Randomized Controlled Trial to Evaluate the Effect of Surface Neuromuscular Electrical Stimulation to the Shoulder After Acute Stroke

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Background and Purpose**—**Surface neuromuscular electrical stimulation (sNMES) after stroke aims to improve upper limb function and reduce shoulder pain, but current evidence of effectiveness is inconclusive. We have undertaken a randomized controlled trial to evaluate sNMES to the shoulder after acute stroke.

Methods**—**One hundred seventy-six patients, within 10 days of stroke onset, were randomized to receive sNMES or placebo in addition to stroke unit care. The primary outcome measure was upper limb function measured by the Action Research Arm Test (ARAT) 3 months after stroke. Secondary outcome measures included other measures of upper limb function, upper limb impairment, pain, disability, and global health status. Outcome assessments were blinded.

Results**—**There was no difference in arm function between groups in terms of the primary outcome measure. The median ARAT at 3 months was 50 in the intervention group and 55.5 in the control group ($P=0.068$). Significant differences were seen at 3 months in favor of the control group for other measures of arm function and impairment: grasp and gross movement subsections of the ARAT, Frenchay Arm Test, and the arm subsection of the Motricity Index. Secondary analysis suggested that these differences were most marked in subjects with severe initial upper limb weakness.

Conclusions**—**A 4-week program of sNMES to the shoulder after acute stroke does not improve functional outcome and may worsen arm function in severely impaired stroke patients. "Routine" use of sNMES to the proximal affected upper limb after acute stroke cannot be recommended. **(*Stroke*. 2006;37:2995-3001.)**

Key Words: arm ■ function ■ randomized controlled trials ■ rehabilitation

Reduced upper limb function is common after stroke and is an adverse prognostic indicator for subjective well-being.[1–3] Poor upper limb function is associated with pain, particularly at the shoulder, which is reported by >50% of patients during the first 6 months after stroke.[4,5]

Surface neuromuscular electrical stimulation (sNMES) has been recommended as a safe method to improve upper limb outcomes after stroke.[6,7] Proposed mechanisms include stimulation of the somatosensory cortex by augmented sensory feedback, and increased proprioceptive stimulation as a result of muscle activation.[8] Repetitive movements induced by sNMES may be important for motor re-learning.[9,10] Other potential benefits include: increased muscle strength, improved joint alignment, reduced spasticity, and modification of visuospatial deficits. sNMES of cutaneous sensory nerves may separately modulate pain via gating pathways and central neuromodulation.[11] It is unclear whether this translates into functional benefit.[7,12] Many previous randomized controlled trials of upper limb sNMES were small and of variable methodological quality.[13–16] A systematic review identified the need for further research.[6]

We undertook a randomized controlled trial to evaluate sNMES to the shoulder after acute stroke. Participants received a 4-week program of sNMES to the shoulder or placebo. Upper limb function, impairment, pain, disability, and global health status were compared between treatment groups at the end of the intervention period and 3 months after stroke.

Methods

Participants

Patients admitted to 2 neighboring stroke units were eligible if they had a new upper limb problem caused by stroke within the previous 10 days. Those with a previous upper limb problem, a cognitive/language impairment likely to influence assessments, another diagnosis likely to interfere with rehabilitation, or a contraindication to sNMES were excluded.

Initial Assessment and Randomization

Participants gave written informed consent. The initial assessment consisted of demographic details, handedness, new neurological

