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0894-9115/04/8308-0592/0
American Journal of Physical Medicine & Rehabilitation
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DOI: 10.1097/01.PHM.0000133435.61610.55

Research Article

Electrical Stimulation of the Upper Limb in Stroke

Stimulation of the Extensors of the Hand *vs.* Alternate Stimulation of Flexors and Extensors

ABSTRACT

de Kroon JR, IJzerman MJ, Lankhorst GJ, Zilvold G: Electrical stimulation of the upper limb in stroke: Stimulation of the extensors of the hand *vs.* alternate stimulation of flexors and extensors. *Am J Phys Med Rehabil* 2004;83:592–600.

Objective: To investigate whether there is a difference in functional improvement in the affected arm of chronic stroke patients when comparing two methods of electrical stimulation.

Design: Explanatory trial in which 30 chronic stroke patients with impaired arm function were randomly allocated to either alternating electrical stimulation of the extensor and flexor muscles of the hand (group A) or electrical stimulation of the extensors only (group B). Primary outcome measure was the Action Research Arm test to assess arm function. Grip strength, Motricity Index, Ashworth Scale, and range of motion of the wrist were secondary outcome measures.

Results: Improvement on the Action Research Arm test was 1.0 point in group A and 3.3 points in group B; the difference in functional gain was 2.3 points (95% confidence interval, −1.06 to 5.60). The success rate (i.e., percentage of patients with a clinically relevant improvement of >5.7 points on the Action Research Arm test) was 27% in group B (four patients) and 8% in group A (one patient). The differences in functional gain and success rate were not statistically significant, neither were the differences between the two groups on the secondary outcome measures.

Conclusion: The difference between the two stimulation strategies was not statistically significant.

Key Words: Chronic Stroke, Upper Limb, Electrical Stimulation Therapy, Rehabilitation

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Most patients with stroke have impairments of the affected arm. As a consequence, functional use of the arm is limited, thereby affecting the activities of daily living. The majority of stroke patients consider impaired arm function to be a major problem,[1] and arm motor impairments are associated with a low level of subjective well-being.[2]

Electrical stimulation (ES) is one of the therapeutic strategies that are applied to improve impaired arm function. ES has been claimed to have a positive effect on spasticity,[3,4] range of motion,[5,6] and muscle strength.[5,7] More recently, studies have mainly focused on the effect of ES on motor control[8,9] and arm function.[10,11] Although these studies suggest a positive effect of ES on motor impairment of the affected upper limb, the evidence is not conclusive,[12,13] and many questions remain with regard to efficacy and optimal stimulation strategy.

One aspect of stimulation strategy concerns the target muscles. In the literature, publications can be found of ES applied to the flexor muscles of wrist and fingers,[4] the extensor muscles,[3,6,8–10] or both flexors and extensors alternately,[14–16] and in all cases, a positive effect of ES was found on one or more outcome measures.

ES of the spastic wrist flexor muscles was compared with passive stretch of the wrist flexors by King,[4] who reported a significantly greater effect of ES on flexor spasticity. However, Alfieri[3] stated that "no direct stimulus must be allowed to reach spastic muscles," and he reported a reduction in flexor spasticity after ES of the extensor muscles. Other studies in which ES was applied to the extensor muscles reported improvement in range of motion of the wrist,[6] wrist extensor strength,[10] and motor impairment.[8,9]

A combination of extensor and flexor stimulation is applied in studies using the NESS Handmaster[14,15] and the mesh glove.[16] These uncontrolled studies report a positive effect on muscle tone,[14,15] passive and active wrist extension,[14,16] motor impairment,[15,16] and arm function.[14]

The exact mechanism underlying the action of ES has not been elucidated, but neurophysiologic models produce arguments in favor of each strategy. Improvement in extensor muscle strength, through ES of the extensors, might provide sufficient power to overcome flexor spasticity. On the other hand, ES of the flexors might cause fatigue in the spastic muscles and thereby reduce spasticity. At the spinal level, ES evokes reflexes;[3,4] reciprocal and recurrent inhibition might explain the reducing effect on flexor spasticity that is achieved by stimulation of the extensors and flexors, respectively. The repetitive movements evoked by ES may facilitate motor recovery by repetitive afferent feedback due to neural plasticity.[8,17] This concept might be valid for the stimulation of both flexors and extensors.

