Intensity of leg and arm training after primary middle-cerebral-artery stroke: a randomised trial

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Summary

Background We investigated the effects of different intensities of arm and leg rehabilitation training on the functional recovery of activities of daily living (ADL), walking ability, and dexterity of the paretic arm, in a single-blind randomised controlled trial.

Methods Within 14 days after stroke onset, 101 severely disabled patients with a primary middle-cerebral-artery stroke were randomly assigned to: a rehabilitation programme with emphasis on arm training; a rehabilitation programme with emphasis on leg training; or a control programme in which the arm and leg were immobilised with an inflatable pressure splint. Each treatment regimen was applied for 30 min, 5 days a week during the first 20 weeks after stroke. In addition, all patients underwent a basic rehabilitation programme. The main outcome measures were ability in ADL (Barthel index), walking ability (functional ambulation categories), and dexterity of the paretic arm (Action Research arm test) at 6, 12, 20, and 26 weeks. Analyses were by intention to treat.

Findings At week 20, the leg-training group (n=31) had higher scores than the control group (n=37) for ADL ability (median 19 [IQR 16–20] *vs* 16 [10–19], $p<0{\cdot}05$), walking ability (4 [3–5] *vs* 3 [1–4], $p<0{\cdot}05$), and dexterity (2 [0–56] *vs* 0 [0–2], $p<0{\cdot}01$). The arm-training group (n=33) differed significantly from the control group only in dexterity (9 [0–39] *vs* 0 [0–2], $p<0{\cdot}01$). There were no significant differences in these endpoints at 20 weeks between the arm-training and leg-training groups.

Interpretation Greater intensity of leg rehabilitation improves functional recovery and health-related functional status, whereas greater intensity of arm rehabilitation results in small improvements in dexterity, providing further evidence that exercise therapy primarily induces treatment effects on the abilities at which training is specifically aimed.

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See Commentary page ???

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Introduction

A collaborative systematic review of randomised trials showed that organised care in a stroke unit results, in the long term, in lower mortality, less dependency in activities of daily living (ADL), and less need for institutional care.[1] The specific components of stroke-unit rehabilitation care that affect outcome, however, remain to be investigated.[1–3]

A research synthesis on the effects of stroke rehabilitation showed small but statistically significant effects of the intensity of rehabilitation on ADL and neuromuscular variables.[4] Sunderland and colleagues concluded that these small positive rehabilitation effects provided ethical justification for a more radical trial.[5] The effects of rehabilitation methods seem to be limited to tasks for which specific training is given, with hardly any transfer to tasks without direct training.[2] Many intervention studies on stroke rehabilitation are hampered by lack of sufficient contrast in amount of rehabilitation between experimental and control conditions, different settings of rehabilitation management, lack of masking procedures, and heterogeneity of the stroke population.[4] In this study, we investigated the differences in efficacy between three rehabilitation programmes with emphasis on arm function, leg function, and immobilisation of arm and leg with an inflatable pressure splint; the primary outcome measures were recovery in ADL, walking ability, and dexterity of the paretic arm.

Methods

Patients

Between Sept 1, 1994, and May 1, 1997, we recruited 101 stroke patients from seven hospitals. Stroke diagnosis was based on the WHO definition.[6] To ensure weekly follow-up assessments, we selected three rehabilitation centres and 15 nursing homes in Amsterdam and Haarlem to participate in this study. The study was approved by the ethics committee of each participating hospital.

Eligibility criteria were: a primary, first-ever stroke in the territory of the middle cerebral artery as revealed by computed tomography or magnetic resonance imaging; age between 30 and 80 years; impaired motor function of the arm and leg; inability to walk at first assessment; no complicating medical history (such as cardiac, pulmonary, or other neurological disorders); no severe deficits in communication, memory, or understanding; written or spoken informed consent; and motivation to participate in the research project.

