Length-specific impairment of skeletal muscle contractile function after eccentric muscle actions in man

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INTRODUCTION

Serial repetitions of maximum voluntary lengthening (eccentric) muscle actions performed with the forearm flexors elicit delayed muscle soreness, efflux of creatine kinase (CK) into the circulation, a decline in elbow joint range of motion and prolonged loss of maximum voluntary force production [1]. The decline in forearm flexor strength immediately after maximal eccentric muscle actions can be extensive, with decrements in excess of 50% being commonly observed [1, 2]. Furthermore, impaired maximum voluntary isometric contraction torque (MVC) has a prolonged time-course and may be apparent for a period of up to 2 weeks without the subjects being aware of their relative weakness [2]. Previous work has not established a relationship between impaired contractile function and observed myofibrillar disruption after eccentric muscular work, since the extent of cellular degradation increases in the days after exercise [3, 4] when muscular strength is beginning to recover [1].

Detrimental changes in the contractile properties of the forearm flexor muscle group are influenced by the active tension generated during isometric and eccentric muscle actions because passive stretching over the same range of motion without activation has no effect [5, 6]. This suggests that structures located in series with the contractile apparatus (e.g. myotendinous attachments, vulnerable sarcomeres) are implicated in the decline in forearm flexor strength after eccentric muscular work as muscle activation presumably unloads the parallel elastic elements [5]. Indirect evidence of myotendinous junction disruption has been observed after stimulated eccentric muscle actions in rabbit tibialis anterior [7]. Furthermore, it has been hypothesized that sarcomeres in the central regions of fibres could be susceptible to over-extension during eccentric exercise (or where isometric contractions occur at long muscle length) due to contraction of relatively shorter sarcomeres at the muscle fibre ends [5].
Alternatively, random variation in sarcomere strength throughout the muscle may increase the susceptibility of certain sarcomeres to rapid overextension (‘popping’) during eccentric muscle actions [8]. This implies that when a sarcomere has yielded its tension generating capacity by becoming overextended, the tension borne by passive components associated with the sarcomere increases suddenly and renders them prone to damage and/or deformation. Disruption within passive cytoskeletal structures (e.g. titin, desmin intermediate filaments), which may function to prevent extreme sarcomere length changes [9], could account for the focal regions of lengthened sarcomeres and Z-line streaming that have previously been observed in rat [10] and human skeletal muscle [3, 4] after eccentric muscular work.

The cumulative effects of regions of lengthened sarcomeres and/or deformed series elastic elements after eccentric muscle actions might be a subtle increase in muscle length, and corresponding shift in the length–tension relationship. A rightward shift in the length–tension relationship of isolated toad sartorius muscle has previously been observed after stimulated eccentric muscle actions, resulting in a disproportionate loss of peak isometric tension at short muscle length [11].

For the forearm flexor musculature in man, this effect would act to accentuate the decline in strength at acute joint angles, i.e. where the muscle group is required to produce tension in a more contracted state. This is because functional sarcomeres would have to shorten further to generate tension (at a given acute joint angle after eccentric muscle actions) to compensate for the increase in overall muscle length. Consequently, it is likely that a greater proportion of functional sarcomeres would be on the ascending limb of their length–tension relationship. The present work was undertaken to test this hypothesis by monitoring the decline in forearm flexor strength at the acute (0.87 rad), mid-range (1.57 rad) and more extended (2.79 rad) elbow angles in the days after a bout of maximum voluntary eccentric muscle actions which evokes indirect evidence of exercise-induced muscle damage.

**Exercise protocol**

Each subject performed a single bout of 70 maximum voluntary eccentric muscle actions using the forearm flexors of a randomly selected arm. The bout was performed on a Kin-Com isokinetic dynamometer (Chattex Corp., TN, U.S.A.) at an angular velocity of 1.75 rad/s allowing a 10s rest interval between each muscle action. The range of motion used for the bouts was from full flexion to almost full extension.

