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Stepwise regression and latent profile analyses of locomotor outcomes post-stroke

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Abstract

Background and Purpose: Previous data suggest patient demographics and clinical presentation are primary predictors of motor recovery post-stroke, with minimal contributions of physical interventions. Other studies indicate consistent associations between the amount and intensity of stepping practice with locomotor outcomes. The goal of this study was to determine the relative contributions of these combined variables to locomotor outcomes post-stroke across a range of patient demographics and baseline function.

Methods: Data were pooled from 3 separate trials evaluating the efficacy of high-intensity training (HIT), low-intensity training, and conventional interventions. Demographics, clinical characteristics and training activities from 144 participants > 1-month post-stroke were included in stepwise regression analyses to determine their relative contributions to locomotor outcomes. Subsequent latent profile analyses evaluated differences in classes of participants based on their responses to interventions.

Results: Stepwise regressions indicate primary contributions of stepping activity on locomotor outcomes, with additional influences of age, duration post-stroke, and baseline function. Latent profile analyses revealed 2 main classes of outcomes, with the largest gains in those who received HIT and achieved the greatest amounts of stepping practice. Regression and latent profile analyses of only HIT participants indicated age, baseline function and training activities were primary

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determinants of locomotor gains. Participants with the smallest gains were older (~60 years), presented with slower gait speeds (<0.40 m/s) and performed 600-1000 less steps/session.

Conclusion: Regression and cluster analyses reveal primary contributions of training interventions on mobility outcomes in patients > 1-month post-stroke. Age, duration post-stroke and baseline impairments were secondary predictors.

Clinical Trial Registration-URL: https://clinicaltrials.gov/. Unique Identifiers: NCT02507466 and NCT01789853

Keywords

gait; rehabilitation; cluster analyses

Introduction

Restoration of locomotor function is a priority for individuals with stroke[1, 2], particularly given the health care and personal costs associated with impaired mobility[3, 4]. Traditional rehabilitation paradigms focus on mitigating the impairments underlying walking deficits post-stroke, or normalizing gait patterns to improve mobility[5, 6]. However, the efficacy of these strategies is limited[7]. Previous studies suggest that the degree of lower extremity impairments and specific demographics (i.e., age, duration post-stroke) are primarily predictors of gains in lower extremity motor recovery[8-12], with uncertain contributions of physical therapy interventions.

Conversely, other studies indicate positive associations between locomotor outcomes and specific exercise strategies[13-17]. Previous studies suggest therapy interventions that focus entirely on providing large amounts of stepping practice at high cardiovascular intensities often result in statistically and clinically significant gains in locomotor function as compared to conventional and/or low intensity strategies[13-15, 17]. Subsequent analyses reveal significant moderate associations between stepping amounts or cardiovascular intensities attained and locomotor gains achieved (i.e., dose-response relationships). More recent data suggest high-intensity training (HIT) performed in variable contexts (treadmill, stairs, obstacles, uneven surfaces) may elicit further gains in postural stability and balance confidence[13], with a small decrease in stepping practice as compared to forward walking alone that does not mitigate gains in locomotor outcomes. The combined data emphasize the influence of exercise dose (i.e., type, amount and intensity) on locomotor responses, which contrast directly with previous findings indicating greater contributions of demographics and initial clinical presentation.

To address these competing hypotheses, details of training interventions from individuals with walking deficits post-stroke across a range of patient demographics and severity of impairments may allow delineation of their relative contributions to mobility outcomes. However, only a few studies have consistently monitored stepping activities during HIT in participants with subacute or chronic stroke[13, 14, 17]. The substantial variability in both patient demographics and interventions across studies may limit the utility of traditional regression analyses, and various cluster analyses may provide greater insight into responsiveness to interventions by identifying potential subgroups categorized by the magnitude of changes across locomotor outcomes. A range of these types of analyses are available, including the use of latent profile analyses[18], which is a mixture model-based technique that hypothesizes there is an underlying hidden (i.e., latent) categorical variable that separates populations into mutually exclusive and exhaustive groups or classes of participants with similar outcomes. This and similar strategies can be used to evaluate differences between classes to evaluate the factors that contribute to responsiveness to training.