A speech therapist assessed the ability to communicate, and accepted a cut-off point of the 50th percentile corrected for age on the Dutch Foundation aphasia test.[7] The mini-mental state examination was used to assess orientation in time and place; only patients with a score of 24 points or more were included in the trial.[8]

Within 24 h after stroke onset, a neurologist assessed the patient to confirm the clinical diagnosis of stroke and to record clinical symptoms such as level of consciousness (on the Glasgow coma scale).[9] Patients were classified according to the Oxford Community Stroke Project as having: infarcts of the total anterior circulation, the partial anterior circulation, or the lacunar anterior circulation.[10] This classification is reliable between observers[10,11] and has a high predictive validity with the side and size of the cerebral infarct on computed tomography.[11] To control for the heterogeneity of the stroke population, muscle strength, balance, proprioception, and cognitive function were assessed with the Orpington prognostic scale.[12]

Design and procedures

Within the first 14 days after stroke, the patients were randomly assigned to one of three treatment groups. The first group was scheduled for immobilisation of the paretic arm and leg by means of an inflatable pressure splint (Svend Andersen, Haarlev, Denmark); the splint was applied with the patient supine for 30 min on 5 days per week (control treatment).[13,14] The other groups were assigned arm or leg training, which was individually applied by local physical and occupational therapists, for 30 min on 5 days per week for 20 weeks after the stroke. In addition, all three groups received 15 min per day leg rehabilitation, 15 min per day arm rehabilitation, and 1·5 h per week ADL training by an occupational therapist. Before randomisation, patients and family were informed that all interventions might improve outcome, but were kept naïve with respect to the assumed efficacy of the experimental condition applied. After enrolment, which included the first assessment of outcome variables, restricted randomisation (permutated blocks of nine) was applied with random number tables for each participating hospital. Allocation was concealed by use of sealed envelopes.

Nurses, speech therapists, and social workers provided usual care depending on patients' needs without knowledge of treatment assignment. With the exception of preventive medication, no other medical interventions or therapies to improve skills were allowed during the first 20 weeks after stroke. From week 20 onwards, decisions about type of treatment and its intensity (average three times, 30 min per week) for each patient were made by the relevant stroke management team.

We wrote a treatment protocol of evidence-based guidelines for stroke rehabilitation. The guidelines were based on patterns derived from findings reported in 165 intervention studies on stroke rehabilitation.[2] They advocated an eclectic approach to neurofacilitation techniques. Arm rehabilitation included functional exercises that facilitated forced arm and hand activity such as leaning, punching a ball, grasping, and moving objects. The key elements in leg rehabilitation were sitting, standing, and weight-bearing exercises during standing and walking, with an emphasis on achieving stability and improving gait velocity. Treadmill training was promoted if equipment was available. If treatment at disability level was not possible, strengthening exercises for arms and legs were promoted. All participating therapists were instructed during a course on rehabilitation of arm and leg function.

Amount of therapy, measured in 15 min time units of one-to-one contact between therapist and patient, was documented in a diary after each treatment session. Content of therapy was reported daily with 25 different codes representing task-specific goals for the arm and leg. In this way, adherence to therapy was assessed. Care of patients was coordinated by two physical therapists.

The three primary outcomes (ADL, walking ability, and dexterity of the paretic arm) were assessed by means of the Barthel index,[15] the functional ambulation categories,[16] and the Action Research arm test,[17,18] respectively. The Barthel index represents a patient's ability to carry out ten everyday tasks (ie, bladder and bowel control, toilet use, dressing, feeding, walking, personal toilet, transfer activities, bathing, and stair climbing).[15] The functional ambulation categories includes six categories of walking ability, according to need for walking aids and help with walking.[16] The Action Research arm test consists of 19 functional movement tasks, in four domains (grasp, grip, pinch, and gross movement).[17,18] The reliability and validity of all three tests have been established.[15,16,18] We assessed the tests for their within-observer reliability in 15 stroke patients with an interval of 1 week between measurements. The Spearman rank-order correlation coefficients (r_s) were 0·97 for the Barthel index and the functional ambulation categories and 0·99 for the Action Research arm test (p<0·001).

