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Research

Early intensive hand rehabilitation is not more effective than usual care plus one-to-one hand therapy in people with sub-acute spinal cord injury ('Hands On'): a randomised trial

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KEY WORDS

Spinal cord injury
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ABSTRACT

Question: What is the effect of adding an intensive task-specific hand-training program involving functional electrical stimulation to a combination of usual care plus three 15-minute sessions per week of one-to-one hand therapy in people with sub-acute tetraplegia? **Design:** A parallel group, randomised, controlled trial. Participants were randomly assigned (1:1) via a computer-generated concealed block randomisation procedure to either a control or experimental intervention. **Participants:** Seventy people with C2 to T1 motor complete or incomplete tetraplegia within 6 months of injury. Participants were recruited from seven spinal units in Australia and New Zealand. **Intervention:** Experimental participants received intensive training for one hand. Intensive training consisted of training with an instrumented exercise workstation in conjunction with functional electrical stimulation for 1 hour per day, 5 days per week for 8 weeks. Both groups received usual care and 15 minutes of one-to-one hand therapy three times per week without functional electrical stimulation. **Outcome measures:** The primary outcome was the modified Action Research Arm Test reflecting arm and hand function, which was assessed at the end of the intervention, that is, 11 weeks after randomisation. Secondary outcomes were measured at 11 and 26 weeks. **Results:** Sixty-six (94%) participants completed the post-intervention assessment and were included in the primary intention-to-treat analysis. The mean modified Action Research Arm Test score for experimental and control participants at the post-intervention assessment was 36.5 points (SD 16.0) and 33.2 points (SD 17.5), respectively, with an adjusted mean between-group difference of 0.9 points (95% CI –4.1 to 5.9). **Conclusion:** Adding an intensive task-specific hand-training program involving functional electrical stimulation to a combination of usual care plus three 15-minute sessions per week of one-to-one hand therapy does not improve hand function in people with sub-acute tetraplegia. **Registration:** Australian and New Zealand Trial Registry ACTRN12609000695202 and ClinicalTrials.gov NCT01086930. **[Harvey LA, Dunlop SA, Churilov L, Galea MP, Spinal Cord Injury Physical Activity (SCIPA) Hands On Trial Collaborators (2016) Early intensive hand rehabilitation is not more effective than usual care plus one-to-one hand therapy in people with sub-acute spinal cord injury ('Hands On'): a randomised trial. *Journal of Physiotherapy* 62: 88–95]**

Introduction

People with tetraplegia consider loss of hand function to be more debilitating and limiting on quality of life than any other consequence of spinal cord injury (SCI), including the inability to walk or control bladder and bowel function.[1] Research attention in recent years has therefore appropriately focused on identifying possible ways of improving the hand function of people with tetraplegia. Intensive task-specific training with sensory or functional electrical stimulation (FES) is one of many interventions that has received research attention, with initial promising results, but it has not been examined within a large, high-quality clinical trial.[2–4] It has been hypothesised that intensive task-specific training with FES improves neural recovery and motor control following SCI. The combination of therapies provides both sensory input from the periphery and motor input from the sensorimotor cortex onto the damaged spinal cord. It is believed that neural bombardment from these two sources may promote neural

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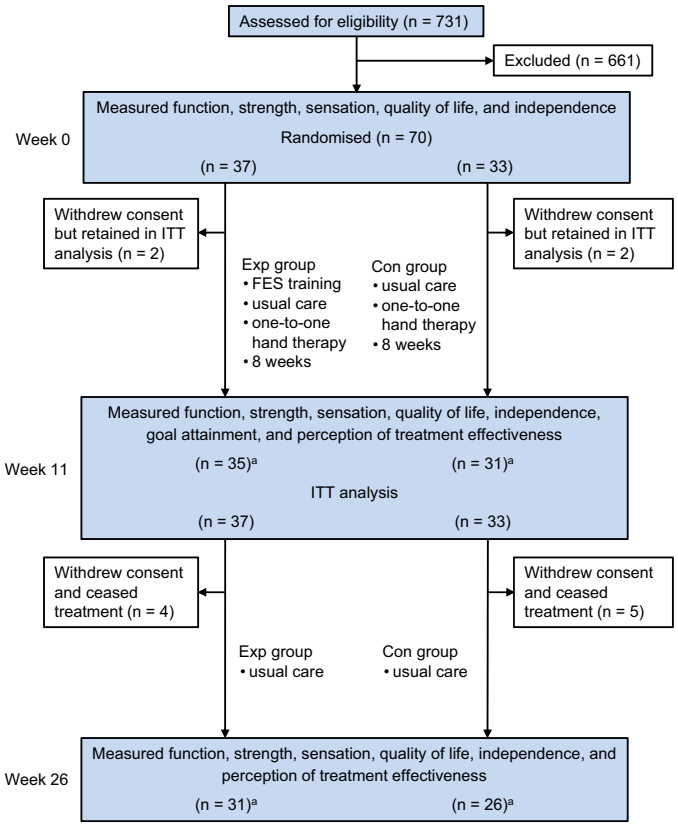
plasticity and provide the critical stimulus required to elicit neurophysiologic and structural re-organisation of the relevant pathways.[5]

