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Higher intensity walking training in individuals with chronic motor incomplete spinal cord injury: A randomized clinical trial

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Abstract

Background: The amount of walking practice may influence locomotor recovery in individuals with motor incomplete spinal cord injury (iSCI), although the contributions of exercise intensity are not well established.

Objective: The purpose of this blinded-assessor randomized trial was to determine the contributions of exercise intensity on locomotor outcomes in individuals > 6 months following iSCI.

Methods: Ambulatory individuals post-iSCI with walking speeds <1.0 m/s were assigned to ≤30 sessions of either high-intensity training (HIT: >70% heart rate [HR] reserve or ratings of perceived exertion [RPE]≥15) or low-intensity training (LIT; <40% HR reserve; RPE≤13). Assessments were performed at baseline, post-training and at 3-month follow-up evaluation, with primary outcomes of fastest walking speeds over 10 m and during graded treadmill exercise tests, and secondary clinical and metabolic outcomes.

Results: Of 65 participants screened, 53 were randomized to HIT (n=28) or LIT (n=25) and completed 1489/1590 (94%) planned training sessions. Peak HRs and RPEs were greater during HIT (both p<0.001). Changes in fastest gait speeds overground were not significantly different between HIT and LIT when using Bonferroni corrections [α=0.025; mean post-training differences: 0.11 m/s (95% CI: 0.04–0.17 m/s), p=0.031], although gains in peak treadmill speed were significant [mean differences: 0.25 m/s (0.15 to 0.34 m/s), p-<0.001]. Secondary outcomes of 6-minute walk test (p=0.002) and combined measures of peak metabolic capacity and efficiency (p<0.001) were also greater with HIT.

Conclusion: Greater gains in peak treadmill speed, 6-min walk, and selected metabolic outcomes were observed with HIT vs LIT in individuals with iSCI.

Trial Registration: https://clinicaltrials.gov/; Unique Identifier: NCT03714997

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Keywords

locomotion; rehabilitation; exercise; aerobic

Introduction

Approximately half of individuals with a spinal cord injury (SCI) present with motor incomplete SCI (iSCI)[1,2], indicating partial preservation of descending supraspinal pathways and the potential to recover independent locomotion. However, optimal strategies to maximize locomotor recovery are uncertain. In animal models[3–5] and individuals with iSCI[6,7], large amounts of task-specific (i.e., walking) practice has been thought to improve locomotor function to a greater extent than providing smaller amounts of walking practice, although strategies to provide such practice vary. Early studies suggested attempts to normalize gait kinematics using manual[8,9] or robotic assistance[10] during training provided repeated, phasic sensory stimulation that could activate spinal circuits underlying locomotion, with sustained practice thought to enhance walking function. Unfortunately, such strategies were shown to be no more effective or worse than other physical interventions[8–11].

One theory to account for some of these findings is that providing substantial assistance during training may allow individuals to “slack”[12], or reduce their volitional effort and engagement[13]. For example, previous studies indicated robotic-assisted treadmill walking reduces neuromuscular and cardiopulmonary demands in individuals with iSCI[14,15] or stroke[16], which likely contributes to limited gains with repeated practice[10,11,17,18]. Conversely, increasing neuromuscular and cardiopulmonary demands during training has been hypothesized to improve locomotor function. In individuals post-stroke, for example, published studies suggest targeting higher exercise intensities, as estimated using heart rate (HR) and subjective ratings of perceived exertion (RPE), can elicit substantial gains in locomotor function[19–21]. Training intensity can be elevated by increasing walking speeds and task demands (i.e., inclined walking or added mass[22]), and attempts to target >70% of age-predicted HR reserve can result in average training HRs that are 110–120% of observed maximum HR at baseline exercise testing[19,22], although achieving higher HRs may be difficult in those with greater impairments (i.e., slower speeds)[23]. Potential mechanisms underlying gains associated with HIT may include greater serotonergic modulation of spinal and supraspinal circuits[24,25], leading to increased synthesis and release of neurotrophic factors (e.g., BDNF)[26,27] to elicit sustained plastic alterations in locomotor circuits[28,29]. Such changes likely contribute to observed improvements in joint powers and neuromuscular coordination[30,31], and greater cardiopulmonary capacity and efficiency[32].

In individuals with SCI, many studies have evaluated the effects of higher-intensity exercise interventions (reviewed in[33]), although most do not focus on locomotor interventions in those with iSCI. More directly, only two pilot randomized cross-over trials have detailed the potential utility of HIT focused on walking as compared to impairment-based interventions, or as compared to lower intensity training (LIT; <40% HR reserve)[6,34]. Differences in outcomes varied between studies, with HIT demonstrating superior gains in fastest walking speed overground and peak treadmill speeds during exercise testing as compared to LIT[34]. Surprisingly, in this latter study, there were no between-group differences in the 6-min walk test, although gains in this outcome are common in HIT studies performed in individuals post-stroke[19–21]. In addition, changes in walking speed and distance were associated with HRs achieved during training sessions[34], despite difficulty in achieving the targeted HR ranges in some individuals. While promising, sample sizes in these cross-over studies were small (n = 15–16), and questions remain as to whether HIT performed in larger populations over extended training durations can elicit similar gains.

The goal of the present study was to evaluate the effects of HIT vs LIT in individuals with iSCI on clinical and metabolic measures of locomotor performance. Using an assessor-blinded randomized controlled design, ambulatory individuals > 6 months post-iSCI were randomized to receive 30 sessions of either HIT targeting >70% HR reserve, or LIT targeting <40% HR reserve. We hypothesized HIT would result in superior gains in locomotor and cardiopulmonary outcomes, consistent with findings from other neurologic populations.

Methods

Study Sample and Design

This trial was conducted from June 2020 to January 2025, with procedures approved by the Indiana University Institutional Review Board with written informed consent. The trial was prospectively registered at ClinicalTrials.gov (NCT03714997), and followed the Consolidated Standard of Reporting Trials (CONSORT) guidelines.

