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Effects of robotic-locomotor training on stretch reflex function and muscular properties in individuals with spinal cord injury

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HIGHLIGHTS

- The ability of robotic-assisted step training (RAST) to reduce neuromuscular abnormalities associated with spasticity was determined.
- RAST reduced the abnormalities in both stiffness magnitude and modulation with position, proportional to the initial level of abnormality.
- These techniques can be used to predict the therapeutic effects of different interventions on neuromuscular abnormalities.

ABSTRACT

Objective: We sought to determine the therapeutic effect of robotic-assisted step training (RAST) on neuromuscular abnormalities associated with spasticity by characterization of their recovery patterns in people with spinal cord injury (SCI).
Methods: Twenty-three motor-incomplete SCI subjects received one-hour RAST sessions three times per week for 4 weeks, while an SCI control group received no training. Neuromuscular properties were assessed using ankle perturbations prior to and during the training, and a system-identification technique quantified stretch reflex and intrinsic stiffness magnitude and modulation with joint position. Growth-mixture modeling classified subjects based on similar intrinsic and reflex recovery patterns.
Results: All recovery classes in the RAST group presented significant ($p < 0.05$) reductions in intrinsic and reflex stiffness magnitude and modulation with position; the control group presented no changes over time. Subjects with larger baseline abnormalities exhibited larger reductions, and over longer training periods.
Conclusions: Our findings demonstrate that RAST can effectively reduce neuromuscular abnormalities, with greater improvements for subjects with higher baseline abnormalities.
Significance: Our findings suggest, in addition to its primary goal of improving locomotor patterns, RAST can also reduce neuromuscular abnormalities associated with spasticity. These findings also demonstrate that these techniques can be used to characterize neuromuscular recovery patterns in response to various types of interventions.

1. Introduction

Two primary clinical sequelae following with incomplete spinal cord injury (SCI) are spasticity and impaired voluntary movement (Barbeau et al., 2002; Drolet et al., 1999; Katz and Rymer, 1989; Lehmann et al., 1989; Thomas et al., 1997). Spasticity is a motor disorder associated with lesions of the nervous system (Lance, 1980), which can lead to changes in mechanical properties of the neuromuscular system (Mirbagheri et al., 2001) and lead to several forms of motor impairment including dysfunction of motor coordination (Burne et al., 2005; Gerhart et al., 1993; Thomas et al., 1998). Many gait impairments are associated with spasticity in

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the lower extremity, including the inability to distribute weight evenly between limbs, reduced step width and length, and abnormalities in step rhythm and function; all of these factors can negatively affect walking capacity (Field-Fote et al., 2001).

Clinical symptoms of spasticity in SCI include hypertonia, uncontrolled spasms, clonus, and the clasp-knife phenomenon (Lance, 1980). Hypertonia is defined as an abnormal increase in resistance to passive movement (Katz and Rymer, 1989; Lance, 1980). Regarded as the defining feature of spasticity (Katz and Rymer, 1989), hypertonia can arise from abnormalities in the mechanical properties of passive tissues, muscle fibers, and stretch reflexes (Dietz et al., 1981; Hufschmidt and Mauritz, 1985; Mirbagheri et al., 2001; O'Dwyer et al., 1996; Sinkjaer and Magnussen, 1994). Since hypertonia manifests as a mechanical abnormality, it is appropriate to characterize it in terms of mechanical properties of the spastic joint (Mirbagheri et al., 2000, 2001). The overall mechanical properties of a joint at rest are determined by the combination of (i) intrinsic mechanisms arising from inertial and viscoelastic properties of the joint and (ii) reflex mechanisms arising from changes in muscle activation due to afferent response to stretch. Hyperexcitable reflexes manifest as a stiffer joint, i.e., a joint more resistant to imposed motion; this quantitative characteristic is defined here as stretch reflex stiffness. This separation is useful for quantifying the nature of abnormalities associated with spasticity, as each abnormality requires its own specific treatments, and thus has a diagnostic and therapeutic significance.