One of the difficulties with providing intensive task-specific practice is that training is not always well tolerated by participants because repeatedly practising the same movement outside a functional context can be tedious. Increasingly, technology has been used to try to overcome this barrier (eg, commercially available, computerised video games that respond to body motion are used to practise balance in people with stroke).[6] For the present trial, a similar concept was wanted for the hand, but since there were no appropriate motion-controlled video devices or games for training hand function in people with tetraplegia, we used FES and an instrumented exercise workstation incorporating several types of manipulanda connected to a computer[a]. Participants triggered FES to drive the different types of hand grasps (eg, pinch, squeeze, grasp, twist, lift, push or pull) required for playing the computer games.[7] The FES was triggered with a behind-the-ear bluetooth device[a] that is sensitive to tooth clicks. The technology thus provided a way of encouraging patients to perform large numbers of different hand movements within a dynamic environment. There is preliminary evidence from five studies to suggest that this technology may be therapeutic.[3,4,8–10] However, all these studies are small and have methodological flaws exposing them to bias.

Therefore, the questions for this parallel group, randomised, controlled trial were:

1. Is adding an intensive hand-training program, with an instrumented exercise workstation and functional electrical stimulation, to usual care more effective than usual care alone in people with sub-acute tetraplegia?
2. What are the possible benefits on muscle strength, sensation, function and quality of life?



ITT = intention-to-treat; con = control, exp = experimental

Figure 1. CONSORT flow chart indicating the number of participants screened, randomised and included in intention-to-treat analysis ([a] some participants did not complete all assessments. See Table 2 for details).

Method

Design

A multi-centre, randomised, assessor-blinded, phase-3 trial was undertaken on inpatients at seven SCI units in Australia and New Zealand. Participants were randomised to the experimental or control group. Experimental participants received an intensive 8-week hand-training program for the target hand. Participant recruitment commenced 23 November 2009 and finished 31 December 2013. The trial protocol (including full details of the study rationale, design and statistical analysis) was published and is available online.[11] The trial was managed by a professional clinical trial management company[b] and overseen by an independent data safety monitoring committee.

Participants, therapists and centres

Seventy participants with sub-acute tetraplegia undergoing inpatient rehabilitation in one of the seven participating SCI units were recruited from a consecutive sample of admissions (Figure 1). The hospital therapists screened participants for suitability and then enrolled them in the study. These therapists provided usual care to all participants but were not otherwise involved in the trial. Instead, specifically designated trial therapists administered the intervention to the experimental participants. One hand of each participant was identified as the target hand according to the criteria below. In situations where both hands met the inclusion criteria, the hospital therapist selected the hand deemed most likely to benefit from intensive training.

Participants were included if they: were 16 years or older and had sustained a motor complete or incomplete SCI at the neurological level of C2 to T1 within the preceding 6 months; were likely to remain in hospital for 12 weeks; had a reduced ability to grasp with the target hand, as determined by the clinical judgement of the hospital therapist; and were able to tolerate sufficient FES to enable the target hand to grasp and release. Participants were excluded if they had a pre-existing injury to the hand or upper limb or any condition that precluded use of the exercise workstation and FES (the full inclusion and exclusion criteria are detailed in the protocol).[11]

The trial statistician used a computer random number generator to create the randomisation schedule, which was stratified by site and the baseline score of the modified Action Research Arm Test (m-ARAT; ≤ 21 versus > 21) using permuted blocks of random sizes. To ensure concealment, block sizes were undisclosed. An independent researcher with no clinical involvement in the trial randomly assigned the participants to either the control or experimental group with a 1:1 ratio. After completion of baseline assessments, randomisation was performed by an administrator who was independent of the recruitment process and located off site[b] to ensure concealment. A participant was considered to have entered the trial once his/her randomisation was allocated.

Trial and hospital therapists and participants were unblinded, but the assessors and statisticians performing the analyses were blinded. The success of assessor blinding was checked by asking assessors whether they had been unblinded.

