Functional Outcomes Can Vary by Dose: Learning-Based Sensorimotor Training for Patients Stable Poststroke

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Functional Outcomes Can Vary by Dose: Learning-Based Sensorimotor Training for Patients Stable Poststroke

Nancy N. Byl, PhD, PT, FAPTA, Erica A. Pitsch, MPT, and Gary M. Abrams, MD

Objective. This study aimed to determine whether the dose of learning-based sensorimotor training (LBSMT) significantly enhances gains in upper limb function in patients stable poststroke.

Methods. A total of 45 subjects stable poststroke participated in a 6-8-week LBSMT program of varied dosage: group I (n = 18; 1×/week, 1.5 hours/visit); group II (n = 19, 3×/week, 0.75 hours/visit); and group III (n = 8; 4×/week, 3 hours/visit). All subjects reinforced their training with home-based practice. The primary outcome measures were functional independence, strength, sensory discrimination, and fine motor skills.

Results. Across all individual subjects, significant gains were measured on the 4 dependent variables (improvement ranging from 9.0% to 38.9%; P < .001). Group III made greater gains than groups I and II on functional independence, sensory discrimination, and fine motor skills, with a significant linear trend by dose for functional independence (P < .001). Only 2-3 subjects in groups I and II, respectively, would need to be treated at the high dosage of group III for one more subject to achieve >50% gain in functional independence.

Conclusions. Learning-based sensorimotor training based on the principles of neuroplasticity was associated with improved function in patients stable poststroke. The gains were dose specific with the greatest change measured in subjects participating in the high-intensity treatment group.

Key Words: Stroke—Neuroplasticity—Sensory training—Sensorimotor training.

No study has examined the effectiveness of different dosages of a well-defined strategy for rehabilitation therapy based on principles of progressive, repetitive task-related practice with a homogenous group of subjects in the late stage of recovery poststroke. Dose–response studies should be as essential to rehabilitation as they are for determining the optimal dose of a new medication prior to initiating a randomized clinical trial for efficacy of the drug.1 The purpose of this study was to compare outcomes associated with different doses of learning-based sensorimotor therapy (frequency and intensity of therapy within a duration of 6 to 8 weeks) in patients >6 months poststroke.

METHODS

Subjects

A total of 52 subjects between the ages of 33 and 80 years (men or women, right or left hemisphere, ischemic or hemorrhagic stroke) were recruited to participate in 3 separate research studies between September, 2001 and April, 2005. Subjects were recruited from physicians and physical therapists practicing in the greater San Francisco Bay Area, stroke support groups, and flyers posted in 4 local hospital clinics.

To be eligible for any of the 3 studies, subjects had to meet all of the following inclusion criteria: (1) be at least 6 months poststroke, (2) have written permission from a physician to participate in an exercise program, (3) speak conversational English or bring an interpreter to the training and testing sessions, (4) be able to arrange transportation to get to and from treatment, and (5) make a commitment to come for all of the appointments. In addition, the subjects had to be able to walk independently at least 100 ft with or without an assistive device, partially open and close the involved hand, elevate the affected arm at least 45° against gravity, and flex the elbow 90° against gravity. Subjects were excluded if they had a degenerative neuromuscular disease, history of a head injury, or any medical condition(s) that could be exacerbated by the training. Subjects with a history of degenerative arthritis and/or high blood pressure were not excluded if considered in control with medications. A series of studies for patients poststroke were approved by the Committee on Human Research at the University of California, San Francisco. All subjects were informed of their rights. Each gave a full, signed consent before participation.
All subjects were instructed in a home program of learning-based sensorimotor training (LBSMT) reinforced with 6 to 8 weeks of supervised LBSMT of varied intensity. Based on random assignment to LBSMT or other intervention strategies in a larger research study, the following intensity groups were selected for this analysis based on dose of LBSMT therapy: group I (21 subjects, participating in supervised exercises 1×/week, 1.5 hours/visit [12 hours]); group II (22 subjects participating in supervised exercises 3×/week, 45 minutes/visit [13.3 hours]); and group III (10 subjects participating in supervised therapy 4×/week, 3 hours/visit [72 hours]). Group II also participated in bodyweight supported treadmill training (3×/week; 45 minutes/visit).