It can be argued that stimulation of the extensors is to be preferred because it is moving the hand opposite the synergistic pattern, as is advocated in neurodevelopment treatment.[18] On the other hand, in functional movements, both flexors and extensors contribute in a balanced way, and this might be regained best by stimulation of both muscle groups. It is not known which argument is the most convincing, and because of the mutual relationship between the mechanisms, the overall benefit is not clear. No clinical study has yet been carried out to compare these strategies. Therefore, the present phase II trial was designed to investigate whether there is a difference in functional improvement in the affected arm of patients with chronic stroke, measured with the Action Research Arm (ARA) test, when comparing alternating ES of the extensor and flexor muscles of the hand with ES of the extensor muscles only.

In theory, stimulation of the extensors *vs.* stimulation of the flexors would be most obvious because this comparison would provide the greatest contrast. However, stimulation of the flexor muscles only is contradictory to the implicit beliefs of clinicians that to focus on the flexor pattern might be potentially harmful to the patient. It was therefore decided to compare the two strategies that are most frequently applied in daily practice and reported in clinical studies: ES of the extensor muscles *vs.* alternating ES of the extensor and flexor muscles.

METHODS

Subject Selection

Subjects were recruited from the outpatient clinics of two rehabilitation centers in the Netherlands. The local ethics committee approved the study protocol, and all subjects who were included gave written informed consent.

Subjects were included if they met the following inclusion criteria: had an interval of >6 mos since unilateral stroke (infarction or hemorrhage) in the territory of the middle cerebral artery, were between 18 and 80 yrs of age, had impaired function of the upper limb due to spastic paresis (spasticity was defined as a synergistic movement pattern or an Ashworth Scale score of ≥ 1; paresis was defined as wrist extensor strength grade 4/5 or less [per the Medical Research Council]), had voluntary extension of wrist (of at least 10 degrees from the resting position) and fingers, and had stable general health status.

Subjects were excluded if they had: a cardiac pacemaker (on demand); an epileptic fit <6 mos before the start of stimulation; metal implants in the affected arm; preexistent functional limitations of the affected

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upper limb; serious contractures of shoulder, elbow, or wrist (clinical assessment); severe cognitive impairments or severe aphasia resulting in an inability to understand the trial; wrist circumference too large for appropriate fitting of the stimulation apparatus; no reaction to the test stimulus; or intensive ES treatment before this trial.

Baseline Characteristics

At baseline, the following data were collected: age, sex, diagnosis (infarction or hemorrhage), hemisphere of stroke, time since stroke, dominant arm prestroke, cognitive function (Mini Mental State Examination), neglect (letter-cancellation test[19]), and sensory function (alternating and simultaneous touching of both hands with eyes closed; thumb-finding test[20]). Neglect was defined as a difference of ≥ 2 between the affected and the unaffected side in the letter-cancellation test. Sensory disorders were considered to be present if a subject's score deviated from normal on one or both sensory function tests.

Intervention

All included subjects received ES. They were randomized to group A (alternating ES of the flexors and extensors of wrist and fingers) or group B (ES of the extensors only). A computer-generated randomization list was used to perform randomization and to guarantee equal group sizes.

The NESS Handmaster was used to apply the ES. The Handmaster is a splint containing five surface electrodes, with an external control box connected to the splint with a cable. On the control box, different stimulation modes can be selected. In this trial, only the exercise mode (alternating extension and flexion) and exercise/open mode (extension only) were used.

The stimulating frequency was 36 Hz. Pulse width and amplitude were individually adjusted to obtain an optimal motor reaction without any side effects such as pain or skin irritation. The duty cycle of the Handmaster was set at 40% and kept constant during the treatment period.

For each subject, a splint was prepared in which the electrode position was individually adjusted to evoke optimal finger movements according to randomization. This fitting of the Handmaster was performed by a trained physiotherapist or occupational therapist. After fitting, the treatment protocol commenced. The subjects in group A received alternating stimulation of the extensor and flexor muscles for 6 wks, and subjects in group B received stimulation of the extensor muscles only for the same period of time.

The subjects were asked to exercise three times a day, starting with 20 mins per session. During the first 10 days, the stimulation time was gradually increased to the maximum of 1 hr per session. The therapist checked the stimulation each week for the first 2 wks and, subsequently, every 2 wks. During these control visits, the therapist scored the subject's opinion with regard to the effect of stimulation on muscle tone and arm function on a 3-point scale: worse, no change, better. The stimulus intensity was adjusted if necessary, and any adverse effects were recorded. Co-interventions were also recorded.