Intervention

Experimental participants received training directed at the target hand five times per week for 8 weeks commencing 3 weeks after randomisation. The 3-week delay in commencing the intensive training was required to allow time for the delivery of the FES garments for the experimental participants. The training consisted of an intensive task-specific hand-training program provided through an instrumented exercise workstation[a] in

conjunction with FES. The hand activities involved playing computer games while practising functional tasks using different manipulanda (including reaching, grasping, manipulating, pulling, rotating and releasing). The exercises and computer games were progressed so that as hand function improved, more difficult hand exercises and games were introduced. Each training session lasted 1 hour and participants were required to use the instrumented exercise workstation and FES as much as possible during this time. A trial therapist directly supervised all sessions, progressed the difficulty of the games, provided encouragement, ensured that participants focused on the quality of their grasp, determined the FES stimulation parameters and provided feedback about performance. The trial therapsits were trained and provided with a written protocol. They recorded details of each training session using standardised recording documents.

The FES was provided through 5-cm diameter electrodes. The electrodes were incorporated into a custom-made garment[a] for each participant, according to the optimal stimulation points and the size and side (left versus right) of the hand. The FES was administered to any two stimulatable key muscles of the hand, including the flexors and extensors of the wrist, fingers and thumb. Participants triggered it by clicking their teeth; this stimulated the hand to open or close, allowing participants to grasp or release the various manipulanda on the workstation independent of assistance from the trial therapists. The intensity of the FES stimulation was determined by the trial therapist to ensure strong contractions of the stimulated muscles, as tolerated by the participant. It was not increased beyond 63 mA (see protocol for full stimulation details).[11]

If participants missed any treatments during the intervention period, additional sessions were offered to them on weekends, at another time during the week or during an optional additional week at the end of the intervention period.

Control participants did not receive the intensive task-specific hand-training program with the instrumented exercise workstation and FES. Instead, both control and experimental participants continued to receive usual care. This included typical inpatient rehabilitation consisting of physiotherapy as well as vocational, recreational and occupational therapy (full details are described in the protocol).[11] In addition, over the 8-week intervention period, both control and experimental participants received at least three 15-minute sessions per week of one-to-one hand therapy for the target hand. This hand therapy was provided by the hospital therapists and individualised to the needs of participants. It consisted of practising functional hand activities and did not involve FES. The hospital therapists used standardised forms to record the duration and type of hand therapy provided to the target hand.

At the end of the intervention period, both experimental and control participants continued to receive usual care by the hospital therapists (patients were discharged between 3 and 9 months after randomisation). Usual care over this period was not standardised or restricted in any way. The only restriction was that neither experimental nor control participants could use the instrumented exercise workstation. In addition, no participant was permitted to practise any aspect of the tests comprising the outcome measures. They could, however, practise activities similar to those included in the hand tests as part of functional training.

Outcome measures

All measurements were taken at baseline, at 11 weeks (ie, at the end of the intervention period) and at 26 weeks after randomisation, except two outcomes that were only taken at 11 weeks: the Goal Attainment Scale and the Participant Perception of Treatment Effectiveness. Most participants were discharged prior to the 26-week assessment and were required to come back to hospital for this assessment. The original protocol included a 12-month follow-up assessment, but the protocol was modified and this final assessment was removed halfway through the trial to reduce participant burden and encourage recruitment.

The primary outcome was the m-ARAT of the target hand, which was measured at the end of the intervention period (ie, 11 weeks after randomisation). The m-ARAT is a standardised measure of unilateral hand and upper limb function. It consists of four sub-tests, including grasp, grip, pinch and gross movement. Participants were required to perform every task in each subtest;[12] all tasks were scored on a scale from 0 to 3 points. Scores were summed to give a total score, where a larger number reflected better hand function.

The m-ARAT was also measured at 26 weeks as a secondary outcome measure. All other outcomes, which were prospectively categorised as secondary or tertiary, are described in detail in the protocol. Each is summarised below:

The Summed Upper Limb Strength of the Graded and Redefined Assessment of Strength, Sensibility and Prehension[13] was measured at the end of the intervention and at 26 weeks; a higher score indicated better strength.

The Sensory Score of the International Standard for Neurological Classification of Spinal Cord Injury[14] for the target hand was measured at the end of the intervention and at 26 weeks; a higher score indicated better sensation.

The AsTex® Sensory Test[15] was measured at the end of the intervention and at 26 weeks. This measured texture discrimination; a lower score indicated better texture discrimination.

The AuSpinal Test of Hand Function[16] was measured at the end of the intervention and at 26 weeks; a higher score reflected better hand function.

The Capabilities of Upper Extremity (CUE)[17] of the target hand was administered at the end of the intervention and at 26 weeks; a higher score reflected better upper limb function.

The Assessment of Quality of Life-8 (AQoL-8)[18] was administered at the end of the intervention and at 26 weeks; a score of 1 reflected perfect health.

