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ORIGINAL ARTICLE

Effects of intense exercise in chronic spinal cord injury

ET Harness[1], N Yozbatiran[2,3], SC Cramer[2,3]

[1]Project Walk Spinal Cord Injury Recovery, Department of Research and Development, Carlsbad, CA, USA; [2]Department of Neurology, University of California, Irvine, CA, USA and [3]Department of Anatomy and Neurobiology, and the Reeve-Irvine Research Center, University of California, Irvine, CA, USA

Background: Exercise has beneficial effects on muscle and motor function after spinal cord injury (SCI). Little is known regarding effects of prolonged intense exercise (IE) in humans with chronic SCI.
Design: Prospective, non-randomized, controlled observational study. The intervention was either a multimodal IE program ($n = 21$) or a control (CTL) intervention consisting of self-regulated exercise ($n = 8$).
Objective: Measure sensorimotor function over 6 months in relation to an IE program.
Setting: Single outpatient center.
Subjects: Subjects with chronic SCI ($n = 29$ total), mainly ASIA Impairment Scale A and B, injury levels C4-T11.
Results: Baseline neurological assessments (for example, ASIA motor score, 39 ± 3 vs 42 ± 5, IE vs CTL, $P > 0.5$, mean ± s.e.m.) did not differ between the two groups. During the 6 months, IE subjects averaged 7.3 ± 0.7 h per week exercise, not significantly different from CTL subjects (5.2 ± 1.3 h per week, $P > 0.1$). However, after 6 months, IE subjects showed significantly greater motor gains than CTL subjects in the main outcome measure, ASIA motor score (change of 4.8 ± 1.0 vs -0.1 ± 0.5 points, $P = 0.0001$). The main outcome measure was calculated by ASIA motor score. These IE subject ASIA motor gains correlated with number of exercise hours per week ($r = 0.53$, $P < 0.02$), and with type of specific IE components, particularly load bearing.
Conclusions: Multimodal IE can significantly improve motor function in subjects with chronic SCI. An organized program may provide greater motor benefits than a self-regulated program; load bearing might be of particular value. IE might have therapeutic value in chronic SCI, and as an adjunct to other restorative therapies.

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Introduction

Spinal cord injury is a common source of chronic disability and is accompanied by a host of health-related issues, many of which are directly related to loss of muscle and related motor functions. This decrease in motor function has been shown to contribute significantly to the cost of care and treatment of people with spinal cord injury.[1] Much of this cost is related to increases in cardiovascular, respiratory and metabolic problems associated with this decrease in activity.[2] Therefore, it may be advantageous to investigate interventions that promote recovery of muscle and motoric functions in subjects with chronic SCI. The current study examined this issue by measuring the effects of an extended course of intense exercise (IE).

Exercise might also have great potential as an adjunct therapy to restorative interventions such as pharmacological and cell-based therapies, as behavioral experience is critical to deriving maximum therapeutic gains.[3–5] In this regard, the specific content or type of physical activity might, therefore, be important. For example, Grasso *et al.*[6] found that training subjects in forward stepping did not translate into proficiency in backward stepping or stepping in place. To date most human studies examining activity-based interventions to promote recovery of function have focused on a singular modality, mainly body weight-supported gait training[7,8] or functional electrical stimulation.[9,10] A few studies have looked at combining the two.[11,12] We are not aware of any studies of human subjects with chronic SCI that have examined the effects of an exercise program that combines multiple therapeutic modalities; this is the focus of the current study.

The primary aim of the current study was to measure effects of a multimodal IE program on motor status in

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Correspondence: Professor SC Cramer, Department of Neurology, University of California, Irvine Medical Center, Building 53, Room 203, Mail code 4280, Orange, Irvine, CA 92868-4280, USA.
E-mail: scramer@uci.edu

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human subjects with complete or incomplete chronic SCI. Secondary aims compared these effects with a non-randomized control group, each of whom dictated their own activity level; examined effects on a wider range of outcome measures; and explored which exercise components accounted for observed gains. The main study hypotheses were that 6 months of IE would improve ASIA motor scores, that this improvement would be greater than that seen in controls, and that the extent of this improvement would be linearly related to amount of exercise performed during the interval.

Materials and methods

Study design

This study used a longitudinal, single center, non-blinded, non-randomized controlled design. Subjects in the IE group were independently enrolled in a single outpatient activity-based recovery center, Project Walk, located in Carlsbad, CA, USA, 58 miles from the University of California, Irvine (UCI), prior to or at the start of participation in the current study. Control (CTL) subjects were recruited through local advertisements as well as websites.

