Robotic-Locomotor Training as a Tool to Reduce Neuromuscular Abnormality in Spinal Cord Injury

The Application of System Identification and Advanced Longitudinal Modeling

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Abstract*—In this study, the effect of the LOKOMAT, a robotic-assisted locomotor training system, on the reduction of neuromuscular abnormalities associated with spasticity was examined, for the first time in the spinal cord injury (SCI) population. Twenty-three individuals with chronic incomplete SCI received 1-hour training sessions in the LOKOMAT three times per week, with up to 45 minutes of training per session; matched control group received no intervention. The neuromuscular properties of the spastic ankle were then evaluated prior to training and after 1, 2, and 4 weeks of training. A parallel-cascade system identification technique was used to determine the reflex and intrinsic stiffness of the ankle joint as a function of ankle position at each time point. The slope of the stiffness *vs*. joint angle curve, i.e. the modulation of stiffness with joint position, was then calculated and tracked over the four-week period. Growth Mixture Modeling (GMM), an advanced statistical method, was then used to classify subjects into subgroups based on similar trends in recovery pattern of slope over time, and Random Coefficient Regression (RCR) was used to model the recovery patterns within each subgroup. All groups showed significant reductions in both reflex and intrinsic slope over time, but subjects in classes with higher baseline values of the slope showed larger improvements over the four weeks of training. These findings suggest that LOKOMAT training may also be useful for reducing the abnormal modulation of neuromuscular properties that arises as secondary effects after SCI. This can advise clinicians as to which patients can benefit the most from LOKOMAT training prior to beginning the training. Further, this study shows that system identification and GMM/RCR can serve as powerful tools to quantify and track spasticity over time in the SCI population.

***Keywords*—locomotor training; rehabilitation; spinal cord injury; robotic; system identification**

I. INTRODUCTION

Robotic technologies are becoming increasingly popular in the field of neuro-rehabilitation [1], particularly in the restoration of gait ability for patients with SCI or other neurological injury. One such device is the LOKOMAT, a driven-gait orthosis that provides gait assistance and body-weight support to a patient over a motorized treadmill, in order to provide the necessary afferent input to improve locomotion [2]. This system has several advantages over the traditional body weight-supported treadmill training (BWSTT) approach. In traditional BWSTT, gait assistance is provided manually by a therapist—a time-consuming and physically-demanding task that often requires multiple therapists to perform effectively [3, 4]. With the LOKOMAT, the gait assistance is provided by the exoskeleton; thus only one therapist is required to operate the robot and monitor patient progress.

While recent studies have suggested that the LOKOMAT can effectively increase walking capacity by improving gait speed and endurance [5, 6], it is unclear whether the LOKOMAT can be effective in reducing the neuromuscular abnormalities that are associated with spastic hypertonia and that typically arise after SCI. The lack of investigation of the effect of the LOKOMAT on neuromuscular abnormality is impeded, in part, by the lack of objective tools in the literature to quantify the neuromuscular properties.

To that end, we have previously developed an advanced parallel-cascade system identification technique to separate the stiffness induced in a joint in response to a position perturbation into its reflexive and intrinsic (musculotendinous) components [7-9]. Such separation is essential, since the two components require separate treatments, and the effect of a particular intervention (i.e. LOKOMAT) may modify these two components in different ways. This system identification technique is robust and validated [10, 11], and has been demonstrated as an effective approach to quantitatively identify the progression and development of neuromuscular abnormalities associated with spasticity [12, 13]. In the current study, this technique was applied to quantitatively model the effect of the LOKOMAT on neuromuscular properties over training time.

In addition, as no intervention affects all patients equally, in this study we used advanced statistical methods used in longitudinal research to classify subjects into distinct subgroups based on common recovery pattern. We then modeled the change over time within each subgroup separately. This innovative approach allows us to, for the first time, track the effect of LOKOMAT training on reducing neuromuscular abnormalities in the SCI population.

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Figure 1: LOKOMAT training system.