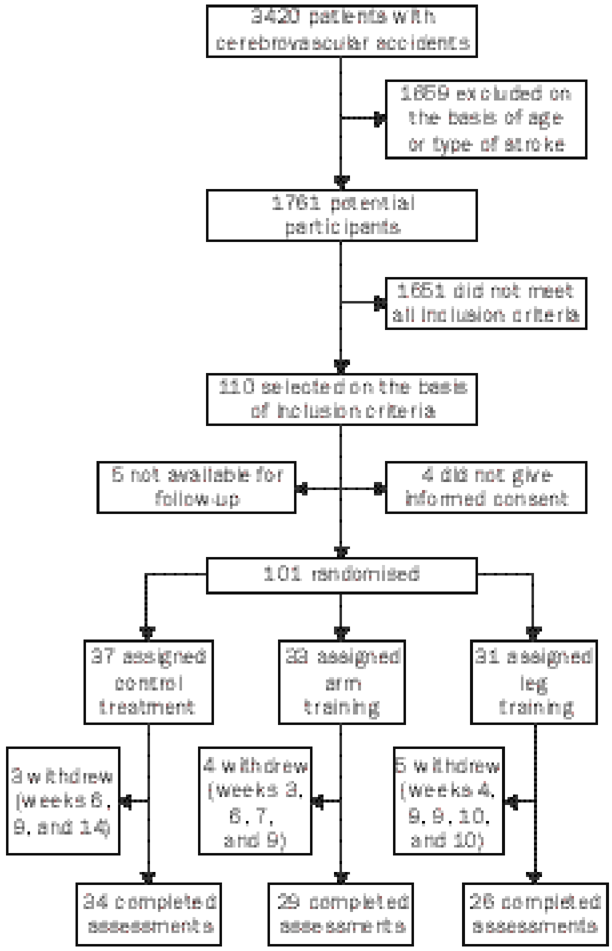

Figure 1: **Trial profile**

Various secondary outcomes were also investigated. Comfortable and maximum walking speeds were assessed by means of a 10 m timed walking test. In this study, a high test-retest reliability has been observed for these tests (r_s=0·97, p<0·001, and r_s=0·96, p<0·001, respectively). In addition, the number of walking devices used was monitored.

Part 1 of the Nottingham health profile and a short generic version of the sickness impact profile were used to assess quality of life. The first part of the Nottingham health profile consists of 38 yes/no questions describing health-related behaviour in six domains of daily life (energy, physical mobility, sleep, pain, emotional reactions, and social isolation).[19] The sickness impact profile (68-item version) assesses six domains of health-related functional status (somatic autonomy, mobility control, psychological autonomy and communication, social behaviour, emotional stability, and mobility range), explaining 94% of the total variance of the original 136-item version.[20] Extended ADL were assessed with the Frenchay activities index.[21] The first part of this index assesses the frequency of performance of ten activities (meal preparation, washing up, clothes washing, light and heavy housework, social outings, local shopping, walking outside >15 min, actively pursuing a hobby, driving a car, travelling by bus) during the previous 12 weeks; the second part assesses five activities (outings and car rides, gardening, household maintenance, reading, and paid work) during the previous 26 weeks. The reliability and validity of these tests have been established.[20,22,23]

All the primary and secondary outcome variables were assessed weekly during the first 10 weeks after stroke onset, then every 2 weeks during weeks 10–20. Final measurements were made at 26 weeks after stroke onset. Quality of life was assessed at 1, 12, and 26 weeks after stroke, and the Frenchay activity index was assessed at baseline and 26 weeks after stroke onset.

