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Effects of inter-synergistic mechanical interactions on the mechanical behaviour of activated spastic semitendinosus muscle of patients with cerebral palsy

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ABSTRACT

Previous physiological experiments and finite element modelling indicate that inter-synergistic epimuscular myofascial force transmission (EMFT) between co-activated muscles has a potential to affect healthy muscle's contribution to joint moment and joint range of movement. This is quite relevant for patients with cerebral palsy (CP) since, amplitude of spastic muscle's force and the joint range of force exertion are central to the joint movement limitation. Stiffness of activated spastic muscle is also a determinant for pathological joint movement. However, assessments of effects of inter-synergistic EMFT on the mechanical behaviour of spastic muscle are lacking. Those assessments require measurement during surgery of activated spastic muscle's forces directly at its tendon and as a function of joint angle. Employing this methodology, the aim was to test the following study hypotheses: added activation of semimembranosus (SM) and gracilis (GRA) muscles of patients with CP changes (1) force, (2) stiffness and (3) joint range of force exertion of activated spastic semitendinosus (ST) due to inter-synergistic EMFT. Isometric spastic ST forces were measured intraoperatively (12 limbs of 7 patients (mean age 8 years 9 months) for knee angles from flexion (120°) to full extension (0°). Conditions I and II: spastic ST was activated alone, and simultaneously with its synergists SM and GRA muscles, respectively. Condition II did increase activated spastic ST's forces significantly (by 33.3%), but did not change its stiffness and joint range of force exertion, confirming only study hypothesis 1. Therefore, we conclude that inter-synergistic EMFT affects forces exerted at spastic ST tendon, but not other characteristics of its angle-force relationship.

1. Introduction

Cerebral palsy (CP) is a movement disorder that occurs secondary to static lesions in the immature brain (Bax et al., 2005). In patients with CP, persistent increased resistance to stretch (Gracies et al., 2010) results in a sustained shortened state of spastic muscle (Botte et al., 1988). This causes soft tissue contracture (Botte et al., 1988; de Bruin et al., 2014; Smith et al., 2011), joint stiffness (Gracies, 2005; Ikeda et al., 1998) and limits joint movement (Fergusson et al., 2007). However, muscle is the motor for movement and patients with CP show muscle hypertonicity (Mirbagheri et al., 2001; O'Dwyer and Ada, 1996). Upper extremity joints being forcefully kept in a flexed position (Van Heest et al., 1999) indicate high force production of spastic flexor muscles in active state. Patients with CP show gait disorders including additional to pathological hip and ankle conditions, crouch gait (Delp et al., 1996) and spastic knee flexion deformity (Bell et al., 2002; Crenna, 1998). Besides, elevated stiffness of spastic muscles has been reported in passive state (e.g., Smith et al., 2011) and is considered highly plausible in active state. Therefore, amplitude of activated spastic muscle's force, stiffness and the range of its active force exertion are central to the joint movement limitation. However, studies quantifying such parameters in intraoperative experiments are sparse (Ates et al., 2013b; Kreulen et al., 2004; Kursa et al., 2005; Smeulders et al., 2004). Moreover, daily activities involve simultaneous activation of several muscles such as co-activation of the semitendinosus (ST) with the semimembranosus (SM) and gracilis (GRA) during walking and sit-to-stand (Arnold et al., 2007; He et al., 2007; Schmitz et al., 2009). Yet, effects of added stimulation of synergistic muscles on spastic muscle's mechanical behaviour are unknown.

Connective tissues linking muscle bellies via e.g., collagen-reinforced neurovascular tracts allow epimuscular myofascial force transmission (EMFT) between synergistic muscles (Huijing, 2009; Yucesoy, 2010). EMFT can change the force amplitude of a muscle held at constant length in response to imposed length changes or activation

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of its synergists (Ates et al., 2013a; Ates and Yucesoy, 2014; Huijing and Baan, 2003; Maas et al., 2001, 2003, 2005; Yucesoy et al., 2005). EMFT effects rely on the connections between the muscle fibres and the extracellular matrix (ECM) along their full peripheral lengths (Berthier and Blaineau, 1997), which can transmit force (Huijing, 1999; Street, 1983). Shear linkage was shown to exist between them (Purslow, 2002; Purslow and Trotter, 1994; Trotter and Purslow, 1992; Trotter et al., 1995). Consequently, forces originating from the synergistic muscles transmitted onto the ECM can affect the force production of a sarcomere by manipulating its length (Yucesoy, 2010). Heterogeneity of sarcomere lengths across muscle fibres affects muscle optimum length (Willems and Huijing, 1994; Yucesoy et al., 2003a, 2003b). Therefore, inter-synergistic EMFT can change muscle's length range of force exertion. In spastic CP this can be a factor affecting the limited joint movement (Huijing, 2007; Yucesoy and Huijing, 2007). The current understanding of tissue adaptations in CP indicates elevated ECM stiffness (Smith et al., 2011). Kreulen et al. (2003) showed that the epimuscular connections of tenatomized spastic flexor carpi ulnaris limit its shortening in response to stimulation. Therefore, also these connections must be highly stiff and overall, stiff muscle related connective tissues in CP suggest that EMFT effects can be more pronounced than in healthy individuals. This not only can limit the passive joint movement, but also can alter activated spastic muscle's mechanical behaviour unfavourably for mobility, which needs to be tested.

Intraoperative testing allows measuring forces of activated knee flexor muscles directly at the tendon (Yucesoy et al., 2010). Employing this methodology, the aim was to test the following study hypotheses: added activation of SM and GRA muscles of patients with CP changes (1) force, (2) stiffness and (3) joint range of force exertion of activated spastic ST due to inter-synergistic EMFT.