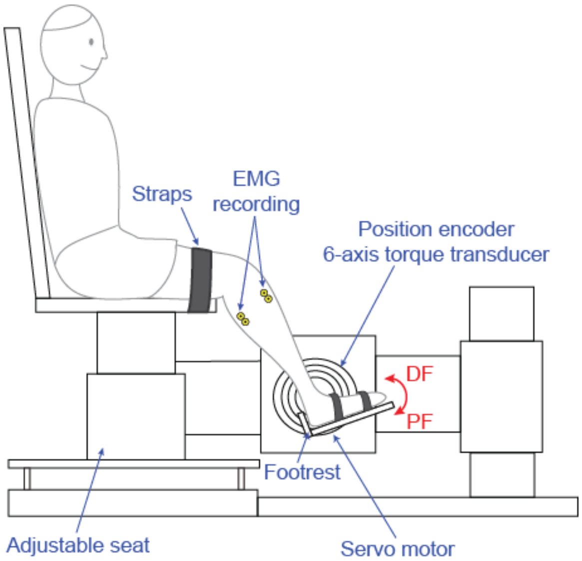

Figure 2: Experimental setup

II. EXPERIMENTAL PROTOCOL

A. *Subject Selection*

Twenty-three chronic incomplete spinal cord injury (SCI) subjects (7 females and 16 males, aged 46.4±12.6 years) with incomplete motor function loss and spasticity at their ankles (average Modified Ashworth Scores (MAS) of 2.2±0.8) participated in this study. Each of the subjects participated in tri-weekly LOKOMAT training sessions for four weeks. The subjects' neuromuscular properties were evaluated at four time points—prior to the start of training, and 1, 2, and 4 weeks after the start of training. An aged-matched group of control subjects (8 females/15 males, aged 47.9±12.2 years, with MAS scores of 2.3±0.6) also participated in the neuromuscular evaluations, but did not receive any LOKOMAT training.

B. *LOKOMAT Robotic Locomotor Training*

In this study, the LOKOMAT, a robotic-gait orthosis, was used to train the subjects in gait patterns [2]. The motorized exoskeleton is attached to the patient's knee and hip and a spring-loaded stirrup supports the ankle, while a harness for the torso and pelvis provides dynamic body-weight support (Fig. 1). The degree to which the exoskeleton assists the gait can be adjusted in real-time by the therapist, as per the subject's ability and comfort.

Subjects received a 1-hour LOKOMAT training session three times weekly for four weeks, with each session containing up to 45 minutes of training. A mirror placed before each subject provided reinforcing feedback to the subject during their gait cycle, and subjects were encouraged to contribute to their walking as much as possible. In particular, subjects were encouraged to flex their ankles during the movement, to prevent the foot-drag syndrome that is common after SCI.

C. *Neuromuscular Properties Characterization*

For the neuromuscular assessments, subjects were seated in front of a custom joint-stretching device that applied a perturbation to the ankle joint (Fig. 2). The device consisted of a position-controlled AC servo motor which tracked a target ankle joint position through an analog input. The subject's ankle was attached to a foot rest which was driven by the motor, with the ankle center-of-rotation aligned with the motor rotational axis. The motor was attached to a screw-driven track to provide vertical adjustment. In addition, the seat was capable of adjustment along three axes of rotation and one axis of rotation; together, these adjustments allowed the system to accommodate a variety of patient sizes.

Joint position was recorded by a rotary encoder, while a six-axis torque transducer recorded joint torque about the center of ankle rotation. Electromyograms (EMGs) placed at the tibialis anterior (TA) and gastrocnemius (GS) were recorded using bipolar surface electrodes. These signals were sampled at 1 kHz by a 16-bit data acquisition card, and low-pass filtered at 230 Hz on-line to prevent aliasing. A custom GUI, written using the MATLAB xPC Target package, was used to control the system.

The servo motor applied a series of pseudorandom binary sequences (PRBS) with an amplitude of 0.03 rad and a switching-rate of 150ms to perturb the ankle at 5^o increments over the ankle range of motion. During this time, the knee was held fixed at 30^o flexion. The ankle anatomic position (90^o) was defined as the neutral position (NP, or zero angle) for this study. Plantarflexion was considered negative by convention.

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The ankle which was considered more spastic— as determined by the MAS [14, 15]— was used for evaluation. Perturbations were performed while the subject was passive, with no active contractions. This was verified with a real-time measure of the EMG with an oscilloscope. Trials in which active contractions were present were repeated.