One physical intervention used to promote gait recovery and improve function is body weight-supported treadmill training (BWSTT) with manual assistance (Barbeau and Fung, 2001; Behrman and Harkema, 2000; Dietz and Harkema, 2004; Wernig et al., 1995). Here, subjects are provided with partial support of body weight over a treadmill and therapists provide assistance to promote foot clearance and to prevent knee buckling during the stance phase of gait. Recently, robotic devices have been developed to assist therapists in the rehabilitation of people with neurological injury (Volpe et al., 2001). One such device is the LOKOMAT (Hocoma, Switzerland), a powered device that provides robotic-assisted step training (RAST) similar to BWSTT, but through a motorized exoskeleton that attaches to the patient's legs, rather than manual positioning by a therapist (Colombo et al., 2000). Recent results have shown that RAST can improve walking capacity by improving gait speed, endurance, or temporal patterns of electromyographic (EMG) activity (Field-Fote et al., 2005; Hornby et al., 2005; Mazzoleni et al., 2011; Schwartz et al., 2011; Wirz et al., 2005). It has also been shown that RAST can improve spasticity as measured by the Pendulum Test (Manella et al., 2010) and reflex excitability (Manella and Field-Fote, 2013), but had no significant impact on hypertonia as measured by the Modified Ashworth Scale (MAS) (Manella and Field-Fote, 2013; Manella et al., 2010). Thus, the effect of RAST on spasticity has been inadequately studied and remains controversial.

While these studies have investigated the effects of RAST on EMGs, gait kinematics, clinical and electrophysiological measures of spasticity, the influence of such training on neuromuscular abnormalities associated with spasticity has been seldom studied, largely due to the aforementioned lack of quantitative and objective clinical tools to characterize the neuromuscular components of hypertonia. Given that alternative physical therapies have been shown to reduce hypertonia, for example passive cycling with and without functional electrical stimulation (Kakebeeke et al., 2005; Krause et al., 2008; Rayegani et al., 2011), we hypothesized that RAST would similarly have a positive effect on reducing hypertonia. One preliminary study found that a single session of RAST could yield a significant reduction in joint stiffness in children with spastic cerebral palsy (Schmartz et al., 2011). However, the long-term effect of this training on joint stiffness, particularly once training is completed, is unclear.

Typically no intervention has a uniform impact across all subjects; rather there is a marked heterogeneity in patient response. However, the standard pre- vs. post-treatment analysis, which uses group-averaging techniques, neglects the substantial heterogeneity among SCI individuals. Consequently, there is a need for the use of advanced statistical methods, such as growth mixture models, that can classify subjects by similar recovery patterns and model these patterns over time.

In this study, we addressed these deficits, for the first time, by characterizing the effects of RAST on stretch reflex and muscular mechanical properties for SCI subjects, using system identification techniques (Mirbagheri et al., 2000, 2001), and by identifying and modeling different recovery patterns for the muscular and reflex stiffness properties over the course of one month due to RAST. We investigated the therapeutic effects of the training on stretch reflex stiffness, which increases abnormally after SCI (Mirbagheri et al., 2001).

2. Methods

2.1. Subjects

Forty-six ambulatory chronic SCI subjects with incomplete motor function loss participated in this single-center, randomized study. All subjects had motor-incomplete SCI with an American Spinal Injury Association Impairment Scale (ASIA) classification of C or D (Kirshblum et al., 2011), a lesion level between C2 and T9, were ambulatory or had a passive range of motion (PROM) within functional limits for ambulation, had ankle spasticity indicated by a MAS score of 1 or greater, and were granted medical clearance to participate. Twenty-three subjects were randomly assigned to the intervention group to receive RAST, while the other half were assigned to the control group and received no intervention. The RAST group (7 females and 16 males) had mean ± SD age of 46.4 ± 12.6 years, were evaluated 10.1 ± 8.3 years after the injury, and had median (interquartile range) MAS scores of 2 (1.8–3). The control group (8 females and 15 males) had mean ± SD age of 47.9 ± 12.2 years, were evaluated 8.9 ± 8.2 years post-injury, and had median (interquartile range) MAS scores of 2 (2–3).

Subjects were draw from the Rehabilitation Institute of Chicago's outpatient service. All provided informed consent and the Northwestern University Institutional Review Board approved the study.

2.2. Robotic-assisted step training (RAST)

The RAST device consists of four motors aligned bilaterally at the hip and knee joints and attached to the patient's legs by fitted cuffs (Fig. 1A). These motors move through physiological gait patterns while the patient walks on a motorized treadmill. The degree to which the device assists gait can be adjusted by the therapist. Dynamic body weight support provides automatic lifting and unloading of the patient through an overhead harness (Colombo et al., 2000). Adjustable elastic stirrups attached to the motorized shank prevented foot-drop and supported the ankles in the neutral (90°) position but allowed ankle movements by the subject (Fig. 1B). During training, subjects were encouraged (through therapist's feedback and a mirror placed in front of the subject) to voluntarily contribute to their ambulation and replicate stepping behavior as much as possible, with particular attention given to activating their ankle muscles.

All participants in the RAST group received training three times a week for 4 weeks (12 sessions in total). Each 1-h session included