, we found that a short-term TS (20 to 30 minutes daily) could maximize functional sensory and motor recovery (Figure). Indeed, increase of functional recovery rate within the therapeutic period is economic and lowers the loading of the family and patients themselves. Accordingly, TS is not only a low-cost treatment (<30 US dollars) but also a potential facilitation. Moreover, TS materials, including water pad and towel, are very easy to make/buy. Therefore, TS can be considered as a part of home therapy program for stroke patients. In this scenario, adequate temperature controlling of TS must be noticed to avoid tissue damage.

A great improvement of functional outcome within a shortest amount of time from stroke onset is beneficial for rehabilitation of stroke patients.[3–5] In this study, we provided evidence for facilitation of several sensory/motor outcomes by TS intervention during a 6-week period without alteration of muscle tone. The recovery rate of functional outcome was stable and significant. Although an ongoing improvement after the 6-week TS may be expected,[4,5,12] whether the facilitation seen in the intervention period is continuous at follow-up, and what the optimal intensity is of TS remain to be studied in the future.

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