Subjects in both groups had chronic SCI and made two visits to the university, separated by 6 months. Each visit included behavioral testing, as described below. All behavioral assessments took place at UCI, and were performed by a single examiner (NY), who is not affiliated with the Project Walk program. Note that the specialists administering the IE program were blinded to the results of behavioral testing. During the 6-month interval, a log of exercise hours per week was maintained, according to exercise type. CTL subjects maintained this log by themselves, whereas for IE subjects, this log was maintained during treatment by Project Walk staff.

Subjects

Entry criteria for all subjects were age 18–70 years, SCI greater than 2 months prior (range 6–255 months) that resulted in paraplegia or quadriplegia between C2 and T12, and American Spinal Injury Association (ASIA) Impairment Scale A, B, C or D. Exclusion criteria included ventilator-dependence, and other major neurological disease including traumatic brain injury operationally defined as trauma associated with loss of consciousness for greater than 24 h. By definition, subjects in the IE group were enrolled in the Project Walk program, and therefore had both physician permission to engage in an IE program as well as financial capacity to pay for the program.

Training program

In the current study, IE refers to regular participation in an individually designed exercise program at the Project Walk Spinal Cord Injury Recovery Center. Each subject's program was based on level of function and was updated daily to build upon new gains. Each subject's IE program focused on attempting to regain voluntary motor function below the level of injury. For subjects with quadriplegia, approximately 80%, and for subjects with paraplegia 100%, of the exercise time was spent on training the trunk and lower extremities. Each exercise program was designed and overseen by one of three specialists, training for each of whom included a Bachelor of Science (B.S.) in an exercise-related field plus greater than 5000 h of experience working with subjects with SCI in an IE program. Each program was implemented by a specialist with a B.S. in an exercise-related field and greater than 900 h of experience working with subjects with SCI in an IE program.

Time spent in the IE program was divided into six categories:

(1) Active Assistive was used when subjects had little to no voluntary movement, and consisted of helping the subject through different ranges of motion and providing a resistance less than gravity. The subjects were instructed to attempt or visualize actively assisting or resisting the movement performed.[13]
(2) Resistance Training was used when subjects demonstrated voluntary motor control, and consisted of concentric or eccentric contraction against gravity, or a resistance greater than gravity.[14]
(3) Load Bearing was used at all levels of motor function, and had hands or elbows and/or feet or knees in contact with the ground, with some percentage of body weight supported through the extremities.[15] If other categories of exercise, for example, active assistive and resistance training were performed in this position, time spent was counted as load bearing.
(4) Cycle Ergometry was used by all subjects, during warm up and cool down periods at the beginning and ending of the session, and involved use of an arm crank ergometer for upper body exercise, or a stationary bicycle for lower body, exercise, at a self-selected rate.[15]
(5) Gait Training/Supported Ambulation was employed by all but two of the IE subjects, who were unable to wear the harness due to skin issues, and included several forms of gait training[7,15,16] including partial body weight-supported mechanized elliptical training and partial body weight-supported treadmill training. This involved assistance by 0–4 specialists based on the subject's ability to control the upper body and lower extremities. Subjects who required no body weight support assistance were advanced to overground walking with a walker.
(6) Vibration Training was included for all IE subjects demonstrating visible voluntary muscle contractions, and places the subject in contact with a platform that generates a vertical sinusoidal vibration up to 40 Hz, which leads to alpha-motoneuron activation and initiates muscle contractions.[6]

Behavioral testing

The same investigator (NY) performed all behavioral testing, that is, upon study entry and again 6 months later, after first undergoing full training on the ASIA Standards Teaching Package (http://www.asia-spinalinjury.org/publications/

store.php). The examiner was not blinded to treatment group. Demographic information including handedness[17] and footedness[18] were recorded at baseline.

Motor and sensory impairment. Injury level was determined as the most caudal segment with normal sensation and motor function. ASIA motor score (total; of the lower extremities (ASIA LEMS); and of the upper extremities (ASIA UEMS)), and combined ASIA pin prick and light touch scores (ASIA Sensory) were determined at both visits.

General health. The EQ-5D thermometer[19] is a visual analogue scale that measures self-rated general health. Subjects were asked to indicate their health on the day of interview from 0 to 100 (0 = worst imaginable health state, 100 = best).

