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Effects of Somatosensory Stimulation on Motor Function After Subacute Stroke

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Abstract

Background—Previous works showed potentially beneficial effects of a single session of peripheral nerve sensory stimulation (PSS) on motor function of a paretic hand in patients with subacute and chronic stroke.

Objective—To investigate the influence of the use of different stimulus intensities over multiple sessions (repetitive PSS [RPSS]) paired with motor training.

Methods—To address this question, 22 patients were randomized within the second month after a single hemispheric stroke in a parallel design to application of 2-hour RPSS at 1 of 2 stimulus intensities immediately preceding motor training, 3 times a week, for 1 month. Jebsen–Taylor test (JTT, primary endpoint measure), pinch force, Functional Independence Measure (FIM), and corticomotor excitability to transcranial magnetic stimulation were measured before and after the end of the treatment month. JTT, FIM scores, and pinch force were reevaluated 2 to 3 months after the end of the treatment.

Results—Baseline motor function tests were comparable across the 2 RPSS intensity groups. JTT improved significantly in the lower intensity RPSS group but not in the higher intensity RPSS group at month 1. This difference between the 2 groups reduced by months 2 to 3.

Conclusions—These results indicate that multiple sessions of RPSS could facilitate training effects on motor function after subacute stroke depending on the intensity of stimulation. It is proposed that careful dose–response studies are needed to optimize parameters of RPSS stimulation before designing costly, larger, double-blind, multicenter clinical trials.

Keywords

stroke; rehabilitation; somatosensory stimulation; motor training; hand function; nerve stimulation

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Declaration of Conflicting Interests

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Introduction

Somatosensory stimulation can be administered in the form of peripheral nerve sensory stimulation (PSS), that is, by bursts of electrical stimuli delivered to the skin overlying peripheral nerves at regular intervals. A single session of PSS applied to a paretic hand leads to transient improvements in pinch force^{1,2} and facilitates training effects on cortical plasticity and on motor function in patients with chronic and subacute stroke.³⁻⁷ The magnitude of the effects reported in these single-session studies differed depending on the intensity of PSS, with some consensus that the higher the stimulus intensity the more prominent the effect at the end of the single PSS session.^{2,8} If this technique is to become useful in clinical practice, it will be necessary to evaluate in more detail the effects of repeated sessions of PSS (RPSS) in association with motor training.

Effects of repeated sessions of other modalities of somatosensory or sensorimotor stimulation on motor function have been previously studied, but the clinical efficacy of different techniques has not been clearly established; while some studies suggested potential benefit of neuromuscular stimulation,⁹⁻¹⁸ cutaneous stimulation,¹⁹ combined neuromuscular and cutaneous stimulation,²⁰ transcutaneous electrical nerve stimulation at constant stimulation frequencies,²¹⁻²⁴ and acupuncture,²⁵ others failed to do so.²⁶⁻²⁹

In this study, we evaluated the effects of the application of RPSS at different intensities over multiple sessions in patients with subacute stroke, at a time when cortical plasticity may be theoretically more prominent and behavioral effects more clinically relevant relatively to the chronic stage. Specifically, we investigated the effects on motor function, disability, and corticomotor excitability of the application of 12 sessions of RPSS at 2 different stimulus intensities in combination with motor training in 2 groups of stroke patients starting within the second month after stroke.

Methods

Participants

Twenty-two patients with a single hemispheric ischemic stroke less than 2 months before entering the study were included from a screening 567 patients admitted to our institution between November 2005 and June 2008. The protocol was approved by the local ethics committee, and all patients provided informed consent to participate. Inclusion criteria were ages 21 to 99 years, right or left hemiparesis after ischemic infarction in a cerebral hemisphere as documented by computed tomography (CT) or magnetic resonance imaging (MRI), stroke onset 30 to 60 days earlier, ability to perform tasks included in the Jebsen–Taylor test³⁰ (JTT), and compliance with the schedule of interventions and evaluations determined in the protocol. Exclusion criteria were previous symptomatic strokes; epilepsy; uncontrolled medical problems, including severe cardiovascular disease, rheumatoid arthritis, active joint deformity of arthritic origin, active cancer or renal disease, end-stage pulmonary or cardiovascular disease; psychiatric illnesses including severe alcohol or drug abuse and depression; neglect; and aphasia or cognitive impairment that interfered with patients' ability to comply with the experimental protocol or provide informed consent. In addition, patients were excluded from transcranial magnetic stimulation (TMS) testing if they had a pacemaker, implanted medical pump, metal plate in the skull, metal objects inside the eye or skull, use of medications that could influence motor excitability, or had undergone decompressive surgery to treat intracranial hypertension.