III. ANALYTICAL METHODS

To quantify the effect of the intervention on the neuromuscular properties, a parallel-cascade system identification technique was used to identify the reflex and intrinsic stiffness. The stiffness trends were then fit to an exponential curve, and the exponential slope (a measure of the modulation of stiffness with ankle position) was tracked over time. Growth Mixture Modeling (GMM) and Random Coefficient Regression (RCR) was used to classify subjects by the slope trends.

A. Parallel-Cascade System Identification Technique

An advanced system identification technique was used to model the measured ankle torque in response to the PRBS inputs. The technique separated the total torque into the sum of the intrinsic (i.e. muscular) pathway and the reflex pathway, using Hammerstein identification methods [7, 9]. The intrinsic pathway was estimated by determined the impulse response function (IRF) between position and torque. A second-order mass-spring-damper model was then fit to the IRF, and the intrinsic stiffness parameter K was calculated and tracked over time. The reflex pathway was modeled as a differentiator (converting position to velocity), a delay, a half-wave rectifier in velocity (static element), and a third-order linear (dynamic) element. The magnitude of the third-order system, reflex gain G, was calculated and tracked over time.

B. Identification of Recovery Patterns

The system identification analysis was performed separately for each of the evaluated ankle positions. This generated stiffness vs. joint angle curves for the intrinsic and reflex stiffness for each evaluated time point. The increasing portion of each curve was then fit to an exponential model, and the slope through the neutral (zero) position was tracked over time for the M_K (intrinsic) and M_G (reflex) curves. The slope is a measure of the modulation of the stiffness with angle, and is thus a physiologically-relevant parameter to track over time.

The change in slope over time (i.e. the recovery pattern) was then determined using GMM and RCR. In this study, we used GMM, an advanced longitudinal statistical technique that was developed to capture heterogeneity in development, for this purpose [16-18]. GMM assumes that the tested subject population can be divided into a finite number of classes such that individuals within each class share the same recovery patterns, but are distinct in these patterns from individuals in other classes [17, 19]. GMM classifies each subject into the class with the highest posterior probability of membership, based on maximizing the likelihood function [20]. We have previously pioneered the use of this technique for the rehabilitation field [21-23]. We then used RCR to model the recovery pattern as an exponential decay over time.

IV. RESULTS

All subjects successfully completed the twelve LOKOMAT training sessions and four neuromuscular evaluations.

Subjects were observed to exhibit multiple recovery patterns for their reflex and intrinsic stiffness vs. angle curves. For example, consider the reflex stiffness (G) vs. joint angle curves for two representative subjects shown in Fig. 3. Both subjects exhibited a similar trend with angle: a region of low reflex stiffness from full plantarflexion (PF) to ~25° to 15° PF, and then an increasing region up to a peak at 10° dorsiflexion (DF), and then a decrease in reflex stiffness up to maximum DF. (The increasing region is what was fitted by the exponential model.) However, Subject 1exhibits a nearly uniform decrease in stiffness over the four weeks of the study, while Subject 2 exhibits a substantial drop in stiffness in the first week of training (i.e. between the baseline and Week-1 evaluations), and then a much smaller change over the subsequent three weeks of training.

For the intrinsic stiffness (Fig. 4), subjects tended to showed a concave-up shaped trend, with a minimum value

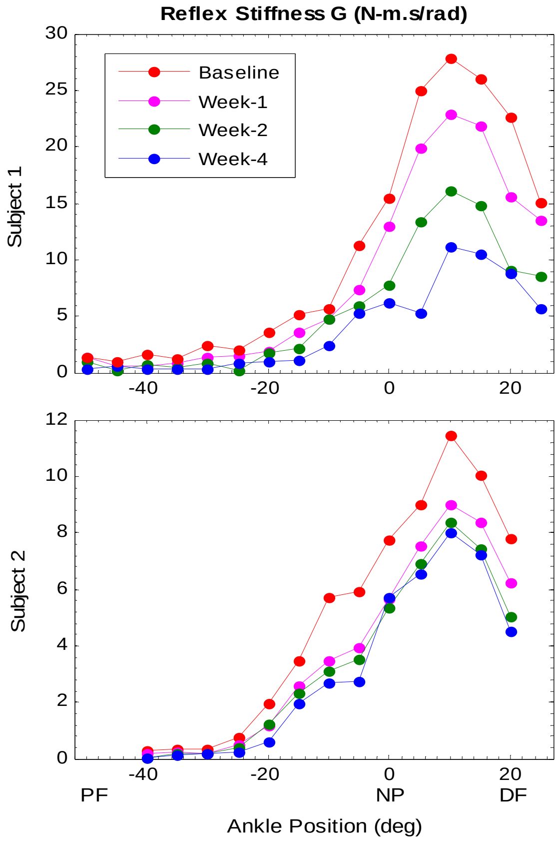

Figure 3: Reflex stiffness *vs.* angle trends for two representative subjects.