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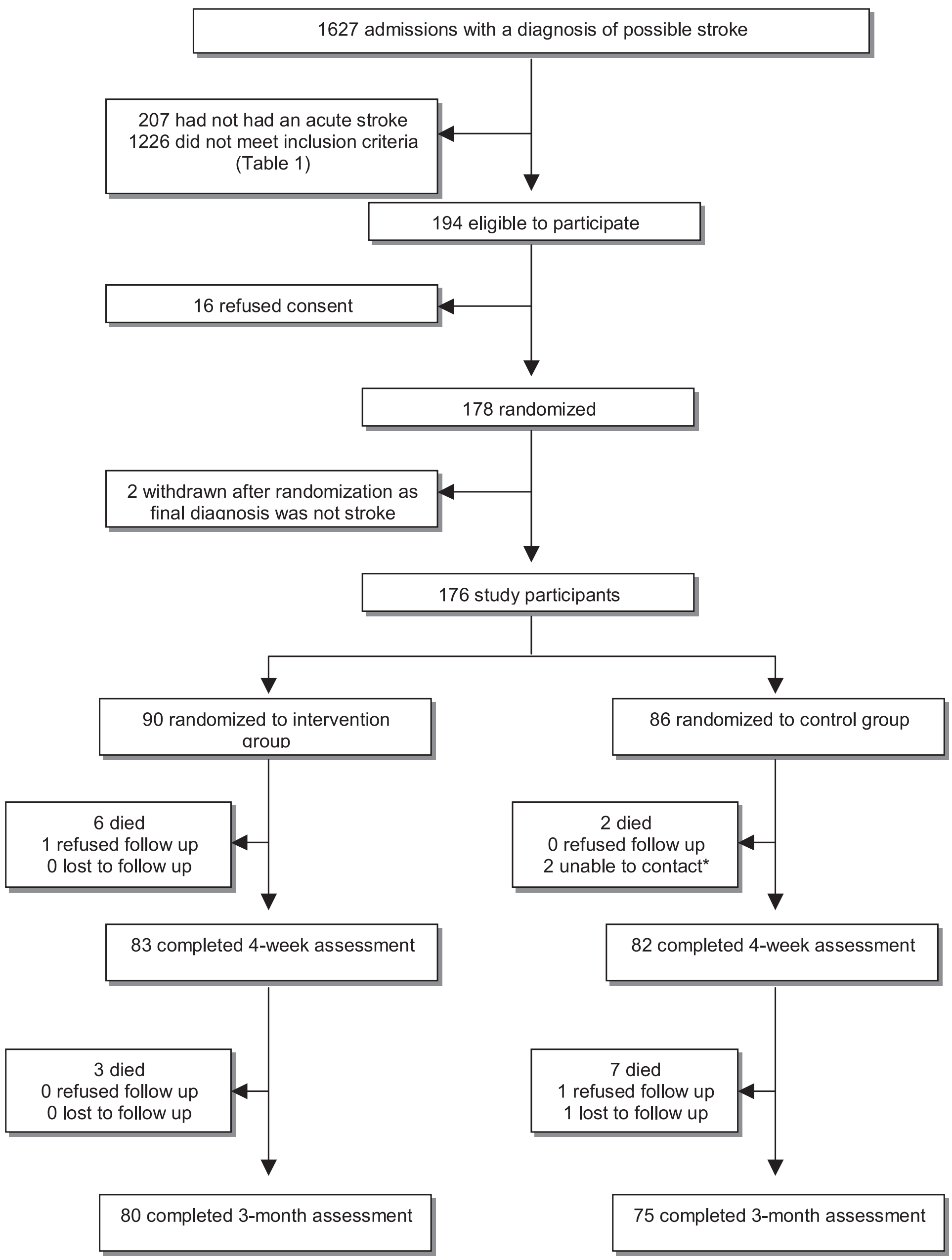
impairment (National Institutes of Health Stroke Scale[17]), stroke subtype,[18] and the following assessments: upper limb impairment and function (Motricity Index;[19] Frenchay Arm Test;[20] Action Research Arm Test (ARAT);[21] upper limb pain (5-point adjectival scale; 0 to 10 numerical rating scale);[22,23] higher cortical function (Star Cancellation Test);[24] Sheffield Aphasia Screening Test;[25] Abbreviated Mental Test Score;[26] and dependency at 7 days (Barthel ADL Index).[27] Participants were randomized by a central independent telephone computerized service and stratified according to severity of upper limb weakness (Frenchay Arm Test[20] score 0, 1 versus 2 to 5).

Intervention

Participants in the intervention group received a 4-week program of sNMES to the shoulder (1 hour, 3 times daily) via surface electrodes over supraspinatus and posterior deltoid. The basic stimulation frequency was 30 Hz. The stimulator on and off time was 15 seconds with a ramp up-and-down time of 3 seconds. The level of stimulation was increased until a comfortable gross muscle contraction was visible. Participants in the control group were given a "sham" stimulator, identical to the intervention, but an internal disconnection prevented any current from being delivered. The sNMES treatment regime and placement of electrodes was undertaken by a single researcher. Compliance was monitored using a diary.

