A Randomized Controlled Trial of Functional Neuromuscular Stimulation in Chronic Stroke Subjects

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Background and Purpose—Conventional therapies fail to restore normal gait to many patients after stroke. The study purpose was to test response to coordination exercise, overground gait training, and weight-supported treadmill training, both with and without functional neuromuscular stimulation (FNS) using intramuscular (IM) electrodes (FNS-IM).

Methods—In a randomized controlled trial, 32 subjects (>1 year after stroke) were assigned to 1 of 2 groups: FNS-IM or No-FNS. Inclusion criteria included ability to walk independently but inability to execute a normal swing or stance phase. All subjects were treated 4 times per week for 12 weeks. The primary outcome measure, obtained by a blinded evaluator, was gait component execution, according to the Tinetti gait scale. Secondary measures were coordination, balance, and 6-minute walking distance.

Results—Before treatment, there were no significant differences between the 2 groups for age, time since stroke, stroke severity, and each study measure. FNS-IM produced a statistically significant greater gain versus No-FNS for gait component execution ($P=0.003$; parameter estimate 2.9; 95% CI, 1.2 to 4.6) and knee flexion coordination ($P=0.049$).

Conclusion—FNS-IM can have a significant advantage versus No-FNS in improving gait components and knee flexion coordination after stroke. (Stroke. 2006;37:172-178.)

Key Words: exercise • gait • rehabilitation

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humans, there was no significant difference in a gait coordination measure.17

The inability, to date, to restore gait components could result from deficiencies in gait practice paradigms available during TT and BWSTT. Specific practice characteristics are critical to reacquisition of coordinated, skilled movement, including: practice of close-to-normal movements, muscle activation driving practice of movement, and repetition of desired movements.18,19 Many stroke survivors are unable to voluntarily activate muscles rapidly or in the proper timing/sequence for practicing coordinated gait components. Rather, patients continually reinforce abnormal movements during walking. Although some stance phase training opportunities were reported for BWSTT, neither TT nor BWSTT provided swing phase practice of normal movement timing, excursion,20 or muscle activations.21 Therefore, these training methods are likely to include repetition of abnormal gait components.

Functional neuromuscular stimulation (FNS) is a promising treatment that can provide critical practice of close-to-normal movements by electrically inducing muscle contractions and coordinated movements not possible voluntarily. Previous FNS gait studies had some limitations. Two RCTs using FNS with surface electrodes showed a significant advantage for FNS versus no-FNS, but in the first study, the gait speed advantage lasted only a number of weeks.22 In the second study, gait energy cost was an outcome measure,23 but subjects did not use methods allowing attainment of steady-state during energy cost data acquisition.24 There has been no documentation that surface FNS can provide a practical system for practice of coordinated movements for >1 lower limb joint.22,23 However, an FNS system with intramuscular (IM) electrodes (FNS-IM) demonstrated the capability to provide practice of close-to-normal gait components at hip, knee, and ankle.20 For chronic stroke survivors (>12 months), case studies showed gains in volitionally executed gait components as a result of FNS-IM treatment,1,25 but FNS-IM alone required >6 months to produce results.

One disadvantage of previous FNS studies was that an optimally synergistic combination of modalities was not tested. FNS-IM, BWSTT, OG, and coordination training together have the potential to target the dyscoordination in persistent stance and swing phase gait components.20 FNS coordination training can target the dyscoordination that prevents normal gait.26 BWSTT can provide the practice of a variety of stance phase gait components.15 FNS can provide the practice of swing and stance phase muscle activations at close-to-normal timings and movement excursions.20 Thus, the combination of FNS-IM+BWSTT has greater gait training practice opportunities than either modality alone.20

No previous study reported significant gains in coordinated gait component movements in response to coordination training, OG gait training, BWSTT, or FNS. The purpose of the current study was to test the effect of FNS-IM according to coordinated gait component movements. The treatment for group 1 was coordination training, OG, and BWSTT. The same treatment was provided for group 2, with the exception that FNS-IM was used in all phases of treatment.