Outcome Measures

A therapist who was blinded for the treatment allocation made three assessments: immediately before the start of the treatment (t0), at the end of the 6-wk treatment period (t1), and after a follow-up period of 6 wks (t2).

Primary Outcome Measure. The ARA test was used to assess manual dexterity of the affected arm.[21] In the ARA test, which consists of 19 items, the subject is asked to grasp, move, and release objects of different size and shape and to perform three gross movements. Each item is scored on a 4-point scale, ranging from 0 (no part of the action can be performed) to 3 (the action is performed completely and within the time limits).[22] The reliability and validity of the ARA test have been confirmed,[21,22] and it has been found to be responsive to improvement in upper limb function in chronic stroke subjects.[23]

Secondary Outcome Measures. Grip strength was assessed with a Baseline hydraulic hand dynamometer (Fabrication Enterprises, New York, NY) with a maximum of 90 kg. The adjustable handle was set in the second position for all subjects. Maximum grip strength of the affected and the unaffected hand were measured in turn, three times each. Grip strength is a sensitive measure of recovery that can span the whole range of recovery.[24] The reliability of grip strength in chronic stroke is good if it is analyzed as the hand ratio (i.e., the ratio of the mean value of the affected hand to the mean value of the unaffected hand).[25] Therefore, hand ratio was used for the analysis and presentation of the results of the grip strength measurements.

The arm section of the Motricity Index was applied for the assessment of motor impairment.[26] In the Motricity Index, pinch grip, elbow flexion, and shoulder abduction are tested; the scoring system is similar to the Medical Research Council grades. The reliability and validity of the Motricity Index have been confirmed, and the test has been found to be sensitive to change.[26] Resistance to passive movement was assessed according to the Ashworth Scale,[27] and a goniometer was used to measure the active range of motion of the wrist joint.

Data Analysis

Baseline characteristics of the two treatment groups were compared to evaluate the success of randomiza-

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tion. Mean and standard deviation values were calculated to summarize scores on the ARA test, hand ratio, Motricity Index, and active range of motion. For the Ashworth Scale, median and range were calculated.

Nonparametric tests were applied to analyze the main effects. Between-group analyses were performed for the time periods t0–t1 and t0–t2 (Mann-Whitney *U* test). If there was a baseline difference in an important prognostic factor for a specific outcome measure, an additional analysis was performed, with this factor as covariable (analysis of covariance).

For the primary outcome measure (ARA test), the percentage of subjects who showed clinically relevant improvement was determined for both groups (the percentage of success with a 95% confidence interval). The minimal clinically important improvement was set at 10% (i.e., 5.7 points on the ARA test).[22] χ^2 tests were applied to evaluate the difference in success rate and the difference between the opinions of the subjects. The statistical analyses were performed with SPSS 11.5 for Windows (SPSS, Chicago, IL). The significance level was set at 0.05.

The objective of the present trial was to investigate whether there is a difference between two stimulation strategies. Therefore, an on-treatment analysis was performed and not an intention-to-treat analysis, which would have been necessary if investigating the effectiveness of ES.[28]

RESULTS

Included Subjects

A total of 30 subjects were included, and 28 completed the treatment program. The characteristics of these subjects are summarized in Table 1. The two groups were comparable with regard to age, time since stroke, percentage with nonhemorrhagic stroke, sex, neglect, cognitive function, and sensory disorders. However, notwithstanding randomization, there were more subjects in group B with right hemiparesis, and thus, there were more subjects with an impaired dominant arm. Grip strength of the affected hand and the hand ratio were also higher in group B. There was no clinically significant difference between the two groups with regard to initial scores for the other outcome measures.

Intervention

One subject dropped out of the treatment program a few days before the final date. Because she only missed a few ES sessions and had completed all assessments, it was decided to include this subject in the analysis. However, two other subjects dropped out much earlier. One dropped out after 1 wk because she experienced an increase in involuntary movements of the arm between the stimulation sessions. In our opinion, this was a result of the way in which she coped with the therapy rather than an effect of the stimulation itself, and the situation normalized as soon as she stopped ES treatment. The other subject dropped out after 2 wks because the 1-hr treatment program three times a day occupied her too much. For these two subjects, the reason why they dropped out early in the treatment period was not related to the specific stimulation method to which they had been assigned. They were both excluded from the analysis (on-treatment analysis).