Procedures

All subjects were evaluated at the beginning and the end of treatment. Testing required 2.5 to 3 hours. All evaluators were trained by the primary investigator and were blinded to group assignment. All tests were administered bilaterally, except for the Wolf Motor Function Test (WMFT). The WMFT was administered only to the affected side because of time constraints and patient fatigue. All other measurements of the upper limb were tracked by affected versus less affected side.

A variety of clinical instruments were used to document performance in the different domains. All tests had standard testing procedures and had acceptable reliability (see previous studies and Table 1). On the timed tests, a ceiling value was established in advance to permit scoring of all tests. For the WMFT, the standard protocol allowed subjects a maximum of 2 minutes to complete each task. For the Digital Reaction Test, the subject had 60 seconds to click a stopwatch on/off one time. Functional independence was measured with the California Functional Evaluation (CAFE 40) and the WMFT. Only items 8 to 16 of the WMFT were used. Items 1 to 6 were required as part of the inclusion criteria, and item 7 was included in strength measurements. Subtests from the Sensory Integration and Praxis Test (kinesthesia, graphesthesia) and the Byl-Cheney-Boczai Discriminator (BCB) were administered to measure cortical sensory discrimination. Without regard to unit, the scores on the sensory tests were added together to create a single sensory score to represent the complex skill of sensory discrimination. Without regard to unit, the scores on the sensory tests were added together to create a single sensory score to represent the complex skill of sensory discrimination. This combined sensory score was correlated (r > 0.35) and the scales were of similar range although different units. This combined sensory score has been shown to be responsive to measuring change, even though it cannot be assumed that one mm of change is the same as 1% change.

Fine motor skills were measured by digital motor reaction time (measured by turning a stopwatch off and on). Grip and pinch strength were tested with handheld dynamometers (Jamar, Clifton, NJ; Hoggan Health Industries, West Jordan, UT). The subjects walked 20 ft and a stopwatch was used to time the walking speed. At least 3 walking trials were made and then averaged for reporting.

Intervention

All subjects received supervised physical therapy at the UCSF Faculty Outpatient Practice. If a subject missed a scheduled appointment, additional visits were added at the end of the treatment up to 2 weeks post usual treatment. If an acute medical event occurred at home between treatment sessions (eg, injury, seizure, arthritic flare), the subject was asked to return to the primary health care provider to obtain clearance to continue in the study.

Learning-based sensorimotor training. The LBSMT was configured to follow the principles of neuroplasticity. All tasks were attended, repeated, purposeful, and progressed in difficulty with performance accuracy positively rewarded. The tasks were functional, with the emphasis placed on haptic activities, graphesthesia (interpreting information delivered to the skin), and adaptation of the hand based on the sensory interface of the object.

Activities emphasized improving sensory discrimination of the cutaneous, muscle and joint receptors by performing matching tasks with the eyes closed (eg, identifying and differentiating various shapes, forms, and textures with the affected hand, reproducing letters and words drawn on the affected hand, discriminating 1 or 2 stimuli, sharpness and dullness or different textures). Training progressed in difficulty to tasks that involved proprioception, kinesthesia, and vibration; then graded movements were practiced (eg, learning to lightly and evenly control the force of the hand on a moving surface, holding a given force on a scale, moving slowly without tremor or unnecessary curling of the digits). The participants were then challenged to integrate sensory and motor function by manipulating objects with varying weights, shapes, and surface textures.