**Muscle soreness, serum CK activity and involuntary elbow flexion**

Immediately before, and on days 1, 2, 3, 4, 7 and 10 after the bout, muscle soreness was monitored by means of a questionnaire consisting of a linear soreness scale for twelve different areas of the arm. The soreness scale ranged from ‘normal’ to ‘very painful’ and subjects were asked to place a mark on the scale with respect to a given area of the arm which best indicated the degree of soreness experienced. Muscle soreness was only reported in five areas of the arm (three regions of the biceps and two regions of the brachioradialis). Muscle soreness scores for these regions were summed each day and the total used as the criterion score.

Ten-millilitre blood samples were drawn from an antecubital vein (n=22). The blood was dispersed into a plain plastic vial containing neutral density beads and allowed to stand at room temperature until clotted before being centrifuged and the serum layer extracted. All the samples were stored at −20°C until analysis. Serum CK activity was assayed by the method of Szasz et al. [12] using an enzymic kit (Sigma No. 47-10; Sigma Chemical Co., Poole, Dorset, U.K.).

Relaxed elbow joint angle was used as a measure of involuntary elbow flexion. Anatomical reference points were marked on the arm at the shoulder, elbow and wrist joints with semi-permanent ink for reproducibility of measurements. A hand-held goniometer was used to measure the angle subtended by the elbow joint with the experimental arm hanging by the subject’s side in a relaxed manner.

**Forearm flexor strength**

Forearm flexor MVC was assessed isometrically before, immediately after and on days 1, 2, 3, 4 and 10 after the bout at elbow angles of 0.87, 1.57 and 2.79 rad (50, 90 and 160°). Testing was carried out in random order using the isokinetic dynamometer in isometric mode. Subjects were seated upright and instructed to place their experimental arm on a rest in front of the torso so that their upper arm was positioned perpendicular to the body and immobilized by the use of straps. The elbow angles to be used for MVC testing were set using the Kin-Com visual display unit after entering a reference datum.

**METHODS**

**Subjects**

Thirty volunteers (28 males and 2 females) aged 18–34 years participated in the study after signing informed consent documentation consistent with University of Wolverhampton guidelines for the protection of human subjects. Subjects had not engaged in any weight training or any other form of regular strenuous physical exercise involving the forearm flexors for at least 6 months before the study. The study was approved by the University of Wolverhampton Ethical Committee.
elbow angle of 1.57 rad (measured with a hand-held goniometer). Two maximum isometric muscle actions of 3 s duration were performed at each elbow angle and the maximum torque elicited was used as the criterion score. A 1-min rest period was allowed between testing repetitions.

**Validity of MVC measurements**

In a subgroup of eight subjects (six males and two females), superimposed percutaneous electrical stimulation during MVC testing was used in addition to the MVC tests in order to examine the possible confounding influence of voluntary inhibition on strength measurements at all elbow angles before and after eccentric exercise. Percutaneous electrical stimulation of the forearm flexor musculature was evoked by a Bioscience Type 200 electrical stimulator (Bioscience, Kent, U.K.) employing a unidirectional 0.5 ms square wave pulse at 100 Hz. Two copper-stimulating electrodes (6 cm x 3 cm) contained within water-soaked felt pouches were attached with Velcro straps proximally and distally to the surface of the forearm flexor musculature of the experimental arm. Subjects were then established in the testing position (as described above) and instructed to relax the forearm flexors of the experimental arm. Voltage was applied and increased in a stepwise manner until there was no further rise in torque elicited. This was established as the voltage to be used for MVC tests containing superimposed electrical stimulation. Subjects were then instructed to perform three MVC tests at each elbow angle in random order and were informed beforehand that one of the MVC tests at each angle would contain superimposed percutaneous electrical stimulation. The experimenter waited for voluntary torque to reach peak values (by observing the Kin-Com visual display unit) before applying percutaneous electrical stimulation for a time period of 1 s. Subjects were instructed to maintain their maximum voluntary contraction for all 4 s of the MVC test.

