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SKELETAL MUSCLE DAMAGE, REPAIR AND ADAPTATION TO UPHILL AND DOWNHILL RUNNING IN HUMANS.

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A Dissertation Submitted to the Department of Physiology,
University of the Witwatersrand, Johannesburg
for the Degree of Master of Science

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SUMMARY

Extensive disruption of muscle fibres has been shown to occur after short term eccentric exercise where high mechanical forces are generated. This study tested whether downhill running acts as a stimulus for inducing eccentric damage, and results in greater muscle damage and deterioration in muscular performance than an equal workload of uphill running. The study aimed at determining whether an adaptation or training effect takes place such that the muscle is more resistant to the damaging effects of a repeated bout of the same exercise. In addition, the study aimed at determining whether the lower muscle volumes and forces of muscular contractions in females compared to males, makes females less susceptible to the damaging effects of eccentric contraction.

Twelve subjects (six males and six females) ran uphill at a gradient of 10 degrees at 10 km/h, for 30 minutes. One week later, the subjects ran downhill (gradient of-10 degrees) at the same workload of 10 km/hr for 30 minutes. After a week of rest, the subjects repeated the downhill run. Pre-exercise, post-exercise, and 24 hours post-exercise, plasma creatine kinase levels as well as strength and endurance values of the hamstrings and quadriceps muscles were measured.

After the eccentric contractions of the first downhill run, the muscles became sore, the hamstring and quadricep muscles lost inherent force and endurance producing capabilities, and showed a marked release of creatine kinase into the blood. The lower muscle volumes and forces of contraction in female subjects, compared to males, does not make females less susceptible to the damaging effect and subsequent plasma creatine kinase response of eccentric exercise. However, with respect to the torque produced at an angular velocity of 180 °/sec, the female hamstrings are more prone to be damaged by uphill running than the male hamstrings. The greater body fat and therefore greater dead weight carried uphill by the female runners could result in greater hamstring strain and and subsequent muscle strain and loss in performance.

The eccentically induced muscle damage is progressive in the post-exercise period before tissues are repaired. Among the factors that may influence the damage and repair processes are calcium, connective tissue, and cyto-skeletal and myofibrillar proteins.

The initial bout of downhill running resulted in a muscular adaptation leading to a reduction in soreness, performance decrements, and a markedly reduced elevation in plasma creatine kinase levels after the second downhill run, one week later. Several hypotheses have been presented to explain the muscle adaptation that occurs after the

initial downhill running session. Stress-susceptible fibres or susceptible areas within a fibre may be eliminated and then regenerated, or muscle fibres and/or connective tissue may be strengthened with an initial bout of downhill running. A creatine kinase inhibitor may have been released along with the creatine kinase into the blood, and the presence of this inhibitor would therefore decrease the amount of creatine kinase released from the muscle after a further eccentric insult. In addition, exercise enhanced endorphin secretion and the subsequent presence of these endorphins could provide an analgesic effect, so minimising the sensation of DOMS after the second downhill run.

DECLARATION

I declare the this dissertation is my own, unaided work except to the extent indicated in the acknowledgement. It is being submitted for the degree of Master of Science to the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination to any other University.

Ingrid Krafft

day of , 1994

I certify that the study contained in this dissertation was approved by the University of the Witwatersrand's Committee for Research on Human Subjects, protocol number 14/6/92.

..... **Date.....**
(Signature of student)

..... **Date.....**
(Signature of Supervisor)

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1. INTRODUCTION

The controversy of whether it is easier to run uphill or downhill has probably existed ever since man began running long distance races against each other, and was possibly even discussed enthusiastically by the ancient Greek athletes.

The Comrades Marathon 'down' run from Pietermaritzburg to Durban takes the form of a gruelling 93 kilometre run and a 914 m descent in altitude to sea level. The 'up' run takes exactly the opposite route, starting in Durban and ending in Pietermaritzburg, but with a climb of 914 m. Again, the debate continues : Is the 'down' run easier than the 'up' run? A conclusion is not drawn easily, since the winning 'up' time is very similar to that of the winning 'down' run. After his first 'down' Comrades victory in 1982, Bruce Fordyce remarked that the 'down' Comrades was not a race, but a "survival trip" (Noakes; 1988).

The natural presumption that it is easier to run downhill is made on the assumption that the runner is "gaining free energy" by converting the free potential energy (free to the runner) into kinetic energy, merely by running downhill. However, the negative effects on the body induced by running downhill have now started to become evident (Armstrong, 1984; Burnes, 1985; Clarkson, 1986; Friden, 1984). It was, therefore, the aim of this study to investigate some of the negative effects that downhill running has on the human body.

The negative external work of continual downhill running, results in temporary, repairable muscle damage with an associated decreased muscle force generation and increased serum creatine kinase activity and muscle soreness (Friden, Sjostrom, Ekblom; 1983). The eccentric muscle contractions of downhill running, are associated with a much lower energy expenditure than the corresponding positive, concentric work of uphill running, and therefore fatigue probably has less of a limiting effect on muscle performance during downhill running than uphill running. Any effect of downhill running on muscular performance is probably more related to mechanical stress than anything else (Armstrong, Asmussen, Davies, Newham; 1986).

Evidence of damage includes disruption of muscle fibres, disturbances of the cross striated band pattern, increased circulating levels of muscle proteins, and changes in voluntary strength and contractile properties in the immediate post-exercise period (Clarkson, Kroll, Graves,

Record; 1982). Based on ultra-structural analyses of sore muscles, Friden, Sjostrom, Ekblom, 1983, have proposed that tearing of the contractile components of the fibres may release protein associated ions. The resultant increased osmotic pressure causes muscle oedema which activates diffuse pain carrying group IV sensory neurones.

The presence of muscle enzymes in the plasma is commonly taken as an indication of some form of muscle damage either in muscle disease (Newham, Mills, Quigley, Edwards; 1983) or following exercise in normal subjects (Fowler, Gardner, Kazerunian, Lauvstad; 1968). The release after exercise is thought to be analogous to the release of cardiac enzymes after an infarct where the magnitude of the release is an indication of the size of the infarct and the plasma levels reach a maximum some hours after the damage has occurred (Gordon, Buncke, Townsend; 1978). Similarly, the release of skeletal muscle enzymes is thought to be proportional to the intensity and duration of the exercise (Apple, Hellsten, Clarkson; 1988), and in the majority of studies, the evidence suggests a similar time course to that seen after cardiac damage (Apple, Rogers, Sherman, Ivy; 1984).

A comparison between concentric and eccentric contractions reveals that at comparable velocities, eccentric contractions can result in far greater external force development (Asmussen; 1956 and Komi, Viitasalo; 1977). Similarly, at comparable force developments, eccentric contractions result in much lower integrated electromyograms (Asmussen; 1956 and Komi, Viitasalo; 1977) suggesting that fewer motor units are recruited in eccentric contractions to produce the same force as concentric contractions. At comparable power levels (work per unit time), the energy cost of eccentric contraction is considerably lower (Amussen; 1956, Davies, Barnes; 1972 and Knuttgen; 1986). In keeping with this, all related physiologic responses are lower, for example, heart rate, cardiac output, pulmonary ventilation, respiratory exchange ratio, muscle blood flow, and muscle temperature (Asmussen; 1977, Davies, White; 1981, Knuttgen; 1986, Thomson, Sweetin, Hamilton; 1975).

Downhill running often results in delayed onset of muscle soreness (DOMS), which is at the least, unpleasant and may at times be debilitating (Friden, Sjostrom, Ekblom, 1983; Friden, Seger, Sjostrom, Ekblom, 1983; Komi, Buskirk, 1972; Newham, 1988; Newham, Jones, Clarkson, 1987; Newham, Jones, Edwards, 1983). Therefore, it would seem to be desirable from a practical and functional point of view to minimise, if not actually prevent, DOMS. It has been observed that exercise-induced DOMS is experienced more often and in greater severity

in individuals who seldom exercise than in regular exercisers. Similarly, performance of an exercise bout that induces muscle damage, results in a rapid adaptation of the muscle, which causes the muscle to be more resistant to the damaging effects of a repeated bout of the same exercise (Friden, Sfakianos, Hargens, Akeson, 1988; Friden, Sjostrom, Ekblom, 1983; Friden, Seger, Sjostrom, Ekblom, 1983; Komi, Buskirk, 1972; Stauber, Fritz, Vogelbach, Dahlman, 1988; Byrnes, Clarkson, White, Hsich, Frykman, 1985; Davies, Qunitanilha, Brookes, Packer, 1982).

Therefore, the aim of the study was threefold :-

(i) **To use the downhill running model to induce eccentric muscle damage so as to investigate the time required, compared to uphill exercise, for changes in serum enzyme activities and delayed muscular soreness to occur, as well as the effect of such an exercise bout on subsequent dynamic skeletal muscle function. Furthermore, the study was designed to determine whether there was a correlation between the amount of increase in serum enzyme activity and the magnitude of muscular soreness sensation.**

(ii) **To determine whether a repeated exposure to eccentric exercise (downhill running) reduces the damaging effects of eccentric exercise.**

(iii) **To determine whether the lower muscle volumes and forces of contraction in female subjects, compared to males, makes females less susceptible to the effects of eccentric damage.**

2. LITERATURE REVIEW

Exercise, especially unaccustomed strenuous activity, can result in damage to muscles. Evidence of damage includes morphological changes (Armstrong et al. 1983; Fridén 1983, 1984; Fridén et al. 1981, 1983b, 1984; Jones et al. 1986; Newham et al. 1983b), delayed-onset muscle soreness and pain (Asmussen 1956; Robbert et al. 1986; Byrnes et al. 1985; Clarkson et al. 1986; Edwards et al. 1981; Schwane et al 1983a), performance decrements (Davies & White 1981; Howell et al. 1985; Jones et al. 1987; Komi & Viitasalo 1977; McCully & Faulkner 1985; Newham et al. 1983c; Talag 1973), and elevation of muscle protein levels in the blood, especially creatine kinase (Byrnes et al. 1985; Clarkson et al. 1985, 1986; Evans et al. 1986; Hunter & Critz 1971; Newham et al. 1983a; Nuttall & Jones 1968; Ross et al. 1983). Exercise-induced muscle damage is not permanent and tissues are repaired (Fridén et al. 1981, 1983a, 1984, Warhol et al. 1985). Moreover, muscles adapt to the stress of repeated exercise such that subsequent bouts of exercise result in little or no damage (Byrnes et al. 1985; Clarkson et al. 1985, 1987b; Clarkson & Tremblay 1988; Newham et al. 1987). Neither the precise cause of skeletal muscle damage induced by exercise nor the mechanism to explain the adaptation to training and repeated bouts of exercise are well understood. This review will outline the proposed mechanisms of exercise-induced muscle damage and repair, the common indicators of exercise damage, and the adaptation response to exercise training.

2.1 INITIAL CAUSE OF EXERCISE DAMAGE

Many types of exercise have been shown to produce muscle damage (Abraham 1977; Apple et al. 1987; Armstrong et al. 1983; Robbert et al. 1986; Byrnes et al. 1985; Clarkson et al. 1985; Davies & White 1981; Fridén 1983; Jones et al. 1987; Knuttgen 1986; Komi & Viitasalo 1977; Newham et al. 1983a). Damage has been observed after isometric exercise (Clarkson et al. 1982, 1985, 1986, 1987a), marathon running (Apple et al. 1984, 1987; Siegel et al. 1981; Warhol et al. 1985), and eccentric muscular activity (Armstrong et al. 1983; Byrnes et al. 1985; Clarkson & Tremblay 1988; Fridén 1983; Newham et al. 1983a, 1986, 1987; Schwane et al. 1983a). Two basic mechanisms have been offered to explain how exercise initiates damage. One mechanism describes a disturbance in metabolic function, and the other addresses a mechanical disruption of the cell.

2.1.1 Proposed Metabolic Mechanisms

During prolonged submaximal exercise, ATP deficiency and waste accumulation have been proposed to explain muscle damage (Armstrong 1984, 1986; Byrnes & Clarkson 1986; DeVries 1966; Irintchev & Wernig 1987).

If metabolic waste products were primarily responsible for exercise-induced muscle damage, then muscles which contract concentrically and fatigue more quickly would show more damage than muscles that develop active tension eccentrically. Armstrong et al. (1983) compared skeletal muscle damage following eccentric (downhill running) and concentric (uphill running) exercise in rats. Running downhill had a lower metabolic cost and produced greater evidence of muscle damage than running uphill. Schwane et al (1983b) compared delayed-onset muscle soreness and blood lactic acid concentrations following level and downhill running in humans. Lactic acid concentration was significantly increased during level running, but subjects did not experience delayed-onset muscle soreness. Contrarily, lactic acid was not elevated in downhill runners, but subjects experienced significant delayed-onset soreness. Also, indicators of muscle damage have been observed in rats following low intensity treadmill exercise with no elevation in blood lactate (Kuipers et al. 1983). Lactic acid does not seem to be a primary agent in the production of muscle damage.

2.1.2 Proposed Mechanical Mechanisms

Many researchers base their arguments against metabolic hypotheses on the finding of greater damage following eccentric muscle actions (negative work) compared with concentric contractions (positive work) [Armstrong et al. 1983; Knuttgen 1986; Newham et al. 1983a,b,c 1986; Talag 1973]. Muscles that develop active tension eccentrically require less energy but experience greater injury than muscles that contract concentrically, as indicated by morphological changes (Armstrong et al. 1983; Newham et al. 1983b), delayed-onset soreness (Newham et al. 1983c, 1986; Talag 1973),

performance changes (Newham et al. 1983c; Talag 1973), and increases in plasma proteins (especially CK) [Armstrong et al. 1983; Newham et al 1983a]. EMG activity also is lower during negative work (maximal and submaximal) suggesting that relatively fewer fibres are recruited to produce large forces (Bigland-Ritchie & Woods 1976; Rogers & Berger 1974). Therefore, under comparable workloads, eccentric actions produce greater tension per cross-sectional area of active muscle than concentric contractions.

To compare eccentric and concentric exercise, several studies have employed a step test (Newham et al. 1983 a,b,c; 1986). During the test, the quadriceps of one leg performed only concentric contractions by stepping up, while the contralateral muscles developed active tension eccentrically by stepping down. Following the step test, no ultra-structural abnormalities were seen in the muscles that had contracted concentrically (Newham et al. 1983b). The muscles that had developed active tension eccentrically, however, showed marked myofibrillar disorganisation (Newham et al. 1983b). Maximum voluntary force decrements and pain were also greater in these muscles (Newham et al. 1983c).

Although there was a greater increase in electrical activation for a given muscle tension following concentric compared with eccentric stepping, there was no evidence of spontaneous electrical activity when the muscles were at rest (Newham et al. 1983c). This observation contradicts the spasm theory of DeVries (1966).

Eccentric muscle actions have been shown to produce more heat than concentric contractions at the same workload (Davies & Barnes 1972; Nadel et al. 1972). These elevated temperatures could damage structural and functional components within the cell. There is evidence from myopathy conditions that elevated temperatures can cause severe rhabdomyolysis (Bartsch et al. 1977). In the case of malignant hyperthermia, muscle temperatures can increase markedly causing degeneration and necrosis of muscle fibres (Gronert 1986).

2.2 MORPHOLOGICAL CHANGES

Histological and ultrastructural analyses of muscle samples provide the most direct evidence of muscle damage (Armstrong et al 1983; Fridén 1983, 1984; Fridén et al. 1981, 1983a,b, 1984, 1986; Hoppeler 1986; Jones et al. 1986; McCully & Faulkner 1985; Newham et al. 1983b). In normal skeletal muscle, the Z-disc appears as a well organised woven basket or square lattice (Hoppeler 1986). Electron micrographs have shown marked broadening, streaming, and, in places, total disruption of Z-discs following eccentric exercise (Fridén 1983, 1984). In fact, changes to the Z-disc are the most commonly found abnormality, and Fridén et al. (1981) have suggested that the Z-disc may be the weak link in the myofibrillar contractile chain. In addition to Z-disc alterations, structural changes include myofibrillar and sarcolemmal disruptions (Armstrong et al. 1983; Fridén et al. 1981, 1983b), widening of the A- and I-bands (Armstrong et al. 1983; Fridén et al. 1983b; Newham et al. 1983b), displacement of organelles (Fridén et al 1983b; Newham et al 1983b), increase in mitochondrial volume density (Fridén 1984; Fridén et al. 1983b), and cytoskeletal changes (Fridén et al 1984). Increased cellular infiltration also has been noted (Armstrong et al. 1983; Jones et al. 1986; McCully & Faulkner 1985; Stauber & Fritz 1988).

2.2.1 Sequence of Events

The sequence of events associated with muscle damage and repair is not well defined, due to different methods used to damage muscle and the variable periods of assessment following the insult. Fridén et al. 1981) obtained biopsies from the soleus muscle 2 and 7 days after an exercise consisting of repeated stair descents. They found markedly less Z-disc disruption on day 7 than on day 2 indicating that repair was taking place. In later studies (Fridén et al. 1983b, 1984), the same researchers found evidence of immediate damage to the vastus lateralis following eccentric cycle ergometer exercise. However, 3 days after exercise the damage had progressed and separated myofibrils, swollen mitochondria, and cytoskeletal

alterations were noted (Fridén et al. 1983b). Lipofuscin granules indicative of lysosomal activity (Fridén et al. 1984) and polyribosome complexes representative of protein synthesis and muscle repair (Fridén et al. 1983b) were seen in areas of disruption. Fibres appeared essentially normal by day 6 after exercise.

Armstong et al. (1983) found sarcomere disturbances, cellular infiltration, and fibre necrosis following downhill running in rats. Immediately after exercise, they observed a disarray of banding patterns and sarcolemmal disruption. Monocytes, macrophages and fibroblasts were evident 1 to 2 days after exercise. At this time, subsarcolemmal mitotic figures, likely to be satellite cells, also were seen. Satellite cells may be sensitive to muscle damage and may increase in number or be activated even when the muscle fibre is only gently compressed (Teravainen 1970). It is possible that satellite cells move to the site of injury, proliferate and become myoblasts. The myoblasts may be transformed into myotubes and ultimately regenerated fibres (Cullen & Mastaglia 1982). In fact, myotubes have provided evidence for regeneration 3 days after downhill running in rats (Armstrong et al. 1983a).

Similar results were reported by McCully and Faulkner (1985) following electrically stimulated eccentric movements of mouse muscle. Structural damage was followed by fibre degeneration and infiltration of macrophages. Four days after damage was induced, myoblasts and myotubes were evident. By 30 days, muscle fibres appeared normal.

Stauber and Fritz (1988) examined cellular infiltration in rat soleus muscle that had been injured by forced lengthening. They reported that mononuclear cellular infiltrates, most evident in damaged muscle between 24 and 48 hours after injury, were not comprised mainly of macrophages, as suggested by others (Armstrong et al 1983). Rather, the cells were myogenic in origin and were most numerous between the torn ends of the fibres. Lymphoid cells were also found, suggesting an involvement of

lymphocytes in muscle repair. At 96 and 120 hours after injury, myofibres were observed in spaces previously occupied by mono-nuclear cells.

Using 2 different eccentric exercise protocols, Jones et al. (1986) observed fibre necrosis and cellular infiltration in humans. Forearm flexors were forcibly extended using a winch with a mechanical advantage of about 10:1. Calf muscles were exercised as the subject walked backward down an inclined treadmill. Although there was variability in the response among subjects, degenerating fibres and infiltrating mononuclear cells were not evident until 7 days after exercise. By 20 days after exercise, many small regenerating fibres with basophilic cytoplasm and internal nuclei were present.

2.2.2 Mechanisms of Morphological Damage and Repair

The preceding evidence suggests that damage progresses in the postexercise period, but is not permanent (Armstrong et al. 1983; Fridén 1983; Fridén et al. 1981, 1983b, 1984; Jones et al. 1986). Among the factors that may influence the damage and repair processes are calcium (Armstrong 1984; Busch et al. 1972; Clarkson & Tremblay 1988; Fridén et al. 1983b; Newham et al. 1983b; Soza et al. 1986), lysosomes (Fridén 1984; Fridén et al. 1981, 1984; Salminen et al. 1984; Salminen & Kihlstrom 1985; Salminen & Vihko 1980, 1983b, 1984; Vihko et al. 1978a,b), connective tissue (Armstrong et al. 1983; Asmussen 1956; Fritz & Stauber 1988; Tullson & Armstrong 1981), free radicals (Alessio & Goldfarb 1988; Cooper et al 1986; Kanter et al. 1986, 1988), energy sources (Noakes 1987; O'Reilly 1987), and cytoskeletal and myofibrillar proteins (Fridén et al. 1984; Lazarides et al. 1981; Reichsman et al. 1988).

2.2.2.1 Calcium

Abnormally high levels of calcium (Ca^{++}) in muscle cells can trigger a series of events leading to necrosis (Baracos et al. 1986; Busch et al. 1972; Duncan 1978; Knochel 1981; Wrogemann & Pena 1976). These increases could result from either lesions in the sarcolemma or a defect in the ability

of the sarcoplasmic reticulum to reuptake Ca^{++}. Investigators have hypothesised that when actin and myosin are pulled apart during eccentric exercise, the surface membrane is damaged, allowing entry of extracellular Ca^{++} (Armstrong 1984; Newham et al. 1983b). There is evidence to suggest an association between Ca^{++} accumulation and sarcolemmal defects in diseased muscle (Bodensteiner et al. 1978; Cullen et al. 1979; Cullen & Fulthorpe 1975; Rowland 1980). In fact, "holes" in the sarcolemma and large areas without any sarcolemma have been observed in overcontracted fibres from patients with muscular dystrophy (Schmalbruch 1975).

