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The Effect of Robot-assisted Lokomotor Training on Gait Recovery: A Multivariate Analysis

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Abstract— **To explore the effect of LOKOMAT and LOKOMAT+Tizanidine on the improvement of walking capacity for people with spinal cord injury (SCI), 20 SCI subjects with hypertonia spasticity at their ankle joints participated in a 12-session Lokomat training; among them, 10 subjects received Tizanidine. 1-hour LOKOMAT training was provided 3 times per week for 4-weeks. Subjects were evaluated 4 times for Timed-Up-and-Go, 10-Meter-Walking, and 6-Minute-Walking testings, at the baseline, 1-, 2- and 4-weeks after training. Latent Class Growth model was used to classify the LOKOMAT training speed, and clinical walking evaluations. Subjects in each treatment group could be classified into two subclasses for training speed and clinical evaluation. It was found that the training speed increased in all treatment group, while the subjects in LOKOMAT+Tizanidine presented a significant improvement of their training speed from the training session. The clinical evaluations classified subjects similarly, and no significant improvement of clinical measurements was observed for either treatment. The MVC dorsiflexion torque at the ankle joint was able to predict the class memberships of subjects for their walking capacity and can be used as a significant predictor for therapeutic functional recovery after spinal cord injury.**

Keywords— **Latent Class Growth Model, LOKOMAT, , Tizanidine, spinal cord injury**

I. Introduction

People with spinal cord injury often suffer from impaired voluntary movement. LOKOMAT training, a typical robot-assisted walking, has been widely used in physical therapy to help persons who suffer from impaired walking ability due to stroke, spinal cord injury (SCI) or brain injury[1], [2]. It helps patients to walk, improve their muscle strength, and prevent from osteoporosis. In the meanwhile, Tizanidine, an anti-spasticity medication has been used to treat spasticity of the lower limbs[3]. It may potentially improve mobility. The combined effect of the LOKOMAT training and Tizanidine on SCI subjects has not been investigated thoroughly.

Accordingly, the overall objective was to investigate the effects LOKOMAT and LOKOMAT+Tizanidine on walking improvement of SCI participants. The specific goals were to find whether,

(1) SCI subjects show significant improvement on LOKOMAT training speed

(2) these subjects present improvement on clinical assessment after physical and pharmaceutical interventions

(3) inter-individual difference of the clinical evaluations can be predicted by other kinetic or kinematic measurements, such as plantar-flexion or dorsi-flexion maximum voluntary contraction (MVC).

II. Experimental Protocol

A. Experimental Procedure

20 incomplete spinal cord injury (iSCI) subjects with hypertonia spasticity in their lower extremity participated in this study. All the subjects were ambulatory and were able to complete the clinical evaluations.

Subjects were assigned into two treatment groups: LOKOMAT (Fig. 1.), and LOKOMAT+Tizanidine. Each group included 10 subjects and used the interventions for 4 weeks. 1- hour LOKOMAT training was provided 3 times a week for 4-weeks. Subjects were evaluated 4 times: at the baseline, 1-, 2- and 4-weeks after training.

The clinical evaluations included Timed-Up-and-Go (TUG)[4], 10-Meter-Walking (10MW)[5], and 6-Minute-Walking (6MINW)[6].

TUG is used to evaluate the functional recovery by measuring time taken by the subject to stand up from and sit back to an armed-chair for a 3-meter walking (T_{TUG}).

10MW is used to evaluate walking speed by measuring time spent for a walking distance of 10 meters (T_{10MW})

6MINW is used to assess walking endurance by measuring distance covered by 6-minute walking (D_{6minw}).

These walking tests have been widely used as guidelines to evaluate functional ambulation capacity and help interpret clinical research results.

In SCI subjects, both sides are typically affected. Thus, the peak torques of maximal voluntary contraction (MVC) generated during dorsi-flexion (Td) and plantar-flexion (Tp) at the ankle joint was measured for the more affected side; the side with higher Ashworth score[7] for the ankle. The measurement was done with the ankle at neutral position (90°). The torque and EMGs were sampled for 5sec.