Participants

Participants were recruited through local and national rehabilitation hospitals via outreach to clinicians. Inclusion criteria consisted of: (1) classified as motor iSCI, or C or D using the American Spinal Injury Association (ASIA) Impairment Scale (AIS), (2) anatomical injury at thoracic level 10 (T10) or above, (3) > 6 months post-SCI, and (4) 18–75 years old, (5) ability to walk overground at self-selected speeds < 1.0 m/s over ~6-m of 10-m walking path (Zeno, Protokinetics, Havertown, PA) without physical assistance with devices and bracing below the knee as needed, and (6) medical clearance to participate. Exclusion criteria included: (1) lower extremity contractures that affected walking function; (2) history of osteoporosis or recent fractures, (3) cardiopulmonary or metabolic instability, (4) unhealed decubiti or heterotopic ossification, (5) history of other neurologic or orthopedic injury affecting walking function; (6) currently enrolled in physical therapy, or (7) history of botulinum toxin injection in leg muscles above the knee < 3 month prior (injections in lower leg were permissible if participants wore an ankle foot orthosis).

Randomization

Participants were stratified by their initial self-selected velocity (<0.5 m/s or 0.5-0-1.0 m/s), and randomized to receive either HIT or LIT using a 1:1 allocation ratio and computer-generated blocked design (8 per block) concealed using the REDCap randomization module.

Pilot data[34] indicated 54 participants would provide 91% power for the primary blinded outcome of fastest gait speed over 10 m at post-training.

Intervention

Training was performed in a laboratory/outpatient clinical setting, and consisted of up to 30 1-hour training sessions over 8–10 weeks, with up to 40 minutes of stepping practice each session. All participants wore accelerometers (StepWatch, Modus, Inc. Washington DC) on their more impaired limb to estimate stepping amount and rate per session. Participant HRs were monitored using pulse-oximeters or chest-worn monitors and documented every 3–5 minutes during stepping tasks, along with RPEs using the Borg scale (range: 6–20). Blood pressures were monitored with training cessation if pressures exceeded 240/110 mmHg.

The goals of HIT were to maximize stepping practice in variable contexts while targeting >70% HR reserve using age-predicted maximum HR [HR_{max}; 208-(0.7*age)[35]] and the Karvonen formula [70% HR reserve =0.70*(HR_{max} – resting HR) + resting HR]. Targeted HR ranges were decreased by 10 beats/min for participants on β-blockers[36,37]. As some individuals with iSCI have difficulty achieving 70% HR reserve due to various factors (e.g., medications, autonomic dysfunction, and gait deficits), RPEs were also utilized with attempts to target ≥15 ("hard") and therapists monitored non-verbal signs of exertion (e.g., increased respiration, sweating)[22]. Stepping tasks performed during each session were divided into ~10-minute increments between speed-dependent treadmill training, skill-dependent treadmill training, overground training, and stair climbing[34,38]. Speed-dependent treadmill training was performed with a fall-arrest harness system, with goals to achieve walking speeds sufficient to reach targeted HRs. Body weight support and swing assistance were provided if needed[38]. Skill-dependent treadmill training was performed by applying perturbations to challenge postural stability, propulsion, stance control, and limb swing as selected by therapists, including walking in multiple directions, over inclines and obstacles, and/or with weighted vests and leg weights, while still attempting to achieve fastest speeds. If HRs decreased substantially during skill-dependent stepping, bouts of speed-dependent training would be interspersed with these variable stepping tasks. Overground training focused on achieving higher speeds or performing variable tasks as described above, and included negotiating uneven, compliant or narrow surfaces, with use of a gait belt or overhead fall-arrest system. Stair climbing was performed over static or rotating stairs (Stairmaster, Vancouver, WA) at faster speeds and/or while attempting variable stepping tasks (e.g., different direction, addition of leg weights/weighted vests).

Participants randomized to LIT performed stepping activities in variable contexts, similar to HIT described above, with attempts to target <40% HR reserve and RPEs ≤13 ("somewhat hard"). The large difference in targeted HRs (>70% vs <40%) was designed to minimize overlap in HR responses between HIT and LIT, as variability in HR responses can contribute to inability to maintain the targeted ranges[34]. During attempts to achieve these lower HRs, the primary strategy was to reduce speeds given the association between speed (power) and HRs, and was utilized during all stepping activities. Other strategies included limited use of weighted vests or leg weights, or providing body-weight support. In addition, stepping tasks could also focus on accuracy of foot placement or provide physical assistance and cueing with attention towards joint kinematics.

Outcomes

Specific primary and secondary outcome measures were performed by blinded assessors at baseline, post-training and 3-month follow-up. Consistent with results of the pilot study, the primary blinded outcome was fastest gait speed during the middle 6-m of 10-m walk tests with instructions to “walk as fast as you safely can”, as well as peak treadmill speed during a graded exercise test, during which 12-lead ECGs were monitored by primary research staff and unblinded. During graded exercise tests, participants walked at 0.1 m/s with a fall-arrest harness for 1 min with speed increased 0.1 m/s every minute until gait instability, abnormal ECGs, symptoms of angina, or participants requesting to stop[23]. Peak treadmill speed was the highest speed achieved for 1 min.

Additional blinded measures included 6-min walk test with instructions to “cover as much ground as possible”, self-selected gait speed with instructions to walk at a “normal comfortable pace”, the Berg Balance Scale (BBS), a 14-item measure of static postural stability, and the 5-times sit-to-stand (5XSTS) performed using an adjustable height chair with 3-in increments (17.5, 20.5, 23.5 inches) for those who could not complete sit-to-stand at the standard 17.5 inch height. Subjective measures included the Activities-specific Balance Confidence (ABC) Scale, and the Medical Outcomes Short-Form-36 questions (SF-36) to assess quality-of-life. The Lower Extremity Motor Score was evaluated by primary research staff using the ASIA standardization to characterize baseline strength deficits.