A total of 12 subjects received other therapy during the ES treatment. This varied from fitness training once a week to more intensive outpatient treatment in the rehabilitation center. Subjects who received co-interventions were equally distributed over groups A and B, and there was a similar distribution of low- and higher-intensity co-interventions (Table 1).

Approximately half of the subjects had some redness of the skin, but only at the beginning of the treatment pe-

TABLE 1
Patients' characteristics and initial values

	Group A (Flexors and Extensors)	Group B (Extensors Only)
n	13	15
Age in yrs, mean (SD)	58 (17.3)	61.7 (9.7)
Months poststroke, mean (SD)	14.7 (11.8)	21.4 (16.1)
Right hemiparesis, *n* (%)	3 (23.1)	8 (53.3)
Dominant arm affected, *n* (%)	4 (30.8)	7 (46.7)
Nonhemorrhagic stroke, *n* (%)	11 (84.6)	14 (93.3)
Female subject, *n* (%)	4 (30.8)	4 (26.7)
MMSE score, median (range)	28 (26–30)	27 (16–30)
Neglect present, *n* (%)	3 (23.1)	3 (20)
Sensory disorder present, *n* (%)	8 (61.5)	7 (46.7)
Co-interventions	6	6
Low intensity/higher intensity	3/3	4/2
ARA test, mean (SD)	28.6 (15.3)	28.9 (13.1)
Grip strength, mean (SD)	11.2 (9.1)	14.8 (7.0)
Hand ratio, mean (SD)	0.25 (0.17)	0.37 (0.15)
Motricity Index, mean (SD)	64.3 (18.1)	60.7 (13.9)
Ashworth Scale, median (range)	1 (0–3)	1 (1–2)
Barthel Index, median (range)	20 (17–20)	20 (16–20)

MMSE, Mini Mental State Examination; ARA test, Action Research Arm test.

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TABLE 2

Results of the assessments immediately before the start of the treatment (t0), at the end of the 6-wk treatment period (t1), and after a follow-up period of 6 wks (t2) and changes in the assessments

	t0 Start of Treatment	t1 End of Treatment	Change from t0 to t1	t2 End of Follow-up	Change from t0 to t2
Action Research Arm test, mean (SD)					
Scale: 0–57, 0 = no arm function					
Flexors and extensors, n = 13	28.6 (15.3)	29.6 (16.5)	1.0 (3.3)	29.6 (17.1)	1.0 (5.3)
Extensors only, n = 15	28.9 (13.1)	32.1 (12.7)	3.3 (5.0)	32.2 (13.5)	3.3 (4.5)
Hand ratio, mean (SD)					
Flexors and extensors, n = 13	0.25 (0.17)	0.31 (0.15)	0.06 (0.07)	0.28 (0.16)	0.02 (0.07)
Extensors only, n = 15	0.37 (0.15)	0.41 (0.18)	0.04 (0.09)	0.40 (0.17)	0.03 (0.09)
Motricity Index, mean (SD)					
Scale: 0–100, 0 = no voluntary movement					
Flexors and extensors, n = 13	64.3 (18.1)	65 (16.6)	0.7 (8.2)	61.9 (15.3)	−2.3 (7.7)
Extensors only, n = 15	60.7 (13.9)	62.7 (12.9)	1.9 (7.6)	62.6 (13.8)	1.9 (9.4)
Ashworth Scale, median (range)					
Scale: 0–4, 0 = normal muscle tone					
Flexors and extensors, n = 13	1 (0–3)	2 (0–3)	0 (−1 to 1)	1 (0–2)	0 (−1 to 1)
Extensors only, n = 15	1 (1–2)	1 (1–2)	0 (−1 to 0)	1 (0–2)	0 (−1 to 1)
Active range of motion of the wrist, mean (SD)					
Measured in degrees					
Flexors and extensors, n = 13	88.2 (27.6)	87.6 (34.9)	−0.5 (19.1)	95.8 (33.6)	7.6 (11.6)
Extensors only, n = 15	94.4 (26.3)	95.1 (24.9)	0.6 (16.4)	103.9 (18.9)	9.5 (15.5)

riod. This was either under the electrodes or where there was pressure from the splint on the wrist. In all cases, the redness disappeared soon after the initial stimulation sessions and did not result in any burns or pressure sores. Four subjects felt pain during the stimulation, but this disappeared as the intensity of the stimulation was decreased. Apart from this temporary redness and pain, no adverse effects were reported.