Increased Ca^{++} may cause mitochondrial swelling that would explain the increase in mitochondrial volume noted by Fridén et al. (1983b). When Ca^{++} levels are high, mitochondria sequester the excess Ca^{++} to maintain homeostasis. Thus, Ca^{++} overload causes reduction in oxidative phosphorylation and a subsequent decrease in ATP (Cullen et al. 1979; Wrogemann & Pena 1976). Low ATP levels may initiate a cycle of events starting with impaired ability to extrude Ca^{++} via ATP-dependent pumps (Armstrong 1984; Wrogemann & Pena 1976).

Accumulation of Ca^{++} in muscle fibres has been shown to induce muscle damage (Baracos et al. 1986; Soza et al 1986). Baracos et al. (1986) noted that Ca^{++} influences protein turnover in incubated rat skeletal muscle. They found that protein degradation was lowest when no Ca^{++} was added to the extracellular medium and increased with increasing Ca^{++} concentrations. In addition, dantrolene, an inhibitor of Ca^{++} release from the sarcoplasmic reticulum, reduced net protein degradation. Thus, it appears that Ca^{++} from both extracellular sources and intracellular reservoirs can affect protein turnover in isolated skeletal muscle (Baracos et al. 1986).

The damage caused by eccentric exercise resembles disruptions elicited by Ca^{++}-activated neutral protease (CANP) [Busch et al. 1972]. After incubating rabbit muscle in a Ca^{++} solution for 9 hours, Busch et al. (1972) noted complete removal of Z-lines. Myofibrils were then incubated in the presence of Ca^{++} and/or sarcoplasmic protein extract. Neither the Ca^{++} nor

the extract alone caused Z-line degradation. However, when myofibrils were incubated with both Ca^{++} and extract, Z-lines were remove. The authors suggested the presence of a Ca^{++}-activated sarcoplasmic factor (referred to above as CANP) capable of selectively degrading Z-lines. This evidence implies that CANP may be involved in the extensive disruption of Z-discs following eccentric exercise.

Ca^{++}-activated neutral proteases may also play a role in the repair process. There are 2 isoenzymes of Ca^{++}-dependent proteases (Mellgren 1980). The type 1 enzyme is activated at micromolar concentrations of Ca^{++}, and the type 2 enzyme requires millimolar concentrations. In the presence of Ca^{++}, both isoenzymes undergo partial autolytic proteolysis. These initial events allow increased Ca^{++} affinity and autoactivation of the proteases. Thus, there is increased proteolytic activity at physiologically attainable Ca^{++} concentrations. Proteins that anchor the cytoskeleton to the plasmalemma are excellent substrates for Ca^{++}-dependent proteases, and Mellgren (1987) has suggested that Ca^{++}-dependent proteolysis may operate in some aspect of cytoskeletal or cell membrane remodeling.

Several studies have reported that exercise-damaged muscles spontaneously shorten and that the shortening is not caused by an increase in electrical activity (Brody 1969; Howell et al 1985; Jones et al. 1987). Clarkson and Tremblay (1988) had subjects perform repetitive eccentric muscle actions of the forearm flexors and then measured the elbow angle as subjects stood with their arm hanging relaxed at their side.

In an attempt to explain the presence of hypercontracted fibres in biopsies from patients with Duchenne muscular dystrophy, Cullen and Fulthorpe (1975) hypothesised that Ca^{++} influx might cause excessive contraction of some sarcomeres. This, in turn, would excessively stretch adjacent sarcomeres. Some of the stretched myofilaments would be disrupted, initiating necrosis.

Brody (1969) reported a case study in which a patient experienced exercise-induced contractures in muscles that were electically normal at rest. Biopsy analysis showed a decrease in Ca^{++} uptake/mg of microsomal protein, and the author suggested a defect in the ability of the sarcoplasmic reticulum to sequester Ca^{++} ions.

It has been hypothesised that the muscle shortening noted after eccentric exercise is due to an accumulation of Ca^{++} in damaged fibres (Clarkson & Tremblay 1988). There is some evidence that eccentric exercise produces damage to the sarcoplasmic reticulum. Significant decreases in force generation, particularly at low frequencies of electrical stimulation, have been noted (Davies & White 1981; Newham et al. 1983c, 1987; Sargeant & Dolan 1987). This low frequency fatigue has been attributed to sarcoplasmic reticulum damage causing insufficient Ca^{++} release for force generation (Newham et al. 1983c).

The Ca^{++} hypothesis for muscle damage is attractive, but more investigation is needed. Increased intracellular Ca^{++} concentrations in exercise-damaged muscle must be documented and the location of the defect identified.

2.2.2.2 Lysosomes

Several studies have noted an increase in activity of lysosomal enzymes in exercised muscle (Salminen et al. 1984; Salminen & Kihlstrom 1985; Salminen & Vihko 1980, 1983b, 1984; Vihko et al. 1978a,b). The activation of these enzymes as well as the role that lysosomes play in exercise-damaged muscle is poorly understood. Invading phagocytes certainly account for a large portion of the increased lysosomal activity noted in histologically prepared tissue from exercised muscle (Salminen & Kihlstrom 1985; Vihko et al. 1987b). However, increased muscle cell lysosomal activity may occur as well (Vihko et al. 1978b). High Ca^{++} levels can increase prostaglandin E_2 production, which is known to increase muscle lysosome function (Baracos et al. 1986).

In several studies utilising a mouse model, investigators have noted an increase in activity of acid hydrolases (most notably ß-glucuronidase) following exhaustive treadmill running (Salminen et al. 1984; Salminen & Kihlstrom 1985; Salminen & Vihko 1980, 1983a,b, 1984; Vihko et al. 1978a,b). Salminen and Kihlstrom (1985) reported significant correlations between ß-glucuronidase and necrotic lesions in mouse muscle following 4 to 9 hours of running at 14.5 m/min. ß-Glucuronidase activity was highest 3 days after exertion and, at this time, a high proportion of lysosomal activity was associated with cellular infiltrates due to inflammation.

Salminen and Vihko (1983b) found that mouse skeletal muscles are selectively susceptible to exercise-induced damage. More necrotic lesions were found in muscles that were located in non-expanding compartments. They hypothesised that more damage may occur in these compartments due to oedema causing tissue pressure, resulting in ischaemic necrosis. Also, correlations between activities of ß-glucuronidase following exhaustive exercise were highest between different muscles within a compartment, rather than between different muscles in different compartments (Salminen & Vihko 1983b). Lysosomal activation seems to accompany oedema and may be involved in the process of ischaemic necrosis.

Contractile proteins also may become exposed to proteolytic attack of lysosomal enzymes after a muscle is mechanically stressed (Friden 1984; Friden et al. 1981, 1984). The increase in lipofuscin granules observed in biopsies of human subjects obtained by Friden et al (1984) 3 days after eccentric exercise when compared with those taken immediately after exercise supports this hypothesis.

To evaluate the role of lysosomes in myofibrillar and total protein breakdown, Lowell et al. (1986) assessed the release of 3-methylhistidine and tyrosine in perfused muscle of starved and fed rats. While 3-methylhistidine is found exclusively in actin and myosin, tyrosine is found in other muscle proteins. Inhibitors of lysosomal proteases did not affect the efflux of 3-methylhistidine but inhibited tyrosine release. Although total

proteolysis, which primarily reflects non-myofibrillar protein degradation, may occur within lysosomes, the data suggest that myofibrillar protein breakdown occurs via a non-lysosomal pathway. Although this study does not support a lysosomal mechanism for myofibrillar damage, the in vitro results cannot be directly compared with exercise-induced damage.

2.2.2.3 Connective Tissue

The high forces associated with eccentric exercise stress the structural elements in series between the cross-bridges and the muscle's bony attachments, including connective tissue (Fridén 1983). Abraham (1977) found elevated levels of hydroxyproline, an amino acid found in connective tissue, in the urine of subjects following soreness-inducing exercise.

Products of collagen breakdown may act as chemotactic agents for monocytes to travel from the blood into the muscle (Armstrong et al. 1983). In fact, a significant decrease in monocytes has been found in the blood of humans at 24 hours following downhill running (Schwane et al 1983a). In rat muscle samples fixed for histology following downhill running, monocytes remained achered to the luminal walls of the venules (Armstrong et al. 1983). These cells may have been fixed in the initial stages of diapedesis into the interstitium. Upon entering the injured area, monocytes are transformed into macrophages which then function in phagocytosis. Infiltrating cells may cause further fibre degeneration as with inflammatory muscle disease (Mastaglia & Walton 1982). However, because tissue infiltration occurs after peak enzyme release, Jones et al. (1986) have suggested that invading cells are a consequence, rather than a cause, of damage and are acting to scavenge and remove debris.

Also, the animal work of Stauber and Fritz (1988) cited above suggests that invading cells may be predominantly myogenic. Proteoglycans, major components of connective tissue, are important for regulating the myogenic process including satellite cell release, myoblast fusion, and myotube

orientation (Fritz & Stauber 1988). Thus, connective tissue may have a regulatory, as well as a structural, role in the damage and repair process.

Fritz and Stauber (1988) used immunohistochemical techniques to monitor changes in proteoglycan localisation following forced lengthening of rat soleus muscle. In the extracellular matrix surrounding fibres from normal muscles, proteoglycans were localised in the endomysium. Between 1 and 3 days after injury, they were absent from this area. However, within 5 days of injury, proteoglycan localisation was essentially normal. The researchers suggested that the extracellular matrix is important in repair by providing structural stability for regenerating cells.

2.2.2.4 Free Radicals

Free radicals are chemical species with one or more unpaired electrons in their outer orbital making them highly reactive (Blake et al. 1987; Machlin & Bendich 1987). Lipid peroxidation initiated by free radicals decreases the barrier function of cell membranes and may be associated with muscle fibre necrosis and enzyme release following damaging exercise. In addition, an increase in the level of free radicals may be related to loss of membrane integrity of the sarcoplasmic reticulum and mitochondria (Davies et al. 1982; Lovlin et al. 1987).

Exhaustive exercise known to induce muscle damage has been shown to increase free radical activity (Alessio & Goldfarb 1988; Cooper et al. 1986; Kanter et al. 1986, 1988). Kanter et al. (1988) recently measured serum malondialdehyde (MDA) and creatine kinase-MB (CK-MB) in the blood of runners following an 80 km race. The presence of MDA was used as an indicator of lipid peroxidation resulting from free radical reactions, and CK-MB was used as an indicator of muscle damage. They found a significant correlation ($r = 0.85$) between MDA and CK-MB. Alessio and Goldfarb (1988) also found an increase in MDA after an acute bout of running in male rats.

Using serum CK, as well as lactate dehydrogenase (LDH) and aspartate aminotransferase (AST), as evidence for muscle damage, Maughan et al. (1988) measured thiobarbituric acid reactive substances (TBARS) following 45 minutes of downhill running. TBARS are products of lipid peroxidation. Subjects with the greatest enzyme increase showed the greatest increase in serum TBARS. The time course of changes in TBARS was also similar to that of serum enzyme activities.

Thus, there is data to suggest a relationship between free radical reactions and loss of membrane integrity following exercise. However, the relationship may not be a causative one (Maughan et al. 1988). In addition, the studies that have shown an increase in lipid peroxidation after exercise have used endurance exercises. The increase in lipid peroxidation could be produced by an increase in catecholamine levels in the blood, an elevation of body temperature, an increased rate of haemoglobin auto-oxidation, or error in oxygen metabolism associated with the increased rate of oxygen utilisation (Kanter et al. 1988). Considering these factors, it is questionable whether the damage induced by high force, short term eccentric exercise would be related to lipid peroxidation.

2.2.2.5 Energy Sources

Only limited data exist concerning the role of energy sources in the damage and repair process. Persons with certain metabolic diseases where muscle glycogen is compromised show severe rhabdomyolysis in response to exercise (Noakes 1987). Thus, it has been suggested that for endurance-type exercise, muscle glycogen depletion may initiate damage (Noakes 1987). Since eccentric exercise generally does not result in total glycogen depletion (O'Reilly et al. 1987), it is unlikely that glycogen depletion would produce the profound damage seen with eccentric work in healthy individuals.

However, glycogen availability may be important for repair. Kuipers et al. (1985b) found that the glycogen content of muscle biopsy samples taken 24

hours after eccentric cycle ergometer work was lower than the glycogen content of samples taken immediately after exercise. O'Reilly et al. (1987) examined muscle glycogen levels of the vastus lateralis after eccentric cycle exercise. They found a 39% reduction in muscle glycogen immediately after exercise. 10 Days after exercise, glycogen levels were not restored and were even lower (but not significantly) than immediately postexercise values. Although glycogen depletion may not initiate damage, the reduced capacity to resynthesise glycogen may play an important role in the repair process.

2.2.2.6 Cytoskeletal and Myofibrillar Proteins

The intermediate filament protein, desmin, also may be involved in muscle repair (Friden et al. 1984; Lazarides et al. 1981). There is evidence that this protein acts as a framework linking Z-discs to one another and to the sarcolemma (Lazarides et al. 1981). Using immunofluorescence microscopy with an antibody specific to desmin, Friden et al. (1984) found longitudinal extensions in biopsies taken 3 days after eccentric exercise. These extensions were taken as indicators of cytoskeletal disorganisation. The authors hypothesised that there is an elevated turnover of cytoskeletal proteins following muscle damage. Increased synthesis of desmin may be important in reorganisation of myofibrillar proteins.

Changes in the electrophoretic banding patterns of the major myofibrillar proteins have not been found with exercise damage. Snyder et al. (1984) examined banding patterns of muscle homogenates prepared from rats that ran downhill for 90 minutes. They observed minimal differences in electrophoretic banding patterns in animals sacrificed 18 or 24 hours after exercise compared with unexercised, control animals. Reichsman et al. (1988) studied biopsy samples from 4 human subjects taken 48 hours after performance of high force eccentric exercise. They also found no change in banding patterns of major myofibrillar proteins. However, they did find a substantial increase in 4 unidentified protein bands representing molecular weights of approximately 95 000 daltons, 76 000 daltons, 33 000 daltons,

and 11 800 daltons. These increases may reflect an enhanced synthesis of certain proteins necessary for repair.

2.2.3 Location and Extent of Damage

There is discrepancy concerning the location of damage, especially when comparing animal models with human models (Armstrong et al. 1983; Fridén et al. 1983b; Jones et al. 1986). Both fast twitch and slow twitch fibres may be injured. Damage occurs prdominantly in the type I fibres of animals (Armstrong et al. 1983) and in the type II fibres of humans (Fridén et al. 1983b, 1988; Jones et al. 1986). Although no clear explanation exists for this difference, it may be attributed to the type and severity of exercise. Individual work periods are much longer in animal studies than in human studies (Fridén 1984).

Recent evidence has shown predominant fast glycolytic (type II) fibre damage in rabbit muscle that had been electrically stimulated during force lengthening (Lieber & Fridén 1988).

Selective damage may be related to motor unit recruitment patterns and/or structural differences between type I and type II fibres (Byrnes & Clarkson 1986; Fridén et al. 1988). However, there is no evidence for selective fibre recruitment on the basis of PAS-staining (Fridén et al. 1983b, 1988; O'Reilly et al. 1987).

It is often difficult to assess the location and extent of damage because of the small specimen size and physiological states of sectioned fibres. Both atrophied and hypertrophied fibres have been identified in damaged muscle at 24 hours after injury (Stauber & Fritz 1988). Since this is too short a time frame for traditional hypertrophy to occur, Stauber & Fritz (1988) have proposed a mechanism to explain these results. The "hypertrophied" fibres may be broken fibres that have retracted, and the "atrophied" fibres may be samples from the end tips of broken fibres. Depending upon where fibres are sectioned, they may appear normal, hypertrophied, or atrophied.

Evidence from several animal studies has suggested that exercise-induced injury is restricted to relatively short segments of few fibres (Armstrong et al. 1983; Kuipers et al. 1983). Kuipers et al. (1983) noted that necrosis was limited to 150 to 1 250 micron segments in rats following treadmill running. Armstrong et al. (1983) found that less than 5% of rat muscle fibres were affected by downhill running.

In the cases of myopathy conditions in humans, it is common to observe areas of necrosis in small segments of one fibre while areas adjacent to the necrotic segments remain viable (Carpenter & Karpati 1984). When this happens, a demarcation membrane forms between the area of necrosis and the healthy adjacent segments (Carpenter & Karpati 1984). Thus, sections of focal necrosis can be "walled-off" from the remaining fibre and then repaired (Carpernter & Karpati 1984).

Armstrong et al. (1983) have hypothesised that necrotic fibres may be suffering from a pathological condition that becomes apparent when the muscles are mechanically stressed. Perhaps all recruited fibres suffer sublethal injury. Those that suffer lethal damage may represent random events in which the damaging process has passed a point of no return. Also, it should be noted that because focal necrosis is probably involved (rather than necrosis of the entire cell), it may be difficult to estimate damage from only a few cross-sections of muscle.

2.3 DELAYED-ONSET MUSCLE SORENESS

Many types of muscle pain and soreness have been documented (Layzer 1986). Hough (1902) first hypothesised that delayed-onset muscle soreness following unaccustomed exercise was a result of muscle damage due to mechanical stress. His theory, which has been supported by the biopsy evidence presented above, is now widely accepted.

Delayed-onset muscle soreness can be distinguished from temporary soreness. Temporary soreness, characterised by only moderate pain, is felt during the final stages of fatiguing exercise (Fridén 1983, 1984; Talag 1973). The primary cause is thought to be metabolic waste accumulation (Fridén 1983; Staton 1951; Talag 1973). In contrast, delayed-onset muscle soreness is unrelated to fatigue and is described as a dull, aching pain combined with tenderness and stiffness (Armstong 1984; Byrnes & Clarkson 1986). Discomfort usually develops during the first 24 to 48 hours following eccentric exercise and peaks between 24 and 72 hours. It then subsides and disappears within 5 to 7 days of exercise (Abraham 1977; Armstrong 1984; Asmussen 1956; Bobbert et al. 1986; Edwards et al. 1981; Fridén et al. 1986; Hough 1902; Jones et al. 1987; Newham et al. 1983a,c; Talag 1973).

2.3.1 Localisation of Discomfort

The method most commonly used to evaluate soreness has been the questionnaire. Subjects are required to rate perceived soreness on a verbally anchored, fixed ordinal scale (Bobbert et al. 1986; Byrnes & Clarkson 1986; Byrnes et al. 1985; Clarkson & Tremblay 1988; Talag 1973). Using such a scale, Bobbert et al. (1986) assessed soreness in the gastrocnemius following repeated lifting and lowering of the body by plantar- and dorsiflexing the ankle of one leg. Twenty-four hours after exercise, subjects located either the proximal or distal parts of the muscle to be most tender upon palpation. However, 48 hours after exercise, all subjects reported that the middle part was as sore as the proximal or distal parts.

Others have quantified tenderness using a roundended wooden probe connected to a strain gauge (Edwards et al. 1981; Jones et al. 1987; Newham et al. 1983c, 1986). The probe with gradually increasing force, was applied to the muscle. When subjects were asked to report the force at which tenderness was first felt, discomfort was most intense in the region of the myotendinous junction of exercise-damaged muscles (Edwards et al. 1981).

There are 2 possible explanations for localisation of pain. Either muscle fibres and/or connective tissue are damaged (Armstrong 1977; Asmussen 1956; Fridén et al. 1986). The fibres just proximal to the musculotendinous junction are oriented obliquely, making them most vulnerable to the high tensions of eccentric exercise (Fridén et al. 1986). However, muscle fibres are highly elastic compared with connective tissue, suggesting that the latter may be even more susceptible to injury (Asmussen 1956).

Jones et al. (1987) observed that muscle stiffness and spontaneous flexion at the elbow developed immediately following eccentric exercise of the forearm flexors. Tenderness when pressure was applied to the affected muscles and pain on extension developed more slowly. Since there was no increase in resting EMG activity, the authors concluded that stiffness and spontaneous flexion may be a result of connective tissue damage causing subsequent sensitising of pain receptors. In a similar study, Howell et al. (1985) also found that flexion deformities were not accompanied by an increase in electical activity. The latter investigators concluded that oedema within the perimuscular connective tissue may alter the elastic behaviour of the muscles and cause restriction of motion. Consistent with this conclusion. Jones et al. (1987) noted that passive movements reduced the flexion deformity possibly by squeezing fluid out of the muscle. Clarkson and Tremblay (1988) suggested that the flexion deformities were due to shortening of fibres by an abnormal accumulation of Ca^{++} in the cells. The shortening would exert a stretch on the connective tissue and tendons, perhaps making receptors more sensitive to pain.

2.3.2 Soreness and Fluid Pressure

The evidence for a relationship between oedema and muscular discomfort is contradictory. Bobbert et al. (1986) found an increase in limb volume relative to the volume of a control limb 24, 48 and 72 hours following eccentric calf exercise. Thus, they hypothesised that an increase in limb volume may be due to oedema formation that results in soreness. However,

Talag (1973) found no significant correlation between limb volume and soreness following eccentric exercise of the forearm flexors.

