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Short communication

Cocontraction measured with short-range stiffness was higher in obstetric brachial plexus lesions patients compared to healthy subjects

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ABSTRACT

We suggest short range stiffness (SRS) at the elbow joint as an alternative diagnostic for EMG to assess cocontraction.

Elbow SRS is compared between obstetric brachial plexus lesion (OBPL) patients and healthy subjects (cross-sectional study design). Seven controls (median 28 years) and five patients (median 31 years) isometrically flexed and extended the elbow at rest and three additional torques [2.1,4.3,6.4 N m] while a fast stretch stimulus was applied. SRS was estimated *in silico* using a neuromechanical elbow model simulating the torque response from the imposed elbow angle.

SRS was higher in patients (250 ± 36 N m/rad) than in controls (150 ± 21 N m/rad, p = 0.014), except for the rest condition. Higher elbow SRS suggested greater cocontraction in patients compared to controls. SRS is a promising mechanical alternative to assess cocontraction, which is a frequently encountered clinical problem in OBPL due to axonal misrouting.

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1. Introduction

Obstetric Brachial Plexus Lesion (OBPL) concerns a closed traction injury of the brachial plexus during birth, with an incidence of 0.5-2.6 per 1000 live births (Walle and Hartikainen-Sorri, 1993). Twenty to thirty percent of cases have a permanent functional deficit (Pondaag et al., 2004). Functional muscle recovery following OBPL depends on the number of outgrowing motor axons that reinnervate muscle fibres, on how many axons are misrouted to the wrong muscles (van Dijk et al., 2001, 2007), and on aberrant central motor programming (Anguelova et al., 2016). Misrouting occurs when a regenerating axonal sprout, which may also be one of several branches, elongates into a basal lamina tube different from the original one (de Ruiter et al., 2013). This may lead to the innervation of an antagonistic muscle and cocontraction. Cocontraction causes joint stiffness, resulting in serious functional problems in OBPL, possibly more so than primary muscle weakness (van Dijk et al., 2007). Cocontraction can be assessed qualitatively

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using electromyographical (EMG) techniques (Anguelova et al., 2014), but quantifying its contribution to motor impairment is difficult due to potential EMG cross-talk (van Vugt and van Dijk, 2001). Cross-talk is the unintended registration of neighbouring muscle activity. Clinical assessment (e.g. joint range of motion, muscle strength) cannot distinguish between weakness of one muscle and cocontraction of its antagonist.

'Short range stiffness' (SRS) is a promising alternative representing the state of the mechanical system including the cocontraction and/or muscle weakness. SRS, i.e. the ratio of a change in torque over change in angle, is assigned to the elastic properties of the cross-bridges in the muscle fibres (Campbell and Lakie, 1998). Both the agonist and antagonist muscles exhibit stiffness and so the total joint SRS is the sum of their stiffness (*SRS_{joint}* = *SRS_{agonist}* + *SRS_{antagonist}*). The actual torque is the difference between agonist and antagonist torque (T_{joint} = $T_{agonist}$ - $T_{antagonist}$) (van Eesbeek et al., 2010). To obtain the same net flexion torque as healthy individuals, patients with biceps-triceps cocontraction will require an increased overall activation to overcome triceps cocontraction, leading to higher elbow stiffness (Fig. 1). Hence, the aim of this pilot study was to quantify elbow SRS and compare









Fig. 1. For the same net flexion torque, obstetric brachial plexus lesion (OBPL) patients (right) with motor misrouting which causes increased triceps activation would have to activate the biceps more than healthy individuals (left). Top: Difference in innervation by nerve roots C6 and C7. (Not shown: theoretically also possible cross-innervation from nerve root C7 to biceps muscle in OBPL.) Bottom: Difference in muscle activation, indicated by the size of the muscles and the arrow thickness (F – force, T - torque). (Not shown: there is some triceps activation in healthy individuals, presumably contributing to joint stability.) In the case of absent misrouting we expect that SRS in patients for a certain torque would be within the healthy individuals range and activation ratio (AR) would be high (i.e. close to 1 as in healthy individuals). In the case of misrouting, SRS in patients would be higher than in healthy individuals and AR would be low (i.e. close to 0). In the case of paresis, certain torque levels may not be reached and SRS in patients for the lower torques are normal compared to healthy individuals and AR will be low with a tendency towards zero due to an unfavourable signal-to-noise ratio. Thus, SRS can potentially distinguish between normal function, cocontraction due to misrouting, and paresis.

it between OBPL patients and controls and we hypothesize that SRS will be higher in patients.