Primary Outcome Measure: ARA Test

Table 2 shows the results of the assessments for both groups on all outcome measures and the changes from baseline to the end of the treatment and to the end of the follow-up. Figure 1 shows the mean ARA scores for both groups. During the treatment period, the mean ARA score in group B improved by 3.3 points (95% confidence interval, 0.51–6.02), whereas the mean score in group A improved only slightly (1.0 point; 95% confidence interval, −0.97 to 2.97). In both groups, there was no deterioration during follow-up. The difference in functional gain between groups A and B was not statistically significant (Mann-Whitney U test: t0–t1, P = 0.25; t0–t2, P = 0.39; 95% confidence interval t0–t1, −1.06 to 5.60; 95% confidence interval t0–t2, −1.47 to 6.14). The baseline difference in hand ratio might bias the outcome on the ARA test. An additional analysis, with the initial hand ratio as covariable, also showed no significant difference between the two groups (analysis of covariance, P = 0.10).

Four of 15 subjects in group B improved more than the clinically relevant difference of 5.7 points (range, 7–12 points), and the percentage of success in group B was 27% (95% confidence interval, 8–55%). In group A, 1 of 13 subjects improved >5.7 points (7 points), resulting in a success percentage of 8% (95% confidence interval, 0–36%). This difference in success is not significant (χ^2 test, P = 0.33). The ratio of the success rates in group B and group A is 3.4, indicating that the chance of success in group B was 3.4 times higher than in group A (95% confidence interval, 0.44–27.24)

Secondary Outcome Measures

Hand Ratio. Table 2 and Figure 2 show that the hand ratio of both groups improved during treatment, but there was some decline during follow-up. The improvement in the flexor-extensor group (group A: 0.06; 95% confidence interval, 0.01–0.10) was somewhat greater than in the extensors-only group (group B: 0.04; 95% confidence interval, −0.01 to 0.09), but the difference in gain was not statistically significant (Mann-Whitney U test: t0–t1, P = 0.27; t0–t2, P = 0.69). An

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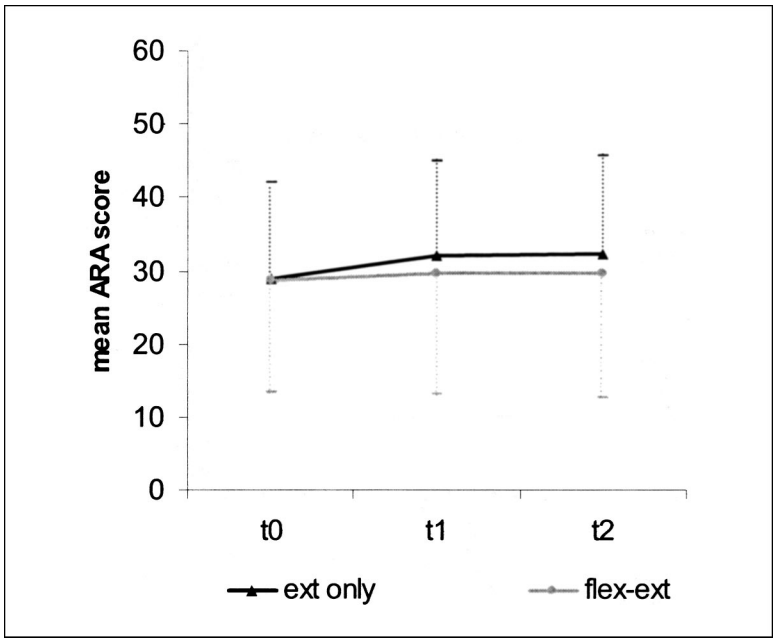

Figure 1: Mean scores and standard deviations on the Action Research Arm (*ARA*) test for groups A (alternating flexion and extension [*flex-ext*]) and B (extension only [*ext only*]). *t0*, immediately before the start of treatment; *t1*, at the end of the 6-wk treatment period; *t2*, after a follow-up period of 6 wks.

additional analysis, with correction for the baseline difference in initial hand ratio, also showed no difference between the groups (analysis of covariance, $P = 0.59$).

Motricity Index. This index for motor impairment showed no treatment effect for either group (Table 2 and Fig. 3) and also no difference between the two groups (Mann-Whitney *U* test: t0–t1, $P = 0.44$; t0–t2, $P = 0.12$).

Ashworth Scale. The median change in Ashworth Scale during treatment and at follow-up was zero for both groups (Table 2). Statistical analysis showed no difference between the groups (Mann-Whitney *U* test: t0–t1, $P = 0.62$; t0–t2, $P = 0.82$).