Methods

Subjects

Subjects were recruited using newspaper advertisements in an urban community and surrounding region with a population of 1.4 million. Fifty-eight candidates were screened from September 1999 to June 2004 by 1 coprincipal investigator. Sample size was limited by time constraints. Candidates were not aware of group assignment. Study criteria included: >12 months after single stroke; inability to clear the floor normally in the sagittal plane; hyperflexion or hyperextension of knee during stance; walking without human assistance; passive joint range of motion of hip, knee, and ankle equal to normal excursion needed for walking; normal corrected distance vision; and not participating in rehabilitation. Exclusion criteria included: inability to follow 2-level commands; pacemaker; peripheral neuropathy; absent proprioception; and acute diagnosis (eg, cancer). Twenty-six did not meet the inclusion criteria, and 5 declined to participate after screening. Thirty-two remaining candidates were accepted, and informed consent was obtained according to the Declaration of Helsinki (supervision by medical center internal review board).

According to principles described in the revised CONSORT statement for clinical trials,27 we allocated either FNS-IM or No-FNS treatment. Two completely independent sets of information were generated by 2 independent individuals, maintaining suggested separation between enrollment and treatment allocation.28 Individual 1 generated an unpredictable treatment allocation sequence and was not involved in enrollment, treatment, or assessment. Individual 2 screened and enrolled subjects, recorded enrollment date, and was not involved in treatment allocation, treatment, or assessment of treatment response. Individual 3 allocated treatment to a given subject based on a cross-matching of enrollment date with the unpredictable treatment allocation sequence (open-list method). We stratified subjects according to moderate and severe motor involvement and used blocking27 to ensure greater probability of balance between the 2 groups. As recommended,28 stroke severity was determined according to Fugl-Meyer lower extremity coordination (FMLE), a 34-point scale: 0 to 19 severe; 20 to 28 moderate; and >29 mild (≥29 not accepted).

Treatment

All subjects were treated 1.5 hours per session, 4 sessions per week, for 12 weeks, including: 0.5 hours coordination exercises, 0.5 hours BWSTT, and 0.5 hours OG. Exercise included coordination of joint movements.20 For BWSTT, we used BODEX500 with handrails. Body weight support was decreased 30% to 0% according to ability to maintain normal, neutral alignment of torso, and stance limb. Chosen walking speed was increased to 0.894 m/s as tolerated. OG included: torso, pelvic, knee, and ankle position control during loading and weight bearing, swing hip, knee, and ankle flexion (manual guidance, as needed), and terminal swing knee extension/ankle dorsiflexion. Home exercises were coordination exercises performed for 1 hour per day.

Exercises, BWSTT, OG, and home exercise were identical for both groups except that FNS was used for all treatment aspects for the FNS-IM group but not the No-FNS group. FNS-IM targeted restoration of voluntary ankle dorsiflexion during swing, knee flexion at toe-off, knee flexion during swing, knee extension before heel strike, and knee and pelvic control during stance.1,20,25,30 Template FNS patterns were individualized.1,20 FNS parameter ranges were: amplitude 4 to 20 mA, pulse width 1 to 150 μs, and frequency 15 to 50 Hz, within comfort. During coordination BWSTT+FNS-IM, FNS activated swing phase movement. As volitional control improved, amplitude of FNS-IM was incrementally reduced. IM electrode construction, safety, performance, and insertion methods are described previously.31 Eight muscles were provided with electrodes: tibialis anterior; peroneus longus; lateral head, gastrocnemius; short head, biceps femoris; semimembranosus; long head, biceps femoris; vastus lateralis; and gluteus medius (except for 2 subjects who received 4 or 7, respectively) and remained in place throughout the treatment protocol. The following criteria were used: ≥3 strength and inability to perform coordinated movements (FMLE). Software and a research stimulator provided FNS patterns for ≤8 muscles in multiple combinations and timings.32

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Outcomes

Measures were obtained the day before and after treatment using volitional movement (no FNS or BWSTT during testing; maximum high score was normal, all measures). To date, there have been few studies reporting interventions that produced significant gains in coordinated gait components. Because the purpose of this study was to test the benefit of FNS-IM in targeting dyscoordination during walking and producing a change in the execution of coordinated gait components, it was important to use a measure of coordinated gait component execution. The primary measure was the Tinetti gait (TG), a 12-point scale assessing these coordinated gait components: (1) gait initiation; (2) walking path; (3) trunk alignment; (4) swing phase limb trajectory; (5) step continuity; (6) step symmetry; and (7) swing limb floor clearance and forward swing limb excursion. In inter-rater (2 raters) and test-retest reliability testing (n = 10 chronic stroke survivors), we found the following: intraclass correlation coefficient (ICC) = 0.85; CI, 0.496, 0.959; P = 0.001; and ICC = 0.91; CI 0.681, 0.977; P = 0.0001, respectively.