Handedness was evaluated with the Oldfield Inventory.³¹ JTT was scored in seconds, as the time required to perform 6 of the 7 activities that comprise the test (turning cards, picking up small objects, stacking checkers, picking up beans with a spoon, moving 5 light and 5 heavy

cans of the same size).³⁰ The sentence writing task was not included in the score to avoid bias in evaluation of patients with mild language impairments. Maximal pinch force³² between the index finger and thumb of the paretic hand (average of 3) was tested with a digital dynamometer while the elbow was stabilized in extension by a splint (Kratos, São Paulo, Brazil). Fugl-Meyer (paretic upper limb),³³ Ashworth Scale,³⁴ NIH Stroke Scale,³⁵ Modified Rankin Scale,³⁵ ³⁶ and Functional Independence Measurement (FIM) scores^{37,38} were also evaluated at baseline. Lesions (Figure 1) were classified as corticosubcortical or subcortical according to presence or absence of involvement of primary motor, primary somatosensory, supplementary motor, or premotor cortices on magnetic resonance imaging (n = 16) or computed tomography (n = 6) scans by an experienced reader blinded to the experimental purposes and study design.

Experimental Design

This investigation was carried out on patients undergoing customary rehabilitative treatment for the appropriate stage of their disease in the department of physical therapy in our hospital. They were pseudorandomly assigned to receive, in addition to such treatment, 2 hours of median nerve stimulation at 1 of 2 different stimulus intensities: *subsensory* (defined as not sufficient to elicit paresthesias) or *suprasensory* (paresthesias elicited in the distribution of the median nerve in the absence of motor-evoked potentials [MEPs] larger than 100 μ V) immediately preceding practice of the JTT task, 3 times a week, for 1 month (total of 12 sessions; see Figure 2, single outpatient visit).

Peripheral nerve stimulation—RPSS was applied according to a technique previously described.^{1,4,39,40} Surface electrodes were optimally placed to stimulate the median nerve at the wrist in the paretic arm. Initially, the minimum intensity of median nerve stimulation at which patients reported paresthesias (mean of 3 trials: sensory threshold) was determined. Trains of 5 electrical pulses (1-ms duration for each) at a frequency of 10 Hz were subsequently delivered at 1 Hz (S48 Square Pulse Stimulator; Grass Instrument Division of Astro-Med, Inc, Braintree, MA) according to a well-described RPSS protocol that elicited changes in motor cortical excitability and in motor functional tests when applied in single-session formats in patients with chronic stroke.^{1,3,4,7,8} For *subsensory* RPSS, stimulus intensity was kept immediately below the sensory threshold ($83.0 \pm 3.0\%$ of sensory threshold in our patients), which did not elicit measurable changes in motor cortical function in previous single-session studies in healthy volunteers and patients with stroke.^{2,8} For *suprasensory* RPSS sessions, stimulus intensity was increased to the level at which patients reported strong paresthesias in the median nerve territory in the absence of pain, while compound muscle action potential amplitudes registered with surface electrodes overlying the APB were smaller than 100 μ V ($207.3 \pm 23.9\%$ of sensory threshold in our patients). This intensity of stimulation is well tolerated and in previous facilitated motor function single-session investigations.^{1-4,7,8,41} In both *suprasensory* and *subsensory* RPSS sessions, a LED seen by patients blinked in the front panel of the stimulator while stimulation was delivered so that patients could see that the stimulator was on and that the intensity of the stimulation was greater than zero. At enrollment, they were told that different intensities of stimulation would be used in the protocol and that they might or might not have tingling sensations in the hand during the procedure. Patients in each group did not have contact with those in the other group in this factorial design.

Compliance with treatment was calculated as follows: (number of performed sessions/number of planned sessions) \times 100. Two questions were asked of all patients in both groups 2 to 3 months after the end of the interventions: “Was your wrist stimulated during the treatment?” and “Do you feel the treatment helped you in any way?”

JTT training—Earlier studies showed that facilitation of motor function after application of a single session of PNS outlasts the period of stimulation by approximately 20 minutes.^{39,40}

Here, patients were instructed to practice 5 different tasks included in the JTT (turning cards, picking up small objects, stacking checkers, picking up beans with a spoon, and moving light cans) in 2 blocks of 5 trials each separated by 1 minute of rest immediately following the end of RPSS. In this way, JTT training was carried out within the time period of RPSS-induced reported changes in cortical excitability as evaluated in previous investigations.^{39,40} During motor training, patients were encouraged to perform the tasks as quickly and accurately as possible as per standardized instructions.³⁰

Customary rehabilitative treatment—Customary outpatient neurorehabilitative treatment was provided immediately following the end of the RPSS + JTT training determinations, once a week. The schedule and treatment types are comparable with those used in other rehabilitation protocols that associated training with application of other techniques, such as motor point stimulation,⁵ functional electrical stimulation,^{9,12} or bilateral arm training.⁴² Therefore, RPSS and JTT training were implemented in addition to the customary rehabilitative treatment (Figure 2). Twenty-six activities were predefined as part of this customary treatment, and the therapist applied them according to each patient's individual needs (Table 1). The numbers of repetitions of each task administered in each therapy session were recorded.

Therapists who administered customary rehabilitative treatment and JTT training also evaluated behavioral endpoints. Neither the therapists nor the patients were aware of the stimulus intensity group to which they belonged. To ensure anonymity, information about randomization and RPSS procedures was kept in printed and electronic formats in a locked cabinet, accessed only by researchers who performed RPSS. Patients did not discuss their experience during RPSS with therapists.