The present study was designed to evaluate contributors to locomotor outcomes post-stroke and characteristics of participants who may or may not respond to specific interventions. Data were utilized from participants with subacute or chronic stroke who enrolled in specific intervention trials evaluating the efficacy of different training strategies on locomotor outcomes. Our primary hypotheses were that training interventions and, more directly, the amount of stepping practice was the primary determinant of responsiveness to training with secondary contributions of baseline function and demographic characteristics.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Participants

Data utilized in this analysis included participants with subacute (1–6 months) or chronic (>6 months) hemiparesis following unilateral stroke previously enrolled in one of three separate trials, including a recent randomized clinical trial in patients with chronic stroke[13], a smaller randomized trial in patients with subacute stroke[14], and a pilot study including participants with either subacute and chronic stroke that served as the pilot study[17, 19]. Four different training strategies were utilized, with the primary experimental group performing HIT focused on stepping activities performed in variable contexts (high-variable)[17]. Comparisons groups included HIT with limited stepping variability (forward walking; high-forward), lower intensity variable walking interventions (low-variable), and conventional physical interventions (conventional). All studies used similar inclusion criteria as follows: 18–85 years old; lower-extremity Fugl-Meyer < 34; over-ground self-selected velocity (SSV) < 1.0 m/s; and medical clearance to participate. Exclusion criteria included: receiving additional physical therapy interventions outside of study interventions, presence of lower-limb contractures that significantly limited locomotor function, cardiovascular, respiratory or metabolic instability, inability to ambulate >150 feet prior to stroke, previous history of additional neurological injury, and inability to adhere to study requirements. Differences in inclusion between studies were related to duration post-stroke and ability to walk with[14, 17] vs without[13] physical assistance as needed, and all ambulatory and non-ambulatory participants were included. All procedures were approved by the local institutional review boards and all participants provided written consent to participate. The initial database of 144 participants with primary locomotor outcomes were included (Table 1; n=22 from the pilot study, n=32 from the randomized subacute stroke trial, and n=90 from the chronic stroke trial).

Interventions

All participants received up to 30–40 1-hr sessions of different interventions over 2–3 months. Participants wore validated accelerometers (StepWatch, Modus, Wash DC) on their paretic ankle to evaluate stepping activity during therapy sessions. Patients received ≤40 min of training per session. The primary goals of all stepping training interventions (high-variable, high-forward, low-variable) were to: 1) maximize the amount of stepping practice; 2) achieve targeted cardiovascular intensities; and, 3) increase difficulty of walking tasks as tolerated. Targeted heart rate (HR) ranges were determined using age-predicted maximum [208-(0.7*age)][20], with high-variable or high-forward targeting 70–80% HR reserve, and low-variable using 30–40% HR reserve.

For high-variable training (n=65), sessions were divided into ~10-min bouts of four different stepping tasks[17]. Speed-dependent treadmill training was performed with an overhead harness system in case of loss of balance, with goals to increase speeds to reach targeted HRs. Criteria for successful stepping included positive step lengths, minimal limb collapse, and sagittal/frontal plane stability, with body-weight support or swing assistance provided only as needed. Minimal consideration was directed towards gait kinematics[17] unless there was a risk for orthopedic injury, with bracing or support provided as needed. Skill-dependent training was performed by applying perturbations to challenge postural stability, propulsion, and limb swing, and included walking in multiple directions, over inclines and obstacles, with leg weight/weighted vests and limited handrail use as tolerated. Over-ground training focused on achieving fastest possible speeds or performing variable tasks as described with use of a gait belt or overhead harness systems. Stair climbing was performed over static or rotating stairs (StairMaster, Vancouver, WA) using reciprocal gait patterns and progression to faster speeds and reduced handrail use as tolerated. For high-forward training (n=30), targeted intensity was also 70–80% HR reserve, although training was limited only to 20 min of forward treadmill training and 20 min of forward over-ground walking. Task difficulty was increased by increasing walking speeds within targeted intensities[13]. Participants in the low-variable group (n=32) performed stepping training similar to high-variable but with targeted intensities set to 30–40% HR reserve[13, 16].