Subjects were asked to “think sensory” as they began to perform fine motor tasks. The quality of movement was emphasized even if only part of the task could be completed. Forced, gross synergistic movements were discouraged. Many fine motor activities were performed with the eyes closed. Subjects were also asked to mentally practice doing skilled movements before actually performing the task. Functional tasks were performed with the subject in good postural alignment encouraging graded, nonstereotypical patterns of movement. The activities in both the supervised therapy sessions and the home program were matched to the ability of the subject. The exact number of repetitions and the
<table>
<thead>
<tr>
<th>Measurement Tool</th>
<th>Dependent Variable</th>
<th>Scoring System</th>
<th>Directions</th>
<th>Reliability</th>
<th>Equipment</th>
</tr>
</thead>
</table>
| Graphesthesi a  
(modified subtest of Sensory Integration Praxis Test [SIPT]) | Sensory performance | 2 = correct 1 = partially correct 0 = incorrect; % error | Tip of a paperclip used to draw designs on subject’s fingers while eyes closed (EC). Subject recreates design with pen with eyes open (EO). Two designs per finger pad | Interrater = 0.95; test-retest r = 0.91 | Paperclip and design sheet |
| Kinesthesia  
(subtest of SIPT) | Sensory performance | Average error (distance from target in mm) | Subject’s hand is moved to target and back to start position; subject attempts to relocate digit, EC; 5 trials per hand | Interrater = 0.95; 6 test-retest r = 0.90 | Target sheet and ruler |
| Byl-Cheney-Boczai Test (BCB) for stereognosis | Sensory performance | 2 = correct 1 = partially correct 0 = incorrect; % error calculated | Subject’s finger is drawn across the shape twice, EC. Subject’s attempts to pick correct shape. 10 trials for 2nd and 4th finger pads | Interrater/intrarate r = 0.995 (ICC), correlation of r = 0.06 b/w BCB and Purdue Test | 20 designs and test sheet of designs |
| Digital reaction time | Fine motor performance | Time in milliseconds, average of all trials (3 trials/digit) | Subject turns stopwatch on/off as quickly as possible; 3 trials per finger | Intrasession reliability range 0.975-0.997 | Stopwatch |
| Finger tapping speed | Fine motor performance | Number of taps in 10 seconds | Subject depresses a mechanical lever attached to a counter | 0.95 in preliminary study with normal adults | Tapper and stopwatch |
| Wolf Motor Function Test | Functional performance | Time multiplied by qualitative score; qualitative score using new inverted functional ability scale (ordinal scale of 1-6): scores totaled for items 7-17 | Functional tasks are timed. Qualitative score (1-6, 1 best). Scale developed from Arm Motor Ability Test | ICC = 0.97-0.99 for repeated measures among subjects | Watch, weights, pencil, paperclip, towel, checkers, key, can, and cards |
| CAFÉ 40 | Functional performance | 7-point Likert scale (1 = least independent, 7 = most independent) | Self-scoring of ability to perform functional activities. Scores inverted for data analysis | Test-retest: r = 0.971 | Written questionnaire |
| Grip and pinch | Strength | Kilograms force, average of 3 trials | Squeeze dynamometer as hard as possible | ICC 0.98-0.99 | Jamar dynamometers |
| Velocity | Gait | Meters/second | Subject walks 4.572 m (15 ft) at self-selected pace | Interrater: 1.009 | Stopwatch |

* All subjects were measured at baseline and completion of treatment.
The progression of difficulty could not be precisely monitored (ie, progression could not be based on minimal detectable differences) because the tasks were not based on robotics or computer control. Progression of task difficulty was based on accurate performance (eg, demonstrating approximately 80% to 90% accuracy before starting a more difficult task).

To reinforce normal movement patterns, some sensorimotor and fine motor functional tasks were performed with a mirror. The affected hand was placed behind a mirror and the unaffected hand was placed in front of the mirror. The mirror image (which looked like the affected hand), guided and reinforced normal patterns of movement. The LBSMT activities have been summarized previously. The emphasis on normal sensory, sensorimotor, graded and quality of fine motor movements distinguished LBSMT from the task-oriented, forced use paradigm of constraint induced movement therapy. The focus was on normal selective fine motor movements rather than gross motor movements.

Body weight–supported treadmill training. Group II also participated in body weight–supported treadmill training (BWSTT). After upper limb LBSMT, subjects were placed in a harness connected to the Lite Gait I body weight support system positioned over the Gatekeeper treadmill (Mobility Research, Tempe, AZ). The amount of body weight support was measured through a BiSym attachment in the yoke of the Lite Gait. Blood pressure and heart rate were recorded prior to during and after training using the Braun PrecisionSensor Pro wrist blood pressure monitor (Braun, Boston, MA) or the Baumanometer Standby Model (W.A. Baum Company, Copiague, NY) standard blood pressure cuff with a ceiling of <70% maximum heart rate and blood pressure >225 mm Hg systolic or >100 mm Hg diastolic set as a guide. Patients tried to walk normally, including spontaneously swinging the arms while the therapist manually facilitated quality of stepping and pelvis stabilization as needed. Up to 40% of body weight was provided and progressively decreased to subject tolerance over 6 weeks. Speed was determined by subject ability (0.8 to 1.0 miles per hour, mph), and then progressively increased to tolerance (1.5 to 2.5 mph). Total time walking was 30 minutes with rest breaks from 2 to 10 minutes as needed to minimize exacerbation of tone and fatigue. Continuous walking increased from 10 to 30 minutes by the end of the study. Subjects were encouraged to talk, spell, and count during training. After walking on the treadmill, all subjects practiced overhead walking for 5 to 10 minutes.