	Control treatment (n=37)	Arm training (n=33)	Leg training (n=31)
Demography			
M/F	14/23	16/17	13/18
Age (years)*	64·1 (15·0)	69·0 (9·8)	64·5 (9·7)
Stroke characteristics			
Left/right	13/24	16/17	13/18
TACI	25	19	17
PACI	9	11	13
LACI	3	3	1
Clinical characteristics			
Glasgow coma scale (0–15)†	15 (15–15)	15 (15–15)	15 (15–15)
MMSE (0–30)†	26 (24–28)	27 (24–29)	27 (26–29)
Urinary incontinence	19 (51%)	19 (58%)	11 (35%)
Sitting balance	26 (70%)	23 (70%)	25 (81%)
Visual gaze deficit	12 (32%)	8 (24%)	5 (16%)
Hemianopia	15 (41%)	11 (33%)	7 (23%)
Visual inattention	20 (54%)	17 (52%)	14 (45%)
TFT score (0–3)†	1 (0·5–2)	1 (0–2)	1 (0–2)
OPS (1·6–6·8)†	4·8 (4·0–5·0)	4·4 (3·6–5·2)	4 (3·6–4·8)
Social support	14 (38%)	15 (45%)	11 (35%)
Outcome variables at baseline			
ADL ability†	5·5 (3–7)	5 (3–7)	6 (3–8)
Walking ability†	0 (0–1)	0 (0–1)	1 (0–2)
Dexterity†	0 (0–0)	0 (0–1)	0 (0–6)
Walking velocity (m/s)*	0 (0)	0 (0)	0 (0)
Frenchay activities index*	26·8 (6·8)	26·5 (6·1)	27·1 (7·0)
Nottingham health profile*	16·5 (6·7)	17·5 (9·3)	14·5 (6·4)
Sickness impact profile*	41·2 (11·7)	38·6 (10·9)	42·5 (6·5)
Time from stroke onset to start of treatment (days)*	7·5 (2·9)	7·2 (2·8)	7·0 (2·5)

TACI=total anterior cerebral infarct; PACI=partial anterior cerebral infarct; LACI=lacunar circulation infarct; MMSE=mini-mental state examination; TFT=thumb-finding test; OPS=Orpington prognostic scale. *Mean (SD). †Median (IQR).

Table 1: **Baseline characteristics of patients**

The test battery took 45–75 min to complete. All measurements were done by one investigator (GK) who was not involved in the patients' care and who was unaware of the assignments of the patients to the various rehabilitation groups.

Statistical analysis

The amount of therapy actually received by the patients was compared with the amount of therapy prescribed by the treatment protocol, with the assumption that a difference of 2 SE would be significant at $p<0·05$. Differences in baseline values between the three groups for independent variables were tested with the χ^2 test, the Kruskal-Wallis (one-way ANOVA) test, or one-way ANOVA. The distribution of interval scaled measurements was first tested for normality with the Kolmogorov-Smirnov test (SPSS, version 7.5).

The Kruskal-Wallis test was used to assess differences between the groups at weeks 6, 12, 20, and 26 for the three primary outcomes, walking velocities, and number of walking devices and the changes from baseline to 12 weeks and from 12 weeks to 26 weeks for the quality-of-life indices. Changes in the Frenchay activities index were evaluated from baseline to 26 weeks.[2] When significant differences between groups were found, a post-hoc analysis was done to test which groups differed significantly from each other, by the Mann-Whitney *U* test. (Outcomes of primary and secondary variables based on a repeated measurement design [ie, generalised estimating equations: GEE] including 15 measurements during the first 20 weeks are available from the investigators.) Each hypothesis was tested with a two-tailed analysis and 0·05 as the level of significance.