Handicap level. The Craig Handicap Assessment and Reporting Technique (CHART)[20] measured handicap level up to 100 points, with higher scores indicating less handicap.

Statistics

Using JMP (SAS, Cary, NC, USA), data were assessed for normality of distribution using the Shapiro–Wilk W test, and when non-normal were transformed, if this could produce a normalized distribution, using logarithmic transform else square root else square. Normally distributed data were analyzed using parametric methods (*t*-test or Pearson's coefficient), and data that could not be normalized were analyzed with nonparametric methods (Wilcoxon test or Spearman's ρ). Categorical variables were compared using χ^2 testing. All analyses were two-tailed, with alpha = 0.05.

Results

Of the 31 recruited subjects (22 IE and 9 CTL), one from each group was not able to return for the 6-month follow-up testing, leaving 21 IE and 8 CTL subjects.

At baseline, the two groups were similar (Table 1) except that IE subjects had shorter time post-injury and lower CHART scores, as compared to CTL subjects. IE subjects had already been participating in IE at Project Walk for 6 ± 6.4 (range, 0–25, mean ± s.e.m.) months.

During the 6-month interval, IE subjects participated 56 ± 6 days in the exercise program. This was significantly less ($P<0.02$) than the 98 ± 23 days spent exercising by CTL subjects. Training time for IE subjects averaged 7.3 ± 0.7 h per week, not significantly different from the 5.2 ± 1.3 h per week by CTL subjects. For IE subjects, greater gains in measures of impairment and handicap were associated with greater time exercising (Table 2); the amount of time spent in each exercise category is shown in Figure 1.

Intense exercise subjects showed greater clinical gains than CTL during the 6-month interval (Table 3), significantly so for total ASIA motor score (4.8 ± 1.0 vs −0.1 ± 0.5, $P=0.0001$). Most of this was due to lower extremity gains, with a significant group difference in LEMS ($P<0.04$) but not UEMS. Among IE subjects, 71% showed an increase in motor score, and 5% a decrease. By contrast, among CTL subjects, only 25% showed improvement in total ASIA motor score, and 25% showed a decrease. Note that these total ASIA motor score gains in IE subjects varied in relation to baseline deficits: subjects who were motor complete (AIS A or B, $n=12$), as compared to subjects who were motor incomplete (AIS C or D, $n=9$), had significantly less gains (2.8 ± 1.2 vs 7.4 ± 1.1, $P<0.02$), a finding entirely attributable to LEMS. Also, subjects with thoracic injury ($n=2$) had significantly less gains than subjects with cervical injury ($n=19$), though small sample size in the former group limits interpretation of

Table 1 Demographic and baseline clinical data

	Intense exercise (n = *22*)	*Control* (n = *9*)	P
Age (years)	37.8 ± 3.6	34.5 ± 2.9	0.23
Gender	19M/3F	9M/0F	0.54
Handedness	1L/19R/2A	1 L/8R/0A	0.41
Footedness	0L/16R/6A	0 L/6R/3A	1.0
Time post-injury (months)	40 ± 7	97 ± 23	0.0057
CHART	444 ± 19	521 ± 23	0.017
EQ-5D	65 ± 4	67 ± 6	0.93
ASIA Total Sensory	94 ± 7	96 ± 15	0.95
ASIA Total Light Touch	59 ± 4	57 ± 9	0.85
ASIA Total Pinprick	36 ± 4	39 ± 7	0.73
ASIA Total Motor	39 ± 3	42 ± 5	0.54
ASIA UEMS	31 ± 2	38 ± 4	0.09
ASIA LEMS	8 ± 2	4 ± 4	0.37

Abbreviations: AISA LEMS, ASIA motor score of the lower extremities; ASIA UEMS, ASIA motor score of the upper extremities; CHART, Craig handicap assessment and reporting technique.
All data are for the baseline exam. All subjects had SCI. Of the 22 IE subjects, ASIA Impairment Scale (AIS) was A in 7, B in 6, C in 8 and D in 1, not significantly different from the CTL group, where AIS was A in 5, B in 2, C in 1 and D in 1. Injury level was C4-T11, being C4 or C5 in 19 and cervical in 23. ASIA scores are bilateral. L = left, R = Right, A = Ambi dextrous/pedal. Values are mean ± s.e.m. For continuous variables, the two groups were compared using Student's *t*-test for normally distributed data, and Wilcoxon test for non-normally distributed data. Categorical variables were compared using χ^2 testing.

