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Effect of botulinum toxin injection on length and lengthening velocity of rectus femoris during gait in hemiparetic patients

N. Lampire [a,b,*], N. Roche [c], P. Carne [a], L. Cheze [b], D. Pradon [c]

[a] Laboratoire d'analyse du mouvement, CMPR L'ADAPT Loiret, Amilly, France
[b] Laboratoire de Biomécanique et Mécanique des Chocs, Université de Lyon, UMR_T 9406, Université Lyon 1, IFSTTAR, Villeurbanne, France
[c] EA 4497 GRCTH, CIC-IT, CHU Raymond Poincaré, UVSQ, Garches, France

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ABSTRACT

Background: In hemiparetic patients, rectus femoris spasticity is one of the main causes of reduced knee flexion in swing phase, known as stiff knee gait. Botulinum toxin is often used to reduce rectus femoris spasticity and to increase knee flexion during swing phase. However, the mechanisms behind these improvements remain poorly understood. The aim of this study was (1) to quantify maximal rectus femoris length and lengthening velocity during gait in ten adult hemiparetic subjects with rectus femoris spasticity and stiff knee gait and to compare these parameters with those of ten healthy subjects and (2) to study the effect of botulinum toxin injection in the rectus femoris muscle on the same parameters.
Methods: 10 patients with stiff knee gait and rectus femoris spasticity underwent 3D gait analysis before and one month after botulinum toxin injection of the rectus femoris (200 U Botox®, Allergan Inc., Markham, Ontario, CANADA). Rectus femoris length and lengthening velocity were quantified using a musculoskeletal model (SIMM®, MusculoGraphics, Inc., Santa Rosa, California, USA).
Findings: Maximal length and lengthening velocity of the rectus femoris were significantly reduced on the paretic side. There was a significant increase in muscle length as well as lengthening velocity during gait following botulinum toxin injection.
Interpretation: This study showed that botulinum toxin injection in the spastic rectus femoris of hemiparetic patients improves muscle kinematics during gait. However maximal rectus femoris length did not reach normal values following injection, suggesting that other mechanisms are likely involved.

1. Introduction

Following stroke, the characteristics of gait are altered in comparison with healthy subjects. Aside from changes in spatiotemporal and postural parameters, there are also alterations in lower limb kinematics such as reduced peak knee flexion during swing phase of the gait cycle, known as stiff knee gait (SKG) (Kerrigan et al., 2001). One of the main causes of SKG is inappropriate electromyographic activity (EMG) of the rectus femoris (RF) muscle, related to spasticity of this muscle (Goldberg et al., 2004). Other causes are reduced peak hip flexion and reduced peak plantar flexion moment (Kerrigan et al., 1999). One of the classic treatments for RF spasticity associated with abnormal EMG activity is botulinum toxin injection (BTI). This neuro-toxin works by blocking neurotransmitter release at the neuromuscular junction. In consequence this treatment induces a paresis of the injected muscle, which is 'voluntary, reversible and transient' (Poulain and Humeau, 2003). Several studies in hemiparetic subjects showed that BTI in the spastic RF muscle significantly increased peak knee flexion during swing phase as well as knee flexion velocity at toe off (Hutin et al., 2010; Robertson et al., 2009; Stoquart et al., 2008). However, the mechanisms behind these kinematic improvements are as yet poorly understood.

It is largely supposed that the focal paralysis which occurs following BTI leads to an increase in maximal muscle length and the muscle's capacity to lengthen during gait. The study of these parameters may help to understand the mechanisms associated with spasticity and the effect of botulinum toxin on spastic muscles. This hypothesis is based on the results of a study by Jonkers et al. (2006) in which a musculoskeletal model (SIMM®, MusculoGraphics, Inc., Santa Rosa, California, USA) was used to quantify RF resting length as well as its length and variations during gait in 35 children with spastic diplegia. The results showed that maximal length and maximal lengthening velocity of the RF were both reduced during gait compared with those of healthy subjects. The SIMM®, MusculoGraphics, Inc., Santa Rosa, California, USA musculoskeletal model has two useful properties: the dynamic module can be used

Abbreviations: RF, Rectus Femoris muscle; SKG, Stiff Knee Gait; BTI, Botulinum Toxin Injection; EMG, Electromyographic; SD, Standard Deviation.

* Corresponding author at: Laboratoire d'analyse du mouvement, CMPR L'ADAPT Loiret, 658D rue des Bourgoins, 45200 Amilly, France.
E-mail address: lampire.nicolas@ladapt.net (N. Lampire).