Home program. Each subject and the family were educated about the benefit of practicing LBSMT activities at home with integrated use of the affected hand in all daily activities to drive reorganization of the brain and improve function. To promote the use of the involved limb in unilateral and bilateral fine motor tasks, each subject was encouraged to wear a “soft” garden glove on the less affected hand during the day. The home LBSMT program was the same for all subjects regardless of group assignment. Each subject recorded home activities on a daily log and turned this into the therapist once a week. Other wellness activities, such as walking, good posture, going to the gym, and involvement in social and community activities were encouraged.

RESEARCH DESIGN AND DATA ANALYSIS

This was a single-blinded 3-group, pre–post test experimental design with groups defined by previous study guidelines under different dosages of LBSMT (frequency, length, and duration of visits). The evaluator was consistent across all studies and blinded to group assignment. For this analysis, the dependent variables were (1) functional independence, (2) grip strength, (3) sensory discrimination, and (4) fine motor skills. Gait speed was considered a control-dependent variable and not expected to change except for subjects in LBSMT II where subjects participated in LBSMT and BWSTT.

Subjects were described by age, gender, ethnicity, side of hemiparesis, length of time poststroke, and group assignment. The dependent variables were described over all subjects and by group in terms of the mean, standard deviation or standard error of measurement (SEM), median and the median pre–post test change score (specifically the mean percent median change score for each subject in each group). In preliminary studies, the dependent variables were not correlated and considered independent families (r < 0.2). Because of high variability of subject performance, pre–post test median gain scores were normalized by ranks and nonparametric statistics were applied for statistical analysis. Nonparametric tests examine the differences in median scores. To determine if significant gains were achieved across all subjects and by each group, the Wilcoxon signed ranks test was applied (P < .0167). The Mann–Whitney U test was applied to determine if there were significant differences between the groups. The Tukey method was used to minimize the experimentwise error (T<sub>.05,10,5</sub> = P < .0167).

For descriptive purposes, across treatment groups, pairwise comparisons were summarized for each dependent variable by side of lesion, length of disability, gender, and age. The Spearman rank correlation coefficient was applied to determine if dosage of therapy (total hours) was correlated with gains in performance. With
results

A total of 52 subjects were admitted with 45 subjects completing the study. In group III, 1 patient did not meet study criteria and 1 decided not to participate after initial baseline measurements were taken but before beginning therapy. All of the remaining dropouts were based on medical or personal problems unrelated to the intervention (group I, 3 dropouts; group II, 4 dropouts).

Table 2. Summary of Subject Characteristics by Group

<table>
<thead>
<tr>
<th>Subject Characteristics</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects, n</td>
<td>18</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Age (years; mean ± SD)</td>
<td>63.2 ± 9.4</td>
<td>62.6 ± 13.6</td>
<td>61.1 ± 13.3</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Female</td>
<td>6</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Affected side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>11</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Left</td>
<td>7</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Years poststroke (mean ± SD)</td>
<td>2.3 ± 1.6</td>
<td>2.3 ± 1.7</td>
<td>2.4 ± 2.1</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>10</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Asian</td>
<td>7</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

* The subjects in all 3 groups were of similar age and on average between 2 and 3 years poststroke. More subjects in group III had a left-sided hemiparesis.