Additional secondary metabolic assessments included estimates of peak O_2 consumption (VO_2peak; ml/kg/min) determined via indirectly calorimetry during graded exercise testing. Metabolic data were analyzed over the last 30 sec of each minute, with VO_2peak defined as the average VO_2 at the peak treadmill speed. In addition, gait efficiency was also assessed, as decreases in VO_2 at similar speeds are often observed with training, which can mask gains in VO_2peak[32]. To quantify these changes, VO_2 at post-training and follow-up assessments were also analyzed at speeds matched to peak baseline speed (VO_2match). Differences in changes in VO_2peak and VO_2match, or VO_2gain (ΔVO_2peak -ΔVO_2match) better reflect gains in metabolic capacity and is strongly correlated with gains in locomotor function[32,34,39].

Fidelity of training interventions was assessed by calculating the number of training sessions, average duration, amount and rate of stepping activity per session, in addition to cardiovascular and subjective intensity measures. Average HRs achieved during sessions are presented as HR reserve using both age-predicted HR_{max} and observed HR_{max} determined at baseline graded exercise testing. Peak speeds achieved during forward treadmill walking were also documented.

Incidence of adverse events during interventions was also tabulated, including serious adverse events such as death, falls with injury, and cardiovascular events requiring hospitalization. Minor events included musculoskeletal pain, falls without injury, dizziness/

loss of consciousness, excessive shortness of breath, or episodes of hypertension, hypotension or angina that limited training session duration[40].

Analysis

Data were tested for normality prior to analyses. Intent-to-treat analyses were utilized for all outcomes using all participants enrolled, with regression imputation for those who could not attend 3-month follow-up assessments. For metabolic outcomes, data were not available for 5 individuals (HIT: n=4; LIT: n=1) who could not complete the slowest treadmill speed (0.1 m/s) at baseline testing. Training variables and baseline locomotor outcomes were compared between treatment groups using unpaired t-tests. Baseline demographics in Table 1 are reported using mean (standard deviations) or proportions, with training variables and changes in outcomes as mean (95% confidence intervals) in text and subsequent tables. Primary and secondary outcomes were analyzed using a 2-way repeated-measures ANCOVA with main factors of treatment (HIT vs LIT) level and repeated for each assessment (baseline, post-training, 3-month follow-up), with baseline scores used as covariates. Significance was set at α=0.025 for the primary outcomes of fastest speeds overground and during graded exercise testing, and α=0.05 for all secondary and post-hoc clinical and metabolic measures. Correlations analyses were used to estimate associations between intensity metrics (% HR reserve using observed maximum HR at baseline and RPE) and selected blinded clinical walking outcomes (fastest speed, 6-min walk test). Differences in the number of individuals who experienced serious and minor adverse events were analyzed using X^2 analyses with subsequent odds ratios determined as indicated.

Results

Sixty-five individuals were screened, with 53 meeting all inclusion criteria, enrolled and randomized (Figure 1). Post-training assessments were collected on all individuals, with 3-month follow-up assessments collected on all but 14 participants who lived out-of-state and were unable to return (Figure 1). Table 1 provides demographic characteristics and baseline locomotor function presented as mean (standard deviation) of all participants, selected demographics include an average age of 53 (14) years old, 77% male, and most presenting with high cervical (C1–4; 43%) or low cervical (C5–8; 23%) SCI.

Details of training interventions (Table 2) indicate 94% (1489/1590) of scheduled sessions were completed [HIT: 769/840 (92%); LIT: 720/750 (96%)] with similar number and sessions between groups, and no differences in duration, amount or rate of steps/session. Conversely, greater HRs and RPEs were observed during HIT vs LIT ($p<0.001$), with training HRs during HIT averaging 70(14) %HR reserve using age-predicted HR_{max}. In the HIT group, average HR responses of 12/28 participants did not reach the targeted 70% HR reserve. Of that group, 4 could not reach above 50% and demonstrated greater locomotor dysfunction (baseline self-selected speeds < 0.20 m/s). The LIT group averaged 40(10) %HR reserve, although mean HRs in 9/25 participants were higher than the 40% HR reserve threshold for “low” intensity. Efforts to reduce walking speeds or task demands did not result in lower HRs. When calculating %HR reserve using observed (vs age-predicted) HR_{max} during baseline testing, the HIT group averaged 110 (21) % HR reserve and the LIT group averaged 72(21) %HR reserve. HIT was also characterized by higher weekly peak treadmill speeds presented as percentage of baseline peak treadmill speed [HIT: 155%, LIT: 84%; Table 2].

Assessments at baseline (Table 3) were not significantly different between groups, although all primary and secondary locomotor outcomes demonstrated differences above thresholds considered clinically significant[41] (gait speed > 0.10 m/s, 6-min walk test > 50 m). Accordingly, baseline outcomes were used as a covariate in the final analysis. Following training, differences for the primary outcome of fastest gait speed were observed favoring HIT (p=0.031; Table 3, Figure 2A–B), although were not statistically significant following Bonferroni corrections. Differences in fastest speeds following HIT at each time point were 0.23 m/s (95% CI: 0.14–0.31 m/s) at post-training and 0.27 m/s (0.17–0.38 m/s) at 3-month follow-up, with changes following LIT of 0.12 m/s (0.07–0.17 m/s) at post-training and 0.13 m/s (0.05–0.20 m/s) at follow-up [mean differences:0.11 m/s (0.04–0.17 m/s) at post-training, p=0.017; 0.14 m/s (0.05–0.25 m/s) at 3-month follow-up]. For the primary outcome of peak treadmill speed during graded exercise testing, changes were significantly different between training groups (p<0.001). Specific changes include gains of 0.30 m/s (0.21–0.37) m/s with HIT at post-training, and 0.23 m/s (0.12–0.33) m/s at follow-up, whereas changes with LIT averaged 0.05 m/s (−0.02–0.12) m/s at post-training and 0.04 m/s (−0.02–0.10) at follow-up [mean differences: 0.25 m/s (0.15 to 0.34 m/s) at post-training, p<0.001; 0.19 m/s (0.10–0.27 m/s) at follow-up].