Participants who received conventional interventions (n=17) continued with concurrent physical therapy as possible, with details of therapeutic activities extracted from medical records[14]. Conventional sessions were supplemented by research staff to achieve up to 40 sessions over 10 weeks, and consisted of conventional therapy activities[14, 21], including specific amounts (repetitions) of strengthening, balance, and transfer tasks, with stepping practice provided on both the treadmill and over-ground/stairs without limitations on cueing and feedback. Training intensity was targeted at 30–40% of HR reserve, consistent with HRs achieved during rehabilitation post-stroke[14, 22]. The treating therapist progressed patients with devices and bracing as appropriate.

Data collection

Participants completed evaluations at baseline and post-training. Primary outcomes included: (1) over-ground SSV and (2) fastest-possible velocity (FV) using a pressure-sensitive walkway (GaitMat, Chalfont, PA or GaitRite, Haverton, PA); (3) 6-minute walk test (6MWT) with instructions to walk at a normal comfortable pace; and (4) peak treadmill (TM) speed during assessments performed on a motorized TM with speeds starting at 0.1 m/s for 1–2 min and increased by 0.1 m/s every 1–2 min. The fastest TM speed that participants could walk for 1 min was considered peak TM speed. For balance measures, the Functional Gait Assessment (FGA) and Berg Balance Scales were used, and preliminary data (n=11) suggest a strong correlation between scores (r=0.95, p<0.01) with regression equations used to convert Berg to FGA (FGA=0.47*(Berg) + 3.12; unpublished results[13]). Balance scores are hereafter referred to as Functional Gait Assessment. Additional tests included the 5-times sit-to-stand test (transformed to repetitions/sec) and lower-limb Fugl-Meyer assessment. Training variables included average steps/sessions recorded by the ankle-worn accelerometers, number of sessions attended, and total number of steps throughout training (steps/sessions * number of sessions).

Statistical analysis

Correlation and stepwise regression and subsequent latent profile analyses evaluated the potential determinants of locomotor improvements and characteristics of responders. Correlations focused on associations between training variables (steps/session, number of sessions, and total steps) and primary walking outcomes (ΔSSV, ΔFV, Δ6MWT and ΔTM speed) with subsequent regressions performed separately for each primary dependent variable. Independent predictors included: age, gender, BMI, and duration post-stroke (1–6 months, >6 months), lesion location, lower-limb Fugl-Meyer, baseline Functional Gait Assessment and sit-to-stand, and the specific dependent variable measured at baseline (i.e., baseline 6MWT for Δ6MWT). Primary training variables utilized in regression analyses focused on number of sessions and mean steps/session (vs total steps) as these former variables may be more readily interpreted by clinicians. Given the findings, stepwise regressions were repeated for only HIT groups (high-variable/high-forward)[13]. Stepwise regressions were performed with α=0.05 using SPSS (v26) with primary associations identified as the independent predictor with the greater association with the dependent variable (i.e., first variable listed in regression equation). Collinearity diagnostics were monitored with variance inflation factors <5.0 considered acceptable.