Across all subjects, significant improvement was expected on the 4 primary dependent variables. By group, subjects in the high-dose therapy group (group III) were expected to make significantly greater gains than subjects participating in the low-dose therapy groups (groups I and II). No significant differences in gain scores were expected between groups I and II. Intensity was expected to be correlated with the dependent variables but not to be correlated with patient parameters. Gains in function, sensation, strength, and fine motor skills were expected to be moderately correlated with intensity of treatment. Younger patients were expected to make greater outcome gains postintervention than older patients.

results

A total of 52 subjects were admitted with 45 subjects completing the study. In group III, 1 patient did not meet study criteria and 1 decided not to participate after initial baseline measurements were taken but before beginning therapy. All of the remaining dropouts were based on medical or personal problems unrelated to the intervention (group I, 3 dropouts; group II, 4 dropouts).

Description of Subjects

The subjects are described in Table 2. The average age ranged from 61.1 years (group III) to 63.2 years (group I). Sixty percent of the subjects were women and 55% had a left hemisphere stroke (right hemiparesis). On average, the subjects were between 2 and 3 years poststroke. There was a larger proportion of subjects with a left hemiparesis in group III, but the differences were not statistically significant.

Baseline Differences: Descriptive Findings

All of the dependent variables are described across all subjects, by treatment group and by less affected side (Figure 1) and affected side (Figure 2, Table 3). Comparing baseline performance parameters by group, on both the affected and less affected sides, there was some variability in baseline performance for sensory discrimination, fine motor control, and strength by group, but the differences were not statistically significant different. However, at baseline, group I walked significantly faster than group II \( (P < .05) \) and had a higher score on functional independence than groups II and III, but due to the large SEM, the differences were not statistically significant.
Table 3. Summary of Outcomes on Affected Side

<table>
<thead>
<tr>
<th>Test</th>
<th>Group I (n = 18)</th>
<th>Group II (n = 19)</th>
<th>Group III (n = 8)</th>
<th>All (N = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Change</td>
<td>Pre</td>
</tr>
<tr>
<td>Functional independence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SEM)</td>
<td>507.4 (35.3)</td>
<td>360.9 (30.2)</td>
<td>−18.9 (9.9)</td>
<td>1179.3 (86.1)</td>
</tr>
<tr>
<td>Median</td>
<td>211.7</td>
<td>178.1</td>
<td>−32.4</td>
<td>404.9</td>
</tr>
<tr>
<td>Sensory discrimination</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SEM)</td>
<td>85.6 (9.7)</td>
<td>71.9 (8.2)</td>
<td>8.9 (7.8)</td>
<td>97.4 (7.13)</td>
</tr>
<tr>
<td>Median</td>
<td>82.5</td>
<td>63.3</td>
<td>−14.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>93.2</td>
</tr>
<tr>
<td>Fine motor control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SEM)</td>
<td>401.3 (64.0)</td>
<td>308.2 (32.9)</td>
<td>−8.6 (1.8)</td>
<td>406.3 (52.3)</td>
</tr>
<tr>
<td>Median</td>
<td>359.2</td>
<td>279.4</td>
<td>−12.0&lt;sup&gt;e&lt;/sup&gt;</td>
<td>332.5</td>
</tr>
<tr>
<td>Strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SEM)</td>
<td>50.9 (5.2)</td>
<td>55.4 (6.41)</td>
<td>7.4 (3.5)</td>
<td>42.8 (7.1)</td>
</tr>
<tr>
<td>Median</td>
<td>52.4</td>
<td>53.2</td>
<td>6.6</td>
<td>36.4</td>
</tr>
</tbody>
</table>

<sup>a</sup>Subjects in the high-dose group generally made the greatest change.
<sup>b</sup>Group I learning-based sensorimotor training (LBSMT) of the upper limb, 1 ×/week for 8 weeks (1.5 hours/session = 12 hours).
<sup>c</sup>Group II LBSMT of the upper limb and body weight supported treadmill training 3 ×/week, 45 minutes of LBSMT, 6 weeks (13.3 hours).
<sup>d</sup>Group III LBSMT of the upper limb, 3 hours/day, 4 days/week for 6 weeks (72 treatment hours).
<sup>e</sup>Significance levels: 1<sup>z</sup> = 3.42, <sup>P</sup> < .0001; 2<sup>z</sup> = 3.40, <sup>P</sup> = .0001; 3<sup>z</sup> = 4.40; <sup>P</sup> < .0001; 4<sup>z</sup> = 4.98, <sup>P</sup> < .0001; 5<sup>z</sup> = 2.32, <sup>P</sup> < .001; 6<sup>z</sup> = 2.71, <sup>P</sup> < .0001; 7<sup>z</sup> = 5.50, <sup>P</sup> < .0001; 8<sup>z</sup> = 3.93, <sup>P</sup> < .001; 9<sup>z</sup> = 2.21, <sup>P</sup> < .001; 10<sup>z</sup> = 2.24; <sup>P</sup> < .0003; 11<sup>z</sup> = 2.21, <sup>P</sup> < .001; 12<sup>z</sup> = 2.05, <sup>P</sup> < .001; 13<sup>z</sup> = 3.30, <sup>P</sup> < .0001.
Gains in Performance: Less Affected Side