2. Materials and methods

Surgical and experimental procedures, in strict agreement with the guidelines of the Helsinki declaration, were approved by a Committee on Ethics of Human Experimentation at Istanbul University, Istanbul. The patients and/or their parents gave informed consent to the work.

2.1. Study design

Seven patients (all male: at the time of surgery, mean age 8 years 9 months, range 5–17 years, standard deviation 5.1 years) diagnosed with spastic CP, however with no prior remedial surgery, were included in the study. The Gross Motor Functional Classification System (GMFCS) was used to assess the mobility of the patients. Those who participated attained scores of at least level II, with four of them attaining level IV (Table 1). The popliteal angle (PA) is a key measurement made in the clinic to characterize passive range of motion. Compared to conventions for abnormality (i.e., PA > 50° (Katz et al., 1992)), the patients' PA values (between 50° and 90°) show their limited knee joint mobility. Overall, pre-operative clinical examinations indicated a severely limited range of knee joint motion and led to a decision that all patients required remedial surgery including release of hamstrings. Six of the patients were operated on bilaterally. For five of them, separate experiments were performed on both legs. For the remainder patients, only one leg was experimented due to time limitations imposed by subsequent multilevel surgery. Therefore, a total of twelve knee angle (KA)-ST muscle force (F_{ST}) data sets were collected. The spastic ST was stimulated exclusively (condition I), and simultaneously with its synergistic muscles GRA and SM (condition II) to assess the effects of inter-synergistic EMFT.

2.2. Surgical and experimental procedures

The patients received general anaesthesia, and no muscle relaxants or tourniquet was used. All experimental preparations and data collection were performed within 30 min (the maximal study duration allowed by the ethics committee), after routine incisions to reach the distal ST tendon and before any other routine surgical procedures. Using a scalpel blade (number 18), a longitudinal skin incision was made immediately above the popliteal fossa.

Table 1
Patient characteristics.

Patient	Limb	Age	L_{thigh} (cm)	$C_{mid\text{-}thigh}$ (cm)	GMFCS	PA (deg)
1	1	5	23.0	26.5	IV	70
1	2	5	23.0	26.0	IV	65
2	3	5	23.0	29.0	IV	70
2	4	5	23.0	28.5	IV	50
3	5	6	27.0	30.5	II	75
3	6	6	27.0	29.0	II	70
4	7	8	27.0	28.0	IV	90
4	8	8	26.0	27.0	IV	90
5	9	17	39.0	39.0	II	90
6	10	15	41.0	39.5	II	80
7	11	5	22.5	24.0	IV	90
7	12	5	22.0	23.0	IV	80

L_{thigh} = thigh length; $C_{mid\text{-}thigh}$ = mid-thigh circumference. GMFCS = Gross Motor Functional Classification System. GMFCS level II: patients in need of physical assistance for walking in order to avoid a fall and rapid build-up of fatigue and a support for sitting and standing. GMFCS level IV: patients in need of additional aids including a wheelchair or a body support walker for mobility. PA = popliteal angle (i.e., the angle between hip and knee at hip in 90° flexion): mean (SD) = 76.7° (12.5°).

After cutting the adipose tissue, the distal ST tendon was exposed. Subsequently, a buckle force transducer (TEKNOFIL, Turkey) (Fig. 1A) was mounted and fixed over the tendon. The key transducer characteristics include S-shape; dimensions: width = 12 mm length = 20 mm and height = 9 mm; maximal force range = 400 N; for test range 0–200 N: accuracy < 3%, (< 0.19% below 100 N); resolution = 0.62 N and high linearity (R^2 = 0.99963, peak nonlinearity = 1.31%). Note that prior to each experiment, the force transducer was (i) calibrated using bovine tendon strips (with rectangular cross section, dimensions $7 \times 2\ mm^2$ representative of that of the ST distal tendon) and (ii) sterilized (using gas sterilization at maximally 50 °C).

The patient was positioned using an apparatus composed of three components (Fig. 1B): (i) The *upper leg component,* (ii) *knee angle adjuster* and (iii) *lower leg component*. The upper leg component was secured with two fixtures to the slot of the surgery table. The knee angle adjuster combining the upper and lower leg components allowed setting the KA and fixing it during the contractions. A circular slot machined in the knee angle adjuster and angles marked on it (in 0.5° increments) allowed adjusting the KA to experimental knee joint positions. The leg holders' position is adjustable on the upper leg component. This allows supporting the upper leg and aligning it based on the following: (a) the hip joint position was set to 0° both in sagittal and frontal planes. (b) the axis of the knee joint rotation corresponded to the center of the rotation of the knee angle adjuster. The *ankle holder*, position of which is adjustable on the lower leg component allowed supporting the lower leg. The leg holder and ankle holder were sterilized components. The non-sterile remainder parts were covered with sterile fabric before an antiseptic agent was applied to the skin and the patient's leg was positioned and secured to the apparatus.

Isometric spastic F_{ST} was measured at various muscle lengths imposed by manipulating the KA. Earlier animal experiments indicated that previous active contraction of muscle at long length affects its forces measured at short length (Huijing and Baan, 2001). Such length history effects were also shown in human (Yucesoy et al., 2010). Taking this into account, before acquiring data, muscle-tendon complexes and their epimuscular connections were preconditioned by isometric contractions, alternatingly at extended and flexed knee positions, until spastic ST forces at flexed knee position were reproducible. In addition, the measurements for data acquisition were started in a highly flexed