More sophisticated methods of measuring intramuscular pressure in painful muscles have also yielded conflicting results (Fridén et al. 1986; Newham & Jones 1985). Fridén et al. (1986) used a slit catheter technique to measure tissue fluid pressure in the anterior tibial compartment of the leg. There was an increase in pressure 2 days following exercise. Thus, pressure elevation may have been a result of fluid buildup associated with delayed-onset muscle soreness. Using a similar technique to study exercise-induced soreness of the elbow flexors, Newham and Jones (1985) found no significant difference in intramuscular pressure between control and exercised muscles. The conflicting results may be due to the compliance of the different compartments (Newham 1988). The tibial anterior compartment is a relatively low compliance compartment whereas the compartment around the elbow flexors is more compliant and distensible (Newham 1988).

Anti-inflammatory drugs are not successful in significantly reducing muscle soreness (Donnelly et al. 1988b; Janssen et al 1983). Either soreness is not related to oedema, or the oedema observed by several investigators is not inflammation in the classical sense. Schwane et al. (1983a) found that increases in neutrophil and total white blood cell counts, which usually accompany inflammation, did not occur in association with soreness following downhill running. In addition, neutrophils were rarely observed in eccentrically exercised rat muscle (Armstrong et al. 1983). Smith et al. (1988) reported a larger increase in neutrophils after downhill running that induced muscle damage compared with uphill running which did not induce damage. Because an increase in neutrophils occurred after both downhill and uphill runs, factors associated with general exercise stress, apart from damage, may have produced the elevated white blood cell counts.

Thus, an alternative sequence of events resulting in oedema has been proposed (Fridén 1983, 1984). Fibre disruption may lead to formation of

degraded protein components, release of protein bound ions, and a subsequent increase in osmotic pressure causing fluid buildup. Fluid pressure may then activate free nerve endings and be perceived as soreness. Fridén et al. (1988) found that muscle fibre swelling was directly associated with delayed muscle soreness after eccentric exercise. Preliminary investigations in our laboratory have suggested that substantial swelling can be present long after soreness has subsided. This may suggest that muscle pain receptors adapt to this stimulus.

Although anti-inflammatory drugs have not proven successful in the alleviation of muscle soreness, there is some evidence from animal models that these drugs may reduce the extent of exercise damage. Kihlstrom et al. (1984) found that prednisolone, a steroidal anti-inflammatory drug, given to mice before exercise reduced inflammation and the lysosomal response. Similar results were found using indomethacin, a non-steroidal anti-inflammatory and prostaglandin inhibitor (Salminen & Kihlstrom 1987).

2.3.3 Soreness Perception

The sensation of pain in skeletal muscle is transmitted by myelinated group III and unmyelinated group IV afferent neurons (Armstrong 1984; Byrnes & Clarkson 1986; Mense & Schmidt 1974, 1977). These fibres are found throughout the muscle but are particularly dense in regions of connective tissue (Mense & Schmidt 1977). Group III fibres carry sharp, localised pain. Since group IV fibres carry dull, diffuse pain and are twice as common as group III fibres, Armstrong (1984) has suggested that they are primarily responsible for the sensation of delayed-onset muscle soreness.

Group IV fibres have been placed into 2 major categories (Mense & Schmidt 1977). There are metaboceptors, which respond to mechanical and/or chemical stimuli, and nociceptors, which respond to noxious stimuli. In addition, some group IV fibres are polymodal and respond to several types of stimuli. Bradykinin, serotonin, histamine, potassium and prostaglandins may activate the free nerve endings of nociceptors (Byrnes

& Clarkson 1986; Mense & Schmidt 1977). The delay in onset of soreness following an acute bout of exercise may be explained by the time required for cells to die and for any or all of these substances to accumulate (Armstrong 1984). It should be noted that while many myopathies are not accompanied by soreness or pain, pain does occur in myopathies where there is rapid breakdown of tissue (Morgan-Hughes 1979).

In addition to peripheral pathways, exercise-induced soreness may be modulated at the spinal level, by the reticular activating system or by the sensory cortex (Byrnes & Clarkson 1986). Variation in receptor types and the ability to modulate pain at multiple levels in the nervous system may explain intersubject variability in soreness perception and the equivocal results obtained by different investigators.

2.4 CHANGES IN FORCE GENERATION

2.4.1 Strength Loss

Exercise-induced damage has been assessed using changes in motor performance, especially functional muscle strength (Clarkson & Tremblay 1988; Newham et al. 1983c, 1987; Sargeant & Dolan 1987; Talag 1973). After eccentric exercise, there is an immediate decrease in maximal force production followed by a slow recovery (Clarkson & Tremblay 1988; Newham et al. 1987; Sargeant & Dolan 1987). Strength may remain depressed for a week or longer (Newham et al. 1987).

The mechanism by which eccentric exercise results in loss of strength has not been clearly identified. Either strength decrements are secondary to soreness perceptions, or the inherent capacity of muscle to produce force is lowered. At present, there is increasing evidence to support the latter explanation (Davies & White 1981; Newham et al. 1983c, 1987).

Investigation of the time courses for development of soreness and for loss of strength suggests little or no relationship between the 2 parameters

(Newham et al. 1983c; Talag 1973). Following eccentric stepping exercise, Newham et al. (1983c) found that maximal voluntary force of the knee extensors had returned to normal by 24 hours after exercise when soreness was most intense. Although Talag (1973) found significant negative correlations between soreness and strength at 48 ($r = -0.61$) and 72 hours ($r = -0.57$) following eccentric arm exercise, the magnitude of the correlations does not suggest a strong relationship.

To determine whether efforts were maximal, Newham et al. (1987) superimposed electrical stimulation on voluntary isometric actions of sore muscles following eccentric exercise of the forearm flexors. Additional force was generated by electrical stimulation only if voluntary force generation was submaximal. Results indicated that maximal voluntary force was generated throughout the testing period.

In an effort to examine the relationship between strength and structural changes. Fridén et al. (1983b) assessed isometric strength and isokinetic strength (at angular velocities of 90, 180 and 300 /sec) at 20 minutes, 3 days and 6 days following eccentric cycle ergometer exercise. Biopsies were obtained at similar time intervals. Isometric strength and isokinetic strength at all angular velocities dropped soon after exercise. By day 6, strength under all conditions, except at 300 /sec, was back to normal. Biopsies revealed disruption in every second to every third fibre up to 3 days after exercise and in one-tenth of the fibres 6 days following exercise. The finding that type II fibres were predominantly affected might explain the slow strength restoration at the highest angular velocity.

It seems that the loss of ability to generate force after eccentric exercise differs from the traditional view of fatigue. As stated above, the strength loss persists for several days or more after exercise. Perplexing, however, is the finding by Clarkson and Tremblay (1988) that subjects were unable to fully flex their forearm immediately after eccentric exercise of the forearm flexors and that this condition lasted for about 48 hours. Whether this indicates profound weakness when the muscle exerts force in a more

contracted state, or may be due to a dysfunction in activation of the muscle, is not known.

2.4.2 Neural Activation

EMG studies also have suggested that strength decrements may be a result of damage to the contractile apparatus (Komi & Viitasalo 1977; Newham et al. 1983c). Newham et al. (1983c) found an increase in integrated EMG activity both during eccentric stepping exercise and when pre- and post-exercise strength tests were compared. A submaximal knee extension test performed at intervals after exercise showed an increase in integrated EMG at all knee joint angels between 0 and 90 . In addition, the neural activation necessary to maintain full extension for 2 seconds was increased. Recovery occurred over 24 hours.

Following eccentric exercise on an electromechanical dynamometer, Komi and Viitasalo (1977) measured isometric knee extension strength and EMG parameters (integrated EMG, averaged motor unit potential). They observed a decrease in maximum strength and an increase in neural activity at a given muscle tension both immediately and 2 days after exercise. Mechanical stress produced during eccentric work may cause structural changes accompanied by neuromuscular performance decrements. Injury to initially recruited motor units may necessitate recruitment to additional units to produce required forces.

2.5 CREATINE KINASE

Because creatine kinase (CK) is found almost exclusively in muscle tissue, serum or plama creatine kinase is considered an indicator of muscle damage (Armstrong 1986; Kagen & Aram 1987; Rogers et al. 1985). While other plama markers of muscle damage, including LDH (Jones et al. 1983; Kanter et al. 1988), myoglobin (Dioszeghy & Mechler 1988; Jorgensen 1987; Smith 1968), and 3-methylhistidine (Dohm et al. 1982) have been used, CK is the most common. Elevated CK activity

in the circulation has been associated with myocardial infarction (Apple et al. 1984; Morelli et al. 1983; Roe et al. 1975, 1977; Sobel et al. 1977), degenerative muscle diseases (Jackson et al. 1987; Kagen & Aram 1987; Rowland 1980; Zundel & Tyler 1965), and exercise-induced skeletal muscle damage (Apple et al. 1984; Byrnes et al. 1985; Clarkson et al. 1985, 1986; Evans et al. 1986; Hunter & Critz 1971; Newham et al. 1983a; Nuttall & Jones 1968; Ross et al. 1983). It should be noted that when measuring CK in the blood, total CK concentration represents both the efflux and clearance of the enzyme. Thus, interpretation of peak changes in CK should be done with caution.

2.5.1 Function and Structure

Creatine kinase has a dimeric structure consisting of M subunits and B subunits (Lang & Wurzburg 1982; Nanji 1983; Wevers et al. 1977). Thus, it exists as 3 different isoenzymes that are specific to different types of tissue. CK-MM, CK-MB and CK-BB are found in skeletal muscle, cardiac muscle (and skeletal muscle, discussed below) and brain tissue, respectively. Isoenzymes are differentiated by electrophoresis based on different rates of migration in an electric field (Apple et al. 1984, 1987; Wevers et al. 1977).

CK-MM, which accounts for 90 to 100% of the total CK activity in skeletal muscle, is primarily responsible for the postexercise rise in seurm or plasma CK activity (Rogers et al. 1985). With isoelectric focusing, CK-MM can be separated into at least 3 isoforms (Clarkson et al. 1987a; Morelli et al. 1983). Following physical exertion, CK is released from damaged muscle as CK-MM_1. This isoform is subsequently transformed in the blood to Ck-MM_2 and then CK-MM_3. The presence of CK-MM_1 in the circulation indicates new release from damaged tissue. CK-MM_1 has been shown to be an earlier indicator of exercise-induced muscle damage for both isometric (Clarkson et al. 1987a) and eccentric (Apple et al. 1988; Donnelly et al. 1988) exercise regimens than total CK activity. A recent study has shown that the time course of the CK-MM_1 response after eccentric exercise closely parallels the development of soreness (Donnelly et al. 1988).

CK-MB has been elevated in the blood of marathon runners following a race (Apple et al. 1984, 1987; Armstrong 1986; Siegel et al. 1981). It is probable that increases resulted from the eccentric component of running and perhaps were exacerbated by ischaemia (Armstrong 1986; Evans 1987). Graves et al. (1987) also reported that plasma CK-MB levels were elevated in 50% of subjects after isometric exercise.

Although high CK-MB levels in the circulation are usually associated with myocardial infarction, the origin of exercise-induced plasma CK-MB is most probably skeletal, not cardiac, muscle (Apple et al. 1984; Graves et al. 1987; Siegel et al. 1981). Siegel et al. (1981) used infarct-avid ("hot spot") scintigraphy to assess myocardial abnormalities in marathon runners showing marked serum CK-MB elevation. However, normal test results were obtained. Moreover, Cummins et al. (1987) reported that cardiac troponin-I and C-reactive protein were not elevated after a marathon when there was evidence of CK-MB in the blood.

CK-MB has been shown to be elevated in the blood of patients who were admitted to an emergency room with severe skeletal muscle injury (Schwartz et al. 1988). Blunt trauma, especially from motor-vehicle accidents, produced higher total CK values and higher CK-MB values than did penetrating wounds. In no case was there myocardial damage.

2.5.2 Time Course and Mechanisms of Efflux

The increase in serum or plasma CK activity after exercise is delayed and the extent of the delay depends upon the type of exercise. After downhill running (Byrnes et al. 1985; Schwane et al. 1983a) or isometric exercise (Clarkson et al. 1982, 1985, 1987a; Kirwan et al. 1986; Triffletti et al. 1988), CK activity significantly increases 3 to 6 hours after exercise and usually peaks 18 to 24 hours after exercise. However, after local muscular eccentric exercise, a significant increase in CK activity may not occur until 48 hours after exercise and may not reach peak values until 7 days [Clarkson & Tremblay 1988; Jones et al, 1986; Newham et al. 1986]. The

difference in the delays may be related to the extent of the damage and will be discussed in the next sections of this review.

After enzymes are released from muscle into extracellular spaces, they are transported to the blood by the lymphatic system (Lindena et al. 1979). Also, the lymphatic system may be important in the inactivation and removal of abnormal enzyme levels (Hsu & Watanabe 1983). Since lymph flow is relatively slow (Hsu & Watanabe 1983), the transport of CK through the lymph could explain part of the delayed appearance of CK in the blood. However, it is unlikely that this would explain delays of 24 to 72 hours observed following high force eccentric exercise (Clarkson and Tremblay 1988; Newham et al. 1987).

2.5.2.1 Early CK Release and Ischaemia

Hypoxia and ischaemia have been popular explanations for changes in membrane permeability resulting in enzyme release (Armstrong 1986; Fowler et al. 1968; Wilkinson & Robinson 1974). With exercise, relative hypoxia and/or ischaemia resulting in energy shortage may occur in skeletal muscle (Armstrong 1986; Fowler et al. 1968). Energy depletion may contribute to increasing membrane permeability and/or muscle damage (Armstrong 1986; Byrnes & Clarkson 1986; Jones et al. 1983; Thomson et al. 1975). Fowler et al. (1968) had subjects perform different types of exercise at various workloads. Blood samples for serum enzyme analyses were obtained 5 and 15 minutes after exercise. Results showed that most serum enzymes increased in proportion to work intensity and that trained subjects had smaller increases in enzyme levels than untrained subjects at progressively higher levels of work. The authors suggested that hypoxia resulted in an increased membrane permeability.

Under hypoxic conditions, elevated intracellular Ca^{++} concentrations may cause skeletal muscle fibre disruption. Jones et al. (1984) found that calcium channel blockers, which are effective in cardiac and smooth muscle, did not prevent muscle damage leading to enzyme release from excised

mouse soleus following excessive electrical stimulation. They hypothesised that with fatigue, Ca^{++} may enter the fibre by a route that is separate from the normal Ca^{++} channel.

Other researchers have suggested that high energy phosphates maintain the integrity of the cell membrane and influence enzyme leakage (Hunter & Critz 1971; Thomson et al. 1975). Employing electrical stimulation of tetanised cat limbs, Thomson et al. (1975) found an inverse relationship between enzyme efflux and ATP depletion determined indirectly by decreased work capacity. They concluded that intracellular ATP must be depleted before enzyme efflux will occur.

Increased CK activity in the blood following isometric exercise suggests that ischaemia may play a role in enzyme release. However, comparison between high and low tension isometric exercise also suggests that mechanical stress may contribute to the response (Clarkson et al. 1982). Subjects performed 2 exercises each consisting of 35 maximal isometric actions of the knee extensors, and serum CK was analysed following each bout (Clarkson et al. 1982). Ten:five (10-second isometric action, 5-second rest) and 10:20 (10-second isometric action, 20-second rest) exercise programmes were performed on different days using contralateral limbs. Serum CK elevation was significantly greater for the 10:20 than for the 10:5 condition. The higher tension may have occluded more blood flow and created greater ischemia. However, since a 20-second rest interval would provide time for resynthesis of creatine phosphate (CP), a greater CP deficit should have occurred with the 10:5 exercise. Histological analysis of isometrically exercised muscle did not show any evidence of fibre damage. The greater CK efflux was probably produced by higher tension levels during the 10:20 exercise resulting in mechanical stress without substantial fibre damage.

Okada et al. (1985) found an increase in serum CK activity after rat hind limbs were exposed to acute and chronic local vibration. Histological analysis showed no pathological change in the muscle. These authors

suggested that the vibration caused an increase in permeability of the cell membrane. Vibration may also serve as a mechanical stress to the muscle, altering membrane permeability of the fibres.

Duncan and Jackson (1987) incubated mouse soleus muscle in 2,4 dinitrophenol (DNP) to induce damage. DNP produced an immediate efflux of CK into the medium that was dependent on extracellular Ca^{++}. DNP also produced ultrastructural damage, but this was not dependent on extracellular Ca^{++}. Using other treatment conditions, CK efflux could be inhibited but myofibrillar damage could not. These researchers concluded that the myofibrillar damage and CK efflux were the result of different mechanisms.

Although changes in membrane permeability associated with metabolic disturbances and unaccompanied by myofibrillar damage may play a role in CK efflux immediately following or for several hours following exhaustive work or high tension isometric exercise, it is unlikely that these factors are a principal cause of the delayed CK efflux following high force eccentric exercise. Peak CK efflux, observed at 5 or more days after high force eccentric exercise (Clarkson & Tremblay 1988; Newham et al. 1987), occurs well after the time it takes for ATP and CP to be resynthesised (Clarkson & Tremblay 1988; Jones et al. 1987; Newham et al. 1983a). The longer delay in the appearance of CK in the blood after high force eccentric exercise has been suggested to be coincident with necrosis (Clarkson & Tremblay 1988).

2.5.2.2 Delayed CK Release and Necrosis

Clarkson and Tremblay (1988) proposed a mechanism to explain the delayed CK release after local muscular eccentric exercise. They suggested that exercise-induced damage may cause an accumulation of Ca^{++} resulting in: (a) production of noxious stimuli such as bradykinin and histamine causing muscle soreness; (b) muscle contractures leading to decreased range of motion; (c) impairment of sarcoplasmic reticulum and

mitochondrial functioning; and (d) activation of sarcoplasmic proteases resulting in loss of sarcolemmal integrity and delayed release of CK. Although there is no direct evidence to support this theory, much indirect evidence exists (Brody 1969; Busch et al. 1972; Cullen & Fulthorpe 1975; Newham et al. 1983c).

Since myofibrillar damage, soreness and strength decrements have been observed prior to release of CK into the circulation, it seems that fibre destruction is progesssive and that sarcolemmal disruption occurs in the final stages of necrosis (Clarson & Tremblay 1988). Fridén et al. (1984) found an increase in the intermediate filament protein, desmin, 3 days following eccentric exercise and suggested that this was evidence for sarcomereogenesis. This observation is consistent with the point at which serum CK just begins to increase, soreness is maximal, and range of motion is most reduced following local muscular eccentric exercise. However, strength is only beginning to recover at this time (Ebbeling & Clarkson 1988).

Perhaps the repair process is initiated by removal of noxious agents and Ca^{++} from the fibre resulting in reduced soreness and greater range of motion. Although sarcomereogenesis may begin as soon as 3 days after exercise, Lazarides et al. (1981) have noted that complete structural reorganisation of damaged muscle fibres may take a week or longer. If strength is dependent on the structural reorganisation of the fibre, this might explain why strength does not return to normal until 7 to 10 days after eccentric exercise.

2.5.3 CK Related to Location and Extent of Injury

Muscular uptake of radiolabelled complexes, such as technetium pyrophosphate, has been used as an indicator of muscle damage (Jones et al. 1986; Newham et al. 1986). Technetium pyrophosphate uptake is related to loss of sarcolemmal integrity (Vita & Harris 1981). Although investigators have found no evidence of increased technetium

pyrophosphate uptake into muscles that have contracted concentrically, the time course of radionucleide uptake by eccentrically exercised muscles parallels that of CK activity in the blood (Jones et al. 1986; Newham et al. 1986). Jones et al. (1986) found a large increase in plasma CK 4 to 6 days after eccentric exercise. Increased uptake of technetium pyrophosphate into the exercised muscles followed a similar time course. Technetium pyrophosphate, therefore, may be valuable in identifying muscles from which CK is being released.

To study the relationship between serum CK and muscle injury, Steiness et al. (1978) gave intramuscular injections of local damaging drugs to rabbits, pigs and humans. They found marked serum CK elevations. In addition, postmortem histological examination of the animal muscle revealed large areas of necrotic fibres at all injection sites. The authors inferred that enzyme activity was related to the severity of the damage and to the volume of tissue affected.

In contrast, although exercise-induced CK elevation may indicate muscle damage, it does not provide an index of the magnitude of the damage. Kuipers et al. (1985a) examined serum CK and amount of muscle damage following exercise in rats. Using serial sections of muscle with light microscopy, a 3-dimensional reconstruction was made and damage was quantified. The correlation between serum CK and percentage of muscle volume affected was $r = 0.04$.

Several investigators have also failed to find a significant relationship between cardiac muscle damage following a myocardial infarction and serum CK activity (Roe et al. 1977; Roe & Starmer 1975; Sobel et al. 1977). The low correlations between CK and histological measurements of infarct size have been attributed to continued release of CK from the damaged tissue and to differing release rates depending on infarct size (Roe et al. 1977; Roe & Starmer 1975; Sobel et al. 1977). These observations on cardiac muscle damage may be applicable to skeletal muscle damage also (Clarkson et al. 1986).