2. Materials and methods

Five adult patients with OBPL, recruited from the Dutch Erb's Palsy Association and earlier research projects of the Leiden University Medical Centre (LUMC) Rehabilitation Department, and seven controls participated. Exclusion criteria were brachial plexus surgery and any other relevant neuromuscular or joint disease. All patients had participated in a previous study (Anguelova et al., 2014). Patients were included when they were able to flex and extend the arm against gravity with a muscle strength of at least grade 3 (Medical Research Council & Committee, 1954). Patients were included who had suffered a traction lesion corresponding to at least the spinal nerves C5, C6 and C7. The study was approved by the Medical Ethics Committee of the LUMC. All participants provided written informed consent.

We adapted the wrist perturbator used by van Eesbeek and colleagues for elbow use (Fig. 2) and adapted the experimental protocol with some alterations described below (van Eesbeek et al., 2010). All variables were transformed in coordinates centred on the elbow (Appendix A). Participants were requested to generate four elbow torque levels in random order for flexion as well as extension, of 0 N m (i.e. relaxed muscles) and on average 2.1, 4.3 and 6.4 N m, depending on arm length. A ramp-and-hold rotation (0.15 radians, 4 radians/s) was automatically started when the difference between the torque generated by the participants and the target level was smaller than 2.5% for 0.5 s. A 15 s rest period was included after each stimulus to prevent fatigue and thixotropic force reduction, a phenomenon affecting resting tension due to earlier muscle use (Campbell and Lakie, 1998). Strain gauge signals were sampled at 5 kHz and low-pass filtered (50 Hz, 3rd order Butterworth filter). SRS was estimated during the first 0.04 s of torque, preventing stretch reflexes to affect the measurements, (Appendix B) (Anguelova, 2012) resulting in 32 trials (4 torque



Fig. 2. Experimental set-up with arrows indicating torque (T) and rotation direction during flexion around the elbow joint. It consists of a handle driven by a position servo-controlled (50 Hz bandwidth) electrical motor delivering a torque of 1000 N m/rad (Schouten et al., 2006; van Eesbeek et al., 2010). To assure that the experimental flexion and extension tasks were within the range of motion for patients with contractures, the posture involved 90° shoulder abduction, 90° elbow flexion, with the palm of the hand facing down. The forearm was fixated at the wrist and elbow joint. The motor lever of the machine was attached to a clamp at the wrist joint, placed over the styloid processes of the radial and ulnar bones. The clamp at the elbow joint was placed over the lateral and medial epicondyles of the humeral bone. Both clamps were covered with elastic foam for comfort. The experiment was performed with the forearm aligned with the moment arm of the motor. The distance along the motor moment arm from the lever axis to the centre of rotation was 7 cm (Schouten et al., 2006). The forearm moment arm length varied per participant and was measured between the ulnar styloid process and the olecranon when the arm was in 90° shoulder abduction, 90° elbow flexion, and the palm of the hand facing down. Angular displacement of the lever was measured and torque exerted at the level of the wrist clamp was measured by strain gauges within the lever between wrist clamp and motor. Visual feedback of elbow torque was provided on a computer screen in front of the participant as described by van Eesbeek et al. (2010).

Table 1

Mechanical model parameters. SRS - short-range stiffness.

Parameter	Unit	Fixed/estimated
Motor lever inertia	kg m ²	Fixed
Motor lever damping	N m s/rad	Fixed
Motor lever stiffness	N m/rad	Fixed
Joint inertia	kg m ²	Estimated
Hand-handle interface damping	N m s/rad	Estimated
Hand-handle interface stiffness	N m/rad	Estimated
Joint damping	N m s/rad	Fixed
SRS	N m/rad	Estimated
Stiffness beyond elastic limit	N m/rad	Estimated
Elastic limit	rad	Estimated

levels, 2 directions, 4 observations) per participant. The median of the four observations was calculated resulting in eight data points per participant for further analysis.