Active Range of Motion of the Wrist. Table 2 and Figure 4 show that the active range of motion of the wrist did not change during the treatment period in either group. However, the active range of motion improved in both groups during follow-up, probably as a result of increased active extension (Fig. 4). No difference was found between the two groups (Mann-Whitney *U* test: t0–t1, $P = 0.79$; t0–t2, $P = 0.79$).

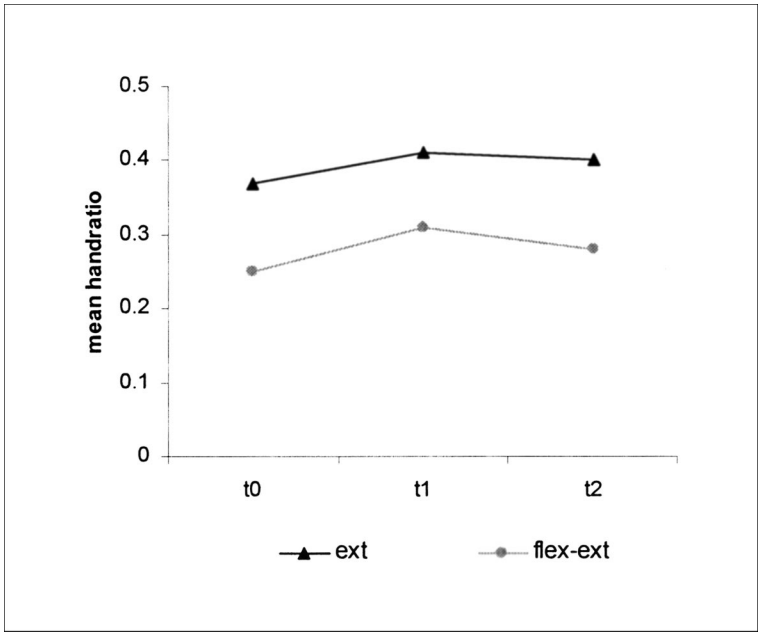

Figure 2: Mean hand ratio for groups A (alternating flexion and extension [*flex-ext*]) and B (extension only [*ext only*]).

Subjects' Opinion About the Treatment

Functional improvement was reported by eight subjects in group A (62%) and 13 subjects in group B (87%). Five subjects in group A and two subjects in group B reported no change in function of the affected arm (38% and 13%, respectively). The subjects mainly described functional improvement as better ability to grasp and release small objects and more functional use of the affected arm in the activities of daily living. In group A, 9 of 13 subjects reported a decrease in muscle tone (69%) and four reported no change (31%). A decrease in muscle tone was reported by 11 of 15 subjects in group B (73%), whereas two subjects reported no change (13%) and two reported an increase in muscle tone (13%). There was no significant difference between the two groups with regard to the subjective score for function and muscle tone (χ^2 test). These subjective opinions did not correspond with the outcomes on the Ashworth Scale and the ARA test.

Donning and doffing of the splint was no problem for most of the subjects. Three subjects needed help; two only initially and one throughout the entire trial.

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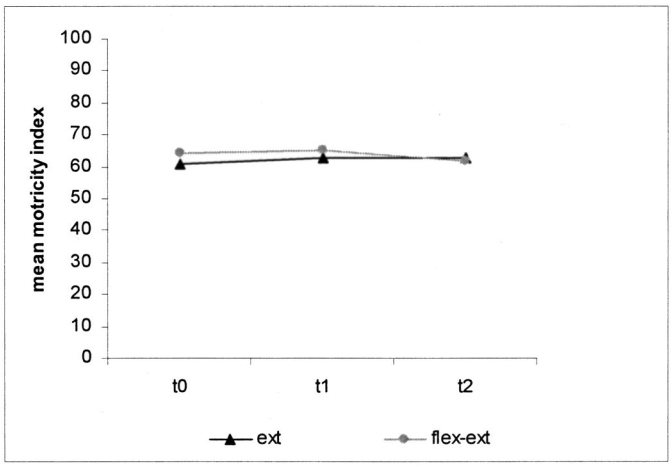

Figure 3: Mean scores at Motricity Index for groups A (alternating flexion and extension [*flex-ext*]) and B (extension only [*ext only*]).