Behavioral outcomes—The primary behavioral endpoint measure was the JTT score, measured as previously described, immediately after the 1-month treatment. Secondary outcomes were pinch force, measured as previously described, and FIM scores. Force measurements were not performed in 3 subjects at baseline and in 1 subject after 1 month of treatment because of technical problems with the measuring device (Figure 2, overall treatment schedule). JTT scores, pinch force, and FIM scores were reevaluated 2 to 3 months after the end of the treatment (except in 3 patients lost to follow-up in each group).

Transcranial magnetic stimulation—TMS was delivered through a figure-of-8-shaped magnetic coil (mean diameter, 70 mm) connected to 2 magnetic stimulators via a Bi-Stim 2002 module. The magnetic coil was placed tangentially to the scalp, with the intersection of both wings at a 45° angle with the midline to optimally stimulate the motor cortex.⁴³ Electromyographic (EMG) activity was recorded from surface electrodes placed over the abductor pollicis brevis (APB) muscle in the paretic hand. EMG responses were amplified (1000), filtered (2 Hz to 2 kHz), and recorded on a computerized data acquisition system built with the LabVIEW graphical programming language (sampling rate, 5 kHz).⁴⁴ Its conditional triggering feature was used to deliver TMS stimuli only when the APB muscle was relaxed. Relaxation was defined as EMG activity at baseline <50 μ V peak-to-peak amplitude for at least 1 second. After identification of the APB hot spot, the following TMS measurements were obtained at baseline and immediately after the last session of treatment:

- Resting motor threshold (rMT), a measure of corticomotor excitability defined as the minimum TMS intensity (measured to the nearest 1% of the maximum output of the magnetic stimulator) required to elicit at least 3 out of 6 MEP \geq 50 mV in consecutive trials.⁴⁵ TMS stimulus intensities were expressed relative to rMT measured from the APB, as widely accepted.⁴⁶

- MEP peak-to-peak amplitudes were measured at rMT, 1.5 rMT, and at 100% of the stimulator's output. Results are expressed relative to the maximal peripheral M response peak-to-peak amplitudes (MEP/M, %). M responses were obtained by supramaximal stimulation of the median nerve at the wrist. This measurement allows controlling for differences in muscle bulk and electrode position across subjects,^{47, 48} reflecting the extent of activation of the spinal motor neuron pool of a target muscle, by a single TMS pulse at a given stimulus intensity.⁴⁹ Ten trials were performed at each stimulation intensity. Three stimulation intensities were chosen to evaluate excitability of high-threshold and low-threshold motor cortical neurons.⁵⁰ All waveforms were evaluated "offline" with a playback program with the LabVIEW graphical programming language. Trials in which pretrigger EMG activity exceeded 50 μ V were excluded.
- Short-interval intracortical inhibition (SICI) and intracortical facilitation (ICF) were measured with paired-pulse TMS. SICI and ICF likely reflect intracortical function in separate excitatory and inhibitory interneurons with a possible spinal contribution to the latter.^{51,52} Conditioning stimulus (CS) intensity was set to 80% of the APB rMT. The intensity of the test stimulus (TS) was that required to evoke MEPs of approximately 0.5 to 1 mV (MEP_{TS}). This procedure was described by Kujirai et al⁵¹ in the classical paired pulse paradigm and has been widely used in healthy volunteers⁵³ and stroke patients⁴⁷ (for review, see Talelli et al⁴⁸). The order of presentation of inhibitory (2 ms), facilitatory (10 ms), and control trials (test stimulus alone) intervals was randomized. Eighteen trials were recorded for each interstimulus interval (ISI). Results were expressed as average percentages of MEP amplitudes in conditioning trials and in test trials (MEP_{CS + TS}/MEP_{TS}, %).

TMS equipment was not available before the fifth patient had been included in the protocol, and the procedure was contraindicated in 3 other patients. Therefore, TMS was studied on 15 patients (8 in the *subsensory* group and 7 in the *suprasensory* group) at baseline and immediately after the last session of treatment.

Data analysis—Distribution of the data was tested with the Shapiro–Wilk test. Baseline differences across groups and compliance with treatment were analyzed with Mann–Whitney tests. Means, standard errors, or ranges are given. Intention-to-treat analysis was performed. ⁵⁴ JTT scores at the end of the 1 month of intervention (n = 22) and 2 to 3 months afterward (n = 18) were analyzed with repeated-measures ANOVA (ANOVA_{RM}) with the factors Group (*subsensory* or *suprasensory*) and Time (baseline, end of treatment at 1 month, 2 to 3 months after end of treatment), assuming a non-structured correlation matrix of longitudinal data. The same analysis was applied for FIM scores (n = 22 at the end of 1 month; n = 18 at 2–3 months), pinch force (n = 19 at the end of 1 month; n = 14 at 2–3 months), rMT, SICI and ICF results (n = 15 at baseline, n = 14 at the end of 1 month; 1 patient started to use citalopram a few days before the end of treatment and did not undergo TMS testing).