For secondary locomotor and other clinical outcomes, changes were observed for the 6-min walk test (p=0.002), with mean differences of 40 m (20–60 m) observed at post-training and 48 m (24–73 m) at 3-month follow-up. Changes in self-selected speeds and other secondary clinical outcomes were not different between groups.

Secondary metabolic outcomes during graded exercise testing revealed selected changes between groups. While differences in changes in VO_2peak were not significant at post-training, changes with HIT were 2.2 ml/kg/min (0–4.4 ml/kg/min) at post-training while changes with LIT were −0.2 ml/kg/min (−2.6–2.2 ml/kg/min; p=0.23). Notably, gains in VO_2peak were masked by 1–3 ml/kg/min improvements in gait efficiency (lower VO_2match) in both groups (Table 1). Calculation of VO_2gain (ΔVO_2peak-ΔVO_2match) revealed significant differences (p<0.001) favoring HIT at post-training [mean difference of 4.2 (2.7–5.7) ml/kg/min] and at 3-month follow-up [mean difference: 3.6 (2.1–5.0) ml/kg/min].

While between-group differences in HRs and RPEs were large, associations between these training variables and changes in fastest speeds or 6-min walk test were limited (Fig 3A–D). Namely, correlations between %HR reserve determined using age-predicted maximum HRs and clinical measures were very low (r=0.15–0.22, p=0.13–0.29), while associations with RPEs were only slightly improved. Namely, only the relation between average RPEs and changes in 6-min walk test were statistically significant (p=0.04), although this association was also low (r=0.29).

Serious adverse events were not observed in either group. Minor adverse events consisted primarily of falls outside of training without injury (HIT:12; LIT: 43) or musculoskeletal pain (HIT:3; LIT:12), with one incidence of diastolic blood pressure > 110 mmHg (HIT). Of those 10 individuals who reported falls with LIT, 32 falls occurred in 2 individuals with a history of recurrent falls prior to enrollment. Conversely, 12 falls in the HIT group occurred across 10 participants. For musculoskeletal pain, 6 participants in LIT accounted for 12 complaints of joint pain or soreness and 2 participants in HIT accounted for 3 reports of pain/soreness. Odds ratios and X^2 analyses were calculated for individuals who experienced each event, resulting in no significant differences between LIT or HIT for falls (1.4, 95% CI: 0.46–4.3, p=0.58) or pain/soreness (4.1, 95% CI:0.74–23, p=0.13).

Discussion

The present data extend upon pilot studies suggesting the comparative efficacy of HIT to improve locomotor outcomes in ambulatory individuals with chronic iSCI[38,42,43]. Cardiovascular intensities averaged 70% during HIT and 40% during LIT, which were the thresholds for high vs low intensity, respectively, although many individuals could not maintain those HRs consistently. Nonetheless both HRs and RPEs were significantly greater with HIT. However, our hypotheses were only partially supported, as gains in peak treadmill speeds during graded exercise testing, but not fastest speeds overground, were significantly greater following HIT vs LIT, with additional gains in secondary outcomes of 6-min walk and VO_2gain.

While the results of the primary outcomes varied, the preliminary data for this trial found similar mixed, but opposite, findings. Namely, the original pilot study hypothesized that gains in 6-min walk test and peak treadmill speed would be greater with HIT vs LIT[34], given the relatively consistent improvements in 6-min walk test observed in aerobic training studies in individuals post-stroke[19–21]. However, the pilot study revealed no differences in the 6-min walk test (p=0.16), but rather differences in fastest speeds and peak treadmill speeds (both p<0.01), which prompted the present hypotheses. While fastest speeds were not statistically significant here when using Bonferroni corrections, gains in 6-min walk test suggest HIT may improve selected clinical measures of locomotor function.

Despite differences in outcomes, the ability to achieve the targeted intensities in the pilot and present study were similar in that participants had difficulty achieving the specific HR ranges. As indicated, 12/28 participants receiving HIT averaged < 70% HR reserve and 11/25 participants receiving LIT averaged > 40% HR reserve. Challenges associated with achieving the targeted HR ranges are likely multifactorial, and may be due in part to altered autonomic function, as patients may present with reflexive tachycardia due to persistent hypotension, or bradycardia with potential interruption of sympathetic drive[44,45]. Additional reasons for not achieving the lower HRs during LIT may be the relative deconditioning of participants. Conversely, the inability to achieve higher targeted HRs with HIT may include use of specific medications (i.e., b-blockers), or could be related to the extent of locomotor deficits, as previous data suggest those with greater gait dysfunction cannot achieve higher HRs during exercise testing[23]. In the present study, for example, 4 individuals in the HIT group presented with self-selected speeds < 0.2 m/s, and averaged < 50% HR reserve. Given these limitations, the use of RPEs is often a surrogate measure to estimate workload, and is common in HIT studies in able-bodied and neurologic populations[46].

Potential mechanisms underlying improved locomotor function following HIT vs LIT are likely multifactorial. Previous data in individuals with iSCI suggest treadmill walking at the fastest possible speeds resulted in increases plasma concentrations of BDNF, which may be consistent with increased BDNF levels in the central nervous system[47,48]. This and other trophic factors may elicit plastic changes throughout the neuraxis[49,50], and may contribute to stepping recovery after SCI[28], potentially through improved neuromuscular powers[30,31] and coordination[51]. Those changes likely contributed to the observed combined gains in ΔVO_2peak and ΔVO_2match (i.e., VO_2gain), consistent with our pilot study[34] and data in both stroke[32] and traumatic brain injury[39]. Future studies may wish to determine the associations between neuromuscular and cardiopulmonary changes, as mechanisms underlying gains in VO_2peak and VO_2match in neurologic populations are uncertain.