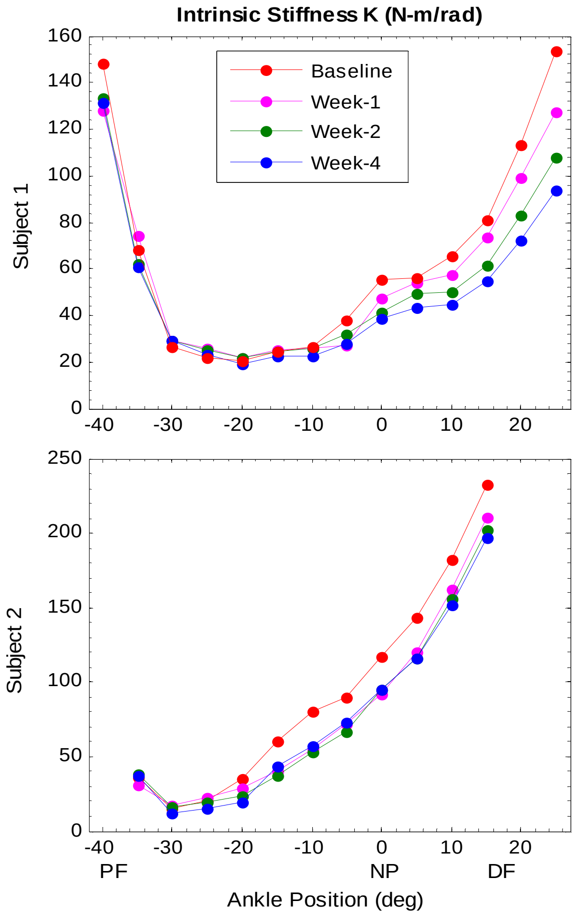

Figure 4: Intrinsic stiffness *vs*. angle trends for two representative subjects.

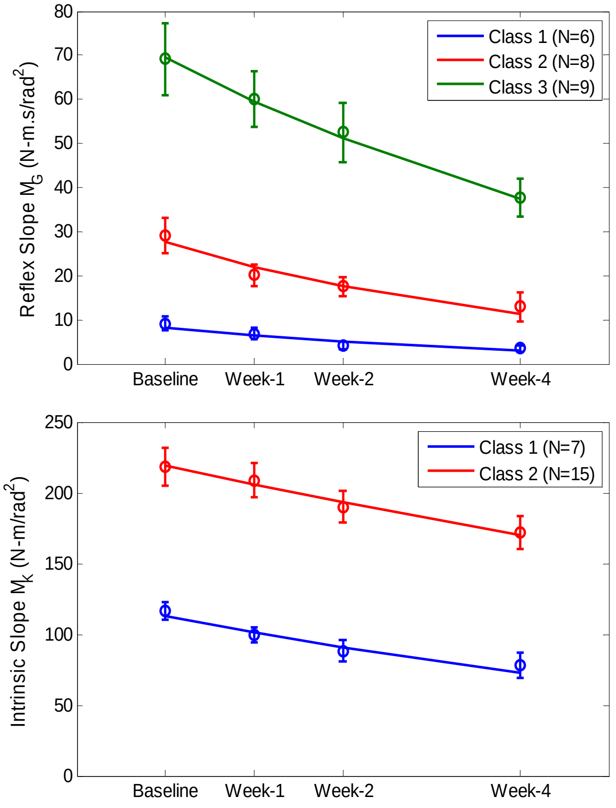

Figure 5: Change in slope for reflex (top) and intrinsic (bottom) stiffness over training weeks.

of stiffness around -30° to -20° PF, with increases in stiffness both for positions further towards maximum PF (i.e., more negative angles) as well as positions towards maximum DF (i.e., more positive angles). However, as before, Subject 1 presented uniform changes over the four weeks of training, while Subject 2 presented most of its change in the first week of training. In other words, Subject 1 benefited from all four weeks of training in terms of reduction of both reflex and intrinsic stiffness, while Subject 2 received most of its stiffness reduction in the first week of training, with little further changes with additional training.