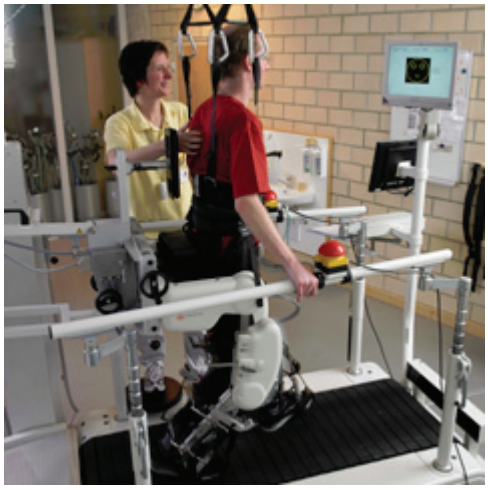

Fig. 1. LOKOMAT, a robot-assisted walking training system, consists of the robotic gait orthosis, body weight support and treadmill (photo courtesy of Hocoma AG, Volketswil, CH).

B. Analytical Procedure

Latent class growth (LCG) model[8], [9] also called Semiparametric Bayesian latent trajectory model, was applied to find the training speed pattern along the 4-week training process for the LOKOMAT and LOKOMAT+Tizanidine treatment groups separately. The LCG model assumes that the population can be divided into a finite number of latent classes (homogeneous inter-subject subpopulations) by inspecting the intra-subject changes. The observations in each subclass are locally independent. The membership of subjects can be associated with continuous or discrete baseline factors (latent variables). Growth model, a random effect model[10], is applied in each latent class to find one of the growth patterns within the population. The number of latent classes and the goodness of fit of the classification model is determined and evaluated by Bayesian Information Criterion (BIC) and entropy. The LCG model with the lowest BIC and largest entropy is selected.

Specifically, the following linear growth model was used in the current study,

$$y_{ijk} = \left[\beta_{00k} + \mu_{0jk}\right] + \left[\beta_{10k} + \mu_{1jk}\right] T_j + e_{ijk} \qquad (1)$$

where i denotes subject number, j is for time (training session number), k corresponds to the latent class number. e_{ijk} is random residual of the model; for other parameters; β_{00k} and β_{10k} are the same for all subjects in subclass k; μ_{0jk} and μ_{1jk} vary among subject k and time point j. The model (1) is similar to a traditional linear regression model except that the individual difference is permitted, i.e., interception ($[\beta_{00k}+\mu_{0jk}]$) and slope ($[\beta_{10k}+\mu_{1jk}]$) in each latent class vary among individuals, j. Equation (1) can be written as

$$y_{ijk} = [\beta_{00k} + \beta_{10k} T_j] + [\mu_{0jk} + \mu_{1jk} T_j + e_{ijk}] \qquad (2)$$

The components of (2) in the first bracket are fixed effect and the rest components are random effect for the current growth model.

Two post-hoc analyses following the LCG were followed.

(1) Different independent variables were inspected by logistic regression[11] to find significant predictors for the membership of subjects in the latent classes;

(2) A linear mixed model with covariance structure of the 1st order auto-regression was performed to inspect the effect of subclass (CLASS) and training session (SESSION) on the training speed in group of LOKOMAT and LOKOMAT+Tizanidine, and check their effects on training speed. The autocorrelation effect from repeated measures of subjects was adjusted.

The standard level of significance was 0.05 during the statistical tests.

III. Results

A. Training speed

LCG model was applied to the training speed in treatment group LOKOMAT and LOKOMAT+Tizanidine. Two sub-classes were found for all treatment groups (Table 1). Regular linear regression was performed to inspect the relationship between training speed and sessions (Fig. 2). It was found that subjects in Class 2 in treatment group LOKOMAT started with 39.65 m/min at the first session, which was higher than the starting speed of 27.01 m/min in Class 1 (Table 1). Similarly, subjects in Class 2 in group LOKOMAT+Tizanidine started with 43.62 m/min, while Class 1 had a lower speed, 29.29 m/min, at the first session.

Linear mixed model showed that, in LOKOMAT group, CLASS had significant effect on the training speed ($F_{[1,16]}$=35.371, P<0.001), while the effect of SESSION and the interaction SESSION×CLASS were not significant. For the treatment group of LOKOMAT+Tizanidine, the effects of SESSION and CLASS were both significant ($F_{[10,58]}$=2.669, P=0.009; $F_{[1,15]}$=84.994, P<0.001 respectively), but with non-significant interaction.