We adapted the wrist SRS model and data analysis (van Eesbeek et al., 2010) for the elbow joint with a varying moment arm per

participant derived from the recorded forearm length. The model (Fig. 2 in van Eesbeek et al., 2010) was implemented in Simulink and the optimization was performed in Matlab (The Mathworks Inc.). In short, a dynamic nonlinear model was used to describe the recorded data (angle and torque) consisting of two masses in series, representing the motor lever and the participants' forearm, each connected by a spring-damper element resulting in three spring-damper elements. Of the corresponding ten model parameters (Table 1) motor lever inertia, damping and stiffness, and joint damping were fixed, and the remaining six were estimated (van Eesbeek et al., 2010). Model parameters were found by minimizing the quadratic difference between the measured and modelled torgues. Goodness of model fit and parameter reliability were checked for with the 'variance accounted for' (VAF) and the normalized standard error of the mean (SEM) (van Eesbeek et al., 2010). The median SRS of all four observations was calculated and presented as a scatter plot against the measured torque in elbow coordinates.

Additionally, we used surface EMG to assess the relative degree of agonist and antagonist activity to support our SRS measurements. Biceps and triceps activity were recorded by EMG electrodes placed over the muscle belly (DelsysBagnoli-4, 20–400 Hz band pass, 10 mm inter-electrode distance), sampled at 5 kHz, full-wave rectified, low-pass filtered (30 Hz, 4th order Butterworth). Muscle activation (*A*) of the biceps and triceps was calculated for each flexion and extension torque task during 0.04 s period prior to the ramp-and-hold perturbation. The mean absolute EMG signal was reduced by the mean absolute EMG at rest. Activation ratio (AR) for the biceps was calculated as follows:

$$AR_{biceps} = rac{A_{biceps}^{flexion} - A_{biceps}^{extension}}{A_{biceps}^{flexion} + A_{biceps}^{extension}}$$

and for the triceps:

$$AR_{triceps} = rac{A_{triceps}^{extension} - A_{triceps}^{flexion}}{A_{triceps}^{extension} + A_{triceps}^{flexion}},$$

where $A_{biceps}^{flexion}$ is biceps activation during flexion, $A_{biceps}^{extension}$ is biceps activation during extension at equal absolute elbow torque conditions (Steenbrink et al., 2010). Calculation of the AR requires a good signal-to-noise ratio, so AR was calculated only when the value of the EMG signal of each of the three tasks was at least twice that of the EMG signal at rest (Henseler et al., 2014).

2.1. Statistical analysis

Generalized linear model for repeated measurements (Generalized Estimating Equations) was used with an unstructured correlation matrix in IBM SPSS Statistics 20.0 (Armonk, NY: IBM Corp.) for the following three statistical analyses. In the first analysis SRS was the outcome and patient and control group the predictor, with confounders: torque, flexion and extension task, the interaction between torque and tasks, and arm mass. SRS corrected for the four confounders is referred to as the 'corrected SRS' in the results, and

Table 2

Demographic details of the participants. MRC – Medical research Council scale. When biceps strength was described as MRC grade '5-', this was noted as 4.75.

	OBPL patients	Controls
Number	5	7
Median age (25th–75th percentile) [years]	31 (24–50)	28 (21-52)
Gender (men)	1	2
Investigated left arm	3	3
Median arm length (25th–75th percentile) [cm]	24.0 (22.8-25.5)	25.0 (24.0-27.0)
MRC biceps (25th-75th percentile)	4.75 (3.50-4.88)	-
MRC triceps (25th-75th percentile)	4.75 (3.88-5.00)	-
Lesion extent: number of patients	C5-C7: 4	-
	C5-C8: 1	

uncorrected otherwise. We checked for other possible causes of stiffness such as joint deformities by comparing SRS for the zero torque level, between patients and controls with the same model. In the second analysis AR was the outcome and patient and control group the predictor with confounders: torque, flexion and extension task, the interaction between torque and tasks, and arm length. AR corrected for the four confounders was referred to as the 'corrected AR' in the results. In the third analysis SRS was the outcome and AR the predictor with confounders: torque, flexion and extension task, the interaction between torque and tasks, arm length, and arm mass. A significance level of 0.05 was chosen.



Fig. 3. Scatter plot of the uncorrected (a) short range stiffness (SRS) and (b) activation ratio (AR) against torque. The lines connect the values belonging to the same subject for flexion and extension separately. Biceps AR is coupled with extension and triceps AR with flexion. Gray circles – controls, black squares – obstetric brachial plexus lesion patients.