MEP/M ratios were analyzed with ANOVA_{RM} with the factors Group (*subsensory* or *suprasensory*), Time (baseline, end of treatment), and Stimulus Intensity (rMT, 1.5 rMT, and 100% of the stimulator's output). Analysis was performed on data from 8 subjects in the *subsensory* group and 5 in the *suprasensory* group (data at 1.5 rMT were not recorded in 2 subjects because of high rMTs and relaxation was not achieved in other subjects in offline inspected data).

Tukey tests were used to perform post hoc comparisons when applicable. *P* values <.05 were considered statistically significant. SAS 8.0 and SPSS 10.0 were used for statistical analysis.

Results

At baseline, there were no significant differences in age, sex, ethnicity, education, time from stroke, side of stroke, handedness, JTT time, pinch force, upper limb Fugl-Meyer, FIM, NIH Stroke Scale, Rankin score, or Ashworth score between the 2 groups (Table 2). Patients' lesion locations are shown in Figure 1. There were no significant differences in the number of repetitions of each customary rehabilitation exercise across groups (*subsensory*, 19.9 ± 14.5 ; *suprasensory*, 17.0 ± 13 ; $P = .420$) nor in the compliance with the RPSS sessions (*subsensory*, $90.2\% \pm 3.7\%$; *suprasensory*, $96.2\% \pm 1.2\%$; $P = .085$) or the number of trials during the JTT training (10 in all patients). All patients answered that their wrists had been stimulated during the treatment and that they felt "electrical stimulation treatment helped" them.

Behavioral Effects of RPSS

Group data are shown in Table 3. RPSS over 12 sessions resulted in an improvement in JTT time in both groups relative to baseline. ANOVA_{RM} revealed a significant effect of Time ($F = 12.8$; $P < .001$) and a significant Group \times Time interaction ($F = 4.4$; $P = .026$) with no significant effect of Group ($F = 0.88$; $P = .359$). Post hoc Tukey tests showed a significant difference in JTT scores in the *subsensory* group ($P = .006$) but not in the *suprasensory* group ($P = .211$) at end of treatment compared with baseline. At month 1, the magnitude of improvement in JTT scores was $43\% \pm 4.5\%$ in the *subsensory* group and $25\% \pm 6.2\%$ in the *suprasensory* group.

Of note is that patients with lower baseline JTT scores (Figure 3) showed greater improvement at the end of treatment ($r = .73$; $P < .001$).

There were no significant differences in JTT scores in the *subsensory* group ($P = .546$) or in the *suprasensory* group ($P = .813$) at 2 to 3 months posttreatment compared with immediately after the end of the treatment (Table 3).

FIM scores improved in both groups over time: ANOVA_{RM} revealed a significant effect of Time ($F = 7.07$; $P = .005$) but no significant effects of Group ($F = 0.51$; $P = .482$) or Group \times Time interaction ($F = 7.07$; $P = .065$). There were no significant effects of Group ($F = 0.13$; $P = .721$), Time ($F = 1.28$; $P = .3$) or Group \times Time interaction ($F = 0.1$; $P = .907$) regarding pinch force.

Corticomotor Excitability

Table 4 shows TMS results. ANOVA_{RM} did not show significant effects of Group, Time, or Group \times Time interaction regarding rMT, SICI, or ICF ($P > .05$). MEP/M ratios increased in the *subsensory* group and decreased in the *suprasensory* group at all TMS intensities, but ANOVA_{RM} revealed only a significant effect of Stimulus Intensity ($F = 36.2$; $P < .001$) and no effects of Group ($F = 0$; $P = .947$) or Time ($F = .13$; $P = .724$), or their interaction on MEP/M ratios.

Contact dermatitis (1 patient) under the stimulating electrodes, local hyperemia (1 patient), and minor wrist discomfort (1 patient) were found as side effects, with all resolving within a session with topical cream or a change in stimulating electrode types.

Discussion

The main results of this study were that repeated sessions of *subsensory* RPSS over 1 month preceding JTT training facilitated motor performance, whereas *suprasensory* RPSS did not have an effect in patients with subacute (<2 months) ischemic stroke undergoing customary

rehabilitative treatment. Greater improvements were noticed in patients with worse JTT scores at baseline, in line with previous results in chronic patients.⁷ Differences in JTT at the end of the month between the 2 groups faded over the subsequent 2 to 3 months. All patients reported that they felt the stimulation, therapists were unaware of the stimulation group patients were assigned to, and overall RPSS was well tolerated in the absence of serious adverse events.