Latent profile analyses were used to identify classes (i.e., subgroups or clusters) of participants with similar changes in primary locomotor outcomes (ΔSSV, ΔFV, Δ6MWT and ΔTM speed). Z-scores were used to stabilize the scales and improve the convergence of the algorithm for estimating the parameters of the Gaussian mixture model. Prior to analysis, a robust variant of the Mahalanobis distance based on the minimum covariance determinant[23] was calculated to detect and delete multivariate outliers, which is an estimate of the relative distance of each specific data point to the normalized mean (z-score) and a procedure recommended prior to using cluster analytic techniques[24]. Four different parametrizations for the covariance structure of the Gaussian mixture model were considered including the following models: 1) equal variances across classes and covariances fixed to 0; 2) varying variances across classes and covariances fixed to 0; 3) equal variances and covariances across classes; and 4) varying variances and covariances across classes. The covariance structure of the mixture model as well as the optimal number of latent classes were determined by considering a range of indices: the Bayesian Information Criterion[25], the sample-size adjusted Bayesian Information Criterior[26], entropy and bootstrap likelihood ratio test[27]. Smaller values of Bayesian Information Criterion (or adjusted for sample-size) indicate a better model fit. The value of entropy between 0.8–1.0 reflects a sound separation of identified classes in relation to the data. The bootstrap likelihood ratio test is used to compare the fit of models that specify different number of classes but utilize the same covariance structure. Latent profile analysis was repeated for only HIT groups given similar locomotor improvements.

Post-hoc analyses assessed differences between latent class membership (independent grouping variable) for training measures, baseline impairments and demographic status (dependent variable). Chi-square tests and one-way ANOVA with post-hoc Tukey's test were used to examine differences among clusters in categorical and continuous dependent variables. All tests were two-sided with $\alpha = 0.05$. Latent profile analysis was conducted using R package "tidyLPA" (version 3.6.1).[28]

Results

Table 1 (1st column) details changes in outcomes, demographics, baseline characteristics, and training interventions of all participants included, demonstrating substantial variability across cohorts. Preliminary correlation analyses revealed the strongest relation between total steps during training (steps/session * number sessions) and primary outcomes (range of r-values:0.48–0.60, all p<0.01), with lower but significant associations between steps/sessions (r-values:0.35–0.50) and number of sessions (r-values: 0.22–0.27; all p<0.01). Given the utility of steps/sessions and number of sessions for clinicians prescribing or providing therapy interventions, these latter data were utilized in regression analyses with associations between steps/sessions with ΔSSV and ΔFV presented in Fig 1A-B. Stepwise regressions for the primary outcomes of ΔSSV, ΔFV, Δ6MWT and ΔTM speed indicate the strongest associations with steps/session (i.e., first independent predictor listed), with secondary contributions of duration post-stroke, age, number of sessions, and baseline assessments (Equations 1-4).

$$\Delta SSV = 0.11 * \left(1000 * \frac{steps}{session}\right) - 0.13 * (> 6\,months) - 0.22 * (baseline\ SSV) - 0.002 * (age) + 0.23;\ r^2 = 0.36;$$

Equation 1:

$$\Delta FV = 0.14 * \left(1000 * \frac{steps}{session}\right) - 0.14 * (> 6\,months) - 0.004 * (age) + 0.007 * (sessions) + 0.031;\ r^2 = 0.42;$$

Equation 2:

$$\Delta 6MWT = 45 * \left(1000 * \frac{steps}{session}\right) + 2.1 * (sessions) - 1.2 * (age) - 0.27 * (baseline\,6MWT) - 41 * (>6\,months) + 103 * (baseline\,sit - to - stand) + 9.2;\ r^2 = 0.46; \qquad \text{Equation 3:}$$

$$\Delta TM\,speed = 0.22 * \left(1000 * \frac{steps}{session}\right) - 0.36\,(baseline\,TM\,speed) - 0.15 * (>6\,months) + 0.11 * (male) + 0.37;\ r^2 = 0.47\,. \qquad \text{Equation 4:}$$

Subsequent latent profile analysis was utilized to differentiate classes (i.e., clusters or groups) of participants based on their responses to training. Prior to this analysis the Mahalanobis distance was calculated to detect 3 outliers with changes that were substantially greater than the population mean (e.g., mean ΔFV=1.24±0.29 m/s). Latent profile analyses on the remaining 141 participants suggested superior fit of a 2-class model. Figure 2A indicates z-scores of changes in locomotor outcomes within each class. Class 1 represents 72% of participants (n=104) with above-average gains (z-scores>0), whereas Class 2 represents 28% (n=37) with below-average changes (z-scores<0).