DISCUSSION

This trial investigated whether there was a difference in functional improvement of the affected arm in chronic stroke patients when comparing two strategies of ES. ES of the extensor muscles yielded a nonsignificant improvement in arm function compared with alternating ES of flexors and extensors. Therefore, the main conclusion of this trial is that there is no significant difference between the two methods of stimulation with regard to functional improvement, as assessed by means of the ARA test.

The fact that the difference between the two groups was not statistically significant is probably due to a power problem (i.e., a type II error). Because this trial was the first to compare these two stimulation strategies, it was not possible to perform a reliable power calculation beforehand. However, the 95% confidence interval for the difference in functional gain (−1.06 to 5.60) does suggest that it is reasonable to assume that a significant effect would have been found if the study had had more power.[28]

Apart from statistical significance, clinical relevance is also important for therapeutic interventions. Neither the difference between the groups nor the improvement in the group that received ES of the extensor muscles only exceeded the minimal clinically important difference of 10% (i.e., 5.7 points on the ARA test).[22] In the present trial, the minimal clinically important difference was also used to calculate success rates with regard to functional improvement in both groups. The percentage of success was 27% in the group receiving ES of the extensors (4 of 15 subjects) and 8% in the other group (1 of 13 subjects). This difference in success rate was not significant either.

The clinician who applies ES to improve arm function might be tempted to choose ES of the extensors only, based on more functional gain, a higher success rate, and more subjects reporting functional improvement, compared with the results of alternating ES of flexors and extensors found in the present trial. However, the lack of a statistically significant difference between the two methods in this respect indicates that this choice would not be based on scientific evidence.

Maximal grip strength, expressed as the ratio between the affected and the nonaffected side, is a valuable marker of hand and arm function in chronic stroke.[25] In the present trial, the hand ratio improved in both groups during the treatment. The improvement in hand ratio was more pronounced in the flexor-extensor group, and this was probably due to the fact that the flexor muscles of the hand were trained in this group but not in the extensors-only group. Although the hand ratio improved in both groups and the gain was greater in the flexor-extensor group, gain in hand ratio was only associated with functional improvement in the group receiving ES of the extensors only. Apparently, gain in grip strength does not guarantee functional improvement.

After the treatment, the hand ratio decreased in both groups, but the decrease was less in the extensors-only group. An explanation might be that the gain in grip strength was maintained by the improvement in function in this group.

This study does not confirm the

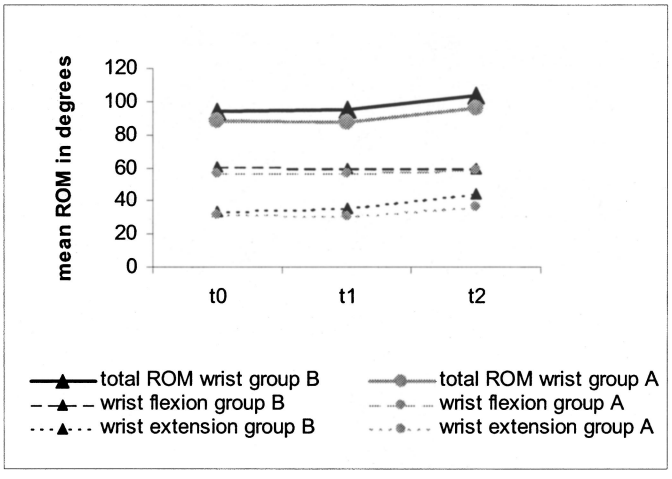

Figure 4: Active range of motion (*ROM*) of the affected wrist in group A (alternating flexion and extension) and group B (extension only).

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tone-reducing effect of ES of the extensor muscles, as claimed by Alfieri,[3] but it seems that the result of flexor and extensor stimulation is not merely a sum of the positive effects of reciprocal and recurrent inhibition.

Assessment of the active range of motion of the wrist resulted in the unexpected finding that, in both groups, improvement in range of motion occurred only in the follow-up period. The meaning and explanation of this finding in relation to the effect of ES are puzzling. However, the improvement found in active extension at follow-up cannot be considered as a measurement error. Measurement errors are random in direction and are not likely to occur only at follow-up.