Tukey post hoc test showed that training speed of class 2 was higher than class 1 for all treatment groups (P<0.001 for all); the training speed in session 2 and 3 were lower than

session 7-11 for treatment group LOKOMAT+Tizanidine (P<0.037 for all pairwise comparisons).

TABLE 1.
Statistical results of LOKOMAT training speed from Latent Class Growth (LCG) model and linear regression

	Lokomat	
LCG model		
Class (# of subjects)	Class 1 (6)	Class 2 (4)
linear regression		
Intercept	26.21 (P<0.001)	39.09 (P<0.001)
Slope	0.79 (P=0.004)	0.56 (P=0.010)
	Lokomat+Tizanidine	
LCG model		
Class (# of subjects)	Class 1 (5)	Class 2 (5)
linear regression		
Intercept	28.78 (P<0.001)	43.07 (P<0.001)
Slope	0.54 (P=0.025)	0.55 (P=0.036)

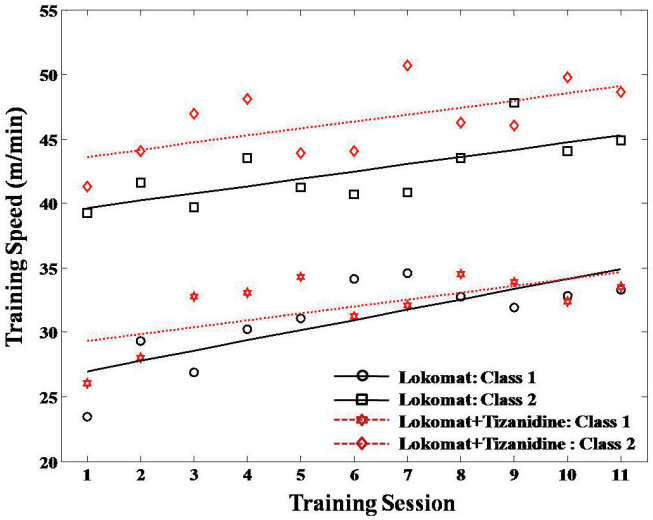

Fig. 2. The training speed as a function of the training sessions for two treatment groups of subjects.

B. *Clinical evaluations*

The Pearson correlation coefficients among the clinical measurements T_{TUG}, T_{10MW} and D_{6minw} were computed for each treatment group over all subjects. They were all significant ($|r|$>0.685, P<0.001 for all). LCG model was applied for all measurements of each treatment group, and two subclasses were found for each group. The membership of subjects into the subclasses was the same for all variables. For example, for treatment group LOKOMAT, baseline T_{TUG} of in Class 2 was 72.72 sec while it was 17.74 sec in Class 1; for treatment group LOKOMAT+Tizanidine, baseline T_{TUG} was 77.32 sec in Class 2 which was higher than 13.32 sec in Class 2.

T_{TUG}, T_{10MW} and D_{6minw} did not change significantly along time in each subclass in each treatment group (P>0.910 for all), therefore, the membership classification of their clinical evaluations was based on the similar intercepts of the time course instead of slope.

C. *Prediction of Functional Recovery*

Logistic regression was used to explore the effects of Td and Tp on class membership. It was found Td was a marginally significant predictor for the classification of subjects in each treatment group (Table 2). While Tp was not significant for LOKOMAT+Tizanidine group (P=0.307). For LOKOMAT group, the subjects with Td>11 Nm were more likely in Class 2 than in Class 1, and the estimated odds ratio was 1.481 which indicates that the probability to be in Class 2 increases with the augment of Td. Similarly, for group LOKOMAT+Tizanidine, the logistic regression showed that the subjects with Td>3 Nm were more likely in Class 2 than in Class 1, and the estimated odds ratio was 1.498.

Other possible factors, injury level, Ashworth scale, and post-injury time, had no significant effect on the class membership of clinical evaluation (P>0.720).

TABLE 2.
Results from logistic regression to inspect the effect of the maximal dorsiflexion torque at ankle joint on the membership of subjects in two subclasses for clinical evaluations

Logistic regression	Class 1	Class 2
	Lokomat	
Odds ratio	Reference	1.481 (P=0.0167)
Td	if ≤11	if >11
	Lokomat+Tizanidine	
Odds ratio	Reference	1.498 (P=0.0556)
Td	if ≤3	if >3

V. Discussion and Conclusions

We used the Latent Class Growth model to classify the LOKOMAT training speed, and clinical walking evaluations for SCI subjects with either LOKOMAT or LOKOMAT+Tizanidine.