Outcome Assessments

The primary outcome measure was upper limb function (ARAT)[21] 3 months after stroke. Secondary outcome measures were undertaken at the end of the 4-week intervention period and 3 months after



*4-week assessment was not completed for 2 of the control participants but 3-month assessment was completed for both.

Study profile.

TABLE 1. Main Reasons for Exclusion (n=1226)

343 (28%) no upper limb deficit
241 (19%) residence outside the area
154 (12%) not within 10 days of stroke onset
106 (9%) significant receptive dysphasia
101 (8%) medically unstable
92 (8%) had another diagnosis likely to interfere with rehabilitation
51 (4%) discharged prior to screening
49 (4%) previous upper limb impairment
40 (3%) significant cognitive deficit
22 (2%) died prior to screening
10 (1%) permanent pacemaker/implantable defibrillator
10 (1%) other eg participation in another research trial
7 (<1%) recent shoulder fracture/dislocation or taking regular analgesia for the upper limb (stroke–affected side)

stroke. These consisted of the ARAT[21] (4-week), Frenchay Arm Test,[20] Motricity Index,[19] Star Cancellation Test,[24] pain scales,[22,23] disability, and global health status (Nottingham E-ADL Index[28]; Nottingham Health Profile)[29] (3 months), Oxford Handicap Scale,[30] and participant views regarding sNMES. The stroke unit staff was not informed of participants' randomization groups. Outcome assessments were undertaken by 2 research nurses who were blinded to each participant's treatment allocation.

Statistical Methods and Sample Size

Using ARAT[21] scores from previous studies[31,32] and allowing for 10% attrition, it was calculated that a total sample size of 168 subjects was needed to give an 80% power of detecting a clinically significant difference of 8 points (0.4 standard deviations). An intention to treat analysis was undertaken. Comparative analyses were made using the Mann-Whitney *U* test. For categorical data, a χ^2 test was used. Significance level was set at $P=0.05$.

Ethical Approval and Data Storage

Ethical approval was obtained and data stored in accordance with the Data Protection Act.

Results

During the recruitment period (January 1, 2002 to February 29, 2004), 1627 patients were admitted with a diagnosis of possible stroke. One hundred seventy-six patients participated in the study (Figure). The main reasons for exclusion to study entry were no upper limb deficit (28%), residence outside the study area (19%), not within 10 days of stroke onset (12%), and significant receptive dysphasia (9%) (Table 1).

The median time from stroke to randomization was 5 days (interquartile range [IQR], 4 to 7) for the intervention group and 4 days (IQR, 3 to 7) for the control group. Groups were well matched for age, gender, stroke subtype, severity, and initial upper limb impairment (Table 2). More control subjects reported prestroke pain, and had a visuospatial deficit on clinical testing, but these differences were not significant.

The median total ARAT[21] score was 55.5 in the control group and 50 in the intervention group at 3 months ($P=0.068$) (Table 3). For other measures of upper limb function and impairment (grasp and gross subsections of the ARAT,[21] Frenchay Arm Test,[20] and the arm subsection of the Motricity Index,[19] the control group achieved statistically significantly higher scores than the intervention group. A greater proportion of participants failed the Star Cancellation Test[24] in the intervention group but this difference was not statistically significant. The prevalence of upper limb pain[22,23] was similar between groups (45% control and 46% intervention). There were no differences in disability and global health status between groups. There were no statistically significant differences between groups at 4 weeks (Table 4).