The Health Utilities Index Mark 3 (HUI3)[19] was administered at the end of the intervention and at 26 weeks. This was scored between –0·36 and 1; a higher score reflected better quality of life.

The Self-Care Subscale of the Spinal Cord Independence Measure (SCIM)[20] was administered post intervention and at 26 weeks; a higher score reflected more independence.

The Goal Attainment Scale (GAS)[21] was scored at the end of the intervention. This was scored from –2 to +2, where +2 reflected attainment of goals ‘a lot better’ than expected and –2 reflected attainment of goals ‘a lot worse’ than expected.

The Participant Perception of Treatment Effectiveness[22] was scored post intervention. This was scored from –7 to +7, where a score of +7 reflected hand function that was ‘a very great deal better’ and –7 reflected hand function that was ‘a very great deal worse’ than at the time of baseline assessment.

At the post-intervention assessment, all experimental participants were asked by the blinded assessors to rate on a 10-point category rating scale their perceptions about the convenience of the hand training. One end was anchored with the words ‘completely inconvenient’ and the other end with the words ‘very convenient’; a higher score reflected more convenience. This was used to gauge the burden of the experimental intervention on participants. It was not used as an outcome measure. All adverse events, whether related or unrelated to the intervention, were collected over the course of the study.

Data analyses

This study was powered to detect a between-group minimum worthwhile treatment effect on m-ARAT scores of 5.7 points at the post-intervention assessment (SD 14 points). A sample size of 78 participants (ie, 39 per group) was estimated to provide 80% power to detect a significant intervention effect (two-sided, $p = 0.05$) using an ANCOVA model that included: baseline m-ARAT score as a covariate, a correlation between baseline and post-intervention m-ARAT scores of at least 0.8 and an adjustment of 10% to allow for dropout rate. These data were based on the results

of a similar pilot study with chronic SCI participants conducted in Canada (personal communication; Prochazka A, 2009, University of Alberta).

Analyses were performed by a blinded and independent statistician according to a pre-specified statistical analysis plan on an intention-to-treat basis,[23] with an assumption for the main analysis that data were missing at random. The sensitivity of the results to plausible departures from the missing-at-random assumption as a part of intention-to-treat analysis was examined using both a selection model (modelling of the missing data mechanism) and a pattern mixture model (modelling of the differences between missing and observed data). Assumptions about the missing data were expressed via a parameter that measures the degree of departure from the missing-at-random assumption. The results were graphed over a range of assumptions.

Analyses of continuous data (m-ARAT, Summed Upper Limb Strength, Sensory score, AsTex Test, AuSpinal, CUE, AQoL-8, HUI3 and SCIM) were conducted using ANCOVA models that included treatment group and the baseline scores as a covariate. The analyses were implemented using multiple linear regression. The corresponding estimates of the treatment effect were calculated as adjusted mean differences with corresponding 95% CIs. Heterogeneity of the treatment effect across multiple participating centres was tested using a corresponding random-effect linear regression model with site as a random effect.

The GAS data were analysed using Wilcoxon-Mann-Whitney rank sum tests to determine the difference between the two groups in GAS across the full ordinal scale. Two analyses were performed: one for participants' first goal and one for participants' second goal. The effect size was presented as a Wilcoxon-Mann-Whitney generalised odds ratio with corresponding 95% CI.[24] In addition, the difference between the two groups in the proportions of patients whose level of achievements were no worse than expected were analysed by dichotomising the GAS scale into 'no worse than expected' (categories of 0, +1 and +2 on the ordinal GAS scale) versus 'worse than expected' (categories of −1 and −2 on the ordinal GAS scale) and using Fisher's exact test. The corresponding effect sizes were calculated as risk differences with corresponding 95% CI.

The Participant Perception of Treatment Effectiveness was analysed in two ways. Firstly, the difference between the two groups in the proportions of participants who felt better/worse was analysed by dichotomising responses into 'feeling better' versus 'feeling worse' and using Fisher's exact test with corresponding effect size presented as risk difference with corresponding 95% CI. Secondly, the difference between the two groups in scores across the full ordinal scale was analysed by transferring responses into a single ordinal scale ranging from −7 to +7 points. This was analysed using a Wilcoxon-Mann-Whitney rank sum test with the corresponding effect size presented as Wilcoxon-Mann-Whitney generalised odds ratio with corresponding 95% CI.

A secondary pre-specified per-protocol analysis was performed to determine the possible effect of trial adherence on the primary outcome (post-intervention m-ARAT). This dataset only comprised participants who adhered to all aspects of the protocol and received at least 80% of training sessions. All analyses were performed using commercially available software[c].

Results

Flow of participants through the trial

A total of 731 participants that were admitted with tetraplegia to the seven SCI units between 23 November 2009 and 31 December 2013 were screened for inclusion. Of these, 70 were eligible, agreed to participate and were subsequently randomised (Figure 1 and Table 1).