Two subclasses were observed for each treatment group in training speed and clinical evaluation. Training speed increased in all treatment group, while it varied between subclasses by different starting speed (intercept of the linear regression), while the rate of training speed increase did not present significant difference between subclasses. The combination of LOKOMAT and Tizanidine presented a significant effect of LOKOMAT training session on the augment of training speed.

In the current study, the improvement from the Lokomat training for either treatment alone was not presented during the clinical overground walking evaluations, such as TUG,

6MW and 10MINW. A similar study for post-stroke patients with hemiparesis also found that the 6MINW did not improve after a 12-session Lokomat training, while the lokomat training speed presented significant increase[12]. The task requirement for the robotic-assisted treadmill training and the level-ground walking are different. The Lokomat training is a sub-maximum task for the participants to improve their functional mobility and motor skills. They are encouraged to increase their training speed and to reduce guidance force, with the help of BWS system. On the other hand, clinical evaluations are self-selected speed, therefore the trial-to-trial variation of clinical evaluations might be higher than the improvement received from the training.

Our results demonstrate the maximal isometric dorsiflexion torque at the ankle joint was able to predict the class memberships of subjects for their overground walking capacity. The MVCs, a routine clinical measure, can be used as a significant predictor for therapeutic functional recovery after spinal cord injury. These findings help to optimize the physical and pharmaceutical treatments for spinal cord injury recovery, and present a novel measurement, doriflexion torque at ankle joint, to be a potential fast and reliable clinical assessment tool.

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REFERENCES

[1] H. Barbeau, *et al.*, "The effect of locomotor training combined with functional electrical stimulation in chronic spinal cord injured subjects: walking and reflex studies," *Brain Research Reviews,* vol. 40, pp. 274-291, Oct 2002.

[2] R. D. de Leon, *et al.*, "Using robotics to teach the spinal cord to walk," *Brain Research Reviews,* vol. 40, pp. 267-273, Oct 2002.

[3] M. M. Mirbagheri, *et al.*, "Quantification of the effects of an alpha-2 adrenergic agonist on reflex properties in spinal cord injury using a system identification technique," *Journal of Neuroengineering and Rehabilitation,* vol. 7, pp. -, Jun 23 2010.

[4] R. W. Bohannon, "Reference values for the timed up and go test: a descriptive meta-analysis," *J Geriatr Phys Ther,* vol. 29, pp. 64-8, 2006.

[5] J. F. Ditunno, Jr., *et al.*, "Walking index for spinal cord injury (WISCI): an international multicenter validity and reliability study," *Spinal Cord,* vol. 38, pp. 234-43, Apr 2000.

[6] H. J. van Hedel, *et al.*, "Assessing walking ability in subjects with spinal cord injury: validity and reliability of 3 walking tests," *Arch Phys Med Rehabil,* vol. 86, pp. 190-6, Feb 2005.

[7] B. M. Haas, *et al.*, "The inter rater reliability of the original and of the modified Ashworth scale for the assessment of spasticity in patients with spinal cord injury," *Spinal Cord,* vol. 34, pp. 560-4, Sep 1996.

[8] T. Jung and K. A. S. Wickrama, "An introduction to latent class growth analysis and growth mixture modeling," *Social and Personality Psychology Compass,* vol. 2, pp. 302-317, Jan 2008.

[9] X. Tan, *et al.*, "How Spacing of Data Collection May Impact Estimates of Substance Use Trajectories," *Substance Use & Misuse,* vol. 46, pp. 758-768, 2011.

[10] P. D. Bliese and R. E. Ployhart, "Growth modeling using random coefficient models: Model building, testing, and illustration," *Organizational Research Methods,* vol. 5, pp. 362-387, Oct 2002.

[11] B. Krishnapuram, *et al.*, "Sparse multinomial logistic regression: fast algorithms and generalization bounds," *IEEE Trans Pattern Anal Mach Intell,* vol. 27, pp. 957-68, Jun 2005.

[12] K. P. Westlake and C. Patten, "Pilot study of Lokomat versus manual-assisted treadmill training for locomotor recovery post-stroke," *Journal of Neuroengineering and Rehabilitation,* vol. 6, p. 18, 2009.