Table 2 Amount and type of intense exercise correlate with behavioral gains

Predictor	*Outcome measure*	R	P
Total hours per week IE	Change in Total ASIA Motor	0.53	0.014
	Change in ASIA LEMS	0.55	0.009
	Change in CHART	0.48	0.027
Load Bearing hours per week	Change in Total ASIA Motor	0.61	0.003
	Change in ASIA LEMS	0.63	0.002
	Change in CHART	0.55	0.01
Active Assistive hours per week	Change in EQ 5D	0.47	0.03
Gait Training hours per week	Change in CHART	0.54	0.016

Abbreviations: CHART, Craig handicap assessment and reporting technique; IE, intense exercise.
Data are for subjects in the IE group only. Outcome measures represent change over the 6 months, that is, exam 2−exam 1. Note that hours per week of vibration training did not correlate with any of these outcome measures. Normally distributed data were analyzed using Pearson's coefficient, whereas non-normally distributed data were analyzed using Spearman's ρ.

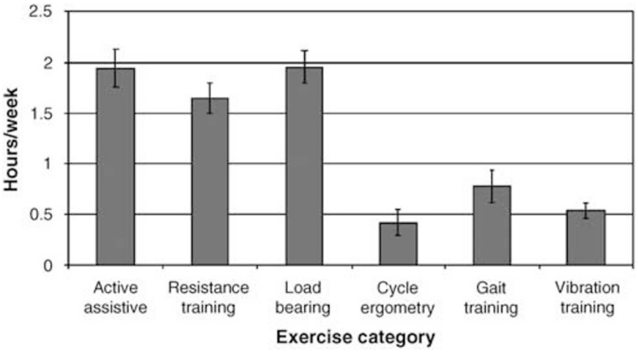

Figure 1 For subjects in the intense exercise (IE) group, the mean ± s.e.m. number of hours per week is shown for each of the six categories comprising the IE program.

Table 3 Change in clinical measures over 6 months

	Intense exercise (n = *21*)	*Control* (n = *8*)	P
ASIA Total Bilateral Motor	4.8 ± 1.0	−0.1 ± 0.5	0.0001
ASIA LEMS	3.3 ± 0.9	0 ± 0.2	0.035
CHART	12 ± 15	0.1 ± 18	0.60
EQ-5D	14 ± 5	3 ± 5	0.14
ASIA Total Sensory	8 ± 3	7 ± 3	0.59

Abbreviations: AISA LEMS, ASIA motor score of the lower extremities; CHART, Craig handicap assessment and reporting technique.
All data are for change over the 6 months, exam 2−exam 1. Mean ± s.e.m.

this finding. Time from injury to study enrollment was significantly related to extent of total ASIA motor score gains for the 21 IE subjects, with longer time associated with greater gains ($r = 0.45$, $P < 0.04$), attributable to LEMS; this is complicated by the fact that subjects with longer time since SCI also had significantly longer amounts of IE prior to study enrollment. The relationship between time post-SCI and motor gains was not significant when the 8 CTL subjects were added ($P > 0.7$).

Changes over the 6 months within individual muscles were examined. Over the 6 months, at least one muscle increased in strength from 0 to 1 or more on the Medical Research Council scale[21] in 15/21 IE vs 0/8 CTL subjects ($P < 0.0001$). In these 15 IE subjects, the mean number of muscles showing such a change was 4.1 (3.2 in lower extremities). Furthermore, over the 6 months, at least one muscle increased strength from <3 (non-functional) to ⩾3 (functional) on the Medical Research Council scale in 7/21 IE vs 1/8 CTL subjects ($P < 0.24$). The average number of lower extremity muscles exhibiting this change was two. The muscles that showed this change most often (unilaterally or bilaterally) were plantar flexor (four subjects), toe extensor (four subjects), elbow extensor (three subjects), knee extensor (two subjects) and wrist extensor (two subjects).

Among the IE subjects, amount and type of exercise correlated significantly with change in behavioral measures (Table 2, Figure 2), with amount of load bearing most often showing such a relationship. Among IE subjects, change in ASIA sensory score correlated significantly with change in total ASIA motor score ($r = 0.70$, $P < 0.008$) and LEMS ($r = 0.69$, $P < 0.01$). Among subjects in the CTL group, no significant relationships were found between amount or type of exercise and change in behavioral outcome measures.