Compliance with the trial protocol

The trial was terminated after randomisation of 70 participants (rather than the intended 78) because recruitment was taking longer than expected and the funding was limited to 5 years. This change to the protocol was made without any knowledge of the results.

Compliance with the study interventions was excellent. The protocol dictated that experimental participants receive 40 1-hour training sessions over 8 weeks with trial therapists, commencing 3 weeks after randomisation. In reality, they received a median of 40 training sessions (IQR 40 to 42) over a median of 8 weeks (IQR 7.6 to 8.6). Only three participants did not receive at least 80% of the 40 interventions. The median length of each training session was 57 minutes (IQR 54 to 59). Control and experimental participants received a mean of 40 (SD 22) and 38 (SD 27) 15-minute hand therapy sessions for the target hand with hospital therapists over the 8-week intervention period, respectively.

Data were missing on four participants at the post-intervention assessment and on 13 participants at the 26-week assessments. Most missing data were due to participants withdrawing consent or not being able to return to the hospital for assessment after discharge. In addition, some participants occasionally declined to complete some measures for various reasons (see Tables 2 to 4 for the exact number of participants who completed each outcome measure). Assessors were inadvertently unblinded for two assessments.

Table 1
Baseline characteristics of the participants included in the intention-to-treat analysis.

Characteristic	Exp (n = 37)	Con (n = 33)
Gender, n male (%)	33 (89)	28 (85)
Age *(y)*, median (IQR)	29 (23 to 45)	29 (22 to 53)
Time since injury *(d)*, median (IQR)	81 (45 to 110)	62 (47 to 87)
ASIA Impairment Scale, n (%)		
A	14 (38)	10 (30)
B	7 (19)	5 (15)
C	3 (8)	9 (27)
D	13 (35)	9 (27)
Target hand, n (%)		
left	16 (43)	12 (36)
right	21 (57)	21 (64)
Upper limb ASIA motor score for both limbs *(0 to 50)*, median (IQR)	25 (17 to 31)	24 (17 to 31)
Upper limb ASIA motor score for limb of target hand *(0 to 25)*, median (IQR)		
upper limb right	12 (8 to 16)	12 (8 to 15)
upper limb left	13 (9 to 16)	12 (8 to 17)
Total ASIA sensation *(0 to 112)*, median (IQR)		
pin prick	26 (20 to 70)	28 (18 to 42)
light touch	49 (29 to 91)	54 (27 to 82)

ASIA = American Spinal Injury Association, con = control, exp = experimental.

Table 2
Results of the intention-to-treat analysis for the primary and some secondary outcomes at 11 weeks (ie, immediately after intervention) and 26 weeks after randomisation.

Outcomes	Groups						Adjusted between-group difference	
	Week 0		Week 11		Week 26		Week 11	Week 26
	Exp (n = 37)	Con (n = 33)	Exp (n = 35)	Con (n = 31)	Exp (n = 31)	Con (n = 26)	Exp minus Con (95% CI)	Exp minus Con (95% CI)
m-ARAT, *(0 to 57)*	24.8 (15.7)	21.2 (15.7)	36.5 (16.0)	33.2 (17.5)	38.7 (17.6)	33.4 (17.4)	0.9 (−4.1 to 5.9)	3.1 (−3.2 to 9.5)
Summed upper limb strength, *(0 to 50)*	21.1 (10.6)	19.2 (8.2)	24.9 (12.5)	23.0 (9.9)	29.5 (13.8) (n = 30)	24.8 (11.0) (n = 25)	0.3 (−2.9 to 3.4)	2.6 (−1.6 to 6.8)
Sensory score, *(0 to 32)*	22.6 (5.8)	22.8 (6.2)	22.7 (6.6)	23.3 (5.3)	20.7 (9.7)	22.6 (6.8)	−0.4 (−2.7 to 1.9)	−1.8 (−5.7 to 2.1)
AsTex index finger, *(mm)*	1.07 (0.76) (n = 35)	0.77 (0.68)	0.66 (0.57)	0.65 (0.48) (n = 30)	0.79 (0.62) (n = 28)	0.62 (0.38) (n = 25)	−0.10 (−0.36 to 0.11)	0.04 (−0.21 to 0.29)
AsTex thumb, *(mm)*	0.87 (0.71)	0.63 (0.58)	0.73 (0.64)	0.58 (0.32) (n = 29)	0.76 (0.62) (n = 30)	0.65 (0.47) (n = 25)	0.02 (−0.18 to 0.23)	−0.02 (−0.23 to 0.19)
AusSpinal, *(0 to 86)*	57.3 (21.7)	52.5 (25.3)	70.8 (20.3)	66.1 (20.5)	70.0 (25.5)	66.7 (22.5)	2.8 (−3.0 to 8.6)	0.8 (−9.0 to 10.5)
CUE, *(0 to 105)*	58.5 (16.3)	54.3 (15.1)	70.3 (16.9)	66.2 (18.8)	69.3 (22.8)	66.2 (18.4)	1.5 (−6.3 to 9.3)	−0.4 (−10.6 to 9.8)
AQoL-8, *(0 to 1)*	0.23 (0.17)	0.24 (0.20)	0.37 (0.24)	0.30 (0.23)	0.41 (0.28) (n = 30)	0.37 (0.25)	0.07 (−0.04 to 0.19)	0.04 (−0.10 to 0.18)
HUI3, *(0 to 1)*	0.18 (0.17)	0.13 (0.15)	0.31 (0.26)	0.22 (0.22) (n = 29)	0.35 (0.31) (n = 30)	0.28 (0.27) (n = 25)	0.02 (−0.07 to 0.12)	0.01 (−0.12 to 0.14)
SCIM, *(0 to 20)*	5.5 (4.6)	4.7 (3.4)	10.1 (5.7)	8.3 (5.9)	10.9 (6.6)	9.5 (7.1)	1.3 (−0.8 to 3.4)	0.8 (−2.1 to 3.8)