2.5.4 CK Variability

Markedly high blood CK values (often over 2 000 U/L) have been found after local eccentric exercise (Clarkson & Tremblay 1988; Jones et al. 1986; Newham et al. 1986), whereas values less than 500 U/L are commonly found after downhill running or isometric exercise (Byrnes et al. 1985; Clarkson et al. 1985; Schwane et al. 1983a). In addition, a large intersubject variability in the CK response to exercise has been well documented (Newham et al. 1987; Noakes 1987; Sargeant & Dolan 1987). For example, in one study where subjects performed an eccentric exercise, some subjects showed increases of CK activity up to 34 500 U/L, while other subjects showed increases of less than 500 U/L (Newham et al. 1983a). This variability is puzzling since in most cases it is unrelated to general fitness of subjects, physical characteristics of subjects, amount of soreness induced by exercise and amount of work done during exercise.

Kagen and Aram (1987) reported that serum from certain patients with muscle disease contained a dialysable inhibitor of CK which resulted in a large underestimation of actual CK levels. They concluded that for certain patients, CK inhibitors may be released into the blood from injured or damaged muscle. Clarkson and Ebbeling (1988) investigated whether the presence of CK inhibitors might explain the large blood CK variability among subjects following an eccentric exercise of the forearm flexors. Subjects were classified as "no CK responders", "low CK responders" (mean peak CK after exercise = 400 U/L), and "high CK responders" (mean peak Ck after exercise = 2 800 U/L). Serum from high responders was mixed with serum from no or low responders. In all cases, the differences between the expected and observed CK activity for the mixes were within expected variability for the assay. Although CK inhibitors have been found in plasma from patients with muscle injury and disease, this study was unable to demonstrate the presence of CK inhibitors in the serum from subjects who showed evidence of severe exercise-induced muscle damage.

Whitfield and Martin (1986) examined genetic variation and serum CK activity. They studied 206 pairs of twins and found that the data were consistent with a simple model of variation in which around 60% of the variation was genetic in origin for the males and 81% of the variation was genetic for the females. While it might be tempting to suggest that CK responses to exercise may have a genetic component, research from Clarkson (1988) shows that some subjects would be classified as high responders when exercising one arm and low responders when exercising the opposite arm. The higher CK response for one arm could not be accounted for by whether the subject performed the exercise with the arm first or second, arm dominance, amount of force exerted during the exercise, or the degree of fatigue experienced during the exercise. At present there is no clear explanation for CK variability.

However, it has been suggested that the low CK response for some subjects may be a consequence of a similar exercise performed prior to the laboratory exercise (Clarkson & Tremblay 1988). A prior exercise may produce a rapid training response that could result in a protective effect lowering the CK response following the laboratory exercise test. This is plausible since laboratory exercises of only one-third (Clarkson & Tremblay 1988) and one-sixth the number of contractions have profoundly reduced the CK response to a subsequent exercise of longer duration employing the same muscles.

2.6 MUSCLE ADAPTATION

2.6.1 Training

Physical conditioning results in reduced morphological changes, delayed-onset muscle soreness, performance changes and CK activity in the blood following an acute bout of exercise (Byrnes et al. 1985; Clarkson et al. 1985, 1987b; Clarkson & Tremblay 1988; Evans et al. 1986; Fridén et al. 1983a; Hunter & Critz 1971; Kirwan et al. 1986; Knuttgen 1986; Komi & Buskirk 1972; Maxwell & Bloor 1981; Newham et al. 1987; Nuttall &

Jones 1968; Schwane & Armstrong 1983). However, the changes that occur with training to protect muscle from subsequent damage are not known. The models used to study the training effect include endurance running (Evans et al. 1986; Maxwell & Bloor 1981), cycle ergometry (Fridén et al. 1983a; Hunter & Critz 1971; Knuttgen 1986), weightlifting (Nuttall & Jones 1968), prolonged isometric exercise (Clarkson et al. 1985; Kirwan et al. 1986), downhill running (Byrnes et al. 1985; Schwane & Armstrong 1983) and novel eccentric exercise (Clarkson et al. 1987b; Clarkson & Tremblay 1988; Komi & Buskirk 1972; Newham et al. 1987). Alterations in energy metabolism and structural adaptations have been proposed to explain the training response.

2.6.1.1 Energy Metabolism

An increased ATP supply is often identified as the reason for reduced CK levels in the circulation of trained subjects following intense exercise (Hunter & Critz 1971; Nuttall & Jones 1968). Hunter and Critz (1971) found that 10 weeks of cycle ergometer training, 3 times per week, reduced CK efflux. Before training, serum CK was elevated after both maximal (36%) and submaximal (18.5%) exercise. Since training increases the number and size of mitochondria, the authors suggested that more ATP was available for maintenance of the cell membrane, resulting in a reduced CK response.

Nuttall and Jones (1968) have implied that a metabolic adaptation also may be responsible for the decreased CK response following weight-training. They found significant increases in serum CK values and delayed-onset muscle soreness following a 6-minute barbell exercise using the forearm flexors and extensors. Subjects then engaged in a training regimen consisting of the same exercise performed 3 times per week for 3 to 5 weeks. The amount of weight lifted by each individual was equal to 15% and 25% of bodyweight. Four days after the conditioning period, the initial exercise was repeated, but serum CK levels did not show the same magnitude of increase and no muscle soreness resulted. The authors

suggested that the muscle cell membrane was in some way protected under conditions of a sudden demand for energy production.

2.6.1.2 Structural Adaptations

Although the energy metabolism explanation for muscle adaptation cannot be rejected, recent evidence involving eccentric training regimens argues against this concept (Fridén 1983; Fridén et al. 1983a; Knuttgen 1986; Komi & Buskirk 1972). Knuttgen (1986) has reported that during the early stages of eccentric cycle ergometer training, subjects were unable to resist the force of the pedals even when ATP and CP values were not different from resting levels. The inability to continue exercise, therefore, may have been the result of fibre damage. Following 6 weeks of training, the subjects could easily perform the exercise for long periods of time.

Using a similar cycle exercise regimen, Fridén et al. (1983a) examined muscle soreness and morphological changes over 8 weeks of training. During the first 1 to 2 weeks, muscles became sore and there was evidence of fibre disruption. Symptoms were reduced following training despite an increase in work.

Komi and Buskirk (1972) assessed the effects of 7 weeks of eccentric conditioning of the forearm flexors using a special dynamometer. During the first week, all subjects experienced muscle soreness that was attributed to overstretching of muscular elastic components. Soreness disappeared after 2 weeks of training. In addition to decreased soreness, there was a significant increase in maximal isometric tension.

Friden (1983) has listed 3 possible mechanisms of structural myofibrillar adaptation that may result from eccentric training to limit damage. First, sarcomere length may be increased. However, this would be only a temporary solution for tension reduction because increased length would

also result in non-optimal overlap between actin and myosin filaments. Second, sarcomereogenesis may result in an increase in the number of longitudinal sarcomeres, the functional units of the contractile system. Third, an increase in synthesis of Z-band proteins or intermediate filaments may strengthen myofibrils.

2.6.2 Repeated Bout or Rapid Training Effect

In all of the studies above, training involved a period of weeks. Recently, investigators have suggested that the prophylactic effect of training may be due to performance of a single initial exercise bout (Armstrong et al. 1983; Byrnes et al. 1985; Clarkson et al. 1985, 1987b; Clarkson & Tremblay 1988; Kirwan et al. 1986; Irintchev & Wernig 1987). The body of research focusing on repeated bouts of exercise has resulted in the development of additional explanations to account for muscle adaptation.

Clarkson et al. (1985) examined the serum CK response to a repeated bout of forearm flexion isometric exercise. Compared with the first bout, a substantial reduction in the serum CK response was found following the second bout which was performed 1 week later. In another study using knee extension isometric exercise, subjects did 4 bouts of exercise each separated by 1 week (Triffletti et al. 1988). Although there was a significant difference in CK and soreness responses between bouts 1 and 2, there were no additional reductions with subsequent bouts.

When a second bout of isometric exercise used a different muscle group from the first, Graves et al. (1987) still found a lower CK response following the second bout. To further investigate this finding, Clarkson et al. (1987b) used an eccentric hamstring exercise. All subjects performed a second bout of exercise 7 days following the first bout. However, some did the second exercise with the ipsilateral limb while others did the second exercise with the contralateral limb. Subjects were positioned to assure that contralateral muscles were not active in isometric stabilisation. Although a repeated bout effect, indicated by a lower CK and soreness response, was

found for the ipsilateral group, no effect was seen when the contralateral limb was exercised. Therefore, the authors concluded that muscle adaptation is more likely a peripheral, rather than a central, response. Perhaps the results reported by Graves et al. (1987) were influenced by stabilising activity in muscles other than those directly involved in the prescribed exercise (Clarkson et al. 1987b).

In both animals and humans, a single bout of downhill running has been sufficient to reduce the CK response on subsequent bouts (Armstrong et al. 1983; Byrnes et al. 1985). When a repeated bout was given to human subjects at 3 or 6 weeks following the first bout, serum CK activity and muscle soreness were significantly reduced (Byrnes et al. 1985). However, when the exercise was repeated at 9 weeks, no significant differences were found between the initial bout and the bout repeated at 9 weeks. Armstrong et al. (1983) have suggested that an initial bout of novel exercise results in a temporary reduction in the pool of stress-susceptible fibres.

Muscle fibres that undergo lethal injury with exercise may be more fragile or more susceptible to damage than other fibres. Fragile fibres may develop through disuse of a given motor unit recruitment pattern or may represent a small percentage of fibres that are constantly degenerating (or ageing) making them more susceptible to stress. Stress-susceptible or degenerating fibres may embody a population of cells that are destroyed by an initial bout of exercise. Strong, healthy fibres that could withstand the effects of repeated bouts would survive. It should be noted that it would not be necessary for a entire fibre to be fragile. Since focal necrosis can occur (Carpenter & Karpati 1984), only portions or small areas of a fibre may be fragile and susceptible to exercise damage. There is evidence from biopsy samples of healthy human subjects that a small percentage of fibres appear disrupted (Meltzer et al. 1976). It may be these fibres that are lethally damaged during exercise.

Although the stress-susceptible fibre hypothesis is plausible, there are data to suggest that fibres are not destroyed but strengthened (Clarkson &

Tremblay 1988; Schwane & Armstrong 1983). If the repeated bout effect were the result of elimination of fragile fibres, injury to this population should be evident after a single initial bout of exercise. Schwane and Armstrong (1983) found that 30 minutes of training in rats protected the vastus intermedius muscle from damage following 90 minutes of downhill running performed 3 days later. However, there was no indication of damage after the 30-minute run suggesting that necrosis did not occur and that lethal damage was not a prerequisite for muscle adaptation.

Clarkson and Tremblay, 1988, suggest that strengthening of the muscle membrane or connective tissue may explain rapid adaptation . Following a forearm flexion exercise regimen consisting of 70 maximal eccentric muscle actions, there was significant elevation of serum CK, increase in soreness and decrease in isometric strength. Prior performance of an exercise consisting of either 12 or 24 maximal eccentric actions (Clarkson & Tremblay 1988) resulted in no CK response, less soreness and smaller strength decrements when 70 actions were performed 2 weeks later. Although the exercises consisting of fewer muscle actions did not produce substantial damage, they did provide protection from subsequent damage.

Newham et al. (1987) have implied that the mechanism responsible for the repeated bout effect may be associated with connective tissue and not muscle fibres per se. Subjects performed 3 repeated bouts of an eccentric exercise of the forearm flexors with each bout separated by 2 weeks. There was an increase in serum CK activity for all subjects following bout 1, but no significant changes in CK values were found following bouts 2 and 3. Each bout produced progressively less soreness. Force decreased immediately following each of the 3 bouts but recovered more rapidly following bouts 2 and 3 compared with bout 1. Stimulated forces also showed a decrement after each bout with a faster return to baseline following bouts 2 and 3. There was no evidence of an increase in strength. In fact, maximum voluntary force was still reduced by approximately 20% 2 weeks after the third bout. Because muscles became neither stronger nor less fatiguable, changes may have occurred in the connective tissue. Any

damage caused by the first bout of exercise might act as a stimulus for new collagen synthesis. In this way, the collagen structure would be strengthened and protected from further damage.

The rapid training effect with regard to serum or plasma CK activity may be influenced by the type of exercise used. Clarkson and Tremblay (1988) and Newham et al. (1987) found that there was absolutely no increase in CK activity following a second bout of eccentric exercise of the forearm flexors. However, Byrnes et al. (1985) noted that although the CK response to a second bout of downhill running was reduced, there was an increase. Likewise, Schwane et al. (1987) found that after 1 week of downhill training there was still a CK response, albeit reduced.

Although prior performance of a local eccentric exercise can prevent release of CK upon a repeated bout, other indicators of damage are only attenuated. For example, following a repeated bout of eccentric arm exercise, soreness develops, and there is loss of strength (Clarkson & Tremblay 1988). However, when compared with the first bout, soreness disappears and strength recovers more rapidly following the second bout. The adaptation must protect against damage in such a way that a final stage in the damage process, necrosis or loss of sarcolemmal integrity (as indicated by CK efflux) is prevented. In light of the theory proposed by Clarkson and Tremblay (1988), a more rapid repair of damage would reduce the likelihood of reaching a critical stage leading to necrosis following a second bout of exercise.

Because recovery from exercise-induced muscle damage is a slow process, a second bout of exercise performed too soon after the initial bout may exacerbate damage and cause a setback in the repair process. Therefore, most researchers who have examined the rapid training effect have given a second bout of exercise after full recovery from the first bout. In contrast, Ebbeling and Clarkson (1988) had subjects repeat an eccentric exercise of the forearm flexors 5 days after performance of the first exercise. When subjects repeated the exercise, muscular discomfort was evident, complete

range of motion and strength were not fully restored, and serum CK was not back to baseline. However, the second bout did not initiate a setback in the repair process. Less damage was produced by the second bout, and recovery time was faster even though the muscles were not fully restored. The results of this study suggest that the adaptation may not be at the site of the contractile elements since isometric strength and the ability to fully flex the forearm had not fully recovered within 5 days following bout 1. At this time, muscle shortening, presumably caused by muscle contractures, was also evident. Complete repair does not seem to be a prerequisite for muscle adaptation to exercise-induced damage. These data may lend support for the hypothesis of a strengthening of the membrane and/or associated endomysium.

2.7 CONCLUSION

This review has focussed on both descriptive evidence and proposed mechanisms for exercise-induced muscle damage, repair, and adaptation. Particular emphasis has been placed on the high mechanical forces associated with eccentric exercise that cause extensive disruption of muscle fibres. Evidence of damage following repetitive eccentric muscle actions includes morphological changes, delayed-onset muscle soreness, performance decrements, and elevation of muscle proteins in the blood, especially creatine kinase. However, the precise cause of skeletal muscle damage and the mechanism of repair are not well understood. Calcium, lysosomes, connective tissue, free radicals, energy sources, and cytoskeletal and myofibrillar proteins may be involved in the damage and repair processes.

Damaged muscles adapt to exercise, and all indicators of damage are reduced following repeated bouts of exercise. Several hypotheses have been presented to explain muscle adaptation. Stress-susceptible fibres or susceptible areas within a fibre may be eliminated and then regenerated, or muscle fibres and/or connective tissue may be strengthened with an initial bout of exercise.

3. METHODS

3.1 SUBJECTS

Twelve recreational joggers, six males and six females, ranging in age from 23 years to 32 years took part in the study. They were healthy and active but none was participating in any training programmes, and they had not previously participated in studies involving eccentric contractions. Their physical characteristics are shown in table 1. The subjects were instructed to refrain from unaccustomed exercise during the course of the study, starting 48 hours before the first exercise session. All the subjects were fully informed of the nature and risks of the procedures to be used and signed an informed consent document. The study was approved by the University of the Witwatersrand's Committee for Research on Human Subjects, protocol number : 14/6/92.

Table 1 : Physical Characteristics of the Subjects Studied

Subject	Height [m]	Weight [kg]	Age [years]
Males			
A	1.60	56.30	28
B	1.71	65.10	29
C	1.80	78.34	31
D	1.66	59.20	32
E	1.76	65.32	28
F	1.79	74.63	26
	Mean : 1.72 Std. Dev. : 0.079	Mean : 66.48 Std. Dev. : 8.567	Mean : 29 Std. Dev. : 2.191
Females			
A	1.72	55.50	27
B	1.70	63.10	23
C	1.59	55.80	26
D	1.64	54.39	24
E	1.62	53.64	25
F	1.68	60.20	23
	Mean : 1.66 Std. Dev. : 0.050	Mean : 57.11 Std. Dev. : 3.720	Mean : 25 Std. Dev. : 1.633

3.2 PROTOCOL

During the first part of the study, each subject ran uphill on a motorised treadmill (gradient of 10 degrees) at 10 km/hr for 30 minutes. After one week of rest, the subjects ran downhill on a motorised treadmill (gradient of -10 degrees), at the same workload of 10 km/hr for 30 minutes.

The subjects then rested for one week before repeating the downhill run on the motorised treadmill (-10 degrees gradient), at 10 km/h for 30 minutes. Subjects were instructed to refrain from any form of physical activity during the weekly rest periods.

In order to determine the effects of uphill and downhill running, as well as the skeletal muscle adaptation to downhill running, it was essential for the protocol design to follow a non-randomised consecutive sequence. Therefore, the uphill running session was followed by the initial and second downhill runs.

During each running session, heart rate was continually monitored using a three lead ECG, and oxygen consumption was determined every 30 seconds using an open circuit on line system (Oxycon 4 : Mynhardt Bunnik, Netherlands). Statistical comparisons were made on the measurements taken at 10 minutes.

3.3 BLOOD SAMPLING

Blood samples were taken prior to exercise, immediately after exercise, and 24 hours after exercise by venipuncture from the cubital fossa into a serum separation tube. The blood was allowed to clot for 10 minutes at room temperature and then centrifuged for 20 minutes to separate the serum. After centrifugation, all serum samples were frozen at -20 degrees Celsius until analysis for creatine kinase activity. The creatine kinase activity was assessed in duplicate samples at 25 degrees Celsius by the method of Szasz and co-workers (1976) with a Boehringer Mannheim Test Kit. Each sample was analysed at least twice.

3.4 MUSCLE SORENESS EVALUATIONS

Subjects responded to a printed soreness questionnaire at the start of each running session, immediately post-exercise, and 24 hours post-exercise. Each subject was given a thorough orientation to the questionnaire, and completed the questionnaire at scheduled times without any involvement from the investigators. Soreness was rated using a scale:

0 = completed absence of soreness.
2 = light pain felt only on palpitation.
4 = moderate pain, stiffness and/or weakness especially during movement.
6 = severe pain that limits the range of motion

Each subject was asked to consider specifically the muscles of the buttocks, quadriceps, hamstrings, shin and calf. Although subjects were necessarily informed that muscle soreness may be encountered at some point during participation in the study, they were not informed of the hypothesis.

3.5 ISOKINETIC MUSCLE TESTING

The muscle performance of the hamstrings and quadriceps of the dominant limb were isokinetically assessed pre-exercise, immediately post-exercise, and 24 hours post-exercise using the Cybex 340 dynamometer. The leg dominance was determined according to the limb preference in kicking a ball and taking - off in jumping.

Prior to testing, each subject underwent a 5 minute warm-up period of aerobic, low resistance ergometer cycling. The subjects were then fixed to the testing device with straps around the chest, pelvis, thigh and ankle. The ankle strap was placed above the ankle. The axis of the knee was placed in line with the axis of rotation of the dynamometer. Subjects were allowed to grasp the handles of the bench during testing.

Each limb was weighed before testing by the Cybex's automatic limb weighing system to correct for the gravitational effect of torque (GET). Each estimate of the GET was added to the quadriceps peak torque and subtracted from the hamstring peak torque. The subjects were then instructed to perform five sub maximal (50%) repetitions at the three isokinetic testing velocities of 60 degrees/second, 180 degrees per second and 240 degrees per second to become familiar with the testing device.

Thereafter, the isokinetic muscle performance test was started. First, two sub maximal repetitions of knee extension and flexion were performed for practice, and then, after a 30 second rest, five maximal voluntary repetitions of alternating knee flexion and extension occurred at an angular velocity of 60 degrees per second. The single highest torque output of the joint produced by muscular contraction as the joint moves through 60 degrees per second can be used to determine the peak torque. In this manner it was possible to determine the peak torque of the hamstring and quadriceps muscle groups. After a two minute rest, the same protocol was repeated at an angular velocity of 180 degrees per second (two submaximal followed by five maximal voluntary repetitions). At a joint speed of 180 degrees per second, torque output at functional velocity of contraction of the hamstring and quadricep muscle groups is assessed. The subject was then allowed to rest for two minutes before the same protocol was repeated for 20 maximal voluntary repetitions at a speed of 240 degrees per second. At a joint speed of 240 degrees per second, the muscular endurance of the hamstrings and quadriceps can be determined. Muscular endurance is defined as the ability of the contracting muscles to perform repeated contractions against a load. The endurance ratio was calculated by expressing the mean torque from the last 5 contractions as a percentage of the mean torque of the initial 5 contractions.

Subjects received consistent verbal encouragement throughout all the tests. Special attention was paid to the instruction to maximally exert each contraction over the full range of motion; that is, from the very beginning to the very end of the movement.

3.6 STATISTICAL ANALYSIS

3.6.1 Males versus Females

After completing the three running sessions, the mean plasma creatine kinase values for both the male and female subjects was expressed as an absolute value (u/l) and as a value standardised to body weight (u/l.kg). In addition, the mean percent change in plasma creatine kinase after each running session was calculated for both the male and female groups.

