39.13

SARCOLEMMA DISRUPTION DURING REPETITIVE MAXIMAL TETANIC CONTRACTIONS IN THE PRESENCE OF A K^+_{ATP} CHANNEL BLOCKER.

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It has previously been reported that the recovery of tetanic force following fatiguing contractions is reduced in the presence of the K^+_{ATP} channel blocker, glibenclamide. We hypothesized that the impairment of force recovery in the presence of glibenclamide could be related to sarcolemma disruption during high intensity contractions. Eight paired diaphragm strips from Sprague Dawley rats were mounted in muscle chambers and attached to a force transducer at L_o. The strips were perfused with oxygenated Kreb's (35°C) containing the molecular tracer procion orange 14 at a concentration of 0.15% and 100 μM glibenclamide was added to the paired treated strips. The strips were supramaximally stimulated (6 V at 100 Hz, single pulse duration 0.3 ms) to elicit 600 ms duration (duty time) maximum isometric tetanic contractions at the following duty cycle (DC, duty time / cycle time): 0.02, 0.15 and 0.30. The presence of glibenclamide during contractions at a DC of 0.02 for 40-50 mins and at a DC of 0.15 for ~3 mins had no significant effect on the percentage of muscle fibres showing sarcolemma disruption in the treated vs untreated groups: 4.9±4.4% (mean±S.D.) vs 4.8±2.4 and 10.1±4.6% vs 12.1±7.8, respectively. At the DC of 0.30 for ~3 mins the presence of glibenclamide showed a significant ($P<0.05$) change in the amount of muscle fibres indicating sarcolemma disruption (34.7±8.9% treated vs 24.2±4.4% untreated). These results indicate that the amount of sarcolemma disruption may be influenced by the modulation of the K^+_{ATP} channel during high (DC=0.30), but not low (DC=0.02 and 0.15) repetitive maximal tetanic contractions. Funded by the MRC of Canada, FRSQ and APQ.

39.14

THE INFLUENCE OF VARIOUS DUTY CYCLES ON SARCOLEMMA DISRUPTION DURING MAXIMAL TETANIC CONTRACTIONS.

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The mechanisms of sarcolemma injury to the diaphragm during resistive breathing are poorly understood. We tested the hypothesis that the amount of sarcolemma disruption in the diaphragm may be associated with the duty cycle (DC), i.e., duty time / cycle time, during high intensity contractions. Eleven paired diaphragm strips from Sprague Dawley rats were mounted in muscle chambers and attached to a force transducer at L_o. The strips were perfused with oxygenated Kreb's at 35°C containing the molecular tracer procion orange 14 at a concentration of 0.15%. One group of strips was not stimulated and served as a paired control. Another four groups of strips were supramaximally stimulated (6 V at 100 Hz, single pulse duration 0.3 ms) to elicit 600 ms duration maximum isometric tetanic contractions at the following DC: 0.02, 0.15, 0.30 and 0.60. The DC of 0.02 did not reach the target force reduction of 50% and was 80% of its initial force after 45-50 min. of stimulation. There was no significant sarcolemma disruption in this group when compared to its paired control, 3.2±0.8 (mean±S.D.) and 0.2±0.4%, respectively. With the DC of 0.15, 0.30 and 0.60, however, the target force reduction of 50% was reached at 1.7±0.3, 0.8±0.02, and 0.3±0.1 min., respectively. At these DC of 0.15, 0.30 and 0.60, sarcolemma disruption was present and was 13.8±3.5, 24.2±4.4 and 10.9±6.9%, respectively. These results indicate that the amount of sarcolemma disruption may be influenced by the duty cycle during maximal contractions of the diaphragm. Funded by the MRC of Canada, FRSQ and APQ.

39.15

MACROPHAGE DYNAMICS AFTER SKELETAL MUSCLE INJURY

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The purpose of this current investigation was to test the hypothesis that the expression of specific macrophage (MØ) maturation markers evolves over time following skeletal muscle injury and that certain MØ markers are associated with the characteristic stages of myofiber necrosis and regeneration. Soleus muscle injury was induced in adult male C57BL/6J mice by using a modified version of the *in vivo* lengthening contraction model developed by Ashton-Miller et al. (1992). Myofiber necrosis peaked at 3 days post-injury, whereas the greatest number of myofibers invaded by ER-MP20-, F4/80-, and acid phosphatase-positive MØ occurred at 1 day post-injury ($P < 0.05$). In addition, invading MØ generally were esterase-, anti-CD11b-, and ER-BMDM1-negative. Myofibers with centrally-located nuclei and positive developmental myosin heavy chain-immunoreactivity appeared at 5-7 days. Inflammatory cells (per mm^2) accumulated in the extracellular matrix (ECM), peaking at 5 days ($P < 0.05$). Elevated concentrations of ER-MP20- and ER-BMDM1-positive cells in the ECM also were greatest at 5 days ($P < 0.05$). CD11b-positive MØ ECM concentrations increased progressively following injury ($P = 0.068$). In contrast, F4/80-positive MØ counts in the ECM were similar to control values. These data suggest that phagocytic macrophages are ER-MP20- and F4/80-positive, whereas ER-BMDM1-positive cells do not invade myofibers and may perform non-phagocytic functions in the ECM. Supported by NR07097 (BAS) and AR39595 (JGC).