AQoL-8 = Assessment of Quality of Life-8, Con = control, CUE = Capabilities of Upper Extremity test, Exp = experimental, HUI3 = Health Utilities Index Mark 3, m-ARAT = modified Action Research Arm Test, SCIM = Spinal Cord Independence Measure (Self-Care Subscale).
Shaded cell = primary outcome.

Participants

The median age of participants was 29 years (IQR 22 to 49) and the median time since injury was 68 days (IQR 45 to 107). The neurological levels of participants' lesions were C1 (n = 2, 3%), C2 (n = 2, 3%), C3 (n = 4, 6%), C4 (n = 38, 54%), C5 (n = 9, 13%), C6 (n = 12, 17%) and C7 (n = 3, 4%). The inclusion of two people with a C1 neurological level was because at the time of inclusion these people had very unusual sensory loss at C2 that was not consistent with their other motor and sensory losses. The examiners attributed this to age in one case and drowsiness in the other. They were both therefore deemed eligible for the trial. However, the present study is reported exactly as per the American Spinal Injury Association (ASIA) charts and does not take these extenuating circumstances into consideration. The ASIA Impairment Scale classifications were AIS A (n = 24, 34%), AIS B (n = 13, 19%), AIS C (n = 11, 16%) and AIS D (n = 22, 31%). There were no clear between-group differences at baseline (Table 1 and the first two columns of Table 2).

Effect of intervention

Primary outcome

The adjusted mean between-group difference for the m-ARAT immediately after the intervention was 0.9 points (95% CI −4.1 to 5.9) favouring the experimental group (Table 2, Figure 2). The result of the per-protocol analyses was very similar (0.9 points, 95% CI −4.5 to 6.4). The sensitivity analysis testing the robustness of the assumptions about missing data indicated very little effect of these assumptions on the primary outcome. There was no statistically significant heterogeneity in treatment effect between the participating centres.

Secondary outcomes

There were no statistically significant mean between-group differences for any of the secondary analyses, including participants' perceptions of treatment effectiveness (Tables 2 to 4). Individual participant data are presented in Table 5 (see eAddenda for Table 5). Experimental participants rated the convenience of the interventions with a median rating of 8 points (IQR 5 to 9), where a score of 10 indicated 'very convenient'.

Twenty serious adverse events (10 in each group) and 738 adverse events were recorded over the 26-week period from randomisation in all participants, but none were related to the intervention.

Discussion

The results of this trial indicate no benefit of adding an intensive task-specific hand-training program involving FES to a combination of usual care plus three 15-minute sessions per week of one-to-one hand therapy in people with sub-acute tetraplegia. The treatment estimate of the primary outcome (post-intervention m-ARAT) was precise, indicating that although the trial was terminated early, the sample size was adequate. The upper end of the 95% CI associated with the mean between-group difference was 5.9 points, suggesting that if the trial was repeated, there would be very little possibility of finding a treatment effect in excess of the pre-determined minimally worthwhile treatment effect of 5.7 points. The results of the secondary analyses and participants' perceptions about the benefits of the treatment also pointed to no between-group differences, although some estimates of treatment effects were imprecise.