As it has been suggested that sNMES may be more beneficial in stroke patients with milder upper limb impairment,[33] 1 preplanned subgroup analysis was undertaken to

TABLE 2. Characteristics at Baseline

	Intervention (n=90)	Control (n=86)
Male, n (%)	42 (46.7%)	47 (54.7%)
Median [IQR] age (years)	75.5 [64–81]	73.5 [65.8–79]
Previous stroke affecting same side, n (%)	7 (4%)	12 (14%)
Side of upper limb impairment, left, n (%)	59 (66%)	53 (62%)
Stroke subtype,[18] n (%)		
Total anterior circulation stroke	29 (32%)	24 (28%)
Partial anterior circulation stroke	23 (26%)	23 (27%)
Lacunar stroke	36 (40%)	37 (43%)
Posterior circulation stroke	2 (2%)	2 (2%)
Stroke type, n (%)		
Infarct	86 (96%)	78 (91%)
Hemorrhage	4 (4%)	8 (9%)
Upper limb prestroke pain,[22,23] n (%)	2 (2%)	6 (7%)
Upper limb poststroke pain,[22,23] n (%)	21 (23%)	22 (26%)
Motricity Index,[19] median [IQR]	61.3 [36–82.4]	63.3 [36.4–78.1]
Frenchay Arm Test,[20] median [IQR]	0.5 [0–4]	0 [0–4]
ARAT[21]*, median [IQR]		
Total	0 [0–45.5]	3 [0–47]
Grasp	0 [0–15]	0 [0–16]
Grip	0 [0–10.5]	0 [0–10]
Pinch	0 [0–12]	0 [0–12]
Gross	0 [0–9]	3 [0–9]
NIHSS†[17], best motor, arm, n (%)		
0, no drift	6 (7%)	8 (9%)
1, drift after brief hold	36 (40%)	37 (43%)
2, cannot resist gravity	15 (17%)	12 (14%)
3, no effort against gravity	33 (37%)	29 (34%)
Cerebellar signs, n (%)	2 (2%)	3 (3%)
Sensory symptoms, n (%)	41 (46%)	41 (48%)
Star Cancellation Test,[24] fail, n (%)	38 (42%)	31 (36%)

*Action Research Arm Test; †National Institutes of Health Stroke Scale.

TABLE 3. Three-Month Outcomes

	Intervention, n=89	Control, n=84	*P*
Dead or dependent (OHS†[30, 3–5])			
n (%)	62 (69%)	59 (69%)	0.903
Length of initial hospital stay (days)	n=89	n=85	
median [IQR]	36 [17–56.5]	25 [12–63.5]	0.131
ARAT*‡[21] median [IQR]	n=79	n=74	
Total	50.0 [0–57]	55.5 [38.3–57]	0.068
Grasp	12 [0–18]	18 [12–18]	0.014
Grip	12 [0–12]	12 [8.8–12]	0.071
Pinch	15 [0–18]	18 [8.5–18]	0.155
Gross	9 [0–9]	9 [9–9]	0.015
Frenchay Arm*	n=80	n=75	
Test[20] median [IQR]	4 [1–5]	5 [3.8–5]	0.012
Motricity Index*[19] median [IQR]	n=79	n=74	
Arm	84 [56–100]	93 [77–100]	0.025
Leg	92 [70–100]	86 [76–100]	0.948
Total	88 [66–100]	89 [76.5–100]	0.248
Star Cancellation	n=80	n=75	
Test[24] fail n (%)	25 (31%)	18 (24%)	0.371
Upper limb pain*[22,23]	n=80	n=75	
n (%)	37 (46%)	34 (45%)	1.000
If pain, median [IQR]			
5-point severity scale	3 [1–3]	3 [2–3]	0.429
0–10 numerical rating scale	6 [3.5–8]	7 [5–8]	0.651
Nottingham-EADL Index[28]	n=80	n=74	
median [IQR]	8 [2–15]	8.5 [2–15]	0.515
Nottingham Health Profile[(29)]	n=76	n=71	
median [IQR]			
Mean of subscales	31.2 [10.4–52.1]	28.1 [15.7–48.2]	0.577

*Upper limb outcomes are affected side; †Oxford Handicap Scale; ‡Action Research Arm Test.