39.16

TIME COURSE OF CHANGES IN ISOMETRIC FORCE AND MUSCLE MASS OF RAT EDL MUSCLE FOLLOWING INTRAMUSCULAR INJECTION OF BUPIVACAINE

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Bupivacaine (BPVC) has a specific myotoxic effect and its intramuscular injection results in a rapid muscle degeneration followed by a regeneration. Although the time course of morphological changes was well-documented, little is known about changes in contractile properties after BPVC injection. It was hypothesized that contractile properties were associated with morphological changes, and the recovery of muscle functions depended on severity of muscle damage. The purpose of this study was to investigate the time course of changes in isometric force and muscle mass of rat extensor digitorum longus (EDL) muscle after intramuscular injection of different amount of BPVC. Either 100ul or 200ul of BPVC was injected into the right EDL, and no injection was made for the left EDL which was served as control. Maximal isometric tetanic force (Po) was measured in situ at 3, 7, 14, 21, 28, 42, and 56 days after injection. Three days after injection, Po decreased significantly, and a larger decrease occurred in the 200ul condition. By 14 days after injection, Po recovered to about 85% of the control level for the 100ul condition and about 75% for the 200ul condition. Po recovered to the control level at 21 days for the 100ul condition and at 42 days for the 200ul condition. Muscle mass significantly decreased 3 days after injection, but returned to the control level by 14 days after injection for both conditions. A significant increase in mass was observed 28-56 days after injection for both conditions. Normalized Po (Po/wt weight) was about 85% for the 100ul condition and about 80% of the control level for the 200ul condition at 14 days after injection, but it should be noted that normalized Po was still lower than control value by 56 days post injection for both conditions. Histological observations demonstrated that more widespread damage occurred for the 200ul condition 3 days after injection. These results suggest that 200ul condition produced a larger damage and slower recovery of the Po. It is concluded that recovery of Po depended on severity of muscle damage.

39.17

CELL PROLIFERATION IN OVER-LOADED RAT SOLEUS MUSCLES: MYOFIBER SPLITTING VS. MYOGENESIS.

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Injury to skeletal muscle has been associated with proliferation and migration of cells into regions with damaged myofibers. Many of these cells have been presumed to be inflammatory cells or phagocytes. Using two types of functional overload we have produced damage to myofibers which mimics overuse syndromes. By applying specific antibodies and using double-labeling techniques, we have identified macrophages, degenerating myofibers, fibroblasts, split myofibers and new myoblasts. Myoblasts can be visualized using desmin and dystrophin or desmin and vimentin. Fibroblasts stain only for vimentin. The location of central nuclei and intracellular deposition of vimentin, desmin and fibronectin appear to be related to myofiber splitting. Some myofibers which appear to have split contain different myosin isoforms whereas others are homogeneous.

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39.18

THE EFFECT OF THE INTRAMUSCULAR TEMPERATURE ELEVATION ON ACTIVE STRAIN INJURY

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The aim of this study was to clarify the effect of intramuscular temperature elevation on active(eccentric) strain injury especially about the length tension curve and segmental length change. Under anesthesia, we stretched the muscle by the speed of 10cm per second to produce strain injury on tibialis anterior(TA) and extensor digitorum longus(EDL) in seventeen rabbits(more than 3kg body weight) with their neurovascular supplies preserved. During the stretch, the peroneal nerves were electrically stimulated simultaneously to evoke muscle contraction with and without previous infrared ray irradiation on muscles. We measured the segmental length change during active strain by two dimensional motion analysis of markers attached on muscles. The length increments of stretch in heated TA and EDL at the time of total disruption were 40.3±13.76% and 43.6±16.62%, respectively. But those of non heated TA and EDL were 36.5±13.13% and 34.4±15.83%, respectively, which were significantly lower than those of heated TA and EDL ($p<0.05$). The absorbed energy in heated TA and EDL until the time of total disruption were 175±39.5N·% and 248±47.0N·%, respectively. But those of non heated TA and EDL were 134±36.1N·% and 184±43.2N·%, respectively, which were significantly lower than those of heated muscles ($p<0.05$, $p<0.01$). The distal muscle segments including distal musculotendinous junction were the most lengthened parts in both muscle groups but the distal muscle segments of heated muscle groups showed more length increment than that of non heated muscle groups statistically. In conclusion, intramuscular temperature elevation has preventive effect on muscle strain injury, not by increasing contractile ability but by improving extensibility of musculotendinous units. And it is the distal muscle segment including distal musculotendinous junction that lengthens and absorbs the energy mostly.