Additional findings included the limited correlations between average HRs or RPEs achieved during training and changes in fastest speeds and 6-min walk tests. In this analysis, we used %HR reserve using age-predicted maximum HRs which was the primary variable differentiating the two training conditions, although the variability in HR responses was fairly substantial. Namely, in many participants receiving LIT, there was difficulty keeping HRs lower than 40% consistent with our preliminary study, and may be due to interindividual variability in heart rate responses to exercise or potential autonomic dysfunction common in this patient population[45]. There was, however, a significant association between average RPEs and changes in 6-min walk tests ($p=0.04$), although this association was low ($r=0.29$). The limited associations between training variables and outcomes is inconsistent with our pilot high- vs. low intensity training study in iSCI[34], or in studies that vary the amount of stepping practice or stepping rates across different interventions[6,19]. Potential reasons may be due to use of a cross-over design in the pilot study[34], where differences in outcomes and training variables were subtracted from high-vs low-intensity conditions since participants received both interventions. That strategy likely minimized the interindividual variability in responses, which was not possible here.

Despite achieving higher HRs in the HIT group, participants in both groups demonstrated no significant adverse events, consistent with other HIT studies in individuals with iSCI[6] or other neurologic populations[19,39,52]. Minor adverse events were observed, including complaints of soreness, particularly in a few participants in both groups, which are likely associated with delayed onset muscle soreness[39]. In addition, while the number of falls were much larger in the LIT group, a small number of participants contributed to the majority of those falls, and analysis focused on individual participants who reported a fall

Limitations of the current study include recruitment only at a single-site and the modest sample size (n=53) particularly as compared to training studies in other neurologic populations (i.e., stroke)[19,53]. While the current sample was larger than many studies in individuals with chronic iSCI[6,9,54], at least one other study has enrolled a larger number of participants (n=74 enrolled, 64 completed), although with 4 vs 2 intervention arms[10]. Nonetheless, assessment of HIT in larger samples would enhance confidence of the efficacy of this training strategy in individuals with iSCI. A potential strength of this study was the ability to complete post-training assessments on all 53 participants, as such retention is uncommon in rehabilitation trials. However, 14 participants could not attend the 3-month follow-up evaluation because of travel limitations. Further, the primary outcome of peak treadmill speed during graded exercise testing was not blinded, as primary research staff were necessary to assess ECGs during testing. Nonetheless, gains in peak treadmill speeds are consistent with substantial changes in fastest speeds overground and the 6-min walk test, as observed in previous studies[6,19,34].

An additional limitation may be the strategy for participant stratification prior to randomization (<0.5 m/s, 0.5–1.0 m/s). While these criteria were utilized in previous studies in stroke[19] and SCI[6,34], there were a larger number of participants randomized to HIT (n=4) vs LIT (n=1) who could not walk at the slowest speed (0.1 m/s) during baseline graded treadmill assessments. These participants also presented with slower overground speeds (all < 0.20 m/s) and 6-min walk distances (all < 15 m). While baseline locomotor outcomes were used as a covariate in the analysis to partially account for this, previous data indicate gains in individuals with iSCI who walk <0.20 m/s can be small[10]. Finally, while the present study did not evaluate HIT in those early following iSCI and in those who are non-ambulatory[8,55], future studies should be directed towards those populations. While HIT has demonstrated some comparative effectiveness when delivered early following stroke[56], similar studies have not been conducted early following iSCI.

Conclusions

Providing HIT focused on walking tasks did not elicit statistically greater gains in fastest walking speeds overground as compared to LIT, although gains in peak treadmill speed and 6-min walk test were observed, in addition to combined measures of peak metabolic capacity and efficiency. No differences in significant or non-significant adverse events were observed in either group. Future studies should continue to evaluate the relative contributions of exercise intensity in this patient population in larger samples.

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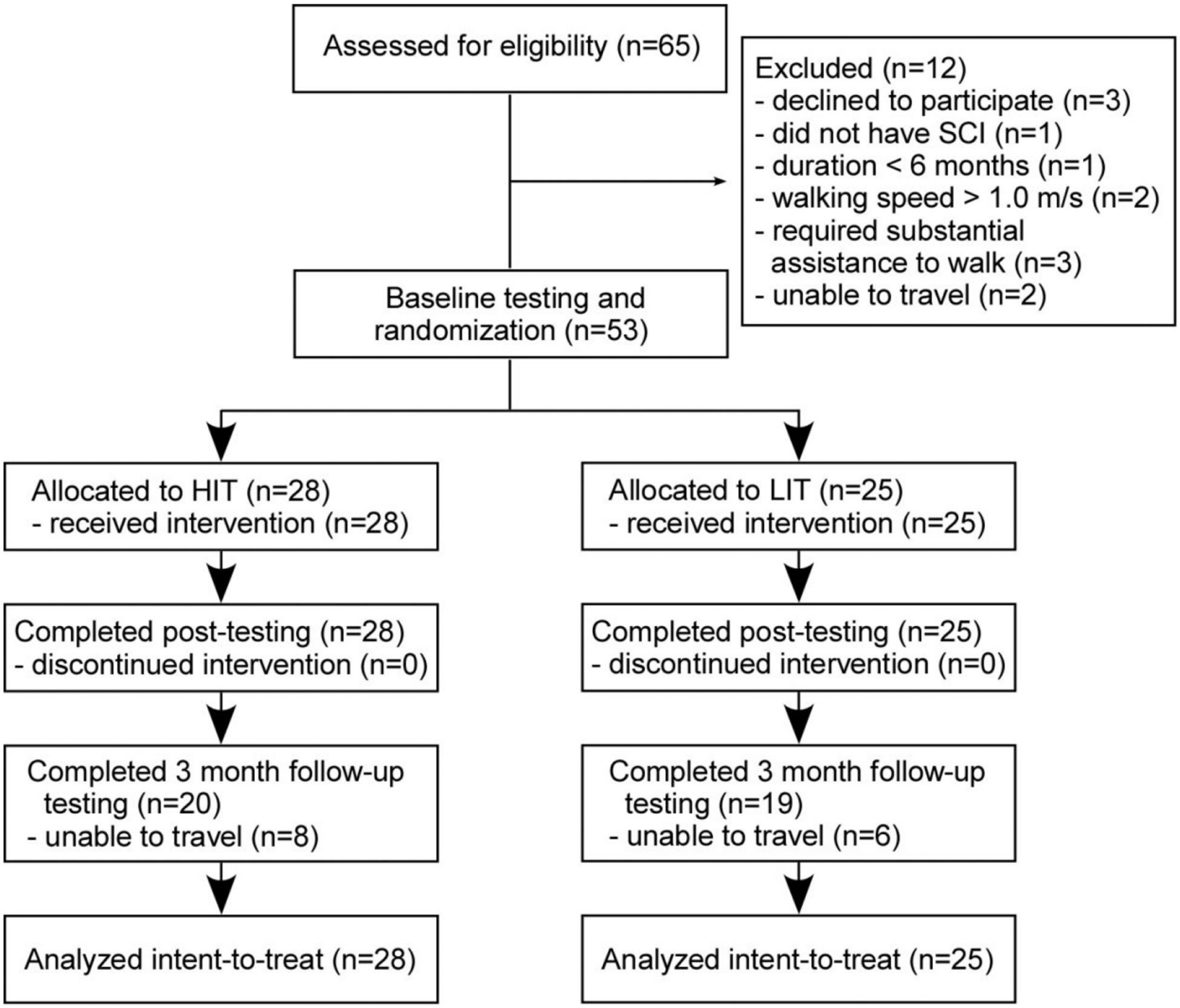