The same subgroup of subjects was used to examine the possible relationship between muscle swelling, the inability to fully flex the elbow and MVC measurements at acute joint angles: (i) fluid accumulation in the arm was assessed by circumstance measurements taken at the mid-belly of the biceps and 2 cm above the humeral epicondyles (anatomical reference points were marked on the skin with semi-permanent ink for reproducibility of measurements), and (ii) impaired muscle shortening ability was assessed by measuring the elbow angle with the subject attempting to fully flex the joint, keeping the arm by the side and the palm of the hand facing the shoulder.

**Statistics and data analysis**

Data for forearm flexor MVC between joint angles (before eccentric muscle actions) were compared using t-tests for correlated samples. Data for serum CK activity, relaxed and flexed elbow angle and muscle swelling were analysed using repeated measures analysis of variance (ANOVA) because comparisons were being made between more than two time-points. Repeated measures ANOVA was also used to compare changes in MVC data over time between joint angles. In this case, where significance was indicated, t-tests were used to highlight differences between mean scores. Non-parametric muscle soreness data were analysed using the Wilcoxon signed-ranks test.

**RESULTS**

**Muscle soreness, serum CK activity and involuntary elbow flexion**

The eccentric exercise induced muscle soreness \((P<0.01)\) and significant changes in serum CK activity \((P<0.01)\) and the relaxed elbow joint angle \((P<0.01)\) from baseline measures (Fig. 1). Muscle soreness developed over time after eccentric exercise, peaking 3 days after the bout. In many subjects, soreness extended into the brachioradialis muscle after peak discomfort had subsided from the biceps region. Serum CK activity increased from a baseline measure of \(66\pm10\text{ i.u.}/\text{l} \) to \(2196\pm572\text{ i.u.}/\text{l} \) 4 days after exercise. A decline in the relaxed elbow joint angle was observed immediately after exercise. Relaxed elbow angle continued to decrease for 3 days after the bout before beginning to recover.

**Forearm flexor strength**

Before eccentric exercise, significantly greater torque was achieved during MVC tests at the mid-range elbow angle (1.57 rad) than was achieved at either shorter (0.87 rad joint angle) or longer (2.79 rad joint angle) muscle lengths \((P<0.01)\) (Fig. 2). There was no difference between MVC measured at the 0.87 rad and 2.79 rad elbow angles. After eccentric exercise, there was a decrease in MVC from baseline measures at all elbow angles \((P<0.01)\) which was followed by slow recovery or further impairment of muscular strength before recovery (Fig. 3). The relative decline in MVC differed between elbow angles \((P<0.01)\) and was observed to be muscle length-specific, with the greatest relative torque loss apparent at the most acute elbow angle (0.87 rad), followed by 1.57 and 2.79 rad respectively (Fig. 3). Ten days after exercise there was no significant difference in MVC (in relation to baseline measures) between joint angles, indicating forearm flexor strength had recovered similarly with respect to pre-exercise measurements while some impaired function was still evident (Fig. 3).

**Validity of MVC measurements**

**Superimposed electrical stimulation.** Superimposed electrical stimulation during MVC testing did not
increase the torque elicited at an elbow angle of 0.87 rad either before or at any time-point after eccentric exercise. However, a non-significant trend for increased torque production at all elbow angles before eccentric exercise (<10%) was observed. After eccentric exercise, this non-significant trend for increased torque production (of similar proportion) continued with the exceptions of 2 and 3 days after exercise at the elbow angles of 1.57 rad and 2.79 rad respectively. Three days after eccentric exercise, significantly more torque (12%) was produced at an elbow angle of 1.57 rad ($P<0.05$) while significantly less torque (6%) was produced at an elbow angle of 2.79 rad with superimposed electrical stimulation.

Arm circumference measurements and ability to flex the elbow joint. After eccentric exercise, an increase in arm circumference was observed at both the mid-belly of the biceps ($P<0.01$) and in the joint region of the muscle ($P<0.01$). Swelling in
both regions of the arm developed gradually over time. Peak recorded values were observed 4 days after exercise although evidence of swelling was still apparent 10 days after the bout (Fig. 4). Significantly greater swelling was observed in the joint region over that observed in the muscle mid-belly 3 days (P < 0.01), 4 days (P < 0.01) and 7 days (P < 0.01) after eccentric exercise. An inability to fully flex the elbow joint was evident immediately after the eccentric bout (P < 0.01) (Fig. 4) and the extent of this impaired muscle shortening ability remained relatively consistent in the 4 days after eccentric exercise. However, despite this, all subjects were able to produce elbow angles that were considerably less than the most acute angle for MVC tests (0.87 rad) in the testing position.