Across all subjects, there were no significant gains on any of the dependent variables on the less affected side (gains ranging from 3.5% to 8.0%). By treatment group, the gains on the less affected side ranged from 0.1% to 22.3% (Figure 1). Sensory discrimination performance was significantly less accurate at posttesting for group I ($P < .019$), but significantly more accurate for group III ($P < .002$). In addition, on the less affected side, group II made significant gains in fine motor control ($P = .007$) and strength ($P < .01$).

Gains in Performance: Affected Side

Across all groups, there were significant post test gains (14.2% to 33.2%) in functional independence, strength, sensory discrimination, and fine motor control ($P < .001$ for each) (see Table 3; shaded area).

Posttreatment gains by group. After intervention, all 3 treatment groups made significant gains in strength, sensory discrimination, and fine motor control ($P < .01$). Groups II and III also made significant gains in functional independence (see Table 3 and Figure 2).

Comparison of gains between treatment groups. Group III made greater gains than groups I and II on all 4 of the primary outcome variables. However, due to the rigorous control of the experiment-wise error the differences were not statistically significant (see Table 3 and Figure 2). The percentage gains in order of group III, II, and I were significantly linear for functional independence ($z_{Page Test} = 3.30; P < .01$) Although the overall changes in the WMFT were otherwise embedded in the score for functional independence, by group, the differences in improved performance between the 3 groups was reinforced by the reduction in performance time averaged across tasks by group (eg, 11 seconds, 6 seconds, and 1 second respectively, for groups III, II, and I).

Gait. The intervention in this study was focused on retraining the upper limb. However, one group also participated in BWSTT. Consequently, gait speed was monitored as a control variable to note the specificity of the effects of the intervention. Groups I and III (LBSMT only) showed no change in gait speed. Group II (LBSMT and BWSTT) made small but statistically significant gains in gait speed (0.52 to 0.65 m/s; $P < .001$).

Correlation analyses: dependent and independent variables. Applying the Spearman rank correlation coefficient for dose (12, 13.3, and 72 hours) with each dependent variable, there was a low moderate correlation between dose and functional independence ($r = -0.313; t = -4.53; P < .0001$) and dose and fine motor skills ($r = -0.292; t = -4.39; P < .0001$). Improvements in function and fine motor skills were measured as negative gain scores (a lower posttest score). Thus, the higher dose of therapy was associated with improved independence in function and more rapid fine motor performance.
In terms of change with intervention across dose, there was a moderate, significant positive correlation between gain in functional independence and gain in fine motor skills ($r = 0.488; t = 6.53; P < .0001$) and a moderate significant negative correlation between gain in strength and gain in sensory discrimination ($r = -0.416; t = 5.66; P < .0001$). In other words, increased efficiency in fine motor skills was correlated with improved functional independence and improved accuracy of sensory discrimination was correlated with increased strength.

Differences in outcomes by age, gender, side of involvement, and time poststroke. Several differences in outcomes by patient characteristics (age, gender, side, and time poststroke) were identified. Posttreatment, subjects more than 65 years of age made less improvement in functional independence and fine motor skills compared with those 51 to 64 years or those less than 50 years of age ($t = 2.77; P < .01$ and $t = 4.40; P < .001$, respectively). In terms of functional independence, subjects more than 5 years poststroke made significantly greater gains than patients less than 1 year poststroke ($t = 3.34; P < .01$). In terms of side of hemiparesis, there were no significant differences in performance.