Figure 1.
CONSORT diagram of enrollment

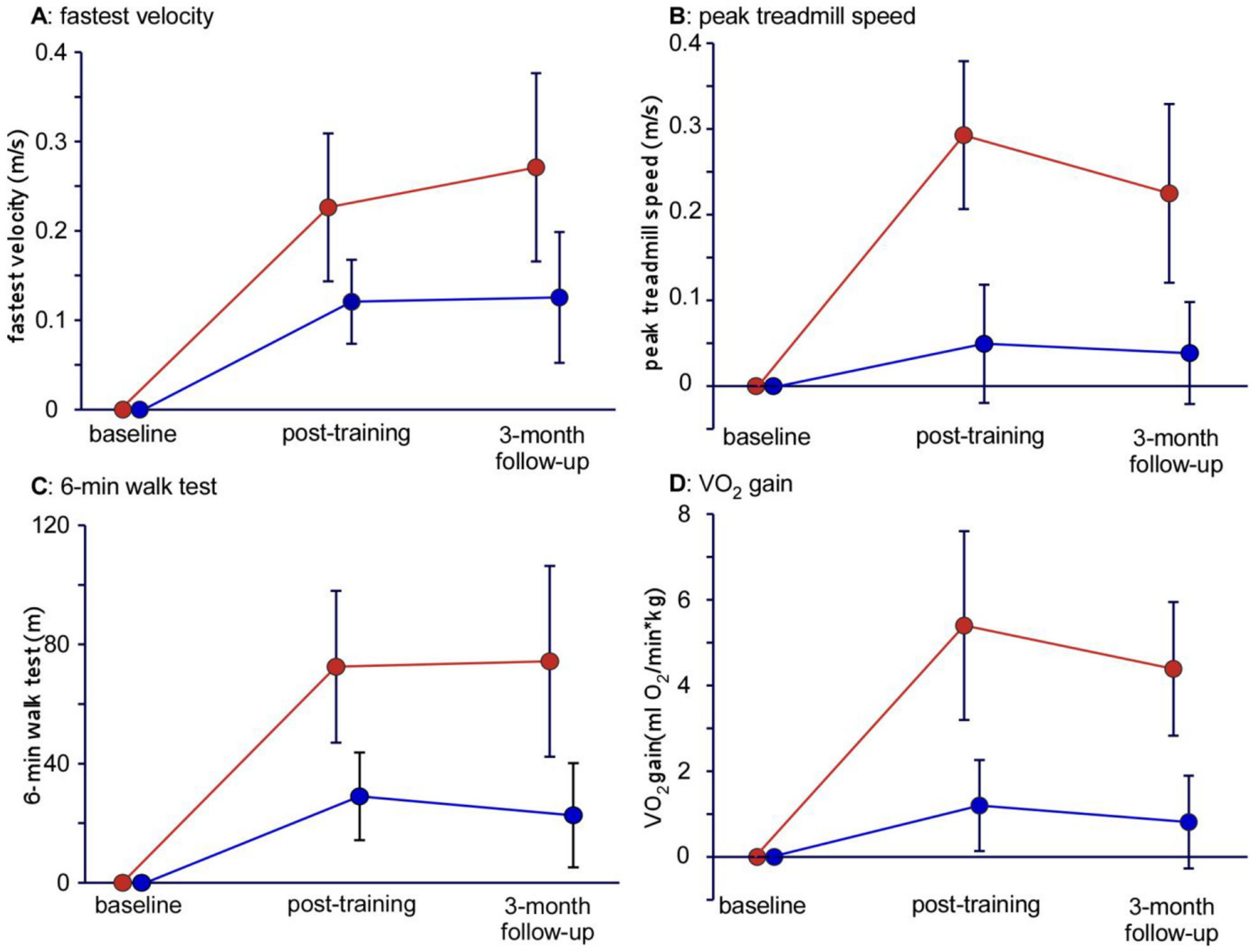

Figure 2.

A-B: Changes in primary outcomes of fastest gait speeds and peak treadmill speeds, (95% CI presented as error bars; HIT: red; LIT: blue). C-D: Changes in secondary outcomes of 6-min walk test and VO_2gain.