3. Results

Characteristics of the groups are shown in Table 2. One patient with triceps weakness (MRC 3) was unable to produce sufficient extension torque in the trials with the highest required torques (levels 4.3 and 6.4 N m); the performed tasks were included in the analysis. A typical raw data recording is shown in Appendix B. The model parameters, their SEM and the VAF are shown in Appendix C. Fig. 3(a) shows uncorrected SRS as a function of torque for flexion and extension and Fig. 4(a) corrected SRS for patients and controls. SRS was significantly higher in patients (250 N m/ rad, standard error [SE] 36 N m/rad) than in controls (150 N m/ rad, SE 21 N m/rad, p = 0.014) and it was higher during flexion (252 N m/rad, SE 29 N m/rad) than extension (148 N m/rad, SE 16 N m/rad, p < 0.001). SRS increased with the level of torque both during flexion (18 N m/rad, SE 6 N m/rad, p < 0.001) and during extension (19 N m/rad, SE 4 N m/rad, p < 0.001). SRS did not differ significantly between patients and controls for torque level zero (p = 0.185). AR was not calculated for the torques of 0 and 2.1 N m, as the EMG signal did not exceed twice the EMG signal at rest. Fig. 3(b) shows uncorrected AR as a function of torque and Fig. 4(b) corrected AR for patients and controls. AR did not differ significantly between patients (0.19, SE 0.43) and controls (0.41, SE 0.36, p = 0.8). SRS was lower when AR was higher, but not significantly so (42 N m/rad, SE 77 N m/rad, p = 0.6).

4. Discussion

We were able to quantify elbow SRS in OBPL patients and controls. We confirmed our hypothesis that SRS would be higher in patients than in controls.



Fig. 4. (a) Bar plot with 95% confidence interval error bars of the corrected short range stiffness (SRS) for controls and obstetric brachial plexus lesion (OBPL) patients. (b) Bar plot with 95% confidence interval error bars of the corrected activation ratio (AR) for controls and OBPL patients.

The amount of VAF by the mechanical model was high and the SEM was low, suggesting that the applied model was sufficiently reliable. SRS was higher during flexion than extension which fits with previous findings for the elbow joint (Cannon and Zahalak, 1982; Perreault et al., 2001; Hu et al., 2011), which may be explained by moment arm, muscle pennation angle, and muscle length differences between the biceps and triceps in healthy subjects. SRS in controls in our study was approximately five times higher than previously reported (Cannon and Zahalak, 1982; Perreault et al., 2001; Hu et al., 2011), which is likely due to the use of continuous perturbations (Perreault et al., 2001; Campbell and Lakie, 1998; Anguelova, 2012) and a smaller angle between both upper arm and forearm, and upper arm and trunk in previous reports (Perreault et al., 2001).

SRS was significantly higher in patients than in controls, suggesting more cocontraction in patients. Previous studies in the same subjects showed that misrouting was present in their biceps and triceps muscles (Anguelova et al., 2014), suggesting that cocontraction exceeding that of controls may be due to misrouting. We feel that the increased stiffness in patients is not affected by joint deformities (Allende and Gilbert, 2004), because SRS did not differ between patients and controls at torque level zero. AR did not differ between patients and controls. This may be because we did not measure brachioradialis muscle EMG which may also explain an outlying value in AR during extension, or because of the small number of participants.

The advantages of SRS compared to EMG for cocontraction measurement is that SRS represents the mechanical state of the elbow including the active contribution of all muscles affecting elbow rotation (Anguelova et al., 2014), is not affected by cross-talk (van Vugt and van Dijk, 2001; Hof, 1984), and has a good signalto-noise ratio. This pilot study was potentially limited by the relatively small number of participants and large number of model parameters. When looking in more detail to the etiological factors further expansion of the mechanical model may be useful, e.g. to distinguish between the different muscular compartments of individual muscles that contribute to joint stiffness (Cholewicki and McGill, 1995; Cashaback et al., 2014).

We conclude that SRS is a promising mechanical parameter to quantify elbow cocontraction in OBPL patients, possibly due to misrouting. The clinical importance is that current cocontraction treatment in OBPL, injection of botulinum toxin in antagonist muscles, based on clinical measures, cannot distinguish between muscle weakness and antagonist cocontraction (Gobets et al., 2010). SRS may be a valuable alternative to tailor OBPL treatment in the future.

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Conflict of interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jbiomech.2017. 08.015.

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