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to perform forward and inverse dynamic simulations on musculoskeletal models. The forward simulation is used for the calculation of the motion and the contact forces resulting from the specified muscle excitation. In contrast, the inverse simulation allows calculation of the muscle activations and forces required to generate a specific motion. The forward model was developed for the prediction of the biomechanical consequences of the modifications of model parameters following a surgical procedure or change in muscle strength (Goldberg et al., 2004; McLean et al., 2004; Neptune et al., 2001; Yamaguchi and Zajac, 1990). The inverse simulation is used for the evaluation of changes in gait resulting from pathology or treatment based on data obtained during 3D gait analysis of a patient (Crowninshield and Brand, 1981; Glitsch and Baumann, 1997; Li et al., 1999). This model is the only tool which allows indirect assessment of muscle strength or lengthening during movement such as gait. Nevertheless it is necessary to keep in mind that it is an indirect approach and that the data obtained result from a simulation. In consequence, the results should be interpreted with caution. However when the inverse simulation is carried out on data from the same subject, the inherent bias of this approach is reduced, therefore, allowing comparison of the modifications induced by a treatment (whatever the type) on muscle strength or length. The present study was based on this method and had two aims. The first was to assess maximal RF length and lengthening velocity during gait in adult hemiparetic subjects with RF spasticity and SKG and to compare these parameters with those of the healthy subjects. The second aim was to evaluate the effect of BTI in the RF muscle on the same parameters.

2. Methods

2.1. Subjects

10 hemiparetic subjects constituted the patient group (Table 1): 4 with right hemiparesis, 6 with left, 8 men, 2 women, average age: 39.6, SD: 9.5 years. Inclusion criteria were the following: a single cerebral lesion of vascular origin (ischemic or hemorrhagic) of more than 6 month duration or more than 4 months since last BTI, a decrease in peak knee flexion during swing phase measured using gait analysis, prolonged RF activity during swing phase determined by EMG and ability to walk 20 min without stopping. Patients were excluded if they had any comorbid disability other than stroke, such as any visual impairment or musculoskeletal, cardiovascular, or pharmacological treatment that could interfere with gait or posture. All patients had previously been treated by BTI in the RF muscle before inclusion in this study.

10 healthy subjects (with no central nervous system lesions; 6 men and 4 women; average age: 32.5, SD: 6 years) were also included as a control group.

All subjects gave informed consent prior to inclusion. This study was carried out according to "The Ethical Codes of the World Medical Association" (Declaration of Helsinki) and was approved by the local ethical committee (CPP Ile de France, Ambroise Paré).

Table 1
Demographic characteristics of the patients.

	Age (years)	Height (cm)	Weight (kg)	Gender	Paretic side	Time since lesion onset (months)	RF spasticity assessed by modified Ashworth scale before and 1 month after BTI
Subject 1	27	180	74	M	L	48	–
Subject 2	40	188	73	M	L	6	0/0
Subject 3	58	160	69	M	R	60	1/1
Subject 4	29	166	72	M	L	60	3/2
Subject 5	33	180	85	M	L	36	–
Subject 6	37	182	82	M	R	60	–
Subject 7	40	181	72	M	R	36	2/2
Subject 8	40	163	51	F	L	84	1/0
Subject 9	52	162	67	F	R	432	2/1
Subject 10	40	173	76	M	L	96	2/1

M = male, F = female, L = left and R = right, RF = rectus femoris, BTI = botulinum toxin injection.

2.2. Protocol

2.2.1. Hemiparetic patients

BT was injected in the spastic RF muscle on the hemiparetic side of all patients included. 200 U of type A botulinum toxin (Botox®, Allergan Inc., Markham, Ontario, CANADA) diluted to 40 U/ml was injected in three anatomical points in the RF muscle using electrostimulation (5 mA) by the same investigator. The technique used was the same to that previously used in Hutin et al. (2010): one point 5 cm under the inguinal crease on a line between the antero-inferior iliac spine and the patella. The second point was ten centimeters above the patella and the third was in the middle of the two others on the same line. The dose used was the same as that in other studies evaluating the impact of BTI in the RF muscle on peak knee flexion in swing phase (Hutin et al., 2010; Robertson et al., 2009; Stoquart et al., 2008).

2.3. Assessments

This was an observational study. Two assessments were carried out: before injection (PRE) and 1 month post injection (POST). The second assessment was carried out one month post injection because this is when the toxin is at maximal effectiveness (Juzans et al., 1996). A clinical assessment and gait analysis were carried out at each assessment.

- Clinical assessment
  Sagittal hip, knee and ankle joint ranges of motion were assessed in order to check for muscle contractures. Spasticity of the quadriceps and RF was evaluated using the modified Ashworth scale. All clinical tests were carried out by the same physiotherapist.
- Gait analysis
  Each patient underwent three dimensional (3D) gait analysis using a Motion Analysis System (Motion Analysis Corporation, Santa Rosa, CA, USA, sampling frequency 100 Hz). Markers were positioned according to the Helen Hays protocol (Kadaba et al., 1990). Subjects walked barefoot at their own comfortable pace. Ten gait cycles, corresponding to those during which the patient walked on the force plate, resulting from ten gait trials were recorded and averaged for each patient. Patients were offered a break after five trials. EMG was recorded simultaneously during the kinematic data collection using bipolar surface electrodes (MA 311) placed on the rectus femoris, vastus lateralis, semimembranosus, tibialis anterior, gastrocnemius medialis and soleus muscles. Vastus lateralis activity was assumed to be representative of the three vastii (Nene et al., 1999). Digitalized EMG, Motion Lab System, LA, USA (1000 Hz) was analyzed to determine the periods of activity of each muscle during gait, and to include them in the model. Moreover, the EMG signal of the RF and VL muscles was used to qualitatively determine if their activation patterns were abnormal during swing phase or not.