Behavioral Measures

One primary conclusion from this study is that results from single sessions of somatosensory stimulation cannot be extrapolated to results from repeated sessions after stroke. Indeed, higher intensities of stimulation have been previously associated with better outcome measures in single-session proof-of-principle studies of PSS relatively early after stroke² and in patients at the chronic stage.^{3,4,6,7} Issues that have not been explored are whether conclusions from these single-session experiments in stroke patients are valid when somatosensory stimulation is applied over multiple sessions (RPSS) preceding motor training, as needed if used as adjuvant strategy in the setting of customarily implemented neurorehabilitative treatments in the subacute stage. Such investigation would be important because, in animal models, structural and functional changes occur in the affected hemisphere from days up to several weeks after stroke (for review, see Cramer⁵⁵). Changes in motor cortical function take place dynamically at this phase,⁵⁶ which may represent a critical period for the application of restorative therapies.^{55,57-59}

We found that *subsensory* threshold RPSS better facilitated the trained JTT task than *suprasensory* stimulation at 1 month. These results, apparently counterintuitive when reviewing the literature on single-session data,^{1-3,7,8} suggest that more work may be needed to determine the optimal stimulation parameters required to facilitate the beneficial effects of training on motor function when applied over multiple sessions. Additionally, it is unclear how these results would fare in a “no stimulation” condition, which was not tested here. Different possibilities could explain our behavioral results at 1 month. First, it is possible that *subsensory* RPSS is more effective than *suprasensory* RPSS in facilitating training effects over multiple sessions than it proved to be in single-session applications. Second, it is conceivable that *subsensory* stimulation can be more effective than suprathreshold stimulation in modulating motor function at earlier stages after stroke, before substantial rewiring of circuits has taken place, an issue that would be of interest to evaluate in animal models.

A disappointing finding, on the other hand, was that the benefits identified at 1 month were not maintained at 2 and 3 months, perhaps pointing to a more transient effect of RPSS on motor function than the effects reported, for example, after cortical stimulation alone in healthy volunteers.⁶⁰ A recent report suggested that the combination of both cortical and peripheral nerve stimulation may evolve as a promising strategy to facilitate motor function after stroke, more than each technique alone.⁴¹ We found no evidence of generalization of the trained task to the FIM or pinch force. It would be important to increase the number of patients tested in order to allow better stratification by impairment levels or lesion sites, an issue poorly explored so far. Finally, it should be noted that direct comparison with previous investigations of somatosensory stimulation is difficult because of the different experimental designs.

Electrophysiological Measurements

Few studies have evaluated changes in motor cortical function after somatosensory stimulation. Increases in MEP/M ratios⁴⁴ or MEP area³⁹ were reported in the stimulated hand in healthy volunteers after a single 2-hour session of ulnar nerve PSS. A single session of median and ulnar PSS led to decrease in SICI in chronic stroke patients.³ The absence of differences in rMT, MEP/M ratios, SICI, or ICF in our study across the 2 interventions may reflect

comparable effects of both on motor cortical excitability, attenuation of the effects reported in a first session over multiple applications of RPSS, or may simply reflect low power.

In summary, our results suggest caution in extrapolating results of single-session interventional studies using somatosensory stimulation after stroke to its use as an adjuvant strategy over multiple sessions in the subacute period. It would be important to implement dose–response studies to optimize parameters of somatosensory stimulation required for the design of more costly, larger, double-blind, multicenter clinical trials in more heterogeneous patient populations.

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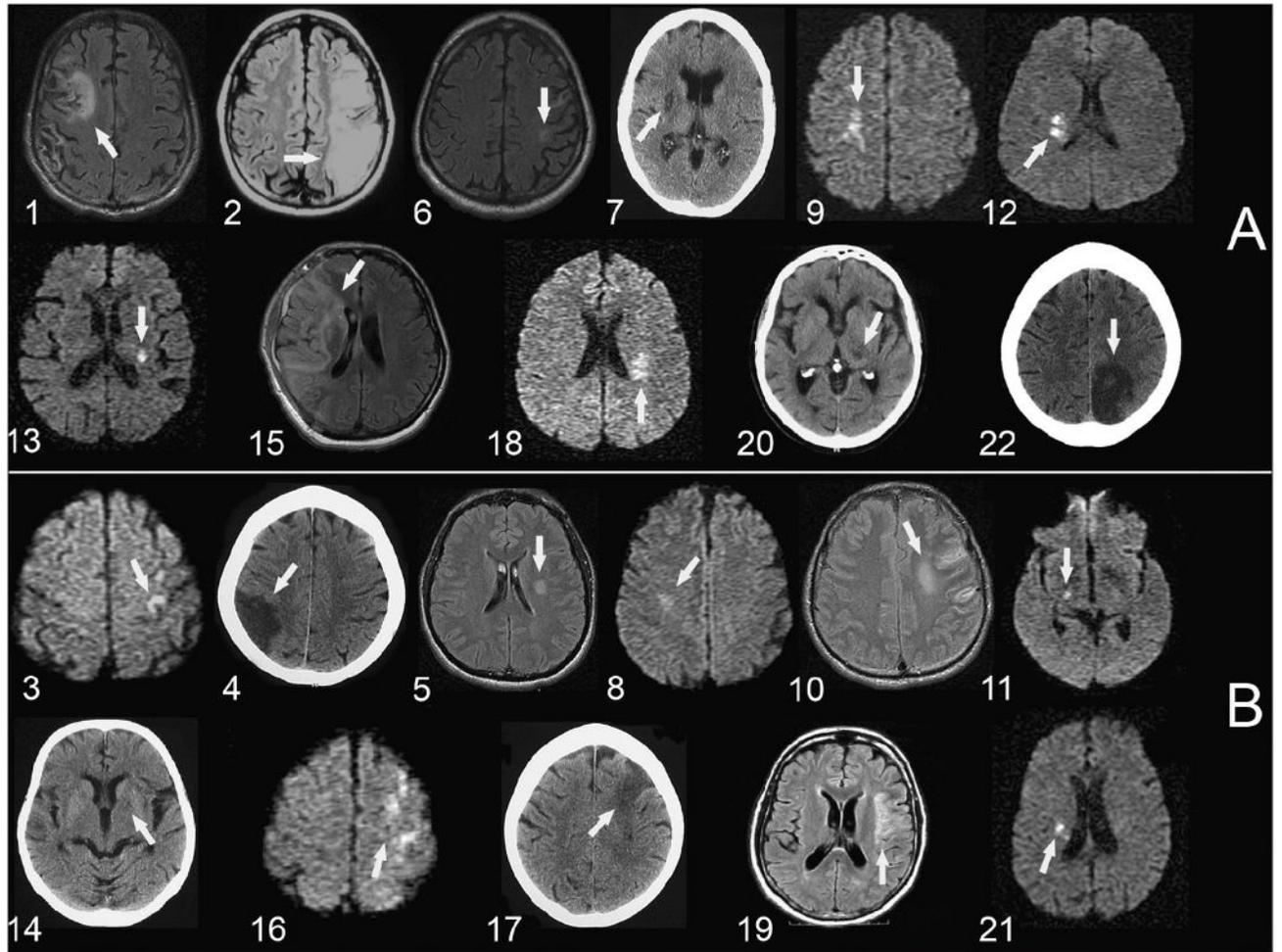