The secondary outcomes were: FMLE, Fugl-Meyer knee flexion coordination (FMKnFx), Tinetti balance (TB), 6MWT, and self-reported functional milestones. Coordination was assessed using FMLE as described above. FMKnFx was a 6-point, ordinal measure comprised of the 3 FMLE items that measure knee flexion coordination under the following conditions: supine/within-synergy, sitting/within-synergy, and standing/out-of-synergy. This measure was important because 1 aspect of treatment targeted the dyscoordination of knee flexion, which may be a critical factor in the stroke "stiff-legged gait." The FMKnFx (26 chronic stroke survivors; >12 months) showed good convergent validity with the FIM mobility scale (r = 0.575; P = 0.001) and divergent validity with FIM communication scale (r = 0.383). In reliability testing, 2 raters independently scored 10 chronic stroke survivors (ICC; inter-rater reliability of the FMKnFx scale = 0.90 [95% CI, 0.64, 0.97]).

TB was a 16-point, ordinal scale assessing balance as follows: sitting, sit-to-stand, standing, response to challenge, eyes closed, turning-in-place, and stand-to-sit. 6MWT measured walking distance within 6 minutes. Subjects used usual assistive device (constant at pretreatment/post-treatment) and a 30.5-m walkway. 6MWT was correlated with activities of daily living, used in the stroke population, and had test/retest reliability of 0.95 for older adults. Subjects were queried bimonthly regarding functional milestones that had been achieved during the previous 2 weeks.

The primary measure, TG, was scored by a blinded examiner who viewed a video record of gait before and after treatment. Independent staff obtained the secondary outcomes, and because they worked in an adjacent clinical area, there is a chance that group allocation may have been unmasked.

Analysis

We compared the 2 groups regarding initial differences for age, years after stroke, stroke severity, and each measure (Mann–Whitney U test). Group comparisons for ordinal measures were made using an ordinal regression model (PLUM Ordinal Regression Model; SPSS) and a general linear model for 6MWT. In all analyses in the study, we used the Sidak stepdown P value adjustment for multiple comparisons.

All results are reported using adjusted P values with critical α = 0.05.

Results

Each of the 2 treatments was allocated to 16 subjects. Subject attrition was 2 (FNS-IM) and 1 (No-FNS), resulting from a compromised social support system (14 FNS-IM and 15

### TABLE 1. Subject Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Stroke Severity</th>
<th>Stroke Type</th>
<th>Years After Stroke</th>
<th>Age</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td></td>
<td>Mean (SD)</td>
<td></td>
<td>Male</td>
</tr>
<tr>
<td>FNS-IM</td>
<td>22.9 (3.5)</td>
<td>11</td>
<td>3</td>
<td>57.7 (11.9)</td>
<td>11</td>
</tr>
<tr>
<td>No-FNS</td>
<td>19.7 (4.3)</td>
<td>12</td>
<td>3</td>
<td>63.6 (10.4)</td>
<td>11</td>
</tr>
</tbody>
</table>