DISCUSSION

The exact cause of the prolonged decline in MVC after eccentric exercise has yet to be established. However, there is evidence to suggest that the inhibitory effects of muscle soreness do not contribute to strength decrements. Using electrical stimulation superimposed onto maximum voluntary contractions, it was shown that subjects were able to fully activate their muscles despite the presence of residual muscle soreness [2]. The results of the present study are not in total agreement with this observation as electrical stimulation superimposed onto MVC measures at 1.57 rad elicited a 12% higher torque than could be achieved voluntarily 3 days after exercise. Interestingly, this was also the day of peak muscle soreness. However, at the most acute joint angle (0.87 rad), superimposed electrical stimulation did not elicit greater torque during MVC testing either before or in the days after exercise despite the presence of residual muscle soreness. Thus, using our experimental design, the present results appear to suggest that the disproportionate loss of strength at shorter muscle length is not due to the inhibitory effects of muscle soreness. Three days after eccentric exercise, less torque was produced at an elbow angle of 2.79 rad with superimposed electrical stimulation than could be achieved in the MVC tests. Although this is difficult to explain, a slight co-activation of the triceps seems unlikely as superimposed electrical stimulation at the other two joint angles produced a trend for increased torque. Interestingly, peak soreness and peak involuntary elbow flexion were also observed 3 days after eccentric exercise. Furthermore, it is a common observation that pain increases when you stretch out an exercise-damaged muscle beyond its comfortable limits. Thus, 3 days after exercise, electrical stimulation may have added to the considerable discomfort already being experienced by the subjects at the elbow angle of 2.79 rad, perhaps inhibiting voluntary contraction of the biceps and/or stabilizing muscle groups.

It appears unlikely that oedema in the joint or belly of the muscle could account for the greater decline in MVC at short muscle length by influencing impairment of muscle shortening ability. Swelling in the joint and mid-belly regions of the muscle developed gradually in the days after exercise with peak recorded values being observed 4 days after the bout. However, the greatest decline in MVC at short muscle length was observed in the first 2 days after exercise when swelling in both regions of the muscle was at relatively low levels. Subjects did exhibit an inability to fully flex the elbow joint on all the 4 days after exercise, but were able to produce elbow angles that were considerably less than 0.87 rad in the MVC testing position.

Regions of lengthened sarcomeres associated with Z-line streaming have been observed in rat [10] and human skeletal muscle [3, 4] after eccentric muscle actions. Furthermore, the extent of this disruption increases in the 3 days after eccentric muscle actions due to some secondary degradation process [3, 4]. The possible mechanisms by which sarcomeres...
might be susceptible to stretching or over-extension are not established. Internal shortening of relatively shorter sarcomeres at the fibre ends at the expense of others within the same fibre could mean that sarcomeres in the central regions of fibres are particularly vulnerable to over-extension during eccentric exercise or where isometric contractions occur at long muscle length [5]. However, Morgan [8] proposed that extreme and virtually instantaneous lengthening of randomly distributed sarcomeres will occur during eccentric muscle actions, in order from the weakest to the strongest, as the fibre force exceeds their maximum tensile stress. Accordingly, sarcomeres will be vulnerable to ‘popping’ or rapid over-extension. This will increase the load borne by passive structures and may render them susceptible to damage with continued contractions. Friden and Lieber [9] proposed that disruption associated with the Z-line region of the sarcomere could directly result from stretched or broken intermediate filaments (linking Z-lines) which may have a mechanical role in limiting extreme sarcomere length changes. Loss of desmin staining in various muscle fibres 1–2 days after cyclic eccentric muscle actions in rabbit ankle flexor muscle, which was negatively correlated with maximum tetanic tension, was recently reported [13]. While it is likely that the tension-generating capacity of over-extended sarcomeres would be impaired (due to the lack of optimal cross-bridge interaction between myofilaments), disruption and continued degradation within cytoskeletal structures before recovery could inhibit the restoration of over-extended sarcomeres to normal functional capacity. This may influence the slow recovery, and perhaps further impairment of muscular strength before recovery after eccentric muscle actions, as was observed in the present study.