Figure 1. Magnetic resonance imaging (FLAIR or diffusion-weighted images) and computed tomography scans in patients in the subsensory (A) and suprasensory (B) groups. Arrows indicate locations of the lesions.

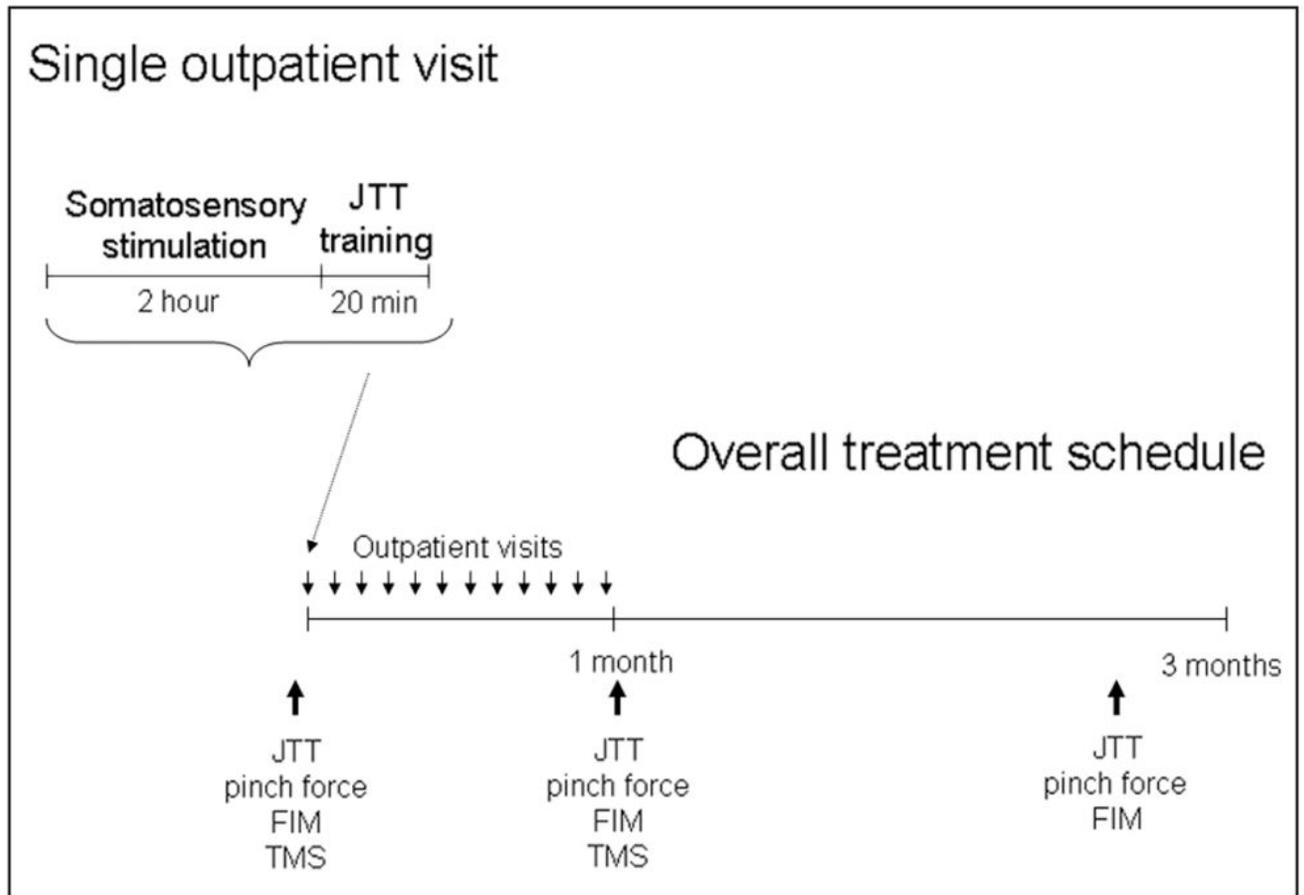


Figure 2. Time line and experimental design. JTT, Jebsen–Taylor test; FIM, Functional Independence Measure; TMS, transcranial magnetic stimulation.