TABLE 4. Four-Week Outcomes

	Intervention n=89	Control n=84	*P*
Dead or dependent (OHS†[30, 3–5])			
n (%)	62 (70%)	62 (74%)	0.663
ARAT*‡[21] median [IQR]	n=81	n=82	
Total	45.0 [0–57]	45.5 [0–57]	0.888
Grasp	15 [0–18]	12 [0–18]	0.853
Grip	12 [0–12]	12 [0–12]	0.523
Pinch	12 [0–18]	11.5 [0–18]	0.818
Gross	9 [0–9]	9 [0–9]	0.885
Frenchay Arm	n=83	n=82	
Test*[20] median [IQR]	4 [0–5]	4 [0–5]	0.923
Motricity Index*[19] median [IQR]	n=83	n=81	
Arm	77 [40–100]	81 [53–100]	0.574
Leg	76 [62–100]	84 [58.5–100]	0.940
Total	80 [52.5–93]	77 [62.5–96)	0.850
Star Cancellation Test[24] fail	n=83	n=82	
n (%)	27 (33%)	28 (34%)	0.870
Upper limb pain*[22, 23] n (%)	22 (27%)	26 (32%)	0.462

*Upper limb outcomes are affected side; †Oxford Handicap Scale; ‡Action Research Arm Test.

examine outcomes according to initial upper limb function (ARAT>0 versus ARAT=0) (Table 5). No differences were seen between intervention and control groups for those with some upper limb function (ARAT>0) at baseline. For those with no arm function at baseline (ARAT=0), there were statistically significant differences for the grasp and gross subsections of the ARAT[21] and arm Motricity Index[19] in favor of the controls at 3 months but not at 1 month.

Participants received 73% (IQR, 53.95 to 90) of intended sNMES. This was similar between groups (73% intervention, 72% control). At the 3-month assessment, 71% of the intervention group and 20% of the control group were able to correctly identify which stimulator (ie, active or sham) they had received. sNMES was well tolerated. The course was discontinued early for 5 (3 intervention and 2 control) participants at their request. In the intervention group, 18% attributed upper limb pain to the stimulator, compared with 1% of the control group.

Discussion

A 4-week program of sNMES to the shoulder did not improve upper limb function when initiated within 10 days of stroke onset. There was no difference in arm function between groups in terms of the primary outcome measure, Action Research Arm Test at 3 months. However, a number of secondary outcomes (upper limb impairment, other measures of arm function) were unexpectedly better in the control group 3 months after stroke, although this did not translate into differences in activities of daily living. There were no differences between randomization groups at 4 weeks.

Previous studies have suggested that sNMES helps to reduce or prevent shoulder subluxation, reduce pain, and improve muscle strength.[7,12] It has been unclear whether this translates into an improvement in arm function.[7,13,14,33] It is unlikely that we have failed to detect a significant treatment benefit. The study design was robust with adequate statistical power, and is the largest study of upper limb sNMES after acute stroke to date. Participants were typical stroke patients treated on stroke units and, there-

TABLE 5. Upper Limb Outcomes, According to Initial Arm Function

	Intervention ARAT=0	Control ARAT=0	*P*	Intervention ARAT>0	Control ARAT>0	*P*
1-month ARAT	n=39	n=37		n=43	n=42	
ARAT*†[21]						
median [IQR]						
Total	0 [0–20.5]	0 [0–43])	0.917	57 [48–57]	53.5 [44.8–57]	0.200
Grasp	0 [0–7]	0 [0–12]	0.702	18 [18–18]	16 [12–18]	0.054
Grip	0 [0–4.5]	0 [0–12]	0.555	12 [12–12]	12 [12–12]	0.937
Pinch	0 [0–1.5]	0 [0–8.5]	0.520	10 [12–18]	18 [10.3–18]	0.547
Gross	0 [0–9]	0. [0–9]	0.844	9 [9–9]	9 [9–9]	0.417
3-month outcomes						
ARAT*†[21]	n=37	n=30		n=42	n=41	
median [IQR]						
Total	0 [0–33.5]	34.5 [0–54]	0.057	57 [51–57]	57 [52.5–57]	0.690
Grasp	0 [0–6]	11 [0–18]	0.049	18 [17.3–18]	18 [18–18]	0.201
Grip	0 [0–12]	9.5 [0–12]	0.124	12 [12–12]	12 [12–12]	0.673
Pinch	0 [0–6]	3 [0–17.3]	0.179	18 [16.5–18]	18 [16–18]	0.963
Gross	0 [0–9]	9 [0–9]	0.034	9 [9–9]	9 [9–9]	0.444
Frenchay Arm Test*[20]	n=37	n=30		n=43	n=42	
median [IQR]	0.0 [0–3.5]	3 [0–4.3]	0.086	5 [4–5]	5 [4–5]	0.134
Motricity Index*[19]	n=36	n=29		n=43	n=42	
median [IQR]						
Arm	53 [15–77]	77 [35–93]	0.039	100 [85–100]	100 [86–100]	0.544
Leg	73 [48.8–92]	76 [41–85]	0.899	100 [92–100]	100 [81–100]	0.792
Total	67 [44–76.5]	76.5 [41.5–86.5]	0.204	100 [88–100]	100 [84.8–100]	0.938
Star Cancellation Test[24]	n=37	n=30		n=43	n=42	
fail, n (%)	15 (41%)	15 (50%)	0.469	10 (23%)	3 (7%)	0.068
Upper limb pain*[22,23] n (%)	23 (62%)	19 (63%)	1.000	14 (33%)	14 (33%)	1.000