Results

101 (about 3%) patients of a total of 3420 admitted to hospital with stroke (International Classification of Diseases, ninth revision; codes 430–438) in our district were eligible for randomisation (figure 1). The distribution of the three treatment conditions did not differ among the seven study sites (p=0·99), and the three treatment groups showed similar distributions of baseline characteristics (table 1). At baseline, all patients had a Barthel index of 9 points or lower and could be classified as severely or very severely disabled.[24] No patient was able to walk unaided. 11 patients (three control, two arm training, six leg training) showed some dexterity (10 points or more on the arm test) at baseline.

12 patients withdrew before week 20 (six had recurrent stroke, two cancer, one carotid endarterectomy, two refused control treatment, and one died from a heart attack). Therefore, 1492 (92·3%) of the planned 1616 measurements were made. No significant differences in number of assessments between the three treatment groups were found (p=0·184). During observation, type of treatment assignment was unintentionally disclosed for one patient in the leg-training group, four in the arm-training group, and five in the control group (most after week 9).

The planned differences between the groups in the amounts of therapy were achieved (table 2). In addition, the arm-training group received a little more ADL training per working day than the control group. The amount of rehabilitation actually applied in each treatment group did not differ significantly from that planned for the group. There was no significant difference between the overall amount of therapy planned and the amount actually applied. Except for the application of the inflatable pressure splint ($p<0·001$), we found no significant differences in the frequency of the various components of arm training (reaching, grasping, and washing) and leg training (sitting balance, standing balance, and walking) between the treatment groups (p values ranged from 0·07 for stair climbing to 0·81 for the use of an arm orthosis or sling).

By Kruskal-Wallis analysis, there were significant differences among the groups in the three primary

Therapy	Mean (SD) amount of therapy (min per working day)					
	Control		Arm training		Leg training	
	Intended	Actual	Intended	Actual	Intended	Actual
Splint immobilisation	30	25·6 (6·0)*	0	0	0	0
Arm training	15	16·5 (2·7)	45	38·6 (10·7)*	15	17·8 (4·1)
Leg training	15	13·9 (4·4)	15	13·4 (4·8)	45	36·6 (9·3)*
ADL training	18	13·7 (4·6)	18	16·7 (5·5)†	18	15·9 (4·6)

*p<0·001 for differences from other two groups.
†p<0·05 for difference from control group.

Table 2: **Intended and actual amount of therapy**

	Median (IQR) value		
	Control group (n=37)	Arm-training group (n=33)	Leg-training group (n=31)
ADL ability (Barthel index)			
Week 6*	8·5 (7–13)	10 (5–13)	13 (8·75–19)||**
Week 12*	11 (8–18)	14 (10·75–18)	17 (13–20)||
Week 20*	16 (10–19)	17 (14·25–20)	19 (16–20)§
Week 26	17 (10·5–19)	17 (11·75–20)	19 (15–20)
Walking ability (functional ambulation categories)			
Week 6†	1 (1–3)	2 (1–3)	3 (2–4)¶**
Week 12‡	3 (1–3)	3 (2–4)	4 (3–5)¶
Week 20*	3 (1–4)	4 (3–5)	4 (3–5)§
Week 26	4 (2–5)	4 (3–5)	5 (4–5)
Dexterity (Action Research arm test)			
Week 6*	0 (0–1)	1 (0–14)	1 (0–43)||
Week 12*	0 (0–1)	3 (0–34)§	2 (0–53)||
Week 20‡	0 (0–2)	9 (0–39)||	2 (0–56)||
Week 26†	0 (0–2·25)	4 (0–38)§	3 (0–56)||

*p<0·05; †p<0·001; ‡p<0·01 for difference among groups (Kruskal-Wallis test); §p<0·05; ||p<0·01; ¶p<0·001 for difference between experimental group and control group. **p<0·05 for difference between leg-training and arm-training groups.