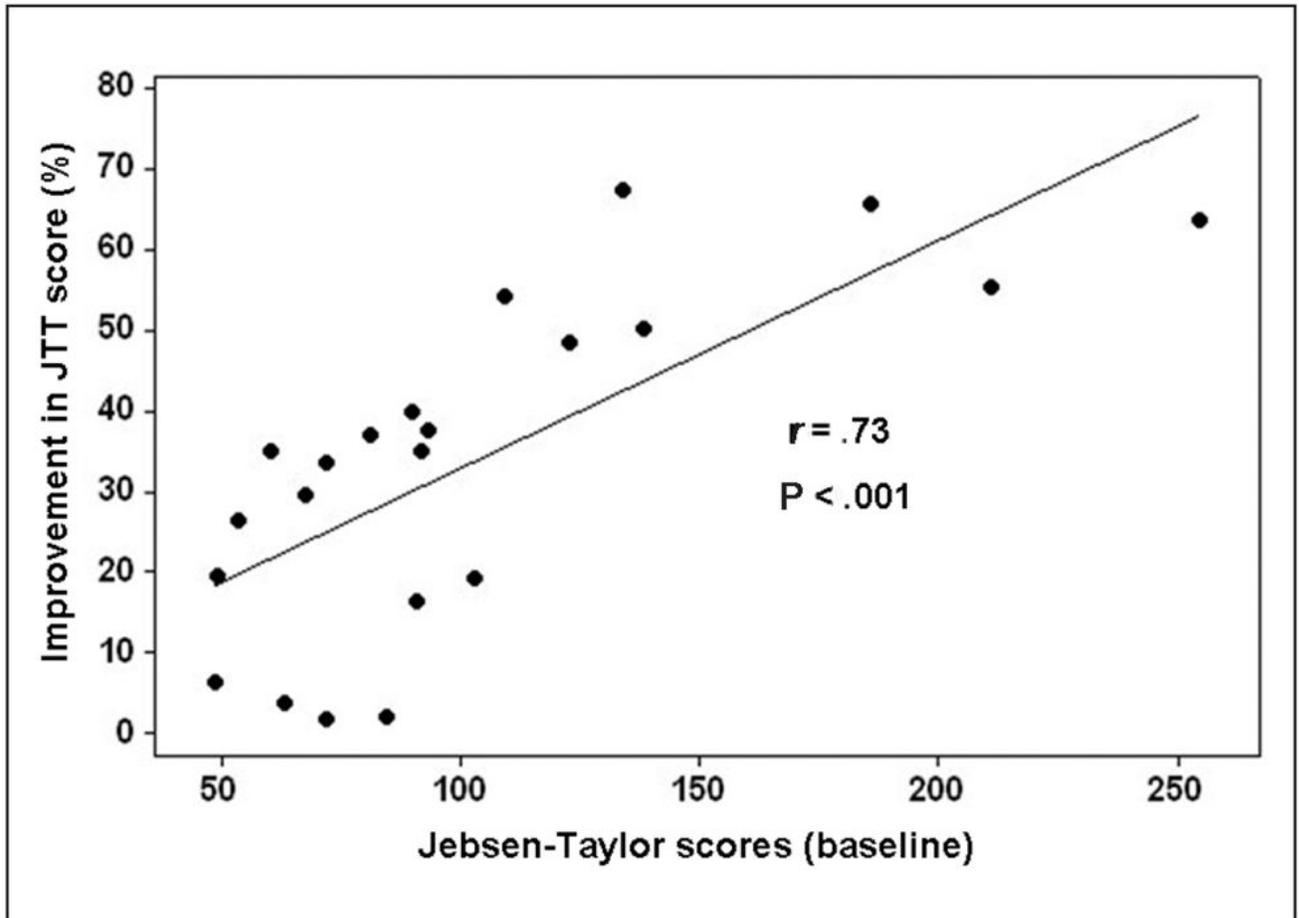


Figure 3. Correlation between Jebsen–Taylor test (JTT) scores at baseline (in seconds) and percentage of improvement in JTT scores at the end of treatment compared with baseline (JTT at baseline – JTT at end of treatment/JTT at baseline × 100).