Percent change was calculated as follows :

$$Percentage\ Change = \frac{24\ Hour\ Post\ Exercise - Pre - Exercise}{Pre - Exercise} \times 100\%$$

The raw data can be found in Table 7, Table 8 Table 9 and Table 10, Appendix A.

A Mann-Whitney Statistical test was then used to test for any significant plasma creatine kinase differences between the male and female subjects after the three running sessions : (uphill vs. downhill 1), and (downhill 1 vs. downhill 2). In all the statistical analyses performed, the null hypothesis was rejected at the 5% level.

Similarly, a Mann-Whitney Test was used to assess the differences between the male and female groups with respect to the percent change in peak torque at 60 °/sec, endurance ratio, and peak torque at 180°/sec of the quadricep and hamstring muscles after uphill and downhill running : (uphill vs. downhill 1), and (downhill 1 vs. downhill 2).
Percent change was calculated as follows :

$$Percentage\ Change = \frac{24\ Hour\ Post\ Exercise - Pre - Exercise}{Pre - Exercise} \times 100\%$$

The raw data can be found in Table 11, Table 12, Table 13, Table 14, Table 15, Table 16, Table 17, Table 18, Table 19, Table 20, Table 21, and Table 22, Appendix A.

3.6.2 Males and Females Grouped Together

As there were no significant differences between the male and female subjects with respect to the absolute, standardised to body weight, and percent change in plasma creatine kinase after uphill and downhill running, it was possible to group the male and female subjects together (n=12).The percent change in plasma creatine kinase for the combined group after the three running sessions was calculated as follows:

$$Percentage\ Change = \frac{24\ Hour\ Post\ Exercise - Pre - Exercise}{Pre - Exercise} \times 100\%$$

A Wilcoxin paired non-parametric test was then used to assess the combined group percent change in plasma creatine kinase differences between the running sessions : (uphill vs. downhill 1), and (downhill 1 vs. downhill 2).

Similarly, as for the plasma creatine kinase values, there were no significant differences between the male and female peak torque and endurance ratios for the hamstring and quadricep muscles, and therefore the male and female data was pooled together (n=12). The percent change in muscle performance for the combined group after the three running sessions was calculated as follows:

$$Percentage\ Change = \frac{24\ Hour\ Post\ Exercise - Pre - Exercise}{Pre - Exercise} \times 100\%$$

A Wilcoxin paired non-parametric test was used to test the percent change differences in the peak torque and endurance ratio for the hamstrings and quadriceps of the combined group (uphill vs. downhill 1, and downhill 1 vs. downhill 2).

3.6.3 Perceived Muscle Soreness in the Combined Group after Uphill and Downhill Running.

A Wilcoxin paired non-parametric test was used to test the statistical difference between the perceived muscle soreness responses immediately before , immediately after and 24 hours after the uphill and 2 downhill runs. The questionnaire responses can be found in Table 23, Appendix A.

3.6.4 Relationship between Percent Change in Plasma Creatine Kinase and the Percent Change in Skeletal Muscle Performance after Uphill and Downhill Running.

The relationship between the percent change in plasma creatine kinase and the percent change in the skeletal muscle performance of the hamstring and quadricep muscles for the combined group was analysed using a Spearman correlation co-efficient (r).

3.6.5 Relationship between Percent Change in Plasma Creatine Kinase and Percieved Mucle Soreness after Uphill and Downhill Running

The relationship between the percent change in plasma creatine kinase and the perceived muscle soreness (questionnaires) for the combined group was analysed using a Spearman correlation co-efficient (r).

3.6.6 Differences in Energy Expenditure during Uphill and Downhill Running

The differences in heart rate and oxygen consumption in the combined group after the uphill and initial downhill running sessions were determined using a Wilcoxin paired non-parametric test.

The raw data can be found in Table 6, Appendix A.

4. RESULTS

4.1 DIFFERENCES IN ENERGY EXPENDITURE DURING UPHILL AND DOWNHILL RUNNING

The initial downhill run, in comparison to the uphill running bout, resulted in a significantly lower mean heart rate and oxygen uptake value in the male and female subjects ($p<0.001$). Figure 1 and Figure 2 illustrate that the negative work associated with downhill running results in a lower energy cost (heart rate and oxygen consumption) than an equal positive workload of uphill running.

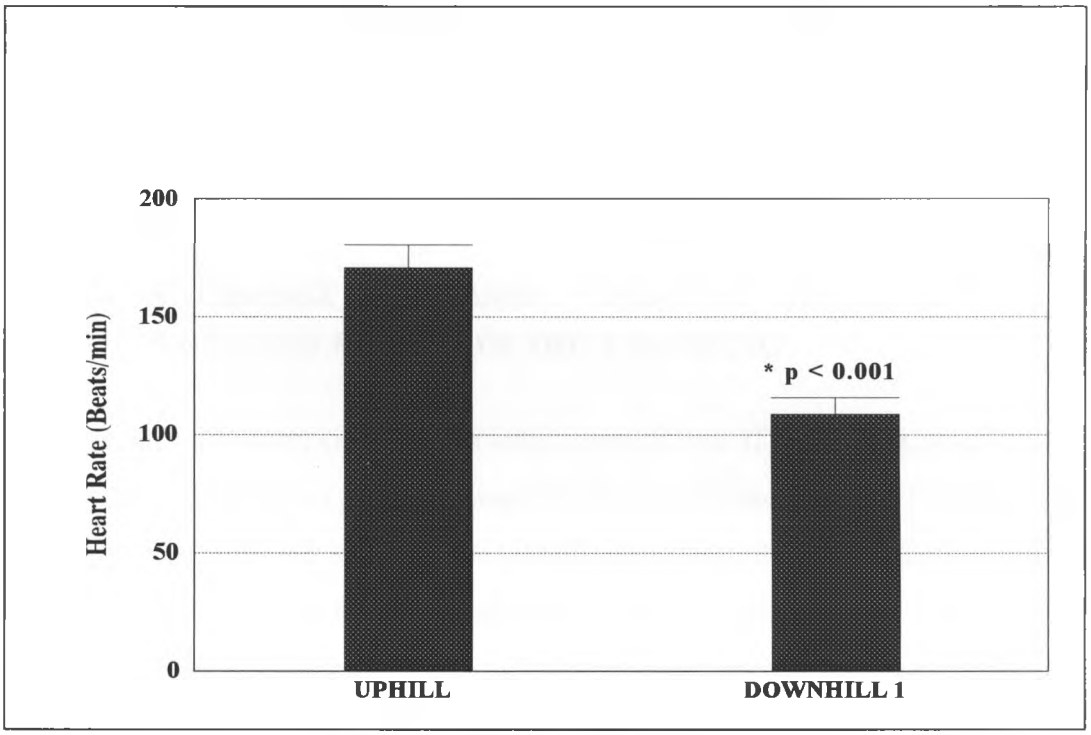

Figure 1: Mean heart rate comparison in the combined group (n=12) during uphill and downhill running.

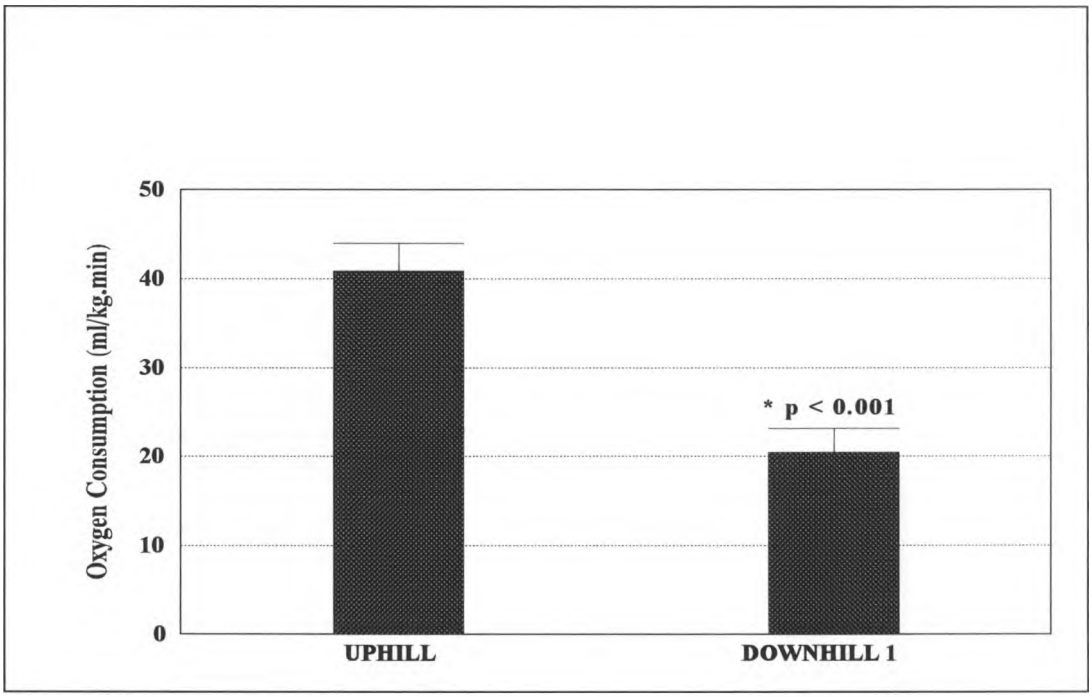

Figure 2: Mean Oxygen consumption (ml/kg.min) in the combined group (n=12) during uphill and downhill running.

4.2 PERCENT CHANGE IN PLASMA CREATINE KINASE AFTER 30 MINUTES OF UPHILL AND DOWNHILL RUNNING

The uphill run, in comparison to the initial downhill run (Downhill 1), resulted in a significantly lower mean percent change in plasma creatine kinase ($p < 0.001$). The mean percent increase in plasma creatine kinase after the uphill run was 23%, whereas the initial downhill run resulted in a plasma creatine kinase mean percent increase of 180% (Figure 3).

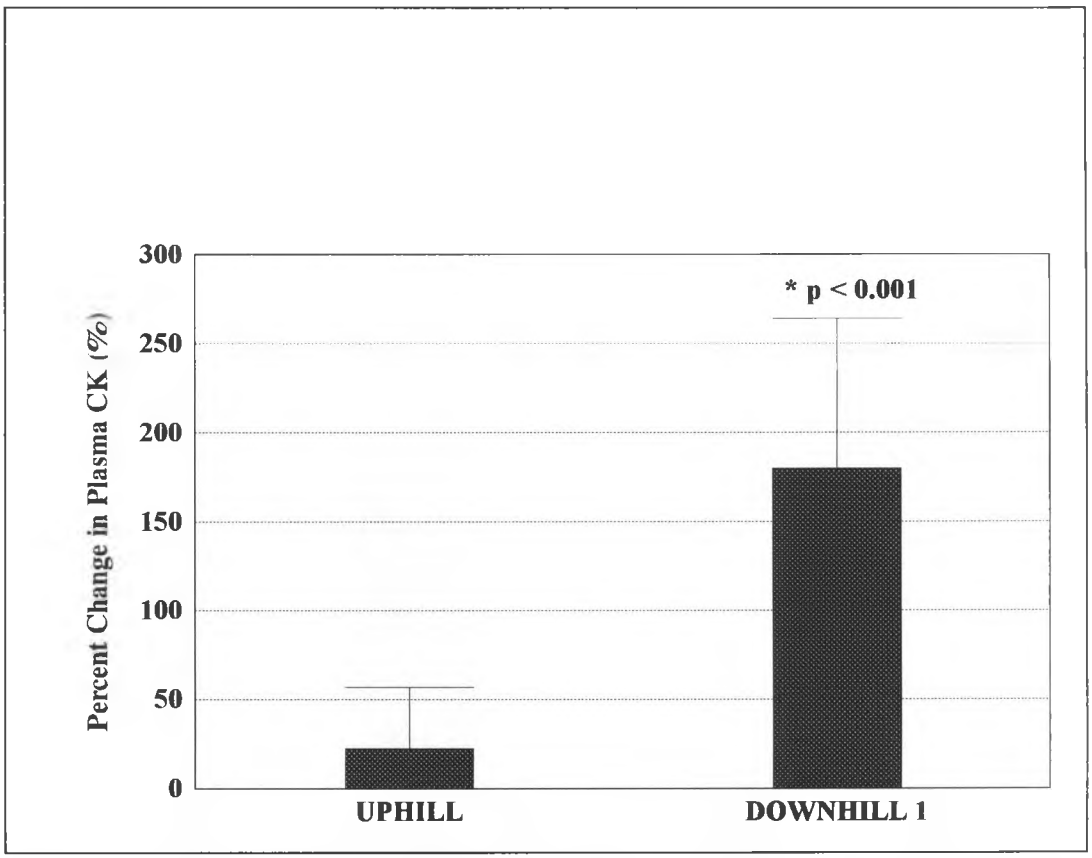

Figure 3: Mean percent change in plasma creatine kinase(CK) in the combined group (n=12) after the uphill and initial downhill running sessions.

When the downhill run was repeated one week after the initial downhill running session, with no intervening exercise, the second downhill run resulted in a significantly lower ($p < 0.001$) percent change in plasma creatine kinase (Figure 4). The initial downhill run (Downhill 1) resulted in a 180 % change in creatine kinase, whereas the repetition of the run one week later (Downhill 2), resulted in a 55% change in plasma creatine kinase (Figure 4).

The percent change in plasma creatine kinase after the second downhill run (Downhill 2) and after the uphill run did not differ significantly.

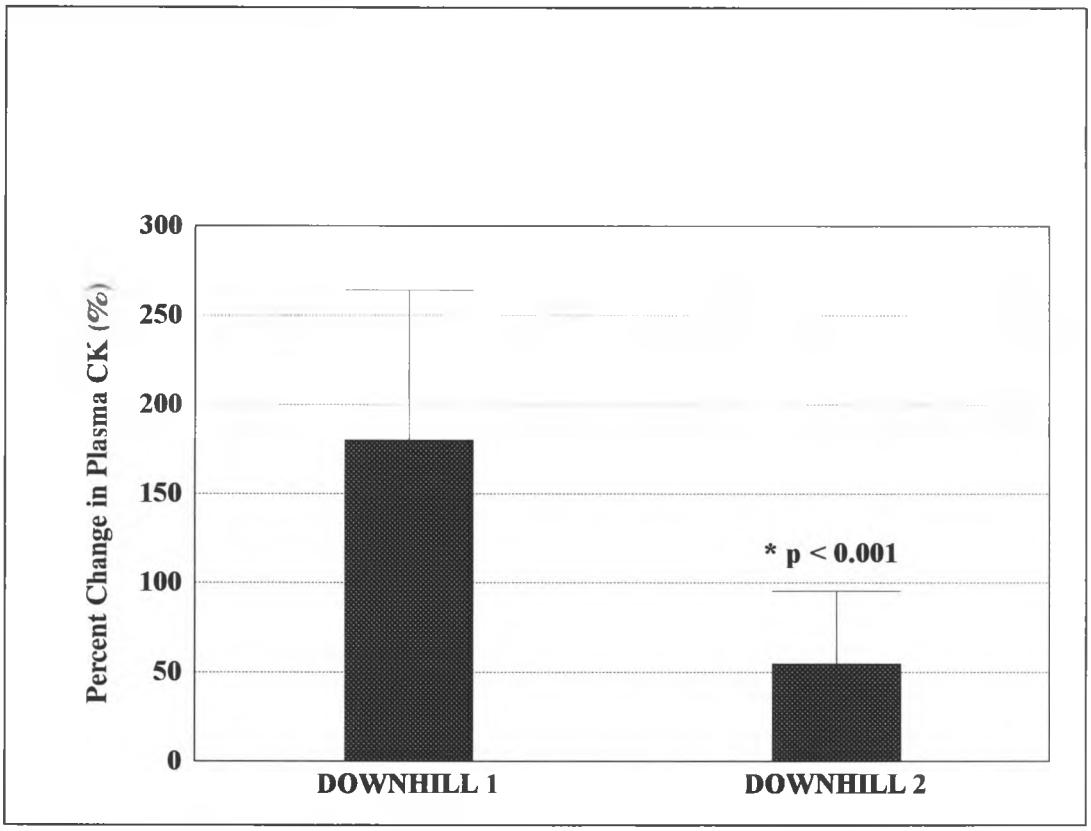

Figure 4 : Mean percent change in plasma creatine kinase (CK) in the combined group (n=12) after the initial downhill and second downhill running sessions. .

4.3 PERCENT CHANGE IN THE ISOKINETIC PERFORMANCE OF THE HAMSTRINGS AND QUADRICEPS MUSCLE GROUPS AFTER UPHILL AND DOWNHILL RUNNING

The initial downhill run, when compared to the uphill run, resulted in significantly larger decreases in the peak torque ($p<0.001$), and endurance ratio ($p < 0.001$) of both the quadricep and hamstring muscles of the combined group.

The mean peak torque of the hamstrings decreased by -3% after the uphill run, whereas the initial downhill run resulted in a -16% decrease in mean hamstring peak torque (Figure 5). The mean peak torque of the male and female quadriceps decreased by -2% after the uphill run, whereas the initial downhill run resulted in a -15% change in mean quadricep peak torque (Figure 6).

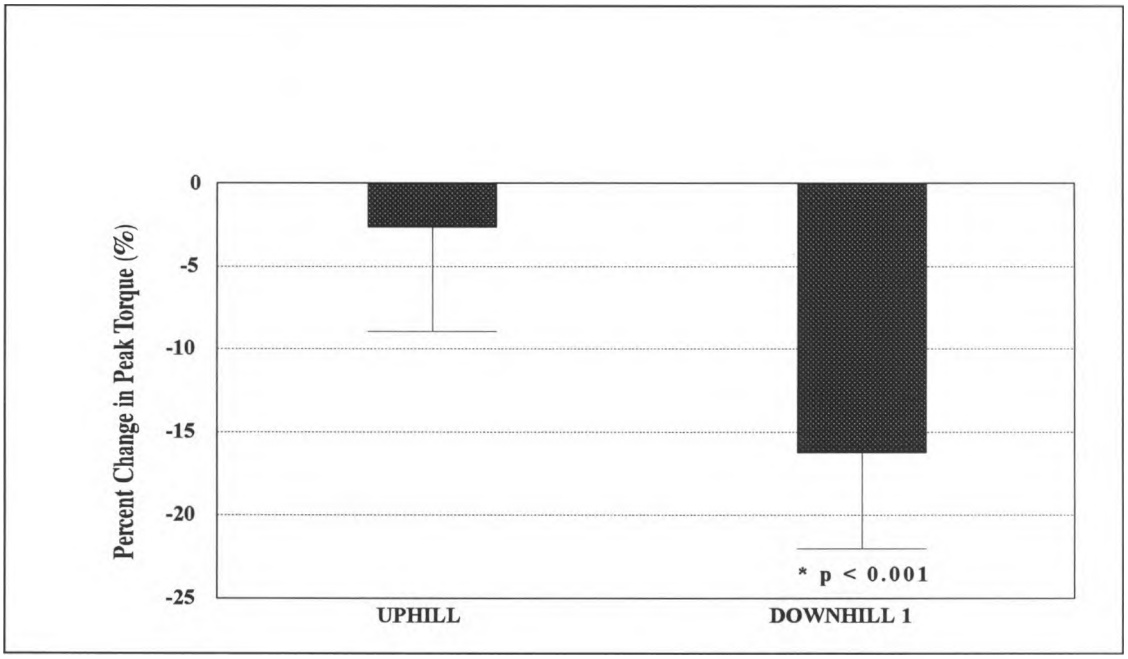

Figure 5 : Mean percent change in the hamstring peak torque of the combined group (n=12) after uphill and downhill running.

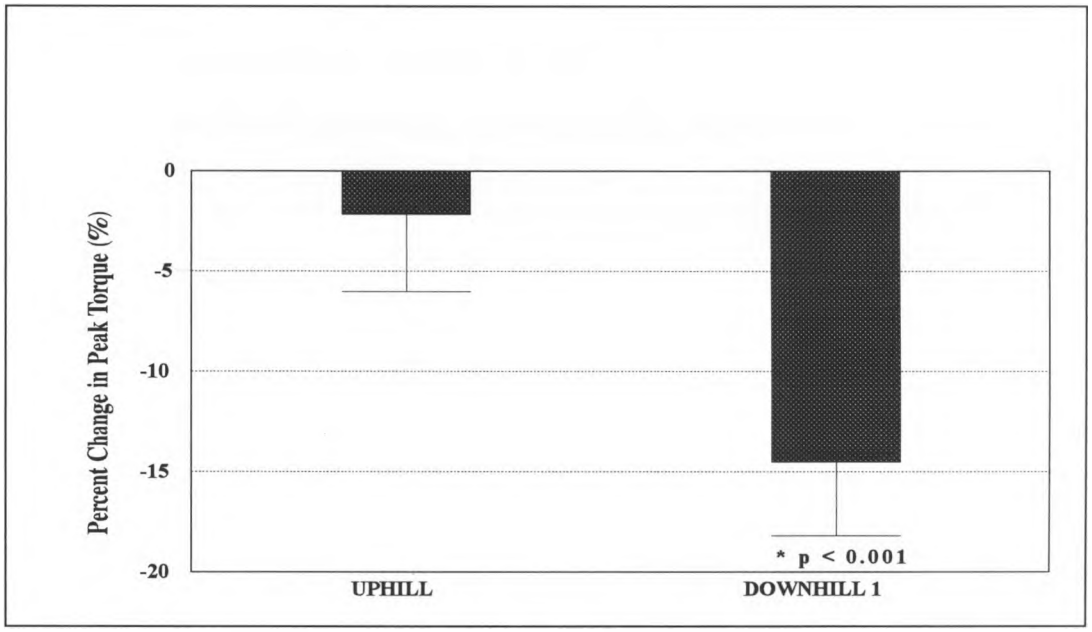

Figure 6 : Mean percent change in the quadricep peak torque of the combined group (n=12) after uphill and downhill running.