*Upper limb outcomes are affected side; †Action Research Arm Test.

fore, results are generalizable to this population. Previous studies recruited patients who were often younger and from neurorehabilitation settings.

It is thought that early intervention offers the greatest opportunity to improve recovery.[34,35] We recruited participants early after stroke but found no benefit. Previous studies predominantly recruited participants months or even years after stroke and therefore may have treated the late complications of stroke rather than influenced recovery.[15,33,36]

We applied sNMES to the shoulder as models of upper limb recovery suggest that proximal precede distal changes.[37] The regime has been shown to be beneficial in previous studies[13,31] and is widely accepted in clinical practice. Unlike most previous studies we measured the amount of sNMES received. Both groups received less treatment than prescribed and it is conceivable that participants in the intervention group received suboptimal sNMES, although this was not significantly different from the control group. This may explain why we have not detected a treatment effect.

A strength of this study was the sham stimulator used by the placebo group. Only 5 previous randomized controlled trials have used sham treatment.[14,36,38–40] As the active stimulator produced visible shoulder movement, complete blinding was not possible. The staff was not informed of participants' randomization groups but may have been aware by their own observations.

The amount of upper limb rehabilitation received during the intervention period was not measured. If the intervention group received less, this may have been because of muscle fatigue or pain, or because therapists were reluctant to interrupt sNMES sessions for those with an active stimulator.

Although there is evidence that sNMES is beneficial in improving joint alignment (ie, reducing or preventing subluxation) and reducing spasticity,[6,7] we did not measure these outcomes. Subluxation is difficult to define,[41] and its measurement is unreliable and often of no clinical significance.[12] There is no validated measure of upper limb spasticity other than at the elbow.[42]

We were surprised to find significant differences in some secondary outcomes at 3 months in favor of the control group. Secondary analysis suggested that these differences were most marked in subjects with severe initial upper limb weakness. The effect was seen after the sNMES had been discontinued ie, after 4 weeks. It is possible that sNMES interfered with motor re-learning processes, influencing and impeding upper limb recovery after the treatment period.

Previous experimental models have suggested that very early constraint therapy and early overuse after cerebral ischemia in rodents may be harmful[43,44] but the clinical relevance of this finding is not known.

The negative effect of sNMES to the upper limb was seen only in those with initial severe impairment. Hypotheses to explain this include:

1. sNMES impedes recovery by producing abnormal afferent stimulation and inhibiting plasticity in a group who are not receiving any other afferent stimulation to the upper limb. It is possible that artificial stimulation proximally interferes with later distal recovery through maladaptive plasticity.
2. The movement produced at the shoulder may have resulted in early over-use of the affected arm.
3. Those with severe impairment may have been less aware of the stimulation and therefore less likely to report adverse events or be aware if the stimulator was wrongly delivered.
4. Overstimulation may have produced tiredness and shoulder subluxation (neither of these effects were measured).
5. As the stimulator produced movement of the shoulder, it is possible that participants used their affected arm less while it was being given, ie, the stimulator promoted learned non-use of this arm.

Those involved in the application of upper limb sNMES after stroke should be aware of its potential negative consequences, and of the lack of evidence to support its routine clinical use. If upper limb sNMES is to be used after stroke, a clearer understanding of its effects on recovery is vital, and further research should consider whether there is benefit for specific patient groups.

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Disclosures

None.

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