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Impaired gait function in adults with cerebral palsy is associated with reduced rapid force generation and increased passive stiffness

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HIGHLIGHTS

- Impaired toe lift during gait was most strongly correlated with increased passive ankle muscle stiffness and reduced rate of force development in ankle dorsiflexors in adults with CP.
- Reduced push-off velocity during gait was most strongly correlated with reduced rate of force development in ankle plantarflexors.
- Spasticity (evaluated clinically or biomechanically) was found not to be a disadvantage for gait.

ABSTRACT

Objective: It is still not clarified whether spasticity contributes to impairments of gait function. Here we compared biomechanical measures of muscle weakness and stiffness of ankle muscles to impairments of gait function in adults with cerebral palsy (CP).
Methods: Twenty-four adults with CP (mean age 34.3, range 18–57 years) and fifteen healthy age-matched controls were biomechanically measured for passive and reflex-mediated stiffness of the ankle plantarflexors at rest, maximal voluntary plantarflexion and dorsiflexion effort ($MVC_{pf,df}$) and rate of force development ($RFD_{pf,df}$). Kinematic analysis of the ankle joint during treadmill walking was obtained by 3-D motion analysis.
Results: Passive stiffness was significantly increased in adults with CP compared to controls. Passive stiffness and RFD_{df} were correlated to reduced toe lift. RFD_{pf} provided the best correlation to push-off velocity, range of movement in the ankle joint and gait speed. Reflex-mediated stiffness was not correlated to any parameters of impaired gait.
Conclusions: Impaired gait function in adults with CP is associated with reduced RFD and increased passive stiffness of ankle muscles.
Significance: These findings suggest that reduced rapid force generation and increased passive stiffness of ankle muscles rather than increased reflex-mediated stiffness (spasticity) likely contributes to impaired gait function in adults with CP.

1. Introduction

Spasticity is usually defined as a velocity-dependent increase in muscle tone related to exaggeration of the stretch reflex circuitry (Lance, 1980), although recent studies have pointed out that this definition may be too narrow to capture the full clinical picture of spasticity (Malhotra et al., 2009). Despite several decades of ever more advanced electrophysiological, biomechanical and clinical studies there is also still no clear consensus regarding the functional

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significance of spasticity defined in this way (Dietz and Sinkjaer, 2007, 2012; Malhotra et al., 2009). This is a concern for antispastic treatment, which is directed at diminishing muscle tone caused by hyperactive reflex activity (Dietz and Sinkjaer, 2007, 2012).

Several studies have documented that reflex modulation is abnormal during gait in spastic subjects with multiple sclerosis (Sinkjaer et al., 1996), stroke (Mazzaro et al., 2007), spinal cord injury (Faist et al., 1999) and cerebral palsy (CP) (Hodapp et al., 2007; Willerslev-Olsen et al., 2014), but it is unclear to what extent this contributes to the impairment of gait observed in these subjects. Although hyperactive reflexes may be elicited by external perturbations in specific phases of the gait cycle, sensory feedback mechanisms seem if anything to contribute less to the muscle activity recorded during gait in spastic subjects with stroke or CP (Mazzaro et al., 2007; Willerslev-Olsen et al., 2014). Other studies on subjects with hereditary spastic paraparesis have also failed to find any correlation between measures of exaggerated reflex activity and impairments of gait (Marsden et al., 2012).

Part of this controversy may be explained by difficulties in distinguishing reflex-mediated stiffness from other causes of pathologically increased muscle stiffness. As pointed out in several recent studies, increased passive stiffness of the muscles, connective tissue, tendons and joints is difficult to distinguish clinically from spasticity and requires a combination of biomechanical and electrophysiological techniques in order to be correctly evaluated (Mirbagheri et al., 2004, 2005; Lorentzen et al., 2010; Willerslev-Olsen et al., 2013). It was suggested already by Volker Dietz and his co-workers more than 30 years ago that such changes in passive muscle stiffness may be the dominant cause of gait impairment in spastic subjects (Dietz et al., 1981; Berger et al., 1982; Dietz and Berger, 1983). Several recent studies have now confirmed Dietz and co-workers original findings of the importance of increased passive muscle stiffness for the gait impairment in subjects with stroke (Lamontagne et al., 2000; Roy et al., 2013) and hereditary spastic paraparesis (Marsden et al., 2012). Impaired gait in adults with cerebral palsy (CP) is usually claimed to be associated to spasticity, but there is little available evidence to support this.