In addition, the initial downhill run, when compared to the uphill run, resulted in a significantly larger decrease ($p<0.001$) in the endurance ratio of the quadricep and hamstring muscles. The mean endurance ratio of the hamstrings increased by 2% after the uphill run ,whereas the initial downhill run resulted in a -13% decrease in the mean hamstring endurance ratio (Figure 7). Similarly, the uphill run resulted in

a 0.1`% increase in the mean endurance ratio of the quadriceps, whereas the initial downhill run resulted in a -32% decrease in mean quadricep endurance ratio (Figure 8).

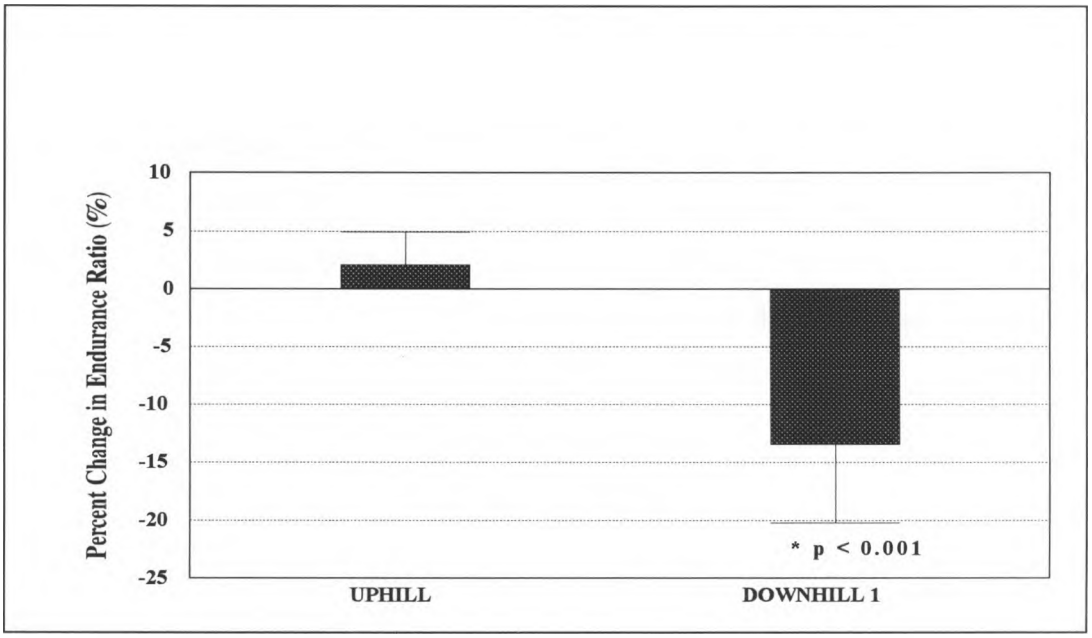

Figure 7 : Mean percent change in the hamstring endurance ratio of the combined group (n==12) after uphill and downhill running.

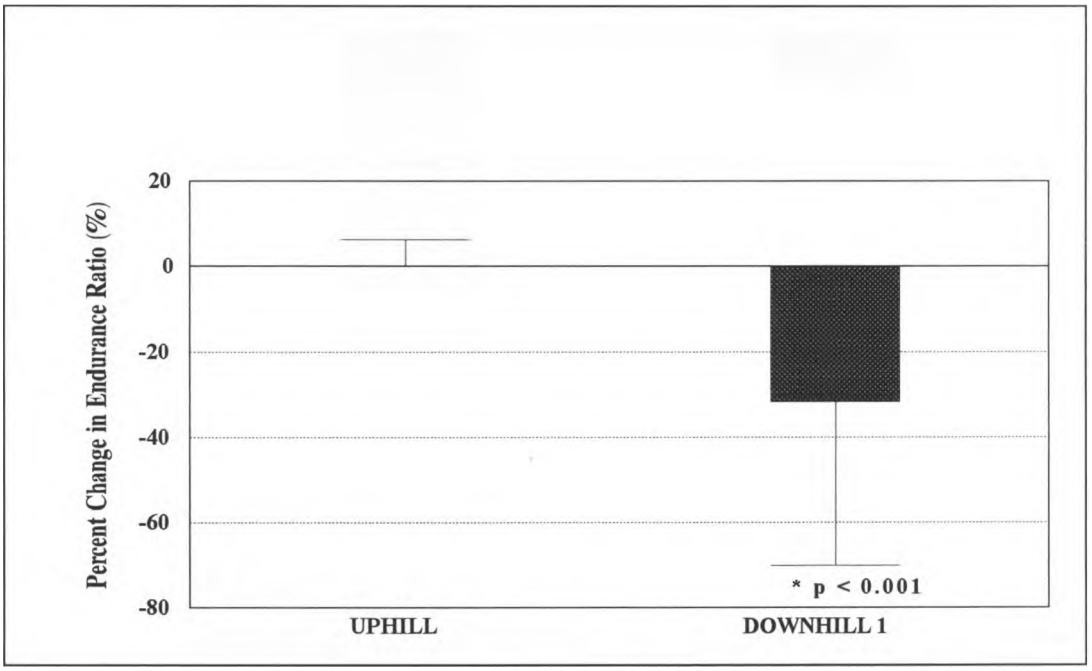

Figure 8 : Mean percent change in the quadricep endurance ratio of the combined group (n=12) after uphill and downhill running.

The initial downhill run therefore resulted in a decreased mean peak torque and endurance performance in the hamstring and quadricep muscle groups

The completion of the second downhill run, one week later, when compared to the initial downhill run, resulted in significantly less decrease in the mean peak torque, and endurance ratio of the hamstring and quadricep muscles in the combined group.

The mean hamstring peak torque decreased by -16% after the initial downhill run, whereas the second downhill run resulted in a significantly lower ($p < 0.001$) change of -3% (Figure 9). Similarly, the mean quadricep peak torque decreased by -15% after the initial downhill run, whereas the second downhill run resulted in a significantly lower ($p < 0.001$) change of -6% (Figure 10).

The percent change in hamstring and quadricep peak torque after the second downhill run and after the uphill run did not differ significantly .

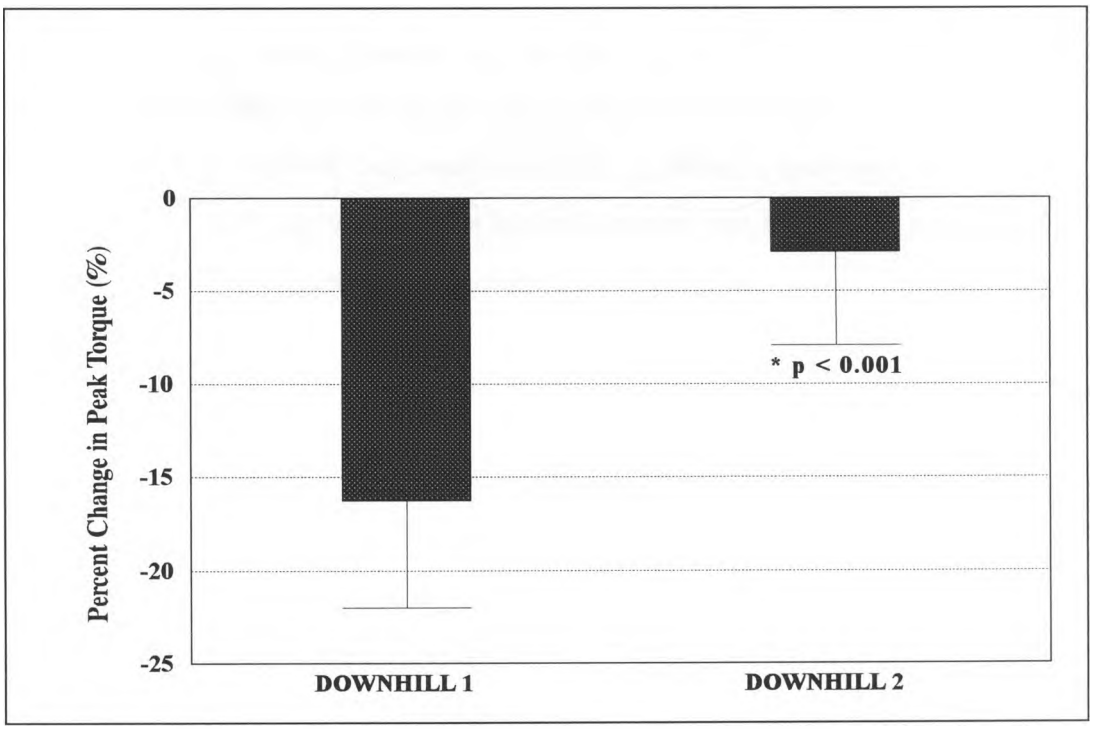

Figure 9 : Mean percent change in the hamstring peak torque of the combined group (n=12) after the initial downhill and second downhill running sessions. .

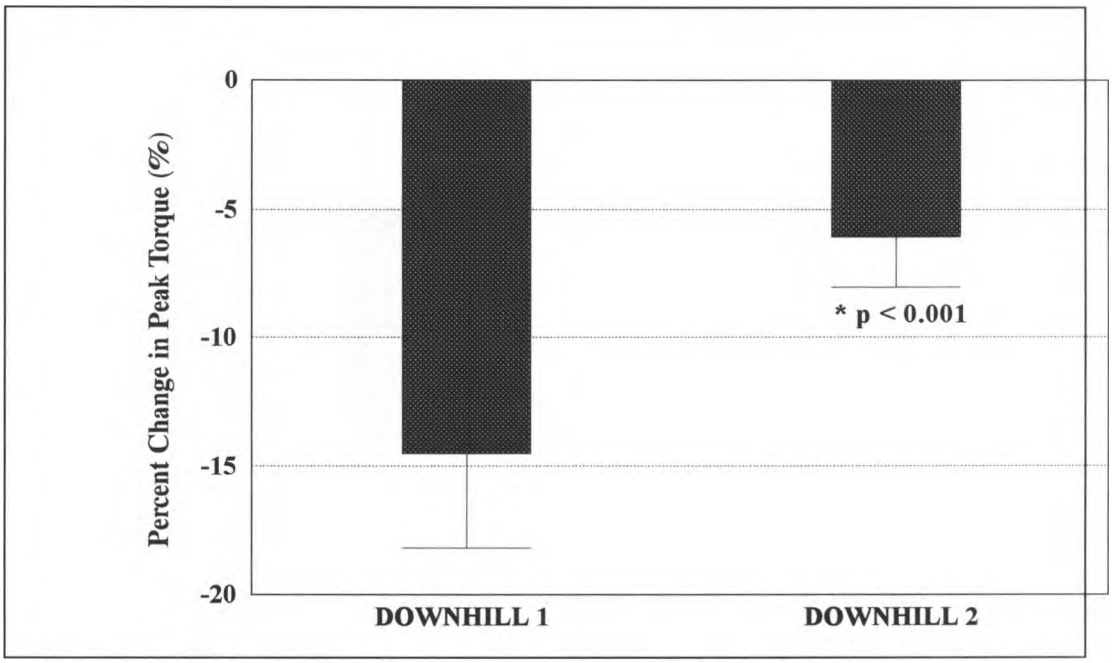

Figure 10 : Mean percent change in the quadricep peak torque of the combined group (n=12) after the initial downhill and second downhill running sessions.

In addition, the mean endurance ratio of the combined group hamstrings decreased by -13% after the initial downhill run, whereas the second downhill run resulted in a significantly smaller ($p < 0.05$) percent change of -7% (Figure 11). Similarly, the mean endurance ratio of the combined group quadriceps decreased by-32% after the initial downhill run, whereas the second downhill run resulted in a significantly smaller ($p < 0.01$) negative percent change of -9% (Figure 12).

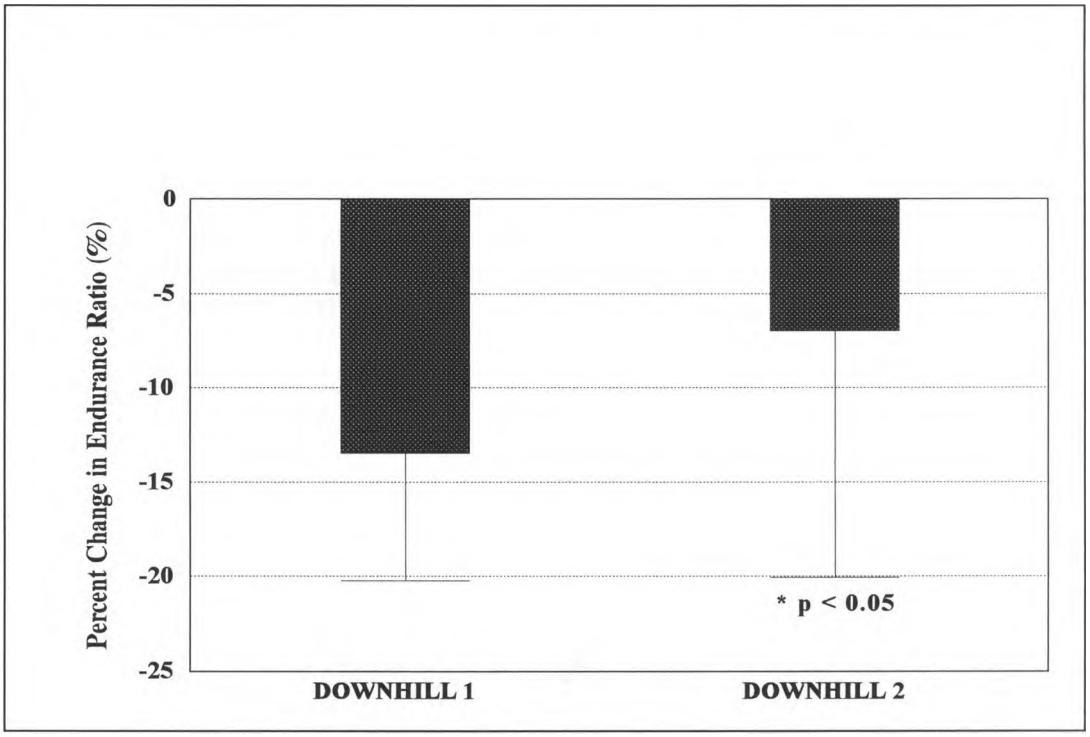

Figure 11 : Mean percent change in the hamstring endurance ratio of the combined group (n=12) after the initial downhill and second downhill running sessions.

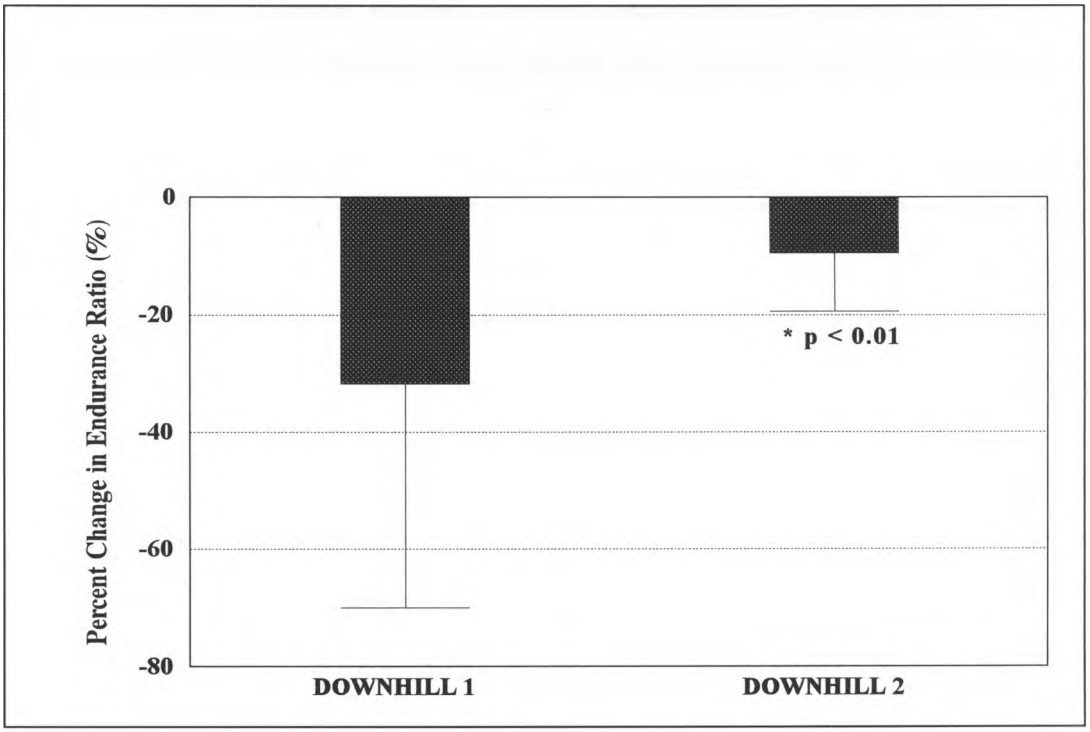

Figure 12 : Mean percent change in the quadricep endurance ratio of the combined group (n=12) after the initial downhill and second downhill running sessions.

The percent change in endurance ratio after the second downhill run and after the uphill run did not differ significantly in both the hamstring and quadricep muscle groups.

4.4 DIFFERENCES IN THE MALE AND FEMALE RESPONSE TO UPHILL AND DOWNHILL RUNNING

4.4.1 Plasma Creatine Kinase Response

The male subjects, when compared to the female subjects, showed no significant differences in the percent plasma creatine kinase changes ($p>0.05$) after the uphill and the two downhill running sessions (Table 2). In addition, there where no significant plasma creatine kinase differences ($p>0.05$) after the uphill and two downhill running sessions when the plasma creatine kinase values where standardised to the subject's body weight (u/l.kg), or presented as absolute values (u/l) (Table 2).

Table 2: Mean plasma creatine kinase response (absolute, standardised to body weight, and percent change) after uphill and downhill running (males vs. females).

MALES	UPHILL		DOWNHILL 1		DOWNHILL 2	
% Change CK	16.9(32.26)		211.38(87.28)		34.57(16.74)	
	Pre-Exercise	24 Hr Post-Exercise	Pre-Exercise	24 Hr Post-Exercise	Pre-Exercise	24 Hr Post-Exercise
CK standardised (u/l.kg)	0.93(0.16)	1.06(0.26)	0.88(0.18)	2.69(0.71)	1.23(0.47)	1.61(0.52)
CK absolute (u/l)	61.2(13.22)	69.4(12.77)	58.32(27.96)	173.37(27.96)	82.05(34.38)	106.43(35.35)
FEMALES						
% Change CK	28.55(38,0)		148.12(75.17)		74.43(49.00)	
	Pre-Exercise	24 Hr Post-Exercise	Pre-Exercise	24 Hr Post-Exercise	Pre-Exercise	24 Hr Post-Exercise
CK standardised (u/l.kg)	1.10(0.14)	1.4(0.37)	1.09(0.21)	2.30(1.25)	1.12(0.2)	1.9(0.4)
CK absolute (u/l)	62.7(8.02)	79.38(19.05)	60.44(9.47)	146.83(38.51)	63.45(10.89)	107.38(21.08)

Values are represented as mean (SD)

There were no significant differences between the male and female subjects with respect to plasma creatine kinase after uphill and downhill running.

4.4.2 Isokinetic Muscle Performance of the Hamstring and Quadricep groups (percent change)

The percent change in peak torque and endurance ratio of the hamstring and quadricep muscle groups of the male subjects, compared to the female subjects, was not significantly different ($p>0.05$) after the uphill and two downhill running sessions (Table 3)

Table 3 : Mean percent change in skeletal muscle performance after uphill and downhill running (males vs. females)

	MALES		FEMALES	
UPHILL	**Hamstring**	**Quadriceps**	**Hamstring**	**Quadriceps**
% Change Peak Torque	1.77 (2.61)	-2.55 (2.70)	-1.9 (5.96)	-1.72 (5.03)
% Change Endurance Ratio	1.85 (2.03)	-0.65 (8.68)	2.35 (3.70)	0.80 (2.84)
% Change in Torque at 180°/sec	***7.48 (5.80)**	-1.98 (10.53)	***-8.50 (9.56)**	-12.20 (9.69)
DOWNHILL 1				
% Change Peak Torque	-15.17 (3.10)	-16.13 (3.41)	-17.33 (7.77)	-12.88 (3.43)
% Change Endurance Ratio	-15.30 (3.36)	-20.55 (5.76)	-11.60 (9.02)	-20.21(5.97)
% Change in Torque at 180°/sec	-20.67 (6.45)	-16.10 (4.10)	-30.88 (12.98)	-19.18 (7.57)
DOWNHILL 2				
% Change Peak Torque	-4.52 (3.44)	-6.27 (2.55)	-1.27 (6.11)	-5.90 (1.39)
% Change Endurance Ratio	-8.08 (2.22)	-11.63 (7.75)	-5.82 (19.24)	-7.35 (12.08)
% Change in Torque at 180°/sec	****-3.68 (2.5)**	-7.08 (3.03)	****-10.70 (5.10)**	-6.63 (9.29)

Values are represented as mean percent change (SD)

**** males and females significantly different after uphill($p< 0.05$)***

***** males and females significantly different after downhill 2($p< 0.05$)***

However, with reference to Table 3, the percent change in torque at an angular velocity of 180 degrees per second for the female hamstrings after the uphill run was significantly worse ($p<0.05$) than that of the male subjects after their uphill running session. The mean female hamstring torque at functional velocity decreased by -9% after the uphill run whereas the males increased by 7% (Figure 13).