Table 1

Customary Rehabilitation Tasks

1	Passive movement: hip flexors
2	Passive movement: shoulder girdle
3	Passive movement: knee flexors and ankle plantar flexors
4	Passive movement: hip adductors
5	Passive movement: brachial biceps, wrist and finger flexors
6	Passive movement: pectoralis major
7	Hip extension exercises
8	Hip extension exercises (with ball)
9	Exercises for strengthening of abdominal muscles
10	Passive movement: flexion and extension, upper limb
11	Exercises: pelvic girdle
12	Rolling
13	Active movements: lower limb (with ball)
14	Transfers
15	Trunk rotation
16	Trunk flexion
17	Assisted active movements: upper limb
18	Balance training while seated
19	“Cat” position
20	Balance training: knees in flexion
21	Balance training: knees in semiflexion
22	Balance training while standing on unstable surface
23	Gait training
24	Gait training with obstacles
25	Gait training on unstable surface
26	Climbing stairs

Table 2**Baseline Characteristics in Patients Receiving Subsensory or Suprasensory Somatosensory Stimulation**

Baseline Characteristics	Subsensory	Suprasensory	P Value
Age (years)	59.3 ± 1.4	64.2 ± 3.7	.431
Sex (male/female)	6/5	5/6	.748
Ethnicity (White/Afro descendents)	7/6	4/7	.197
Education (years)	4.0 ± 0.95	4.0 ± 0.43	.949
Time since stroke (days)	53.1 ± 1.8	53.5 ± 2.6	.889
Side of stroke (right/left)	7/6	6/7	.748
Handedness (right/left)	10/1	11/0	.748
Jebsen–Taylor test (seconds) ^a	102.9 (53.3–211.1)	84.3 (48.2–254.9)	.217
Pinch force (N, obtained in all but 3 patients)	0.43 (0.05–0.79)	0.56 (0.14–0.67)	.683
Fugl-Meyer, upper limb ^b	83.3 (65–93.5)	90.9 (67.7–93.5)	.332
Functional Independence Measure	110 (75–119)	112 (103–121)	.562
NIH Stroke Scale	4 (1–8)	3 (0–9)	.562
Modified Rankin Scale	3 (1–4)	2 (1–3)	.116
Ashworth ^c	0 (0–2)	0 (0–2)	.519
Lesion location (CS, S)	6/5	3/8	.478

Abbreviations: NIH, National Institutes of Health; CS, corticosubcortical; S, subcortical.

^aThe item “writing a sentence” was not included in the Jebsen–Taylor score.

^bPercentage of the maximum score (126) is given.

^cMedian of score of elbow, wrist, and fingers.

Table 3

Jebsen–Taylor (JTT) Scores (Seconds), Pinch Force (N), and Functional Independence Measure (FIM) Scores in Both Groups^a

Endpoint	Subsensory Group	Suprasensory Group
JTT		
At baseline	113.9 ± 14.6	92.8 ± 16.4
After 1 month	49.5 ± 5.1	61.4 ± 4.9
After 2–3 months	64.7 ± 5.2	54.6 ± 4.8
Pinch force		
At baseline	4.7 ± 0.5	4.4 ± 0.7
After 1 month	4.9 ± 0.4	4.9 ± 0.6
After 2–3 months	5.6 ± 0.5	5.3 ± 0.7
FIM		
At baseline	105.5 ± 3.7	111.2 ± 2.0
After 1 month	114.7 ± 2.3	113.7 ± 2.5
After 2–3 months	114.4 ± 0.9	114.7 ± 2.8

^aData are presented as mean ± standard errors of the mean.

Table 4

Transcranial Magnetic Stimulation Results at Baseline (D_0) and After 1 Month (1m) in Patients Receiving Subsensory or Suprasensory Somatosensory Stimulation^a

TMS Measure	Subsensory, D_0	Suprasensory, D_0	Subsensory, 1m	Suprasensory, 1m
rMT (% s.o.)	52.6 ± 5.0	50.7 ± 6.1	49.5 ± 3.7	52.6 ± 1.6
SICI (%)	81.3 ± 16.0	90 ± 23	78.1 ± 9.8	65.7 ± 9.5
ICF (%)	172.6 ± 25.4	155.3 ± 12.0	164.6 ± 22.5	149.5 ± 6.4
MEP _{TS} (μV)	716.3 ± 137.3	741.2 ± 110.0	760.2 ± 212.0	724.6 ± 68.7
MEP/M at rMT (%)	1.7 ± 0.5	2.1 ± 0.6	2.0 ± 0.5	1.5 ± 0.3
MEP/M at 1.5 rMT (%)	12.4 ± 4.5	17.7 ± 3.3	23.3 ± 7.8	11.4 ± 2.1
MEP/M at 100% s.o. (%)	21.4 ± 5.9	36 ± 8.3	29.7 ± 9.1	28.6 ± 7.3

Abbreviations: TMS = transcranial magnetic stimulation; rMT = resting motor threshold; s.o., stimulator's output; SICI, short-interval intracortical inhibition; ICF, intracortical facilitation; MEP_{TS}, motor-evoked potentials elicited by test stimuli; MEP/M, motor-evoked potential amplitude, given in percentage supramaximal M response amplitude.

^aTMS was studied on 15 patients (8 in the subsensory group and 7 in the suprasensory group). Data are presented as mean ± standard errors of the mean.