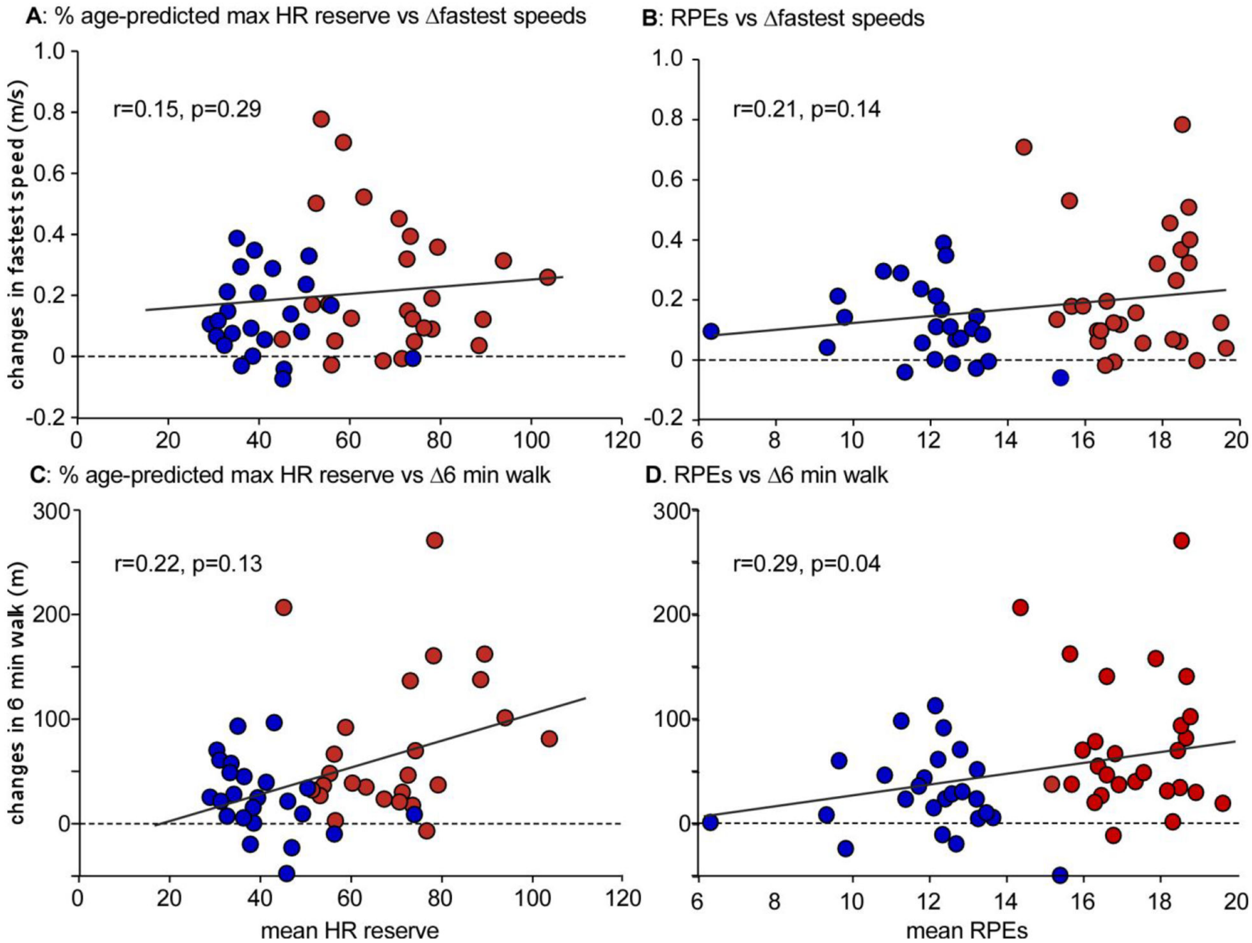

Figure 3.

Associations between average %HR reserves using observed baseline HR max and RPEs with changes in fastest speeds (A-B) and 6-min walk test (C-D; HIT: red; LIT: blue).

Table 1.

Demographic and baseline characteristics; mean (SDs) or number (%).

Demographics	**HIT (n=28)**	**LIT (n=25)**
Age (years)	51 (14)	55 (15)
Gender, male	23 (82%)	17 (68%)
Body mass index (kg/m^2)	28 (5.9)	29 (8.0)
Race		
Asian	0 (0%)	2 (8%)
Black/African American	11 (39%)	9 (36%)
White	17 (61%)	14 56%)
Ethicnitiy: Hispanic/Latinx	3 (11%)	0 (0%)
Charlson Comorbidity Index (a.u.)	1.2 (2.0)	0.7 (0.93)
Duration post-injury (years)	3.5 (4.2)	3.5 (3.6)
Level of injury		
High-cervical (C1-4)	12 (43%)	11 (44%)
Low-cervical (C5-C8)	7 (25%)	5 (20%)
Thoracic (T1-T10)	9 (32%)	9 (36%)
Mechanism of Injury		
Traumatic	15 (54%)	18 (64%)
Non-traumatic	13 (46%)	7 (32%)
Ankle foot orthosis		
None	17 (61%)	17 (68%)
Unilateral	8 (38%)	5 (20%)
Bilateral	3 (11%)	3 (12%)
Assistive device		
None	6 (21%)	5 (20%)
Single cane	4 (18%)	3 (12%)
Bilateral canes	8 (29%)	4 (16%)
Walker	9 (32%)	13 (52%)
Medications		
Antidepressants	14 (50%)	11 (44%)
Antihypertensive agents	9 (32%)	8 932%)
Antispastic agents	19 (68%)	21 (84%)
Baseline impairments		
ASIA Impairment Scale (AIS)		
AIS C	2 (7%)	2 (8%)
AIS D	26 (93%)	23 (92%)
Lower extremity motor score (a.u.)	42 (7.8)	44 (9.2)
Self-selected velocity(m/s)	0.45 (0.28)	0.55 (0.27)
Fastest velocity (m/s)	0.61 (0.38)	0.78 (0.39)
6-min walk test (m)	176 (130)	228 (128)
Peak treadmill speed (m/s)	0.66 (0.51)	0.81 (0.42)

Table 2:

Training parameters with mean (95% CIs) with p-values indicated unpaired t-tests between groups.