This trial is important because it is one of the largest non-pharmaceutical trials conducted in people with SCI and the largest trial involving any type of hand intervention for people with tetraplegia. The trial was conducted according to Good Clinical Practice standards,[25] which is uncommon for non-pharmaceutical trials involving people with SCI. Trials involving training are

Table 3
Results of the intention-to-treat analysis for the Goal Attainment Score and the dichotomised[a] Perception of Treatment Effectiveness score at 11 weeks (ie, immediately after intervention) and 26 weeks after randomisation.

Outcomes	Groups				Generalised odds ratio (95% CI)	Risk difference (95% CI)	
	Week 11		Week 26		Week 11	Week 11	Week 26
	Exp (n = 35)	Con (n = 31)	Exp (n = 30)	Con (n = 26)	Exp relative to Con	Exp relative to Con	Exp relative to Con
Goal Attainment Score not worse than expected, n (%)							
goal 1	27 (79) (n = 34)	23 (74)			1.2 (0.7 to 2.1)	0.1 (–0.2 to 0.3)	
goal 2	24 (71) (n = 34)	19 (61)			1.1 (0.6 to 1.9)	0.1 (–0.1 to 0.3)	
Perception of Treatment Effectiveness score[a], n (%)							
better	34 (97)	30 (97)	30 (100)	25 (96)		0.0 (–0.1 to 0.1)	0.04 (–0.0 to 0.1)

Con = control, exp = experimental.
[a] Dichotomised as better or worse.

Table 4
Results of the intention-to-treat analysis for the Perception of Treatment Effectiveness scores at 11 weeks (ie, immediately after intervention) and 26 weeks after randomisation.

Outcomes	Groups				Generalised odds ratio (95% CI)	
	Week 11		Week 26		Week 11	Week 26
	Exp (n = 35)	Con (n = 31)	Exp (n = 30)	Con (n = 24)	Exp relative to Con	Exp relative to Con
Perception of Treatment Effectiveness scores, n (%)					1.4 (0.8 to 2.5)	1.2 (0.7 to 2.3)
a little worse	1 (3)	0 (0)	0 (0)	1 (4)		
almost the same (if worse)	0 (0)	1 (3)	0 (0)	0 (0)		
almost the same (if better)	4 (11)	2 (6)	4 (13)	3 (13)		
a little better	6 (17)	6 (19)	2 (7)	2 (8)		
somewhat better	3 (9)	7 (23)	2 (7)	3 (13)		
moderately better	1 (3)	6 (19)	4 (13)	2 (8)		
a good deal better	12 (34)	6 (19)	6 (20)	5 (21)		
a great deal better	6 (17)	3 (10)	7 (23)	5 (21)		
a very great deal better	2 (6)	0 (0)	5 (17)	3 (13)		

Con = control, exp = experimental.

notoriously difficult to complete because they require the administration of complex interventions over an extended period of time. For example, experimental participants required 40 hours of training with the instrumented exercise workstation and FES. These training sessions required direct supervision from a trial therapist. The training was often difficult to deliver because of participant illness, staff shortages and equipment failure. In addition, it was often difficult to find 1 hour during a participant's day that was not already scheduled for some other type of therapy (eg, vocational training, education, mobility training or hydrotherapy). Regardless, all but three participants received 40 treatments. Sometimes, however, more than one treatment was provided per day to meet the target of 40 treatments. More than 1 hour a day of training may have compromised the effectiveness of the intervention because the hand training required considerable concentration and co-operation from participants.

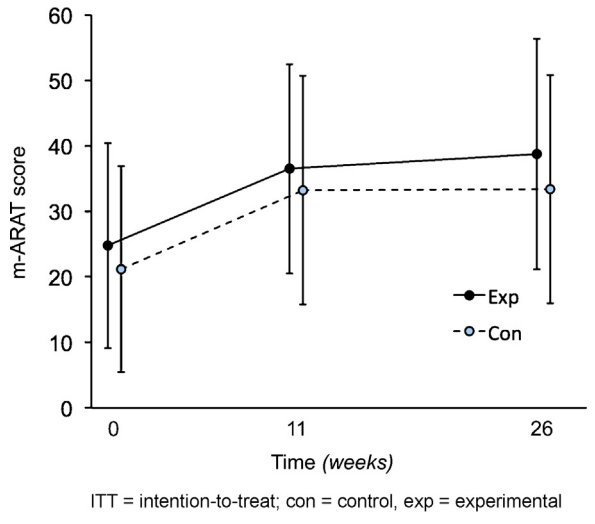


Figure 2. m-ARAT (/57 points) results for experimental and control groups at baseline (week 0), after the intervention (11 weeks) and at follow-up (26 weeks).