As illustrated by these two exemplar subjects, not all subjects responded the same way to the training, and thus subjects had to be separated into distinct classes in order to model their recovery patterns separately. The slopes of the exponential fit, i.e. M_K and M_G, were used to classify subjects using GMM. Three classes were identified for the reflex slope, while two classes were identified by the intrinsic slope (Fig. 5). The RCR fits to the recovery pattern are also shown. Classes are numbered by increasing baseline value.

For the reflex slope, it was observed that the class with the highest baseline value (Class 3) exhibited the largest reduction in reflex slope (32.1 N-m.s/rad^2), while the class with smallest baseline value (Class 1) exhibited the smallest reduction in slope (5.2 N-m.s/rad^2). The class with the intermediate value of baseline slope (Class 2) also had an intermediate value of slope reduction (16.3 N-m.s/rad^2). These changes were all significant ($p < 0.05$). Also, Class 1 showed almost no change in slope between the Week-2 and Week-4 evaluations, suggesting that LOKOMAT training during these latter two weeks was minimally effective at reducing reflex slope (i.e. modulation).

For the intrinsic stiffness, again Class 1 (the higher baseline stiffness) exhibited a larger reduction over four weeks of training (46.5 N-m/rad^2) than Class 2 (38.7 N-m/rad^2), although the differences in reduction between classes were not as pronounced as with the reflex slope, although both were significant ($p < 0.05$). Notably, neither class showed an asymptotic limit at four weeks, suggesting that additional LOKOMAT training beyond the four-week period would yield further reductions.

The control subjects presented no significant change in either reflex slope or intrinsic slope over time (P = NS for all groups).

A one-way ANOVA between MAS scores and reflex class membership indicated no significant relationship between these quantities (P = NS). There was a significant relationship between intrinsic class membership and MAS scores (P = 0.004), with subjects with larger MAS scores belonging to the higher-slope class. However, there was substantial overlap between the class memberships, and this may not indicate a general finding.

V. DISCUSSION

In this study, for the first time, the therapeutic effects of a robotic locomotor intervention (the LOKOMAT) on reducing neuromuscular abnormality were quantified in SCI subjects. The parallel-cascade system identification technique was successfully used to characterize the neuromuscular abnormalities associated with spasticity in terms of reflex and intrinsic stiffness, and the changes of stiffness slope (i.e. modulation with ankle position) over training time was quantified. GMM was then used to effectively separate subjects into different classes of recovery and to track the recovery over time.

Both reflex and intrinsic stiffness, increased abnormally in SCI, were significantly reduced following four weeks of LOKOMAT training. The fact that subjects with initially higher values of slope prior to training suggests that subjects with greater amounts of abnormality can realize greater improvements from the training, while subjects with lower initial slopes can receive less benefit. Also, subjects with larger abnormalities require more than four weeks of LOKOMAT training in order to achieve the maximum possible benefit.

We characterized the ankle joint in this study because of its pivotal role in locomotion [24, 25], and because modifications to the intrinsic and reflex stiffness properties in the ankle can affect walking patterns [26]. In the present study, we showed that such modifications were the consequence of LOKOMAT training. This could be due to the following mechanism: during the training, as previously mentioned, the subject’s ankles were supported in a spring-loaded stirrup to prevent foot drop. This support breaks the spasticity patterns and modifies the functional condition under which the ankle acts, by stretching the ankle. This in turn leads to a reduction in both the abnormal reflex stiffness and the intrinsic stiffness.

These findings demonstrate that LOKOMAT training has the potential to modify neuromuscular properties in neurologically-impaired subjects, thus facilitating greater recovery. Further, this study shows that the system identification technique can be an effective method to characterize the progress of neuromuscular modifications during treatment in spastic populations. Finally, the results demonstrated that the GMM approach can be used to successfully model the disparate recovery patterns of patients. Such an approach is highly innovative and clinically-significant since it can help clinicians to identify which patients are most likely to benefit from LOKOMAT training prior to the start of therapy, minimizing time, effort, and costs while maximizing successful outcomes.

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