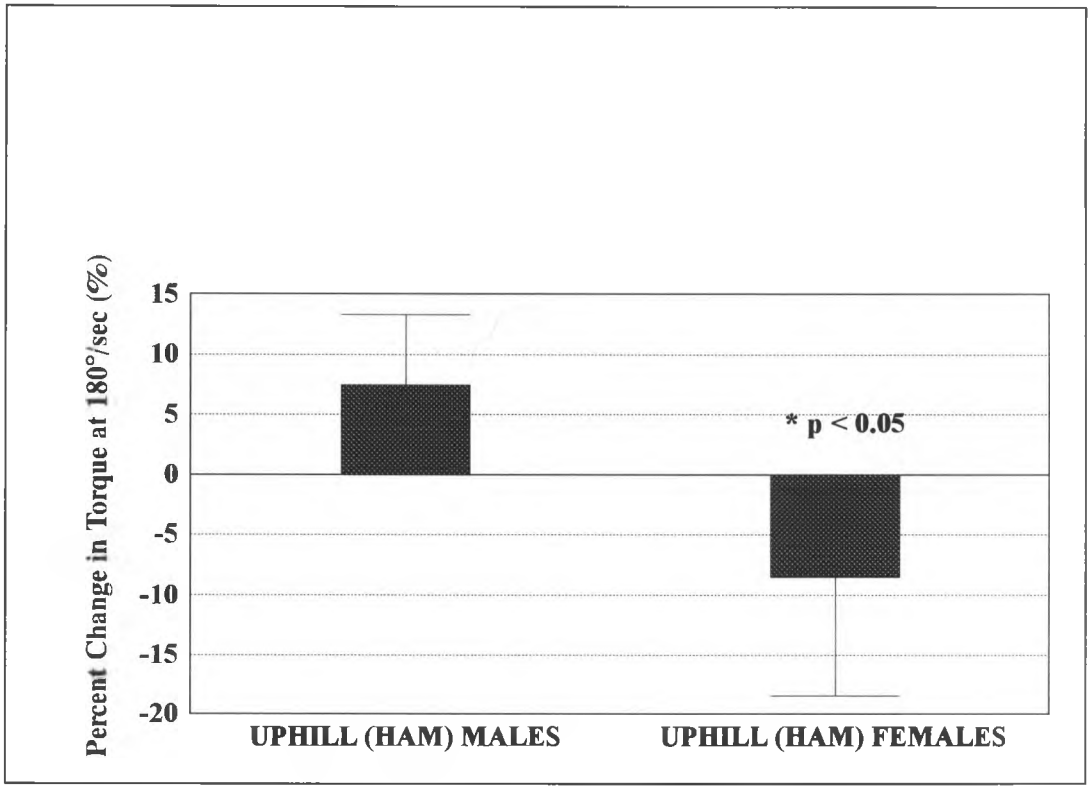

Figure 13 : Male and female mean percent change differences in hamstring torque at 180 degrees per second after uphill running.

In addition, the percent change in the torque at an angle of 180 degrees per second of the female hamstrings was significantly higher ($p<0.05$) after the second downhill run when compared to the percent change in the male hamstrings after the second downhill run (Table 3) The mean torque at an angle of 180 degrees per second of the female hamstrings decreased by -11% after the second downhill run, whereas the male subjects decreased by -4% (Figure 14).

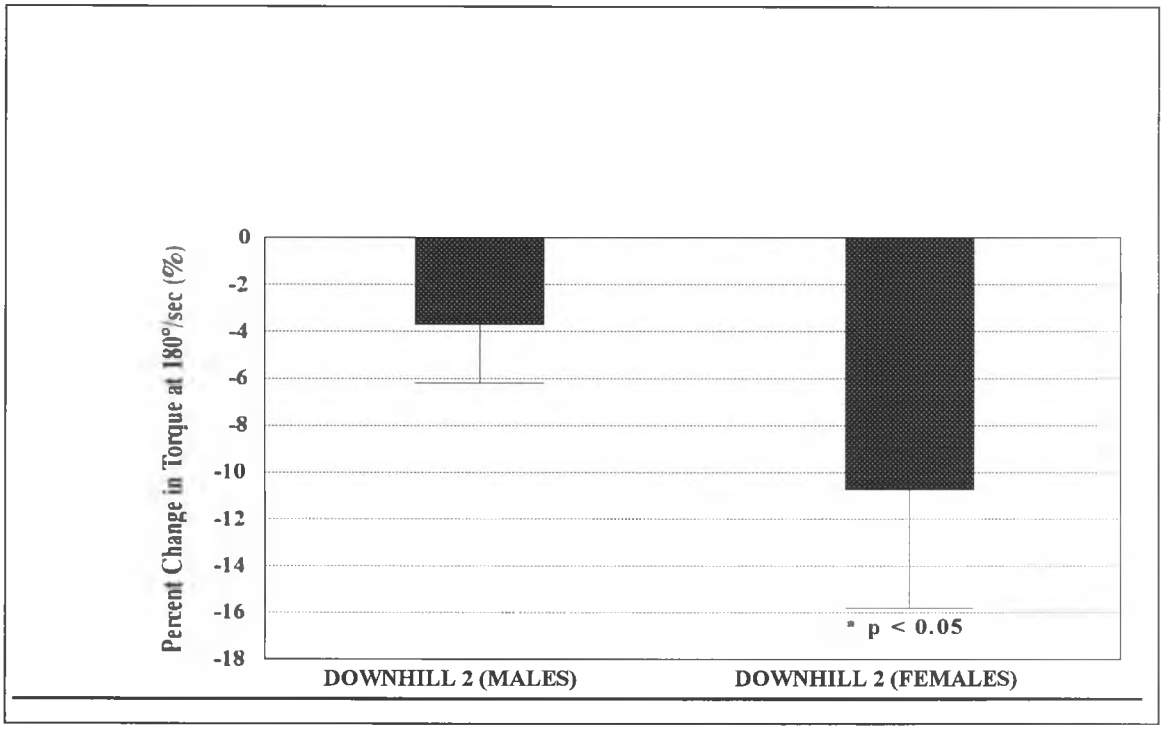

Figure 14 : Male and female mean percent change differences in hamstring torque at 180 degrees per second after the second downhill run

4.5 RELATIONSHIP BETWEEN PERCENT CHANGE IN PLASMA CREATINE KINASE AND SKELETAL MUSCLE PERFORMANCE (QUADRICEPS AND HAMSTRINGS).

The relationship between plasma creatine kinase percent change and skeletal muscle performance was not correlated when the male and female data was viewed separately. However, when the male and female data was pooled together (n=12), the percent change in plasma creatine kinase after the second downhill run was significantly correlated (r=0.7343) to the percent change in the endurance ratio of the quadricep muscle group after the second downhill run (Table 4). Therefore, the decrease in endurance ratio of the quadricep muscle group was highly related to the percent change in plasma creatine kinase which occurred as a result of the second downhill run.

Table 4 : Relationship between percent change in plasma creatine kinase and skeletal muscle performance in the combined group after uphill and downhill running

	Peak Torque (Nm)		Endurance Ratio (%)		Torque at 180°/sec (Nm)	
UPHILL	**Hamstrings**	**Quadriceps**	**Hamstrings**	**Quadriceps**	**Hamstrings**	**Quadriceps**
Spearman Correlation Coefficient	r = -0.09	r = -0.24	r = 0.32	r = 0.35	r = 0.34	r = 0.28
DOWNHILL 1	**Hamstrings**	**Quadriceps**	**Hamstrings**	**Quadriceps**	**Hamstrings**	**Quadriceps**
Spearman Correlation Coefficient	r = -0.24	r = -0.08	r = -0.59	r = 0.45	r = 0.05	r = -0.38
DOWNHILL 2	**Hamstrings**	**Quadriceps**	**Hamstrings**	**Quadriceps**	**Hamstrings**	**Quadriceps**
Spearman Correlation Coefficient	r = 0.04	r = -0.32	r = 0.20	*** r = -0.74**	r = -0.15	r = 0.30

The data is presented as a Spearman correlation co-efficient (r)

** **Significant correlation.***

4.6 PERCEIVED MUSCLE SORENESS AFTER UPHILL AND DOWNHILL RUNNING.

The perceived muscle soreness immediately after the initial downhill run was significantly greater ($p < 0.05$) than that perceived by the subjects immediately after the uphill run.

The perceived muscle soreness immediately after the initial downhill run was significantly greater ($p < 0.05$) than that perceived by the subjects immediately after the second downhill run.

Similarly, the muscle soreness perceived by the subjects 24 hours after the uphill run was significantly less ($p < 0.001$) than that experienced 24 hours after the initial downhill run.

In addition, the 24 hour post initial downhill run yielded significantly more muscle soreness ($p < 0.05$) than 24 hours after the second downhill run.

4.7 RELATIONSHIP BETWEEN PERCENT CHANGE IN PLASMA CREATINE KINASE AND PERCEIVED MUSCLE SORENESS AFTER UPHILL AND DOWNHILL RUNNING

The percent change in plasma creatine kinase 24 hours after the initial downhill run was significantly correlated (r = 0.85) to the perceived muscle soreness 24 hours after the second downhill run (Table 5).

Therefore the increase in plasma creatine kinase 24 hours after the initial downhill run was highly related to the perceived muscle soreness 24 hours post exercise.

Table 5 : Relationship between percent change in plasma creatine kinase and perceived muscle soreness in the combined group after uphill and downhill running

	Pre- Exercise	Post-Exercise	24 Hours Post-Exercise
UPHILL			
Spearman Correlation Coefficient	r = 0.34	r = 0.28	r = 0.15
DOWNHILL 1			
Spearman Correlation Coefficient	r = 0.34	r = 0.5	**r = 0.85 ***
DOWNHILL 2			
Spearman Correlation Coefficient	r = 0.09	r = 0.4	r = 0.45

The data is presented as a Spearman correlation co-efficient (r)

*** *Significant correlation.***

5. DISCUSSION

5.1 ENERGY EXPENDITURE

The present study supports previous research showing that negative work (downhill running) results in a decreased energy cost when compared with positive work (uphill running). The magnitude of the changes in heart rate and oxygen uptake are similar to the changes reported by others investigators who have used uphill and downhill running as part of their research protocols (Clarkson et al, 1985). The reduced energy expenditure for eccentric exercise compared to comparable levels of concentric exercise suggest huge increments in performance. That this does not occur underlines the extreme debilitating effects of the ultrastructural muscle damage associated with eccentric exercise.

5.2 DELAYED ONSET OF MUSCLE SORENESS (DOMS)

The results of this study indicate that subjects perceive a significantly greater amount of muscular soreness and stiffness immediately after and 24 hours after an initial bout of downhill running, when compared to a corresponding workload of uphill running. Therefore, downhill running can be considered to induce muscle soreness due to the bias towards eccentric contractions.

In a previous study, Schwane et al (1983), examined plasma creatine kinase levels following 30 minutes of eccentric cycling on a specially adapted bicycle. Although the eccentric workload set by Schwane was similar to that of this study, the time course of delayed onset muscle soreness (DOMS) differed. Schwane reported greatest perceived soreness at 12 hours post exercise, whereas in this study the highest perceived soreness values were recorded 24 hours post-exercise, with no indication that peak values had been achieved at this time (Table 23, Appendix A). Utilising different exercise regimes, other investigations have reported peak soreness to occur at 30 hours post exercise or longer (Newham et al, 1983; Schwane et al, 1983; Tiidus et al, 1983). The present study has found that the soreness ratings were quite variable among subjects, with some subjects reporting little to no soreness, and others reporting intense soreness (Table 23, Appendix A). This finding is consistent with other studies (Newham et al, 1983; Schwane et al, 1983), yet no explanation presently exists for this phenomenon. The positive

correlation between perceived muscle soreness and increased plasma creatine kinase 24 hours after the initial downhill run supports plasma creatine kinase as a marker of muscle tissue damage and subsequent muscle soreness.

The soreness and stiffness experienced by the runners immediately after and 24 hours after the exposure to the first downhill run, is hypothesised to have occurred as a result of an influx of calcium ions into the sarcoplasm which causes excessive contraction (Cullen et al, 1975). Generally, subjects experienced pain in all the major extensor and flexor muscles of the hip, thigh, and leg. The tenderness was described as being localised in the distal portion of the muscle in the region of the muscle -tendon junction. This could be due to the fact that muscle pain receptors are most concentrated in the regions of the tendons and connective tissue, or due to a localisation of the damage in the distal muscle-tendon region, or to a combination of these factors (Schwane, 1983).

5.3 PLASMA CREATINE KINASE RESPONSE

When active muscle fibres are stretched, as occurs during downhill running, the fibres generate greater tension than when allowed to shorten (uphill running). In addition, the metabolic cost of generating a given tension is also lower during eccentric contractions (downhill running), when compared to the concentric contractions of uphill running (Smith, 1988). Consequently, not only may there be fewer motor units active during eccentric contractions, but the metabolic cost of performing the same work is much less, In these circumstances, the delayed rise in plasma creatine kinase which occurred after the first downhill run cannot have been a consequence of the energy expenditure of downhill running.

It is known that eccentric contraction causes morphological damage to skeletal muscle (Clarkson et al, 1987b). Friden et al (1981), found extensive areas of Z-line streaming after downhill running. To produce a given muscle force, fewer motor units are activated in an eccentric than in a concentric contraction (Asmussen, 1956). Therefore, in downhill running, the force is distributed over a smaller cross-sectional area of muscle and the tension per active cross-sectional area is greater .It seems probable that this increased tension per unit area could cause mechanical

disruption of structural elements in the muscle themselves or in the connective tissue that is in series with the contractile elements (Davies, 1981). This may lead to the release of algesic substances causing the pain and tenderness, and initiate a process leading to the release of large quantities of creatine kinase into the plasma. The creatine kinase proteins are too large to escape from muscle unless there is either a membrane disruption or change in the membrane permeability. The delay in appearance of creatine kinase activity in the blood after the initial downhill run might be due to the slow lymphatic system which clears the creatine kinase from the extra cellular spaces. However, it is unlikely to be the only explanation. Levels of creatine kinase activity in the blood reflect a balance between efflux and clearance, so therefore the results must be interpreted cautiously. What is clear, is that the creatine kinase is escaping from the damaged tissue. This statement is reinforced by the results of research conducted by Martin et al (1983), in which a radio-active substance (technetium 99M pyrophosphate) was injected into the blood of ultra-marathoners. After 80 and 160 km it had been taken up by the damaged tissue - the highest tissue levels occurring in the lower limbs, and those runners with the highest values having the worst DOMS.

5.4 SKELETAL MUSCLE FUNCTION AFTER UPHILL AND DOWNHILL RUNNING

Warhol et al (1985), have reported that ATP concentration remains unchanged following negative work, creatine phosphate decreases within normal limits and lactate accumulation is unexceptionable. These results argue in favour of the maintenance and efficacy of the muscle chemical processes responsible for energy supply during and following negative work (downhill running). It may well be, therefore, that repeated stretching of the muscle actually damages the contractile protein machinery directly and affects the cycling of cross-bridges within the muscle fibre resulting in a loss of efficiency of the normal contraction process.

According to Kuipers (1985a), eccentric muscle exercise may generate higher local temperatures than concentric contractions. Kuipers postulated that the elevated temperatures in the muscles could conceivably damage the structural elements of the muscle, resulting in necrosis of muscle fibres and breakdown of connective

tissues. This theory could therefore be used to explain the decreased muscle performance of the hamstrings and quadriceps after the initial downhill run.

An electromyograph has revealed that during downhill running the forward swing of the lower limb is initiated by the hip flexors, and the knee extensors (quadriceps) act initially to prevent the leg from folding up too much as the thigh is pulled forward (De Vries, 1983). During mid-recovery, there is a brief period of power production of the quadriceps (a concentric action), but then the knee flexors (hamstrings) dominate and provide a vigorous eccentric effort to control an otherwise excessive whip-like action, absorbing the energy acquired by the leg and slowing it down in preparation for foot strike (De Vries, 1983). Clearly, the repetitive eccentric muscle contractions of 30 minutes of downhill running places a large eccentric strain on both the quadricep and hamstring muscle groups, and as a result, muscle performance can be impaired.

According to Cullen (1979), structural damage to the sarcolemma or alterations in permeability of the cell membrane resulting from the high mechanical forces generated during downhill running, is accompanied by a net influx of calcium ions from the interstitium. When abnormally high levels of calcium ions exist in the cell, the mitochondria accumulate the ion, which inhibits cellular respiration and initiates a cycle of events in which the cells lowered ability to produce ATP compromises the cells ability to actively exclude calcium ions (Wrogemann, 1976). This destructive cycle could possibly result in impairment of oxidative phosphorylation and abnormally high calcium ion concentrations in the cell. According to Davies (1982), high calcium ion concentrations in muscle cells have been shown to activate a calcium-dependent proteolytic enzyme that preferentially degrades Z-discs as well as troponin and tropomyosin. Therefore, the above theories of Wrogemann and Davies could be used to explain the decrease in muscle performance of the hamstrings and quadriceps as shown by the subjects in this study after the initial downhill run.

After the initial downhill run, there was a significant decrease in the peak torque, endurance ratio, and torque at an angular velocity of 180 degrees per second of the hamstring and quadricep groups of muscle in the combined group. A previous

eccentric study by Hough(1964), suggests that the diminished muscular performance resulted both from reduced voluntary effort due to the sensation of soreness and to a lowered inherent capacity of the muscle to produce force. Therefore, in the present study, 24 hours after the first downhill run, when the muscles were sore from the previous day's exertion, the subjects produced considerably less force than the pre-exercise values. These results suggest that performance may be reduced during the period of DOMS both through reluctance to use the muscle because of the pain, and through loss of inherent force-producing capability in the muscle.

5.5 ADAPTATION TO DOWNHILL RUNNING

Certainly, one of the most important findings of this study is the brief time of training required to decrease the extent of the exercise induced muscle damage. It is clear from the results of this study that after the first exposure to the eccentric exercise(downhill running), the muscles seem to have an adaptive response, as evidenced by much lower levels of plasma creatine kinase activity in response to the same exercise bout and less of a fall in muscle performance. In addition, the muscle soreness perceived by the subjects immediately after and 24 hours after the second downhill run was significantly less than that of the initial downhill run. The above information suggests the prophylactic effect of a single bout of eccentric exercise with regard to the subsequent development of muscle soreness. Clearly, this phenomenon of adaptation has great practical application for runners who are attempting to reduce the amount of muscle damage experienced after training and racing. For example, the Comrades Marathon runner facing the 'down' run should be able to substantially decrease the amount of muscle injury caused by eccentrically-biased downhill running.

What then is the mechanism(s) of this muscular adaptation if the adaptation observed is a tissue training response?

Previous studies (Byrnes et al, 1985; Clarkson et al, 1986; Norton et al, 1985), have found that the increase in plasma creatine kinase activity is unrelated to either the development of muscle soreness, the amount of strength loss after eccentric

exercise, fitness level of the subject, or lean body weight. Similarly, in this study, the only correlation between percent change in plasma creatine kinase and skeletal muscle performance occurred in the endurance ratio of the quadricep muscles after the second downhill run. Reasons for the absence of a correlation may include individual variations and/or inhibition of creatine kinase activity. Jackson et al (1987), attributed the large creatine kinase variability in patients with Duchene dystrophy to individual differences in the release of enzymes from the muscle. On the other hand, Kagen and Aram (1987), found a dialysable inhibitor of creatine kinase activity present in plasma obtained from patients with muscle disease or injury, but not in the plasma of other individuals. They suggested that the creatine kinase inhibitor may be released along with the creatine kinase into the blood as a result of the muscle fibre damage.

Therefore, the lower plasma creatine kinase response after the second downhill running bout may be due in part to an adaptation resulting in the release of creatine kinase inhibitors from the muscle tissue. It still remains unclear why inter-subject variability exists in the creatine kinase response to exercise induced muscle damage. Apparently some subjects may be more resistant to damage, although the explanation for this is unclear.

In addition, there are other possibilities to account for the muscular adaptation that has occurred. Firstly, there might be a change in the pattern of motor recruitment, and secondly, there might be some intrinsic adaptation to the muscle fibre.

Thirdly, fibres may be nearing the end of their postmitotic growth or a small part of stress susceptible fibres are destroyed at the first exposure. At this stage, it seems that the latter two points are more likely explanations because the EMG pattern does not change, suggesting that muscle recruitment is unaltered (Davies, 1981).