Subject self-reported compliance with home therapy. Each week, participants completed a reporting form describing time invested in task practice and time donning the garden glove. Subjects frequently forgot to bring this information to the therapist. Thus, the therapist had to take a verbal summary. Across subjects, by group, the average time reported for wearing the glove each day was 4.5, 2.1, and 3.65 hours for groups III, II, and I, respectively. The reported time for practicing the exercises at home varied by subject by day and did not necessarily correlate with wearing the glove. On some days, the subjects reported doing no exercises at home and other days they reported doing 2 to 3 hours of practice. The hours the subjects committed to doing specific sensorimotor exercises appeared to be independent of their other activities of daily living or community-based activities.

Cost–benefit analysis. Comparing the gain scores in functional independence for the 3 groups, the event rates, the absolute risk reduction (ARR), and the number needed to treat (NNT) were calculated based on the proportion of subjects in each group who achieved $>50\%$ improvement on functional independence. The event rates were 0.278 for group I, 0.158 for group II, and 0.750 for group III. The ARRs were calculated as follows: ARR group I versus...
group II = 0.12; ARR group I versus group III = –0.545; and ARR group II versus group III = –0.665. Compared with group I, to have 1 more subject in group II achieve a gain of >50% on functional independence, 9 subjects would need to be treated following the group I dose of therapy. Compared with group III, 3 subjects in group I or 2 would need to be treated at the intensity of group III for 1 more subject to achieve >50% improvement in functional independence.

If $100 was billed for each hour of physical therapy, the estimated costs of the 3 intervention paradigms for groups I, II, and III would have been $1200, $1330, and $5300, respectively. The cost–benefit analysis based on the ratio of the costs and the proportional benefit of achieving >50% improvement in functional independence was calculated for group I versus groups II and III and group II compared with group III using the following formula:

\[
\text{costs group I} - \text{costs group II} = \text{proportion group I > 50% improvement} - \text{proportion group II > 50% improvement}
\]

Compared with group II, $100 was saved for 12% more subjects in group I to achieve >50% improvement in functional independence. Compared with group I, an estimated $4130 was invested to have 47.3% more subjects in group III to achieve >50% gain in functional independence and compared with Group II an estimated $4030 was invested for 59.2% more subjects in group III to achieve >50% gain in functional independence.

A cost effectiveness analysis can also estimate the benefits of the differences in the intensity of intervention therapy. This was calculated based on the following formula:

\[
\frac{\text{\$ invested for group I}}{\text{proportion group I achieving 50% improvement in FI}} - \frac{\text{\$ invested for group III}}{\text{proportion group III achieving 50% improvement in FI}}
\]

where FI denotes functional independence.

This analysis indicates it would save $2790/subject in group I to be treated at the intensity of group III to achieve comparable outcomes in functional independence. It would cost $1311 per subject in group II to be treated at the intensity of group III to have comparable outcomes in functional independence. When the NNT is factored in for 1 more subject to achieve the beneficial outcomes of group III (3 subjects in group II and 2 subjects in group I), $8370 would be saved for a subject in group I and it would cost $2622 more for a subject in group II. Because the time difference is inconsequential for groups I and II and the NNT was high, this calculation was not carried out.

**DISCUSSION**

This study provides evidence for measurable improvement in function following 6 to 8 weeks of different doses of LBSMT in subjects in a stable state of recovery poststroke. These findings are consistent with other studies reporting on the effectiveness of learning-based rehabilitation with similar subjects.\(^4,17-23\) However, this study provides unique information on the specificity of effects by dosage of training. Training dosage was positively correlated with greater gains. Subjects training 72 hours made greater gains in functional independence, sensory discrimination, and fine motor control compared with subjects training 12 to 13.3 hours. Although the gains were not necessarily linear by dose or frequency of weekly visits (4×, 3×, or 1× per week) increasing the dose to 72 hours of therapy more than doubled the functional gains compared with subjects training a total of 12 to 13 hours. This investment of 60 additional hours was more than 4 times the minimal addition of 16 hours needed to significantly improve gains based on intensity of intervention as reported by Kwakkel et al\(^24\) during the acute phase of recovery. Moreover, a cost effectiveness analysis suggested periodic intense rehabilitation in the late stages poststroke may help patients maintain function. The question that was not answered is whether the >50% gain in function would allow an individual to remain independent at home instead of requiring residential care.