Table 3: **Primary outcomes**

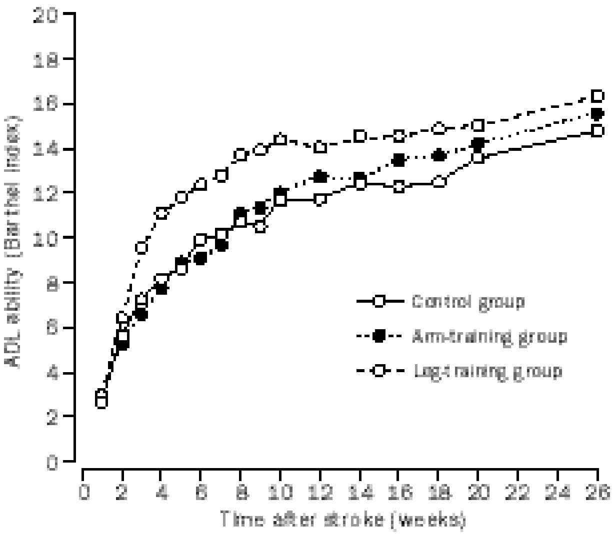

Figure 2: **Mean recovery patterns of Barthel index**

outcome measures at 6, 12, and 20 weeks after stroke (table 3, figure 2). At 26 weeks, only the Action Research arm score showed a significant difference between the groups. Post-hoc analysis showed that the leg-training group had significantly higher values of the Barthel index and functional ambulation categories than the control group during the first 20 weeks, and higher scores than the arm-training group at 6 weeks. Action Research arm scores were higher in the leg-training group than in the control group from week 6 onwards, and in the arm-training group than in the control group from week 12 onwards.

Secondary outcome data are given in table 4. For comfortable and maximum walking speeds, small but significant differences were found between the groups: post-hoc analysis showed significant differences in comfortable and maximum walking speed between the leg-training and control groups at 6, 12, and 20 weeks after stroke, but no significant differences between the leg-training and arm-training groups or the arm-training and control groups.

We analysed the changes in recovery during the first 12 weeks and found a significant difference between the groups in improvements on the sickness impact profile (table 4). Post-hoc analysis again showed significant differences between the leg-training and control groups but not for the other comparisons. Differences in the Nottingham health profile approached significance (p=0·065). Separate analyses of the six domains of the sickness impact profile showed significantly larger improvements in the leg-training than the control group for mobility control ($z=-4{\cdot}16$; $p<0{\cdot}001$), mobility range ($z=-2{\cdot}49$; $p=0{\cdot}013$), and social behaviour ($z=-3{\cdot}36$; $p=0{\cdot}001$). The improvements in quality-of-life measures and Frenchay activities index did not differ significantly between the treatment groups.

	Mean (SD) value		
	Control group	Arm-training group	Leg-training group
Comfortable walking speed (m/s)			
Week 6*	0·17 (0·37)	0·21 (0·39)	0·40 (0·45)†
Week 12*	0·31 (0·39)	0·46 (0·47)	0·58 (0·50)†
Week 20*	0·37 (0·41)	0·55 (0·46)	0·65 (0·46)†
Week 26	0·44 (0·44)	0·55 (0·44)	0·63 (0·47)
Maximum walking speed (m/s)			
Week 6*	0·22 (0·50)	0·33 (0·60)	0·55 (0·65)†
Week 12*	0·41 (0·55)	0·55 (0·63)	0·79 (0·65)†
Week 20*	0·52 (0·58)	0·76 (0·64)	0·88 (0·66)†
Week 26	0·57 (0·60)	0·73 (0·62)	0·85 (0·65)
Used walking aids			
Week 6	6 (16%)	11 (36%)	10 (32%)
Week 12	14 (40%)	12 (40%)	12 (47%)
Week 20	17 (49%)	14 (47%)	12 (47%)
Week 26	17 (49%)	17 (57%)	14 (53%)
Sickness impact profile‡			
Week 12§	36·8 (11·7)	31·1 (11·4)	26·9 (12·5)‖
Week 26	32·9 (12·0)	27·9 (13·1)	25·7 (12·7)
Nottingham health profile‡			
Week 12	14·5 (5·6)	10·4 (7·3)	9·4 (6·1)
Week 26	11·6 (7·9)	9·5 (5·9)	9·8 (8·1)
Frenchay activities index			
Week 26	8·2 (7·8)	10·9 (8·3)	13·7 (9·5)

*p<0·05 for difference among groups.
†p<0·05 for difference from control group.
‡High scores indicate poor status.
§p<0·05 for difference in improvement among groups.
‖p<0·05 for difference in improvement from control group.