Table 1 delineates the clinical and demographic characteristics and changes in outcomes in the two classes. Between-class analyses indicated locomotor gains were significantly different as anticipated, with 0.20–0.35 m/s differences in gait speed changes (ΔSSV, ΔFV, ΔTM speed) and 70 m differences in Δ6MWT. Age was the only demographic variable that was statistically different between classes, although all measures of baseline function and Fugl-Meyer were significantly lower in Class 2. For training characteristics, a greater proportion of non-HIT training (low-variable/conventional) was observed in Class 2, and differences in total steps and steps/session (Class 1 > Class 2).

Given the significant contributions of training interventions to outcomes, regression and latent profile analyses were repeated with only HIT (high-forward/high-forward) groups. Table 2 (1^{st} column) delineates the demographics, clinical characteristics, training activities and locomotor outcomes in HIT groups combined. Correlations again indicate total steps were better correlated with primary outcomes (r-valus:0.40–0.58), with significant associations with other training variables (steps/session, 0.24–0.45; number sessions, 0.28–0.35; all p<0.01). Retaining both steps/session and number of sessions as independent predictors in the stepwise regression revealed primary associations between age and locomotor outcomes (Equation 5-8), with secondary contributions of training variables or other demographics or clinical characteristics.

$$\Delta SSV = -0.007 * (age) - 0.008 * (sessions) + 0.007 * (Fugl - Meyer) + 0.20;\ r^2 = 0.31; \qquad \text{Equation 5:}$$

$$\Delta FV = 0.12 * \left(1000 * \frac{steps}{session}\right) + 0.012 * (sessions) - 0.008 * (age) + 0.07;\ r^2 = 0.39; \qquad \text{Equation 6:}$$

$$\Delta 6MWT = -2.7 * (age) + 3.9 * (sessions) + 22 * (1000 * \frac{steps}{session}) + 60;\ r^2 = 0.48; \qquad \text{Equation 7:}$$

$$\Delta TM\ speed = -0.009 * (age) - 0.012 * (BMI) + 0.20 * (1000 * \frac{steps}{sessions}) - 0.41 * (baseline\ TM\ speed) + 0.18 * (male) + 0.85;\ r^2 = 0.48; \qquad \text{Equation 8:}$$

Latent profile analysis of only the HIT groups (n=92) suggested good fit of a 3-class model. Class-specific mean z-scores are presented in Figure 2B, with classes ranked by their relative responsiveness (HIT1>HIT2>HIT3; Table 2). Substantial differences in locomotor gains were observed between HIT1 and HIT2, with smaller but significant differences between HIT2 and HIT3 except TM speed. Post-hoc ANOVA revealed younger participants in the highest responders (HIT1>HIT2/HIT3). Differences in baseline function and impairments were consistently lower in the lowest responding group (HIT3). Additional differences in training sessions were observed between HIT1 vs HIT2, with lower steps/session and total steps in HIT3.

Discussion

The present study details the relative contributions of physical interventions, demographics, and clinical presentation on locomotor outcomes in individuals post-stroke using both regression and latent profile analyses. Variables thought to contribute primarily to recovery (age, duration post-stroke and baseline deficits)[9, 10] were important contributors to locomotor gains. However, training-related variables, namely total steps and steps/sessions during HIT, were strong predictors of gains in primary locomotor outcomes as previously shown[29, 30]. While total steps throughout the duration of training demonstrated greater association to locomotor outcomes, steps/sessions and number of sessions may be more tangible training parameters that clinicians can readily interpret and apply in clinical practice. Subsequent latent profile analyses resulted in two classes of participants based on responses to training, and revealed between-group differences in training characteristics, age, and baseline clinical presentation.