When the results of the present trial are compared with those of previous trials in chronic stroke patients, it is striking that the previous studies reported improvement in passive range of motion,[14,16] active range of motion,[14,16] muscle tone,[3,14,15] and motor control,[15] whereas in the present trial, no effect of the treatment was found on range of motion, muscle tone, or motor control in either of the two groups. One explanation is that this might be due to subject characteristics. Comparison of baseline characteristics with those in previous trials revealed that the subjects in previous trials were, in general, more severely affected than the subjects included in the present trial. It is possible that more severely affected subjects benefit more from ES with regard to muscle tone and range of motion. The present trial specifically focused on less severely affected subjects (i.e., subjects with active voluntary wrist extension). This was based on previous subgroup analyses suggesting that less severely affected subjects might benefit more from ES with regard to motor control and function.[9,15] Based on these subgroup analyses, improvement in motor control was expected to be found in the present study population.

The previously mentioned studies were mainly nonrandomized trials, and their positive results might therefore be biased. Pocock and Elbourne[29] state that only randomized, controlled trials can provide a reliably unbiased estimate of treatment effect. To date, three randomized, controlled trials focusing on ES in chronic stroke patients have been published.[9,11,30] Sonde et al.[9] reported an improvement in motor control without any reduction of muscle tone; functional abilities and strength were not assessed in this trial. The lack of improvement in motor control that was found in the present trial is not in accordance with the results of the trial carried out by Sonde et al.[9]

Cauraugh et al.[11] focused on less severely affected subjects, like those in the present trial. Spasticity and range of motion were not assessed, but they reported improvement in sustained contraction of the wrist extensor muscles and in function (box and block test) but no effect on motor control. From the publication, it is not clear whether there was no gain in motor control or no difference in gain. In a later trial, functional improvement was confirmed,[30] but the clinical relevance of this improvement was not discussed. From the present trial, it seems that functional improvement can be clinically relevant for some subjects.

The results of the present trial and previous randomized, controlled trials on ES are therefore inconclusive with regard to motor control, but functional improvement can be achieved by ES in chronic stroke patients, at least in those with residual voluntary wrist extension. The exact mechanism underlying this functional improvement is still unclear. However, the results of the present study and the study carried out by Cauraugh et al.[11] suggest that improvement in motor control is not a prerequisite for functional gain. It can be hypothesized that functional gain is achieved by improvement in movement strategies or enhanced movement efficiency. The clinical opinion is that improvement in movement strategy is associated with reduction in muscle tone,[18] but that is not in accordance with the findings of the present trial. It is more likely that muscle strength is a crucial factor in movement efficiency. Grip strength is shown to be a good marker of hand function, but the results of the flexor-extensor group in the present trial show that an increase in grip strength alone is not enough to achieve functional improvement. Strength of wrist and finger extension might be more important. The stabilizing effect of extension power to the wrist is a component of grip strength, and extension power itself is important for use of the fingers in most functional hand activities.[11] In the studies carried out by Cauraugh et al.[11] and Cauraugh and Kim,[30] functional improvement is associated with increased sustained contraction of the stimulated wrist extensors. We hypothesize that this is also true in the present trial. Although muscle strength of the finger extensors was not assessed, it can be assumed that extensor muscle strength increased most in the extensors-only group because these muscles were trained most in this group and because it was this group in which most functional improvement was found.

It might therefore be argued that the difference between the extensors-only group and the flexor-extensor group with regard to functional improvement is merely a result of the difference in intensity (i.e., duration of extensor stimulation between the two groups). In our opinion, this argument is only valid if ES of the flexors is believed to be completely neutral. However, the theories described in the "INTRODUCTION" indicate that flexor stimulation is bound to have some influence on the impaired arm. Therefore, the present trial is not just a dose-effect study of extensor stimulation but a comparison of two different stimulation strategies. The exact influence of flexor stimulation is still not known, but the trial showed that the addition of flexor stimulation to extensor stimulation had no additional value.

In conclusion, there was no statis-

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tically significant difference between ES of the extensor muscles of the hand and alternate ES of flexor and extensor muscles. Functional improvement in chronic stroke patients can be achieved by ES, but at the group level, the functional gain did not exceed the minimal clinically relevant difference. Future studies should focus on patient characteristics to identify patients who might benefit in a clinically relevant way. Given the importance of arm function improvement, more research is needed to elucidate the determinants of functional recovery and the specific mechanisms underlying the action of ES.

ACKNOWLEDGMENTS

We thank the rehabilitation centers 'De Vogellanden' in Zwolle and 'Het Roessingh' in Enschede for their cooperation in the recruitment of subjects, Ms. M. T. Hartlief for coordinating the trial in Zwolle, the therapists for their expertise in supervising the patients in the application of the stimulation throughout the trial, the therapists who performed the outcome measures with such care, and all the subjects who participated in the trial.

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