### TABLE 2. Comparison of Pretreatment/Post-Treatment Measures for FNS-IM and No-FNS

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pretreatment Median or Mean† ([interquartile range** or SD‡])</th>
<th>Post-Treatment Median or Mean† ([interquartile range** or SD‡])</th>
<th>Group Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary measure</td>
<td></td>
<td></td>
<td>P = 0.0003*</td>
</tr>
<tr>
<td>TG (n = 14)</td>
<td>6.5* (3)**</td>
<td>3–10</td>
<td>9* (1)**</td>
</tr>
<tr>
<td>No-FNS (n = 15)</td>
<td>6* (4)**</td>
<td>3–10</td>
<td>7* (3)**</td>
</tr>
<tr>
<td>Secondary measures</td>
<td></td>
<td></td>
<td>P = 0.182</td>
</tr>
<tr>
<td>FMLE</td>
<td></td>
<td></td>
<td>P = 0.049*</td>
</tr>
<tr>
<td>FNS-IM</td>
<td>22* (5)**</td>
<td>16–28</td>
<td>28* (6)**</td>
</tr>
<tr>
<td>No-FNS</td>
<td>20* (4)**</td>
<td>11–28</td>
<td>23* (8)**</td>
</tr>
<tr>
<td>FMKnFx subscale</td>
<td></td>
<td></td>
<td>P = 0.133</td>
</tr>
<tr>
<td>FNS-IM</td>
<td>4* (2)**</td>
<td>1–5</td>
<td>5* (0)**</td>
</tr>
<tr>
<td>No-FNS</td>
<td>3* (2)**</td>
<td>0–5</td>
<td>4* (2)**</td>
</tr>
<tr>
<td>TB</td>
<td></td>
<td></td>
<td>P = 0.184</td>
</tr>
<tr>
<td>FNS-IM</td>
<td>13.5* (4)**</td>
<td>10–15</td>
<td>15* (2)**</td>
</tr>
<tr>
<td>No-FNS</td>
<td>10* (5)**</td>
<td>6–14</td>
<td>13* (4)**</td>
</tr>
<tr>
<td>6MWT distance (m)</td>
<td></td>
<td></td>
<td>P = 0.05.</td>
</tr>
<tr>
<td>FNS-IM</td>
<td>186.6† (±75.6)‡</td>
<td>75.6–309.7</td>
<td>252.2† (±101.6)‡</td>
</tr>
<tr>
<td>No-FNS</td>
<td>128.3† (±83.8)‡</td>
<td>14.6–285.9</td>
<td>165.9† (±98.8)‡</td>
</tr>
</tbody>
</table>

*Adjusted P values reported.

Significant P value, P < 0.05, with adjusted P values shown.
No-FNS completed treatment, according to their treatment allocation. Reported data are exclusively from those who completed the study (Table 1). There was no baseline difference between groups for the following: age ($P=0.166$), years after stroke ($P=0.701$), and stroke severity ($P=0.089$). Among 4 FNS-IM subjects, there was a total of 7 instances of erythema on the skin surface at lead exit sites. All were treated with topical antibiotic and resolved in $\leq 3$ days. There was no statistically significant baseline difference between the 2 groups for TG ($P=0.533$), FMLE ($P=0.089$), FMKnFx ($P=0.291$), TB ($P=0.078$), and 6MWT ($P=0.145$).

For the primary measure, TG, FNS-IM produced a statistically significant greater gain versus No-FNS ($P=0.003$; Table 2). The statistically significant model coefficient indicated a difference in slope of 2.9 points for FNS-IM versus No-FNS (while accounting for pretreatment scores; 95% CI, 1.2 to 4.6). The difference in distribution of gain scores for the 2 groups (Figure 1) underlies the statistically significant group difference in treatment response. For FNS-IM, 64% had gains of 2 to 6 points; whereas, only 13% of No-FNS had gains of $\geq 2$. In fact, $\approx 50\%$ of No-FNS had no gains; whereas only 14% of FNS-IM subjects had no gains. Figure 2a shows an example of pretreatment abnormal swing phase using a stiff-legged pattern. Figure 2b shows the identical point in the gait cycle and restoration of volitional swing phase flexion at post-treatment after FNS-IM treatment (no FNS during video).

In secondary analysis, gains in TG items were calculated (Figure 3). FNS-IM demonstrated gains for all items, and the gain for each item was greater than that exhibited by No-FNS (except item 1). For No-FNS, there were no gains in 3 items, and for 1 item, there was a worsening.

For FMKnFx, FNS-IM had a statistically significant greater gain than No-FNS ($P=0.049$; Table 2). Figure 4a and 4b show changes in individual scores that underlie the group difference.

For the remaining measures, after accounting for pretreatment scores, there was no statistically significant difference between groups in response to treatment, according to the following: FMLE ($P=0.182$), TB ($P=0.133$), and 6MWT ($P=0.184$; Table 2).

Both groups subjectively reported gains in walking endurance and functional milestones. Figure 5 shows that functional milestones were reported in 11 instances for No-FNS and 53 instances for FNS-IM. Milestones of greater motor complexity were demonstrated more frequently for FNS-IM versus No-FNS.