Regression analyses performed in only those participants who performed HIT revealed greater primary contributions of age and training activities, with additional influences of baseline function. In this latter analysis, HIT1 demonstrating the largest improvements was younger than HIT2 but with similar baseline function, while HIT3 with the smallest gains were older and presented with the lowest baseline function. Despite attempts to provide similar interventions in all HIT participants, this latter group also received the least amount of stepping practice. Reduced stepping activity in HIT3 may be due both to initial baseline function or other factors not captured here (e.g., exercise tolerance and willingness to participate). While gains in HIT3 approached thresholds for small minimally important clinical differences (0.05 m/s for speed, 20 m for 6MWT)[31], the changes as compared to those observed in HIT1/HIT2 emphasize the limitations of performing HIT in selected individuals.

The present findings contrast with studies emphasizing the primary contributions of demographics and baseline function to resultant neurologic or functional recovery and little association with therapy activities[9]. Differences between these competing hypotheses may be due to two factors. First, few studies measure the amounts and intensities of interventions performed, and their assessment may be important to delineate the contributions of physical therapy strategies[29, 30]. In addition, the primary measures to evaluate recovery post-stroke vary between studies. Specifically, many researchers focus on the assessment of the Fugl-Meyer or other paretic limb impairments[9] as a measure of recovery. While valuable, these measures do not directly assess activity limitations. Conversely, clinical locomotor outcomes are used prominently in studies evaluating the efficacy of different physical interventions given their relation with health, participation and mortality[4, 32]. Both types of measures are important for determining recovery post-stroke, although estimate different constructs that require differentiation by the neuroscience and rehabilitation community.

Limitations of the current study include the relatively small sample size, although the pooled data represent the largest cohort of participants post-stroke with accurate stepping data during physical therapy interventions. While a potential strength of the current analyses is the use of similar inclusion criteria and outcomes across studies, the present sample excluded patients early post-stroke (< 1 month) during which larger gains are typically observed and the benefits of rehabilitation may be greater[12]. Similar types of analyses are possible on those populations with availability of data detailing demographics, baseline function, and therapy activities.

Another primary limitation is the inability to provide precise lesion locations or estimates of the integrity of descending pathways using imaging or electrophysiological measures (e.g., transcranial stimulation). The importance of the magnitude and location of lesions is well-recognized[33-35], and detailed anatomical or electrophysiological measures of corticospinal integrity may serve as biomarkers for predictive algorithm of motor recovery post-stroke. Interestingly, however, recent studies of the lower limb recovery suggest evaluation of corticospinal integrity through selected imaging analyses or with transcranial stimulation may be of limited utility of to predict or estimate motor function[9, 36]. Continuing work related to this area of research should provide valuable insight into brain-behavior relations for lower limb recovery and locomotor function post-stroke.

In summary, correlation, regression and latent profile analyses suggest that participation in HIT providing substantial amounts of stepping practice at higher cardiovascular intensities were primary determinants of changes in locomotor function in ambulatory individuals > 1-month post-stroke. Secondary analysis of only those participants who performed HIT reinforce the important contributions of age and baseline function. Given these findings, the possibility of more widespread clinical implementation of HIT in patients > 1-month post-stroke may be warranted with appropriate safety considerations[37] and with explicit understanding that specific patient populations may demonstrate smaller gains with such training. Further research is necessary to evaluate the comparative efficacy of this strategy to other treatment protocols < 1-month stroke.

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Abbreviations

6MWT	6-min walk test
FV	fastest velocity
HIT	high-intensity training
HR	heart rate
SSV	self-selected walking velocity
TM	treadmill
FGA	Functional Gait Assessment

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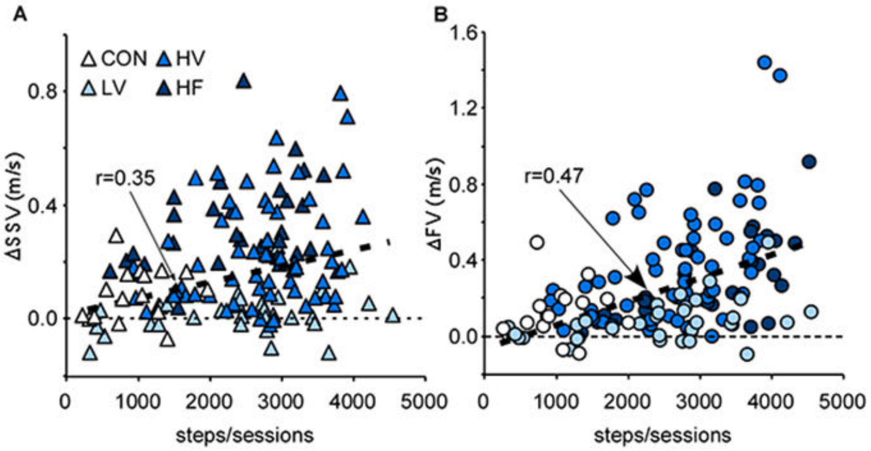