The force generated by cross-bridge cycling is transmitted along the length of the fibre to ultimately act on the myotendinous junction [14]. Thus, disruption and/or deformation in this region of the musculature would severely affect the transduction of force from muscle to tendon, and could significantly alter the biomechanical properties of the joint. Tendinous attachments could be susceptible to exercise-induced damage [5] as this region of the muscle is often the main site of pain and tenderness [15]. In the present study, subjects experienced considerable soreness in the joint region of the muscle. We also observed a significantly greater degree of swelling in the joint region over that observed in the mid-belly region 3–7 days after exercise, perhaps adding some support to the hypothesis that tendinous attachments are implicated in the damage response. However, the possibility that swelling in the joint region could be the result of inflammatory fluid draining down the arm under the influence of gravity cannot be discounted. Despite limited research, contraction-induced damage within the myotendinous regions should not be overlooked since Lieber et al. [7] found evidence to suggest that myotendinous junction disruption may have accounted for some 13% of the 69% decline in maximum tetanic tension observed after stimulated eccentric (rabbit tibialis anterior) muscle actions of 25% strain.

On the basis of our results, we propose that the greater relative decline in MVC observed at shorter muscle length could be attributable to a shift in the length–tension relationship resulting from the cumulative effects of regions of lengthened sarcomeres and/or deformed series elastic elements (e.g. myotendinous attachments) after eccentric muscle actions. Restricted cross-bridge interaction between myofilaments in over-extended sarcomeres and disruption within tendinous attachments would affect the generation of tension at all muscle lengths, but these structural changes could also evoke a subtle increase in muscle length. A consequent shift in the length–tension relationship resulting from an increase in muscle length would further reduce MVC at acute joint angles because functional sarcomeres would have to shorten further in order to generate tension. It has previously been argued that disruption of the myofilament lattice occurring at the sites of over-extended sarcomeres could provide a weak point for areas of injury to spread across myofibrils as well as along them with continued contractions [11]. By this reasoning, the load borne by the sarcolemma could increase dramatically, rendering it prone to disruption and perhaps influencing release of intramuscular enzymes such as CK into the blood after eccentric exercise as was observed in the present study.

The concept of regions of over-extended sarcomeres and deformed series elastic elements may appear to be inconsistent with the decline in relaxed elbow angle observed after eccentric exercise in the present study. However, explanations for the protracted decline in relaxed elbow angle observed after eccentric exercise have included shortening of connective tissue structures in parallel with the contractile machinery [16] and swelling within the connective tissue structures of the muscle [17]. Thus, it would not be inconsistent to hypothesize that regions of lengthened sarcomeres and/or deformed series elastic elements (bringing about an increase in muscle fibre length) could coexist with different pathological changes eliciting a delayed decline in resting elbow angle, such as those previously speculated upon by other workers. In functional terms (i.e. in terms of torque measurements), our data suggest that the muscle has lengthened and it is a common observation that the decline in relaxed elbow angle can be transiently alleviated by passive extension of the affected joint. Thus, a longer muscle (in terms of functional capacity) could simultaneously appear to be in a shortened state due to the palliative shortening of connective structures and/or decline in extensibility of connective tissue structures with swelling. However, it is also possible
that the remaining functional sarcomeres could shorten to some degree to counteract the overall increase in fibre length.

In conclusion, severe and prolonged loss of strength is commonly observed after serial repetitions of eccentric muscle actions. We have observed a disproportionate decline in MVC at short muscle length after eccentric muscular work which may yield interesting clues about the nature of the muscle fibre damage. The data presented support the hypothesis that series structures (e.g. vulnerable sarcomeres, myotendinous attachments) are implicated in the impaired contractile function observed after eccentric exercise.

REFERENCES