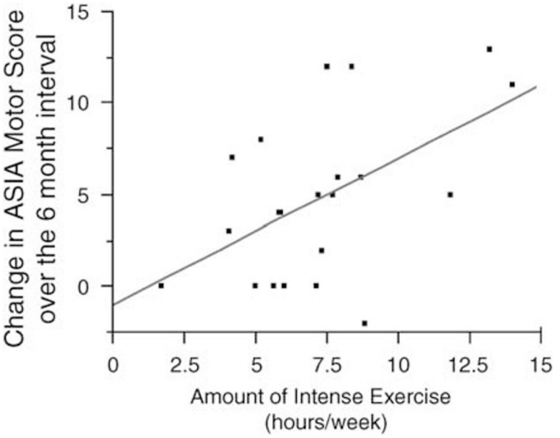

Figure 2 For subjects in the intense exercise (IE) group, the total amount of intense exercise, expressed as hours per week averaged across the 6 months, was linearly related to the change in Total ASIA Motor Score over the same interval ($r = 0.53$, $P < 0.02$).

Discussion

In subjects with SCI, decrease in motor function impacts a number of health, quality of life and other issues.[2] Limited data exist examining the effects that a prolonged multimodal IE therapeutic program has on muscle and related motoric functions, as well as behavioral recovery, in this setting. In the current study, a 6-month IE regimen was associated with significant great gains in ASIA motor score, particularly in the lower extremity, among subjects with chronic SCI. These gains correlated with the amount of time spent performing IE. These gains were not seen in subjects in a control regimen of self-regulated exercise, despite the controls spending a greater number of days exercising, with comparable number of hours per exercise day. Together, these results support the study hypotheses.

A period of 6 months of IE was associated with motor gains in paralyzed or severely paretic limbs in chronic SCI. Most of this change was due to gains in the lower extremity, consistent with IE therapy content. Motor gains were seen in 71% of IE subjects, which compares favorably with the natural history of chronic SCI,[22] where one study reported that 40% of subjects with SCI have show motor improvement over a 5-year period, though no information was available regarding therapy during that study. Importantly, in approximately one-third of subjects in the current IE group, motor gains included having at least one muscle change from non-functional to functional.

Among the IE subjects, the number of hours per week exercising correlated significantly with impairment and handicap improvements. This might indicate that larger amounts of IE is a direct contributor to behavioral gains, or, because amount of IE was set by individuals, this might reflect a third factor pertinent to both, such as motivation. In IE subjects, greater time since SCI correlated with larger motor gains, possibly suggesting an accumulation of learned nonuse over time, as has been suggested in patients with weakness due to stroke.[23]

Interestingly, CTL subjects, despite reporting significantly more days—almost twofold—engaged in exercise than subjects in the IE program, did not show motor gains. Thus, while subjects in the IE group gain approximately 5 points in total ASIA Motor score, the larger number of exercise days in CTL subjects was associated with no change in this score. This suggests that unstructured exercise might have less value for return of motor function in the setting of chronic SCI.

Amount of time spent by IE subjects in the two most common activities, load bearing and active assistive exercise, correlated with gains over the 6 months. Out of all the modalities, amount of time spent in load bearing had the most significant relationship with LEMS.

Weaknesses of the study include the non-randomized assignment of study treatment, the bias introduced by capacity to enroll in the IE program, the small size of the CTL group and, thus, limited study power, the possibility that CTL subjects were relatively highly motivated as based on the large number of days and hours per week reported for self-regulated exercise, some imbalances in baseline measures between groups, the fact that subjects in the IE group had in most cases been participating for several months in the IE program prior to study initiation and inclusion of many subjects in the first 2 years after SCI. The latter point is of potential concern given that subjects with SCI can take 18–30 months to reach a stable ASIA motor score.[24] The significant difference between subject groups in time post-injury might, therefore, have influenced study results.

The current results describe motor gains associated with 6 months of multimodality IE, an intervention that might be useful to improve impairment and disability after SCI as a primary treatment or as an adjunct[3–5] to other restorative therapies. There are scant data available on such an intervention. Future studies might examine the extent to which such therapeutic gains are related to changes in related factors such as cost of care, metabolic status and quality of life. The current report is a useful first step to understand extent, nature and correlates of behavioral gains related to 6 months of IE.

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