Training characteristics	HIT	LIT	Mean differences (95% CI)	p-values
sessions	27 (25–29)	27 (26–29)	0.2 (−1.7–2.2)	0.54
duration/session (min)	35 (33–37)	37 (35–38)	−2.4 (−6.4–1.6)	0.30
steps/session	2293 (1837–2750)	2169 (1332–2981)	137 (−954–1228)	0.67
steps/min	53 (45–59)	47 (41–53)	5 (−3.1–12)	0.23
HR reserve (predicted)	70 (65–76)	40 (36–44)	31 (23–38)	<0.001
HR reserve (observed)	110 (101–118)	72 (57–79)	38 (30–47)	<0.001
RPE (a.u.)	17 (17–18)	12 (11–13)	5.6 (4.8–6.3)	<0.001
peak speeds (% baseline)	156 (132–180)	81 (60–103)	71 (45–98)	<0.001

Table 3:

Primary and secondary outcomes with mean (95% CIs) with baseline scores and changes at post-training and 3-month follow-up with results (p-values) of the group-by-time interactions provided.

	HIT (mean, 95% CI)	LIT (mean, 95% CI)	Between-group mean differences (95% CI)	p-values
Primary outcomes				
fastest speed (m/s)				
BSL	0.61 (0.46–0.71)	0.78 (0.62–0.93)	−0.17 (−0.38–0.03)	0.101
ΔPOST	0.23 (0.14–0.31)	0.12 (0.07–0.17)	0.11 (0.04–0.17)	0.031
ΔF/U	0.27 (0.17–0.38)	0.13 (0.05–0.20)	0.14 (0.05–0.25)	
peak treadmill speed (m/s)				
BSL	0.66 (0.46–0.86)	0.81 (0.65–0.98)	−0.15 (−0.37–0.06)	0.248
ΔPOST	0.30 (0.21–0.37)	0.05 (−0.02–0.12)	0.25 (0.15–0.34)	<0.001
ΔF/U	0.23 (0.12–0.33)	0.04 (−0.02–0.10)	0.19 (0.10–0.27)	
Secondary clinical outcomes				
6-min walk test (m)				
BSL	176 (125–225)	228 (178–278)	−52 (−118–14)	0.127
ΔPOST	73 (47–98)	32 (17–47)	40 (20–60)	0.002
ΔF/U	74 (42–106)	26 (8.0 to 44)	48 (24–73)	
Self-selected speed (m/s)				
BSL	0.45 (0.34–0.56)	0.55 (0.45–0.66)	−0.10 (−0.24–0.04)	0.154
ΔPOST	0.18 (0.10–0.26)	0.11 (0.07–0.15)	0.07 (0.01–0.13)	0.112
ΔF/U	0.17 (0.10–0.24)	0.09 (0.04–0.13)	0.08 (0.02–0.14)	
Berg Balance Score (a.u.)				
BSL	31 (24–38)	34 (28–40)	3.1 (−11–4.8)	0.440
ΔPOST	2.0 (0.1–3.9)	0.5 (−1.7–2.6)	1.5 (−1.4–4.4)	0.462
ΔF/U	3.1 (0.4–5.7)	1.4 (−0.9–3.8)	1.6 (−1.5–4.7)	
5X sit-to-stand (s)				
BSL	12 (7.5–16)	12 (8.4–15)	0.2 (−4.2–4.5)	0.994
ΔPOST	0.6 (−3.2–4.3)	−0.4 (−2.4–1.7)	0.8 (−1.9–3.6)	0.649
ΔF/U	1.5 (−2.1–4.9)	−0.3 (−1.8–1.1)	1.7 (−0.3–3.8)	
Activities-specific Balance Confidence scale (%)				
BSL	50 (40–59)	52 (42–62)	−2.4 (−15–10)	0.670
ΔPOST	9.7 (6.0–13)	5.8 (2.4–9.1)	4.0 (−0.5–8.4)	0.284
ΔF/U	8.4 (3.1–14)	4.6 (0.6–8.7)	3.8 (−1.6–9.2)	
Medical Outcomes Short-Form – 36 (a.u.)				
BSL	36 (32 to 39)	36 (32–39)	0.2 (−4.4–4.8)	0.989
ΔPOST	5.0 (1.4–7.7)	4.3 (2.0–6.7)	0.2 (−2.9 to 3.3)	0.742
ΔF/U	5.9 (2.4–9.3)	5.0 (1.5–8.6)	0.9 (−3.8–5.6)	
Secondary metabolic outcomes				
VO_2peak (ml/kg/min)				
BSL	16 (13–18)	16 (14–18)	0.3 (−3.5–2.8)	0.850
ΔPOST	2.2 (0–4.4)	−0.2 (−2.6–2.2)	2.3 (−0.8 to 5.5)	0.275
ΔF/U	2.1 (−0.3–4.4)	0.4 (−1.8–2.7)	1.6 (−1.4–4.6)	

	HIT (mean, 95% CI)	LIT (mean, 95% CI)	Between-group mean differences (95% CI)	p-values
ΔVO_2match (ml/kg/min)				
BSL	16 (13–18)	16 (14–18)	0.3 (−3.5–2.8)	0.850
ΔPOST	−3.2 (−5.5– −1.0)	−1.4 (−3.4–0.9)	−1.9 (−4.6–0.9)	0.270
ΔF/U	−2.3 (−4.2– −0.5)	−0.4 (−2.5–1.7)	−2.0 (−4.7–0.8)	
VO_2gain (ml/kg/min)				
BSL	-	-	-	-
ΔPOST	5.4 (3.2–7.6)	1.2 (0.1–2.3)	4.2 (2.7–5.7)	<0.001
ΔF/U	4.4 (2.8–5.9)	0.8 (−0.3–1.9)	3.6 (2.1–5.0)	