The results of this trial are also important because they conflict with the results of all other trials involving hand training in people with tetraplegia. Other trials have examined hand training with FES (versus hand training alone[2] or no intervention[3,8,9]) or FES and biofeedback (versus usual care[10]) or repetitive practice on a workstation[a] with FES (versus usual care[4]). All have reported therapeutic effects. However, these trials were small, with methodological flaws. For example, the median PEDro score[26] of these trials is 3.5/10 (IQR 3 to 4) and few trials blinded assessors or concealed allocation, whereas the PEDro score of the present study was 8/10. In addition, none of those trials was prospectively registered nor had an accompanying protocol. All these design weaknesses increase susceptibility to bias and, in the light of our starkly different findings, raise questions about the robustness of the results of those studies. This should prompt researchers and clinicians to re-examine some widely held assumptions about the effectiveness of repetitive practice with FES. The idea that recovery and return of hand function are not necessarily influenced by intensive practice, as has been assumed, may need to be entertained. But of course, the contrast between the present results and those of all previous trials may not reflect bias. Instead, it may point to some fundamental difference between the present trial and previous trials. For example, past trials have solely focused on people with chronic SCI, while the present trial was restricted to people with sub-acute SCI. Perhaps those with chronic SCI respond better to FES-based intervention than those with sub-acute SCI. In addition, the present control and experimental participants received 40 and 38 sessions of individualised one-to-one hand therapy for the target hand plus usual care, respectively. This additional hand therapy may have rendered the FES-based hand training for the experimental participants redundant.

It is possible that the training was ineffective because there was insufficient opportunity to individualise training. While the exercise workstation provided practice with different manipulanda,

the FES stimulated a gross grasp and release. Perhaps participants would have benefitted from practice of isolated finger and thumb movements as well as practice of various hand grasps in many different contexts. Alternatively, perhaps the games encouraged participants to rely on the FES and perform the hand activities quickly and without care. Perhaps participants needed to practise slowly with maximal voluntary effort and focused concentration. It is also possible that contamination diluted the contrast between the two groups. This may have occurred if control participants practised hand movements and grasps each day outside formal therapy in response to the trial or if the hospital therapists inadvertently provided more attention to control participants. The only way that this could have been safeguarded against these factors was to blind the participants and the hospital therapists, but this was not possible because of the nature of the intervention.

This trial did not explore other possible therapeutic benefits of FES. For example, studies in the lower limb of people with SCI provided initial evidence that FES helps prevent atrophy and maintains stimulated strength of paralysed muscles.[27,28] Recent evidence has also suggested that FES maintains the excitability of peripheral nerves affected by SCI.[29,30] It is argued that all of these therapeutic effects may be important for future recovery,[31] although these claims are yet to be verified in high-quality clinical trials.

The findings of the present study are notable because it is believed that repetitive task-specific practice with FES will lead to improved hand function in people with tetraplegia. The results of this study challenge these beliefs and indicate that an 8-week intensive hand-training program with FES in people with recent SCI does not provide added benefit over and above the combination of usual care and three 15-minute hand therapy sessions per week. While it is tempting to suggest that a trial with an even more intensive training regimen is now required, it is difficult to know whether it is realistic to provide an even more intensive hand-training program than already provided in this trial. One hour a day is a considerable time commitment for people with recently acquired tetraplegia undergoing rehabilitation because they invariably have busy schedules with many skills to learn and therapies to attend. However, future trials are required to clarify other possible therapeutic effects of FES and the effects of intensive practice provided in different ways. Nonetheless, the results of this study indicate that adding an intensive task-specific hand-training program involving FES to a combination of usual care plus three 15-minute sessions per week of one-to-one hand therapy does not improve hand function in people with sub-acute SCI.

What is already known on this topic: Loss of hand function is a very debilitating consequence of tetraplegia after spinal cord injury. The use of functional electrical stimulation triggered by tooth clicks at a workstation with a range of hand grasp tasks allows patients to independently undertake intensive task-specific hand rehabilitation.

What this study adds: Adding an intensive task-specific hand-training program involving functional electrical stimulation to a combination of usual care plus three 15-minute sessions per week of one-to-one hand therapy does not improve hand function in people with sub-acute tetraplegia.

Footnotes: [a]Rehabtronics Inc, Edmonton, Canada. [b]Neuroscience Trials Australia, Melbourne, Australia. [c]Stata IC 13 statistical software, StataCorp, College Station, USA.

eAddenda: Table 5 can be found online at doi:10.1016/j.jphys.2016.02.013

Ethics approval: Ethical approval was obtained from the University of Melbourne (HREC 0932764.1) and the Human Research Ethics Committee at each site. All participants were provided with an approved participant information sheet and signed a consent form before data collection began.

Competing interests: The authors declare no competing interests, however an associate investigator on the original funding application (but not on this publication) has commercial interests in the instrumented exercise workstation and FES technology used as part of this trial. MPG has a commercial interest in the AsTex®.

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