**Discussion**

This study extends the literature and adds to the totality of gait training information by showing that FNS-IM produced a statistically significant greater gain versus No-FNS in a measure of coordinated gait component execution. Restoring normal coordinated gait component execution can reduce the frequency of falls, reduce energy cost, increase endurance,
Greater safety and reduced gait energy cost can result in greater functional ability. FNS-IM subjects demonstrated not only greater gains in coordinated gait components but also greater gains in self-reported functional mobility (Figure 5). In contrast, 87% of No-FNS had minimal or no gain (0 to 1 points). Multiple gait deficits can elevate energy cost 1.5 to 2.0x normal.36 For example, lack of normal movement at the knee or ankle during swing phase can reduce gait efficiency to 76% or 92% of normal, respectively.2,3 With improvement in each gait component, safety and energy cost can improve.35,36

Greater safety and reduced gait energy cost can result in greater functional ability. FNS-IM subjects demonstrated not only greater gains in coordinated gait components but also greater gains in self-reported functional mobility (Figure 5). In contrast, 87% of No-FNS had minimal or no gain (0 to 1 points) in gait component execution and fewer demonstrated functional milestones.

FNS-IM produced a significantly greater gain in knee flexion coordination versus No-FNS. This could have occurred because FNS-IM provided the training advantage of electrically induced, coordinated muscle contractions and joint movements that closely approximated normal. Without FNS-IM assistance, practice of coordinated movements among hip, knee, and ankle were not possible. Practice and motor relearning of coordinated movements were important because isolated joint movement control and coordination among hip, knee, and ankle movements are critical to execute the movement components inherent in normal gait.37

Similarly, the FNS-IM advantage in the TG measure could have occurred because FNS-IM uniquely targeted gait components including joint movement excursion, sequence, and timing of movements.20 First, FNS-IM activated knee flexors and ankle dorsiflexors during swing phase at normal timing and at normal joint movement excursions so that the normal sagittal plane trajectory (TG item 4) could be practiced.20 Second, FNS-IM smoothly transitioned changes in knee flexor and ankle dorsiflexor muscle activations across the phases of swing phase to enable practice of a smooth, continuous swing phase pattern closely approximating normal step continuity (TG item 5). Third, during loading and throughout stance phase, FNS-IM activated hip abductors for pelvic control and knee flexors/extensors for knee control, assisting in weight shift and balance, and further facilitating step continuity (TG item 5). Stable support of the body in the upright position precluded abnormal compensatory trunk movement (TG item 3). As volitional control of the gait components was reacquired, FNS-IM amplitude was reduced in a finely graded manner so that volitional muscle activation was increasingly required and practiced. FNS-IM advantages, reflected in the gait component scale and knee flexion coordination, are generalizable to stroke survivors with the following characteristics: >12 months after stroke, ambulating at least short distances without human assistance, and moderate to severe coordination and gait deficits.

Figure 4. Individual FMKnFx scores are shown for pretreatment/post-treatment, separately for No-FNS and FNS-IM. Each line illustrates the direction of change from pretreatment to post-treatment. Numbers on each line illustrate number of subjects having a given pattern of change in pretreatment/post-treatment score. More subjects had gains in the FNS-IM group (78%) vs the No-FNS group (60%). Greater total gains were produced by FNS-IM (14 points) vs No-FNS (9 points).
Figure 5. Functional milestones reported by study participants.
21 visits. The combined cost of the FNS-IM system and electrode placement would be $4960. Because results of this study showed that FNS-IM treatment of persistent gait deficits could produce statistically significantly greater gait improvements, the relatively small incremental cost of the FNS-IM system justifies additional investigation of the use of FNS-IM in gait training. The nature of individual functional gains in the FNS-IM group suggests a potential for improvement in quality of life. A formal cost/benefit analysis might be useful in determining whether functional changes in response to FNS-IM gait training would mitigate expenses incurred by disability across the lifespan of stroke survivors.

**Summary**

There was a statistically significant greater gain in gait components and in knee flexion coordination in response to FNS-IM versus No-FNS. FNS-IM gait practice advantages could explain the group differences. There was no statistically significant difference between the 2 groups in measures of overall limb coordination, balance, and 6-minute walking distance.

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**References**

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