Muscle weakness is another factor that is often discussed in relation to gait function in CP (Dallmeijer et al., 2011; Eek et al., 2011; Thompson et al., 2011). Many everyday activities allow a limited time to develop muscle force (up to 200 ms) whereas the time required to develop maximal force takes considerably longer (Aagaard et al., 2002). Interestingly, the rate at which force or torque is produced, known as the rate of force development (RFD), have been shown to be a good predictor of functional performance in elderly (Bassey et al., 1992; Skelton et al., 1994) and recently also in children with CP (Downing et al., 2009; Moreau et al., 2011). Nevertheless, the importance of RFD for gait function has been largely overlooked in adults with CP.

It was therefore the purpose of the present study to investigate the relationship between muscle weakness (MVC and RFD), passive and reflex-mediated muscle stiffness to impairments of gait function in adults with CP.

2. Methods

2.1. Participants

Twenty-four adults diagnosed with CP (age 34.3, range 18–57 years; 15 men, 9 women) were recruited through the Danish Cerebral Palsy organization. Fifteen subjects were diplegic, eight hemiplegic and one quadriplegic and their Gross Motor Function Classification System (GMFCS) scores ranged from I-III (I: $n = 9$, II: $n = 8$, III: $n = 7$; Table 1). All subjects were described as spastic and most of the subjects had previously received anti-spastic medication for shorter or longer periods. Two subjects received anti-spastic medication (Chlorzoxazone) at the time of the study. Many subjects had a history of multiple surgeries (Table 1). They were all community ambulators except for two subjects, who both required personal assistance.

As a control group, 15 age-matched (age 32.9 years, range 23–47; 9 men, 6 women) neurologically healthy adults were recruited.

The study was approved by the local ethics committee (H-4-2012-107) and all procedures were conducted within the standards of the Helsinki declaration. Prior to the experiments all the participants received written and verbal information, and signed consent-form for participation was obtained.

2.2. Neurological examination

The neurological examinations were performed bilaterally for both knee- and ankle joints by trained clinicians (two of the authors: JL, HK). The clinical tests were performed at the ankle- and knee joint with the subject at rest lying comfortably on an examination-bed. The tests were performed in the following order: Passive range of motion (ROM) was measured with a handheld plastic goniometer by moving the foot slowly from a neutral position (90° position in relation to the tibia) and as far as possible in both plantar- and dorsiflexion direction. The largest excursion was measured and noted in both directions. Modified Ashworth Scale (MAS) (Bohannon and Smith, 1987; Bakheit et al., 2003) and Modified Tardieu Scale (Gracies et al., 2000) was evaluated by moving the joint passively from a neutral position. The investigated joint was first moved 2–3 times as slow as possible to evaluate the stiffness/resistance without the presence of stretch reflexes. Afterwards, the investigated joint was moved with a speed compared to the speed of gravity and finally it was moved as fast as possible to evaluate the reflex contribution to the stiffness/resistance of the joint.

2.3. Experimental set up

2.3.1. Measurement of passive and reflex-mediated stiffness

In order to objectively assess the passive and reflex-mediated stiffness components of the ankle plantarflexors, biomechanical and electrophysiological evaluations were performed on the leg that the subject reported to be the most affected (Lorentzen et al., 2010; Willerslev-Olsen et al., 2013). The subject was at rest throughout all measurements. Subjects were seated in a reclining armchair with the examined foot attached to a foot plate, which could be rotated by a motor (CEM model 26) causing a stretch of the plantarflexors. The motor was driven by a DC power amplifier (Brüel & Kjaer; model 2708) and could deliver maintained torques up to 80 Nm and peak torques up to 120 Nm. An electro-goniometer, connected to the foot plate, measured the angle of the ankle joint and a torque meter measured the torque exerted on the foot plate prior to and during the stretch perturbations. The subject was positioned with the hip joint in 80° flexion, the knee in 55° flexion and the ankle joint in 20° plantarflexion. Five subjects, in whom their passive, ankle ROM (Table 1) did not allow this ankle position, were instead positioned in 10° (subject 7, 15, 18 and 24) or 0° (subject 8) plantarflexion. The perturbations consisted of ramp and hold dorsiflexion with an amplitude of 6° at 17 different velocities between 5 and 220°/s and with a hold time of 460 ms. Perturbations were delivered in a software generated, pseudo-random order until 10 trials per velocity were collected. The interval between perturbations was 1 s. This short interval was chosen based on the observation by Grey et al. (2008) that the largest difference in reflex excitability between a group of subjects with