Table 4: **Secondary outcomes**

Discussion

In this small but homogeneous group of stroke patients, leg rehabilitation training improved functional recovery in terms of ADL, walking ability, and walking speed, compared with a control condition in which the arm and leg were immobilised by means of an inflatable pressure splint. In addition, leg rehabilitation improved the health-related functional status. Arm rehabilitation training had a small but significant effect on the functional recovery of dexterity of the paretic arm. The experimental control of duration for attention and treatment goals, the compliance with treatment, and the masked assessments in this study support the conclusion that the observed differences in efficacy are due to greater intensity of leg and arm rehabilitation. The differences in efficacy were most pronounced within the first 12 weeks after stroke. From week 12 onwards, the differences in recovery patterns became smaller. These findings support early initiation of intensive stroke rehabilitation as an important feature of specialised stroke care.[2,25–27] Significant differences in primary outcomes between the arm-training and control groups were detectable only at 3 months after stroke, whereas differences between the leg-training and control groups were apparent at 6 weeks after stroke. The recovery patterns of arm function showed a slower improvement than those of leg function, as has been reported previously in patients with middle-cerebral-artery strokes.[18]

The small but significant effects of arm training on arm function in this study support the results of Feys and colleagues,[28] who reported significant interaction effects between time and group on the motor recovery of the paretic arm in a study comparing a sensorimotor stimulation programme for a period of 6 weeks with placebo treatment. Contrary to our findings, the effects did not generalise to an improvement in dexterity of the paretic arm.[28] We found, however, that leg rehabilitation training resulted in improved motor function and dexterity of the arm, compared with the control programme, despite the same intensity of arm rehabilitation. This finding may be due to the facilitation of arm function during gait training.[2] Alternatively, the apparent improvement may be related to the higher proportion of patients with some dexterity at baseline in the leg-training than in the arm-training and control groups.

Recovery in ADL was faster with leg rehabilitation than with arm rehabilitation or control, whereas we found no differences in ADL scores between the arm-training and control groups. This finding suggests that stroke patients compensate the loss of function in the paretic arm by using the non-paretic arm during ADL. In addition, it suggests that the Barthel index largely assesses mobility. However, the difference in recovery rate may also show that improvements in mobility are more easily established than improvements in dexterity, or that larger improvements in dexterity are needed before any detectable change or difference can be noted.

Several outcome measures of degree of disability showed no significant follow-up effects at 26 weeks after stroke, which suggests that intensity of leg and arm rehabilitation for patients with severe disability at onset should be continued for longer. We plan analyses of follow-up measurements at 9 months and 12 months after stroke.

In this study the Barthel-index score showed larger overall effect-sizes in the comparison between leg-training and control groups at 6 weeks and 12 weeks after stroke (Hedges's g 0·63 [SD 0·43] and 0·73 [0·43], respectively), than effect-sizes reported in a meta-analysis (0·28 [0·12]).[4] The larger summary effect-size in our study may be explained by a greater contrast in intensity of rehabilitation between experimental and control condition (since the paretic arm and leg were immobilised in the control group), the inclusion of a homogeneous subgroup of stroke patients according to specific neurological and functional selection criteria fit to receive an intensive rehabilitation programme,[25,29] or the inclusion of severely impaired and disabled stroke patients showing remarkable, but not maximum, improvement according to the Barthel index. The scaling properties of most assessment measures used in the study were, therefore, optimally used, and ceiling effects were limited.[30] Also, the rehabilitation programmes were founded on evidence-based physical and occupational therapy, irrespective of specific neurological treatment approach.[2] Before the start of the study, all participating therapists took a specially designed course on formulating task-specific goals for improving functional exercise therapy for the arm and leg and evidence-based practice.