Figure 1.

Dose-response relationships between stepping activity (steps/sessions) and changes in SSV (A) and FV (B) across 144 participants with subacute and chronic stroke.

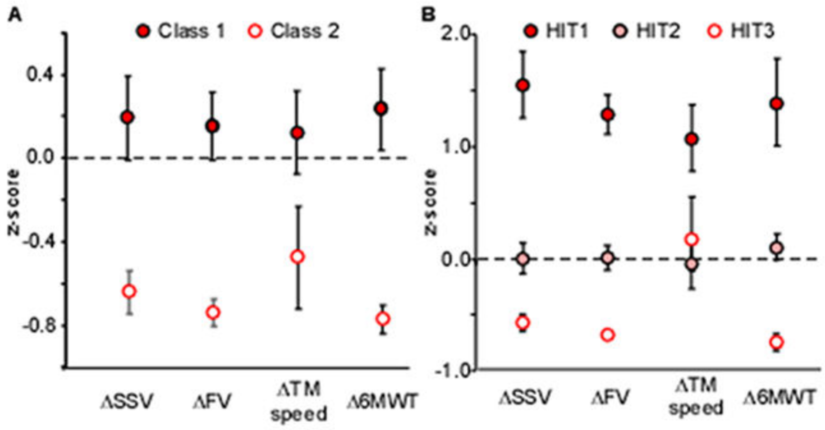

Figure 2.

A) Mean z-scores for primary locomotor changes for 141 participants classified into Class 1 and 2. B) Mean z-scores of primary locomotor changes for 92 HIT participants classified into HIT1, HIT2, and HIT3 (errors bars indicate confidence intervals).

Table 1.

Demographics, training characteristics, baseline and changes in primary (ΔSSV, ΔFV, Δ6MWT and ΔTM speed) and secondary outcomes (sit-to-stand, ΔSTS; Functional Gait Assessment: ΔFGA) outcomes in all participants and each class identified through latent profile analyses [conventional, CON; high-forward, HF; high-variable, HV; low-variable, (LV)]. Classes did not include the 3 outliers.

	All (n=144)	**Class 1 (m=104)**	**Class 2 (n=37)**	**p-values**
Changes in outcomes				
ΔSSV (m/s)	0.15±0.17	0.19±0.18	0.04±0.05	<0.01
ΔFV (m/s)	0.24±0.26	0.28±0.22	0.05±0.05	<0.01
Δ6MWT (m)	71±73	88±73	15±14	<0.01
ΔTM speed (m/s)	0.30±0.25	0.33±0.26	0.18±0.16	<0.01
ΔSTS (reps/s)	0.05±0.12	0.04±0.12	0.07±0.13	0.26
ΔFGA (a.u.)	2.3±3.6	2.4±3.8	2.0±3.3	0.55
Demographics				
age (yrs)	58±11	56±11	62±8.9	<0.01
BMI (kg/m^2)	29±6.7	29±6.7	29±7.1	0.89
gender (F/M)	48/96	37/67	11/26	0.52
duration (1-6/>6 mo)	99/45	30/74	12/25	0.68
side of paresis (R/L)	55/89	41/63	13/24	0.65
lesion site: cortical	68	49	16	
subcortical/lacunar	49	37	12	
brainstem/cerebellum	9	6	3	0.39
multiple/diffuse	8	7	1	
not reported	10	5	5	
Baseline assessments				
Fugl-Meyer (a.u.)	22±5.1	22±4.8	19±5.9	<0.01
AFO (N/Y)	46/98	34/70	9/28	0.34
SSV (m/s)	0.45±0.28	0.51±0.26	0.26±0.24	<0.01
FV (m/s)	0.60±0.39	0.68±0.36	0.31±0.33	<0.01
6MWT (m)	156±106	178±101	85±90	<0.01
TM speed (m/s)	0.65±0.44	0.74±0.41	0.37±0.38	<0.01
STS (reps/s)	0.28±0.15	0.31±0.13	0.18±0.14	<0.01
FGA (a.u.)	12±5.8	13±5.1	8.1±6.0	<0.01
Training activities				
CON/HF/HV/LV	17/30/65/32	10/25/51/18	7/4/12/14	0.01
number of sessions	30±7.2	30±7.6	30±6.3	0.83
steps/session	2460±1057	2677±947	1708±847	<0.01
total steps (x10^3)	74±36	78±36	48±30	<0.01