**Training Specificity**

This study contributes evidence that rehabilitation outcomes are training specific. Gains in functional independence, sensory discrimination, and fine motor skills were measured in all 3 groups performing LBSMT. In contrast, strength only improved in the group assigned to the high dose of therapy. In this group, more than 75% of the subjects increased functional independence by >50%. Increasing physical activities could have contributed to the increase in strength. In addition, improvement in gait speed was only measured in subjects participating in LBSMT supplemented with BWSTT. These findings are consistent with other treadmill training studies.\(^25-27\)

**Variations in Performance by Age, Side of Stroke, and Time Postinjury**

Younger patients (<50 years) walked faster than older subjects and tripled their gains in fine motor skills compared with subjects more than 65 years of age. On the other hand, the younger subjects did not make significantly greater gains in functional independence, strength, or sensory discrimination compared with those older than 65 years. Although this was not what was expected, these findings may have been confounded
by time poststroke. Several of the younger subjects were less than 1 year poststroke.

In this current study, the subjects less than 1 year poststroke were weaker and demonstrated more compromised functional independence than subjects >1 year poststroke. The more recent stroke survivors made greater gains in fine motor control but less gains in strength and functional independence postintervention. Although differences in gain scores for subjects between 0 and 6 months and those 6 to 12 months poststroke were not analyzed because small numbers, visual data analysis suggested that subjects less that 6 months poststroke made greater gains than subjects 6 to 12 months poststroke. Gender appeared to interact with physical gains. For example, compared with men, at baseline, women demonstrated reduced strength, fine motor control, and functional independence. After treatment, women made greater gains than men in fine motor performance and functional task performance. This finding could be related to the role of women in personal care (eg, makeup, hair styling, dress styles) and household chores.

Limitations

The design of the study had limitations in both internal and external validity. Random assignment was not employed and we had no untreated control group. Although selection criteria remained consistent, the sequential admission of subjects was associated with some differences in subjects. This may have been related to chance alone in terms of the subjects referred or the increased experience of study investigators and the application of the criteria. The size of the treatment groups was not homogeneous, which contributed to the variance in measurement and may have limited the power of finding a difference when a difference was actually present. Compliance was monitored by self-report rather than a reliable unobtrusive measurement (eg, compliance monitor). In addition, no objective measures of patient cognition, depression, motivation, or expectations were made to assess whether these characteristics interacted with the response to the intervention. A confounding interaction between the intervention strategies is possible. For example, fatigue from gait training could have interfered with the solidification of sensorimotor learning. The study design did not factor in prior rehabilitation, community activities, family support, or compliance with home training. The difference in the dose of therapy between groups I and II was small (1.3 hours) whereas the dose of therapy for group III was more than 50 hours greater. This limited the power of finding a difference when a difference was actually present. Compliance was monitored by self-report rather than a reliable unobtrusive measurement (eg, compliance monitor). In addition, no objective measures of patient cognition, depression, motivation, or expectations were made to assess whether these characteristics interacted with the response to the intervention. A confounding interaction between the intervention strategies is possible. For example, fatigue from gait training could have interfered with the solidification of sensorimotor learning. The study design did not factor in prior rehabilitation, community activities, family support, or compliance with home training. The difference in the dose of therapy between groups I and II was small (1.3 hours) whereas the dose of therapy for group III was more than 50 hours greater. This limited options for trend analysis.

Future Research

For patients in the late phase of recovery poststroke, the importance of the intensity of therapy on recovery of function needs further validation. Given that controlled, randomized, multicenter, clinical efficacy, and effectiveness studies are expensive, controlled randomized experimental trials with moderate size samples could serve as a cost-effective research model to analyze the relative benefits of different intervention strategies at different intensities of intervention for patients poststroke.

CONCLUSION

This study provides evidence supporting the functional benefits of learning-based training in the late stage of recovery poststroke. Functional gains were positively enhanced with an increased intensity of therapy. To maintain, if not improve, patient function and independence, perhaps patients in the late stage of recovery poststroke should be encouraged to seek periodic, intense learning-based training.

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