The differences in efficacy between the groups in this study are small, but the effect on functional dependency of patients was greater. 20 weeks after stroke, only 35% of the patients in the control group were fully or nearly independent in ADL (Barthel-index scores $\geqslant$95%), compared with 43% and 62% of the arm-training and leg-training groups. 47% of the patients in the control group were able to walk independently on flat surfaces (or had better ability) compared with 64% and 72% in the arm-training and leg-training groups. The better walking performance can be explained to a certain extent by a difference in the prescription of aids such as canes and (knee)-ankle-foot orthosis within the first 12 weeks after stroke (table 3). This finding suggests that compensatory mechanisms contribute to the improvement of walking ability observed in the leg-training and arm-training groups. 21% of the patients in the control group achieved at 20 weeks after stroke some dexterity (arm test score 10 points or more) compared with more than 40% of the other groups. These findings correspond to the significant positive effects of leg rehabilitation training on the recovery observed in the domains related to physical health status 3 months after stroke.

A larger contrast in intensity of arm and leg rehabilitation than that achieved in this study might result in even larger differences in efficacy. However, ethical concerns about withholding of therapeutic exercises, and organisational constraints on the application of more intensive rehabilitation, precluded the use of a larger range of intensities. We believe that the use of an inflatable pressure splint as a control treatment was ethically justified in this study by the small effect sizes reported in studies that investigated an intensity-effect relation in rehabilitation of stroke patients.[4,5] No adverse effects of the application of the pressure splint for 30 min have been reported.[14] All patients in this study received therapy additional to the usual daily therapeutic input of 30 min one-to-one contact between therapist and patient.

An important limitation of this study is the generalisation of the reported effects to other stroke populations. However, recruitment of patients with the same stroke type, with respect to highly restricted lesional and functional categories, is extremely difficult. In addition, the division of arm and leg treatment is artificial, and outside the study the content of the treatment remains heterogeneous and mainly based on old-fashioned treatment concepts. Furthermore, differentiation between the functional improvement caused by rehabilitation and the effects of spontaneous neurological recovery is impossible.[25,26] ADL, walking ability, and dexterity 6 months after stroke could, to a certain extent, be accurately predicted within 2 weeks after stroke (the explained variance ranged from 42% for walking ability to 66% for dexterity of the paretic arm),[31] whereas the summary effect-sizes were small to moderate, suggesting that reported effects of intensive treatment are limited compared with the amount of improvement due to spontaneous neurological recovery. Another limitation of the study is the use of the Kruskal-Wallis test on repeated within-person measurements, which may have introduced false-positive results through the play of chance. For that reason, we also analysed the time series with the GEE model. In the GEE model, all data are tested simultaneously. The findings confirmed those obtained with the Kruskal-Wallis test.

Which processes bring about spontaneous neurological recovery and can they be enhanced by arm and leg rehabilitation? Possible mechanisms include: recovery of penumbral tissue around the infarcted area;[32] subcortical reorganisation by means of tissue repair caused by denervation supersensitivity, axonal growth, and synaptogenesis;[33] reduction of temporarily deactivated intact brain regions, remote from, but anatomically connected to the area of primary injury (deactivation of diaschisis),[34] including reinforcement of ipsilateral motor pathways such as thalamus, caudate, lentiform nuclei, and premotor cortex;[35] and behavioural compensations. The optimum selection of stroke patients capable of receiving early applied intensive rehabilitation, and the development of new rehabilitation strategies, require better understanding of mechanisms of recovery after stroke and motor relearning processes.

Contributors

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