Table 2.

Demographics and baseline/change in outcomes for participants who performed HIT and each class identified through latent profile analyses; * indicates significantly different from other groups; † indicates differences between two groups. Classes did not include the 3 outliers.

	All (n=95)	**HIT1 (m=26)**	**HIT2 (n=44)**	**HIT3 (n=22)**	**p-values**
Changes in outcomes					
ΔSSV (m/s)	0.21±0.17	0.42±0.15*	0.15±0.09*	0.05±0.04*	<0.01
ΔFV (m/s)	0.32±0.27	0.58±0.13*	0.24±0.10*	0.07±0.03*	<0.01
Δ6MWT (m)	92±76	172±83*	78±32*	17±16*	<0.01
ΔTM speed (m/s)	0.39±0.24	0.57±0.22*	0.29±0.19	0.34±0.22	<0.01
ΔSTS (reps/s)	0.05±0.13	0.07±0.15	0.05±0.11	0.02±0.15	0.44
ΔFGA (a.u.)	2.3±3.5	3.2±3.2	2.2±3.8	1.6±3.3	0.29
Demographics					
age (yrs)	58±11	51±10*	60±9.3	62±8.0	<0.01
BMI (kg/m^2)	29±6.8	28±6.6	31±6.8	29±7.1	0.25
gender (F/M)	29/66	11/15	14/30	4/18	0.20
duration (<6/>6 mo)	27/68	10/16	9/35	6/16	0.26
side of paresis (R/L)	38/57	11/15	19/25	7/15	0.65
lesion site: cortical	46	11	19	13	
subcortical/lacunar	32	11	16	5	
brainstem/cerebellum	6	1	4	1	0.53
multiple/diffuse	5	2	3	0	
not reported	6	1	2	3	
Baseline assessments					
Fugl-Meyer	22±5.2	22±5.1	23±4.8	19±5.4*	<0.01
AFO (N/Y)	36/59	10/16	17/27	6/16	0.63
SSV (m/s)	0.45±0.29	0.45±0.29	0.50±0.27†	0.30±0.28†	0.02
FV (m/s)	0.60±0.39	0.60±0.39	0.68±0.37†	0.38±0.38†	0.01
6MWT (m)	156±105	166±113	172±100†	99±91†	0.02
TM speed (m/s)	0.65±0.42	0.72±0.41	0.73±0.41	0.35±0.34*	<0.01
STS (reps/s)	0.29±0.15	0.32±0.13	0.30±0.16	0.24±0.14	0.16
FGA (a.u.)	12±5.6	13±5.8	13±5.1	9.3±5.8*	0.02
Training activities					
HF/HV	30/65	7/19	16/28	6/26	0.63
number of sessions	31±7.3	34±5.2†	29±8.1†	30±6.1	<0.01
steps/session	2826±865	3144±683	2844±848	2234±740*	<0.01
total steps (x10^3)	87±32	106±25*	76±36	67±25	<0.01