According to Carpentar and Karpati (1984), muscle fibres that undergo lethal injury with exercise may be more fragile or more susceptible to damage than other fibres. Fragile fibres may develop through disuse of a given motor unit recruitment pattern or may represent a small percentage of fibres that are constantly degenerating (or ageing) making them more susceptible to stress. According to

Carpentar and Karpati (1984), stress-susceptible or degenerating fibres may embody a population of cells that are destroyed by an initial bout of exercise with the strong, healthy fibres withstanding and surviving the effects of repeated contraction. It should be noted that it would not be necessary for an entire fibre to be fragile (Carpentar et al, 1984) . Since focal necrosis can occur (Carpenter & Karpati 1984), only portions or small areas of a fibre may be fragile and susceptible to exercise damage.

Therefore, in this study, a pool of fragile or stress susceptible muscle fibres might have been lethally damaged and eliminated by the first bout of downhill running. Injury to these stress susceptible fibres would result in a release of creatine kinase from the damaged tissues and a production of noxious stimuli leading to the sensation of pain (Byrnes et al, 1985). The noxious stimuli, which could be products of the inflammatory response or release of endogenous chemicals, excite free nerve endings in the muscle. Lethal injuries from the first bout of downhill running could have resulted in a temporary reduction in the stress susceptible fibres so that performance of the second downhill run would result in a reduced plasma creatine kinase and soreness response (Armstrong, 1984).This could also explain the plasma creatine kinase adaptation to downhill running in our group of subjects.

Fridén (1983), has listed 3 possible mechanisms of structural myofibrillar adaptation that may result from eccentric training to limit damage. Firstly, sarcomere length may be increased. However, this would be only a temporary solution for tension reduction because increased length would also result in non-optimal overlap between actin and myosin filaments. Secondly, sarcomere-ogenesis may result in an increase in the number of longitudinal sarcomeres, the functional units of the contractile system. Thirdly, an increase in synthesis of Z-band proteins or intermediate filaments may strengthen myofibrils. Therefore, it is possible that the above three mechanisms could result in a structural myofibrillar adaptation that would protect the muscle from subsequent eccentric damage.

A central neural mechanisms may also play a role in explaining the muscular adaptation that occurs after the initial downhill run. The adaptation could, in part, result from endorphin release by neurones in the central nervous system (Kelly,

1982). These endogenous opiods (example, beta-endorphin), which are more potent than morphine in inducing analgesia, are secreted by neurones in the brain and spinal cord with the overall effect of inhibiting transmission of pain (Goodman, 1983; Kerr, 1978). It has been suggested that endorphin release is increased during exercise (Kelly, 1982), so exercise enhanced endorphin secretion could potentially provide an analgesic effect, minimising the sensation of DOMS after the second downhill run.

5.6 MALE VERSUS FEMALE RESPONSE TO UPHILL AND DOWNHILL RUNNING

It was surprising to see that there was not a significant difference between the plasma creatine kinase response in the male and female subjects after uphill and downhill running, since data from previous studies have suggested a lack of creatine kinase response to moderately strenuous exercise in females, but a brisk creatine kinase deviation in men (Griffiths, 1965; Hunter et al, 1971).

If creatine kinase release indicates damage to muscles, as commonly assumed, the results from this study imply that the muscles of males and females are equally sensitive to adverse factors.

Although there is a great range and overlap of strength abilities in men and women, when the measure is the absolute amount of force exerted or weight lifted, the average woman is about two-thirds to four-fifths as strong as the average man (Laubach, 1976; Hudson, 1978). In this study, the above phenomenon is clearly indicated by higher peak torque values (at an angular velocity of 60°/sec), endurance ratio values (angular velocity of 240°/sec), and torque values at an angular velocity of 180°/sec for the hamstring and quadricep muscle groups when compared to the female subjects.

It would therefore seem that the greater muscle volumes exhibited by the male subjects would result in a greater plasma creatine kinase response after uphill and downhill running. However, this was not the case - the male and female subjects cannot be differentiated with respect to the amount of muscle damage and

subsequent plasma creatine kinase levels after uphill and downhill running. Therefore, the smaller muscle volumes in the female subjects does not make them less susceptible to the damaging effects of downhill running, and therefore a decreased plasma creatine kinase response.

With respect to skeletal muscle performance, the female hamstrings, in comparison to the male subjects, are more susceptible to be damaged by uphill running when torque at an angular velocity of 180 degrees per second is used as a measure of muscle performance. According to Noakes (1983), females have twice as much body fat as do equally active men, and this could present as a possible explanation for the loss in torque at an angular velocity of 180 degrees per second in the female hamstrings after uphill running. During uphill running, the hamstring muscles reach a peak of activity in extending the hip joint just as the heel strikes the ground (De Vries, 1983).The greater non-metabolising tissue or dead weight carried by the female subjects during uphill running could therefore account for the greater hamstring strain, muscle damage and subsequent loss in muscle performance experienced by the female subjects after uphill running.

6. CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSIONS

The results of this study indicate that downhill running, characterised by a large eccentric component, produces greater skeletal muscle damage than does concentric work of a considerable higher metabolic cost. Evidence of damage following repetitive eccentric muscle actions (downhill running), include delayed-onset muscle soreness, hamstring and quadricep muscle performance decrements, and elevation of plasma creatine kinase. The lower muscle volumes in female subjects, compared to males, does not make females less susceptible to the damaging effects of eccentric exercise. However, with respect to the torque produced at an angular velocity of 180 °/sec, the female hamstrings are more prone to be damaged by uphill running than the male hamstrings. The greater body fat and therefore dead weight carried uphill by the female runners could result in excessive hamstring strain, and subsequent loss in muscle performance.

The precise cause of skeletal muscle damage and the mechanisms of repair are not well understood. Calcium, connective tissue, and cyto-skeletal and myofibrillar proteins may be involved in the damage and repair process. Damaged muscles adapt to downhill running, and all indicators of damage (plasma creatine kinase, soreness and muscle performance) are reduced following a repeated bout of downhill running, one week later. Several hypotheses have been presented to explain the muscle adaptation that occurs after the initial downhill running session. Stress-susceptible fibres or susceptible areas within a fibre may be eliminated and then regenerated, or muscle fibres and/or connective tissue may be strengthened with an initial bout of downhill running. A creatine kinase inhibitor may have been released along with the creatine kinase into the blood, and the presence of this inhibitor would therefore decrease the amount of creatine kinase released from the muscle after a further eccentric insult. In addition, exercise enhanced endorphin secretion and the subsequent presence of these endorphins could provide an analgesic effect, so minimising the sensation of DOMS after the second downhill run.

6.2 RECOMMENDATIONS

The results of this study have a number of practical implications related to exercise prescription and leadership in fitness and rehabilitation programmes.

Firstly, some protection against exercise-induced DOMS is provided by little training. This study has shown that performance of a single 30 minute bout of eccentric exercise, which itself elicits DOMS, results in reduced DOMS following repetition of that same activity. Also, several investigators have reported progressively decreasing soreness after the first several days of repeated intense eccentric exercise (Friden et al, 1983b; Komi et al, 1972). These observations are of interest physiologically, but such regimes are not of practical use if avoidance of all soreness is the objective.

Therefore, by combining the results of this study and those of Schwane et al (1987), more than two weeks of training involving very gradual progression of exercise load are indicated if DOMS is to be avoided. Furthermore, incorporation of exercise involving a substantial eccentric component (example, downhill walking or jogging) should be incorporated into an exercise program of an individual who is training for an event that involves stressful eccentric work. The Comrades Marathon runner who is facing the eccentric load of the 'down' run from Pietermaritzburg to Durban, is advised to incorporate different forms of eccentric training into his/her training. For example, hill training (both uphill and downhill) is essential. In addition, a weight training program which emphasises eccentric contractions is important. The runner is helped to lift a weight concentrically, but has to lower the weight eccentrically without assistance. This action can be performed on a seated leg extension machine for the quadriceps, and on a lying leg flexion machine for the hamstrings.

One must recognise that large differences exist among individuals in terms of their responses to eccentrically biased exercise and training, and therefore the frequency, intensity, nature, and duration of an eccentric training program should be tailored to meet the needs and responses of the individual.

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8. APPENDIX A : DETAILED MEASURED RESULTS AND STATISTICAL CALCULATIONS

Table 6 : VO2 and heart rate values in male and female subjects after uphill and downhill running. The table shows individual as well as mean and SD values

	MALES			FEMALE		
	Heart Rate	VO2		Heart Rate	VO2	
	[beats/min]	[ml/kg]	[l/min]	[beats/min]	[ml/kg]	[l/min]
	156	41.3	2.69	168	44.3	2.38
	172	42.2	2.41	181	37.5	3.10
	165	42.4	2.50	176	35.4	2.30
UPHILL	166	43.8	2.85	182	36.8	2.06
	151	43.2	3.16	180	40.2	2.01
	178	44.4	2.53	172	38.9	1.97
Mean	165*	42.9*	2.69	177*	38.9*	2.30
Std. Deviation	9.95	1.1	0.28	5.58	3.1	0.42
	112	20.8	1.35	102	17.5	0.98
	120	22.1	1.26	110	18.1	1.02
	114	22.2	1.31	98	15.3	0.99
DOWNHILL-1	106	22.8	1.46	100	17.8	1.01
	104	21.2	1.51	118	23.6	1.35
	112	23.6	1.35	109	20.2	1.32
Mean	111	22.1	1.37	106	18.8	1.11
Std. Deviation	5.75	1.0	0.09	7.55	2.8	0.17
	104	19.4	1.26	100	15.1	0.83
	118	23.0	1.29	103	17.7	0.97
	106	22.8	1.31	96	16.2	1.06
DOWNHILL-2	112	23.2	1.40	98	16.6	0.91
	103	19.2	1.38	110	22.1	1.26
	107	22.7	1.27	112	19.6	1.17
Mean	108	21.7	1.32	103	17.9	1.03
Std. Deviation	5.68	1.9	0.06	6.52	2.6	0.16

Table 7 : Plasma creatine kinase values (u/l) in male subjects after uphill and downhill running. The data is shown as individual absolute results as well as mean, standard deviation, and percent change in plasma creatine kinase after upfhill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	48.14	50.89	5.7%	86.66	80.0%	61.56
	57.74	56.54	-2.1%	63.65	10.2%	
	53.65	31.64	-41.0%	64.20	19.7%	
	63.32	54.23	-14.4%	61.23	-3.3%	
	58.20	50.28	-13.6%	56.39	-3.1%	
	86.12	80.97	-6.0%	84.27	-2.1%	
Mean:	61.20	54.09	-11.9%	69.40	16.9%	
Standard Dev.:	13.22	15.86		12.77		
Down-hill 1	46.25	58.36	26.2%	196.32	324.5%	102.24
	64.75	74.26	14.7%	201.65	211.4%	
	56.21	62.31	10.9%	130.61	132.4%	
	60.11	68.23	13.5%	192.32	219.9%	
	42.35	93.21	120.1%	162.60	283.9%	
	80.27	93.74	16.8%	156.70	95.2%	
Mean:	58.32	75.02	33.7%	173.37	211.2%	
Standard Dev.:	13.65	15.28		27.96		
Down-hill 2	64.36	66.37	3.1%	83.76	30.1%	94.13
	110.62	140.65	27.1%	150.70	36.2%	
	130.31	131.73	1.1%	142.60	9.4%	
	90.23	111.65	23.7%	115.62	28.1%	
	40.61	50.66	24.7%	64.67	59.2%	
	56.22	62.36	10.9%	81.20	44.4%	
Mean:	82.06	93.90	15.1%	106.43	34.6%	
Standard Dev.:	34.38	38.87		35.35		
MEAN	67.19	74.34		116.40		

Table 8 : Plasma creatine kinase values (u/l) in female subjects after uphill and downhill running. The data is shown as individual absolute results as well as mean, standard deviation, and percent change in plasma creatine kinase after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	53.65	55.62	3.7%	60.23	12.3%	72.58
	68.81	62.83	-8.7%	64.72	-5.9%	
	54.76	96.32	75.9%	110.30	101.4%	
	74.32	95.23	28.1%	92.10	23.9%	
	63.70	68.70	7.8%	68.72	7.9%	
	60.92	75.32	23.6%	80.23	31.7%	
Mean:	62.69	75.67	21.7%	79.38	28.5%	
Standard Dev.:	8.02	16.88		19.05		
Down-hill 1	45.26	64.36	42.2%	154.24	240.8%	96.19
	61.30	72.49	18.3%	98.36	60.5%	
	60.20	68.23	13.3%	197.65	228.3%	
	73.33	98.36	34.1%	182.32	148.6%	
	66.23	99.22	49.8%	115.66	74.6%	
	56.29	85.16	51.3%	132.76	135.9%	
Mean:	60.44	81.30	34.8%	146.83	148.1%	
Standard Dev.:	9.47	15.25		38.51		
Down-hill 2	56.62	69.64	23.0%	123.69	118.5%	81.48
	57.32	92.98	62.2%	94.33	64.6%	
	51.32	52.36	2.0%	120.62	135.0%	
	69.98	84.17	20.3%	132.70	89.6%	
	64.17	63.17	-1.6%	79.61	24.1%	
	81.29	79.32	-2.4%	93.35	14.8%	
Mean:	63.45	73.61	17.3%	107.38	74.4%	
Standard Dev.:	10.89	14.80		21.07		
MEAN	62.19	76.86		111.20		

Table 9 : Plasma creatine kinase values standardised to body weight (u/l.kg) in male subjects after uphill and downhill running.The data is shown as individual absolute results as well as mean, standard deviation, and percent change in plasma creatine kinase after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	0.86	0.90	4.7%	1.54	79.1%	0.89
	0.89	0.87	-2.2%	1.00	12.4%	
	0.69	0.40	-42.0%	0.81	17.4%	
	1.07	0.10	-90.7%	1.03	-3.7%	
	0.89	0.77	-13.5%	0.87	-2.2%	
	1.15	1.09	-5.2%	1.13	-1.7%	
Mean:	0.93	0.69	-24.8%	1.06	16.8%	
Standard Dev.:	0.16	0.37		0.26		
Down-hill 1	0.82	1.04	26.8%	3.49	325.6%	1.57
	0.99	1.14	15.2%	3.10	213.1%	
	0.71	0.80	12.7%	1.67	135.2%	
	1.02	1.15	12.7%	3.25	218.6%	
	0.65	1.43	120.0%	2.50	284.6%	
	1.08	1.26	16.7%	2.10	94.4%	
Mean:	0.88	1.14	34.0%	2.69	211.9%	
Standard Dev.:	0.18	0.21		0.71		
Down-hill 2	1.14	1.18	3.5%	1.48	29.8%	1.42
	1.70	2.16	27.1%	2.31	35.9%	
	1.67	1.68	0.6%	1.82	9.0%	
	1.52	1.89	24.3%	2.00	31.6%	
	0.62	0.78	25.8%	1.00	61.3%	
	0.75	0.84	12.0%	1.10	46.7%	
Mean:	1.23	1.42	15.6%	1.62	35.7%	
Standard Dev.:	0.47	0.57		0.52		
MEAN	1.01	1.08		1.79		

Table 10 : Plasma creatine kinase values standardised to body weight (u/l.kg) in female subjects after uphill and downhill running.The data is shown as individual absolute results as well as mean, standard deviation, and percent change in plasma creatine kinase after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	1.00	1.00	0.0%	1.09	9.0%	1.23
	1.10	0.10	-90.9%	1.03	-6.4%	
	1.00	1.73	73.0%	1.98	98.0%	
	1.37	1.75	27.7%	1.70	24.1%	
	1.13	1.28	13.3%	1.29	14.2%	
	1.01	1.25	23.8%	1.30	28.7%	
Mean:	1.10	1.19	7.8%	1.40	27.9%	
Standard Dev.:	0.14	0.61		0.37		
Down-hill 1	0.81	1.16	43.2%	2.78	243.2%	1.61
	1.10	1.15	4.5%	0.15	-86.4%	
	1.07	1.22	14.0%	3.54	230.8%	
	1.40	1.81	29.3%	3.36	140.0%	
	1.23	1.90	54.5%	1.81	47.2%	
	0.93	1.41	51.6%	2.20	136.6%	
Mean:	1.09	1.44	32.9%	2.31	118.6%	
Standard Dev.:	0.21	0.33		1.25		
Down-hill 2	1.02	1.25	22.5%	2.23	118.6%	1.44
	0.90	1.47	63.3%	1.50	66.7%	
	0.92	0.93	1.1%	2.16	134.8%	
	1.30	1.55	19.2%	2.40	84.6%	
	1.20	1.18	-1.7%	1.50	25.0%	
	1.40	1.32	-5.7%	1.60	14.3%	
Mean:	1.12	1.28	16.5%	1.90	74.0%	
Standard Dev.:	0.21	0.22		0.41		
MEAN	1.11	1.30		1.87		

Table 11 : Peak torque values (N.m) in the male hamstrings after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running.

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	138.00	142.00	2.9%	139.00	0.7%	
	134.00	138.00	3.0%	142.00	6.0%	
	140.00	144.00	2.9%	138.00	-1.4%	
	148.00	158.00	6.8%	148.00	0.0%	140.00
	130.00	128.00	-1.5%	134.00	3.1%	
	138.00	140.00	1.4%	141.00	2.2%	
Mean:	138.00	141.67	2.6%	140.33	1.8%	
Standard Dev.:	6.07	9.75		4.68		
Down-hill 1	130.00	125.00	-3.8%	108.00	-16.9%	
	132.00	118.00	-10.6%	111.00	-15.9%	
	126.00	116.00	-7.9%	105.00	-16.7%	
	125.00	120.00	-4.0%	113.00	-9.6%	119.94
	137.00	115.00	-16.1%	112.00	-18.2%	
	131.00	122.00	-6.9%	113.00	-13.7%	
Mean:	130.17	119.33	-8.2%	110.33	-15.2%	
Standard Dev.:	4.36	3.78		3.20		
Down-hill 2	126.00	124.00	-1.6%	123.00	-2.4%	
	140.00	136.00	-2.9%	134.00	-4.3%	
	138.00	140.00	1.4%	136.00	-1.4%	
	142.00	136.00	-4.2%	140.00	-1.4%	131.11
	134.00	122.00	-9.0%	122.00	-9.0%	
	129.00	120.00	-7.0%	118.00	-8.5%	
Mean:	134.83	129.67	-3.9%	128.83	-4.5%	
Standard Dev.:	6.34	8.62		8.95		
MEAN	134.33	130.22		126.50		

Table 12 : Peak torque values (N.m) in the female hamstrings after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	83.00	81.00	-2.4%	78.00	-6.0%	82.39
	79.00	78.00	-1.3%	72.00	-8.9%	
	92.00	93.00	1.1%	84.00	-8.7%	
	79.00	82.00	3.8%	82.00	3.8%	
	86.00	84.00	-2.3%	77.00	-10.5%	
	89.00	86.00	-3.4%	78.00	-12.4%	
Mean:	84.67	84.00	-0.7%	78.50	-7.1%	
Standard Dev.:	5.32	5.18		4.18		
Down-hill 1	92.00	82.00	-10.9%	76.00	-17.4%	83.00
	80.00	77.00	-3.8%	73.00	-8.8%	
	98.00	93.00	-5.1%	81.00	-17.3%	
	82.00	80.00	-2.4%	75.00	-8.5%	
	94.00	83.00	-11.7%	70.00	-25.5%	
	98.00	88.00	-10.2%	72.00	-26.5%	
Mean:	90.67	83.83	-7.3%	74.50	-17.3%	
Standard Dev.:	7.87	5.78		3.83		
Down-hill 2	88.00	89.00	1.1%	86.00	-2.3%	90.50
	87.00	89.00	2.3%	84.00	-3.4%	
	94.00	96.00	2.1%	95.00	1.1%	
	92.00	98.00	6.5%	96.00	4.3%	
	93.00	90.00	-3.2%	82.00	-11.8%	
	89.00	88.00	-1.1%	93.00	4.5%	
Mean:	90.50	91.67	1.3%	89.33	-1.3%	
Standard Dev.:	2.88	4.23		6.06		
MEAN	88.61	86.50		80.78		

Table 13 : Peak torque values (N.m) in the male quadriceps after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running.

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	224.00	228.00	1.8%	216.00	-3.6%	
	221.00	224.00	1.4%	218.00	-1.4%	
	233.00	233.00	0.0%	216.00	-7.3%	
	240.00	246.00	2.5%	234.00	-2.5%	225.89
	211.00	213.00	0.9%	209.00	-0.9%	
	230.00	239.00	3.9%	231.00	0.4%	
Mean:	226.50	230.50	1.8%	220.67	-2.5%	
Standard Dev.:	10.13	11.61		9.71		
Down-hill 1	234.00	214.00	-8.5%	196.00	-16.2%	
	223.00	208.00	-6.7%	198.00	-11.2%	
	235.00	204.00	-13.2%	187.00	-20.4%	
	242.00	216.00	-10.7%	201.00	-16.9%	211.11
	218.00	200.00	-8.3%	189.00	-13.3%	
	234.00	211.00	-9.8%	190.00	-18.8%	
Mean:	231.00	208.83	-9.5%	193.50	-16.2%	
Standard Dev.:	8.81	6.08		5.61		
Down-hill 2	230.00	226.00	-1.7%	214.00	-7.0%	
	220.00	214.00	-2.7%	208.00	-5.5%	
	228.00	226.00	-0.9%	213.00	-6.6%	
	231.00	236.00	2.2%	226.00	-2.2%	218.78
	211.00	208.00	-1.4%	198.00	-6.2%	
	228.00	216.00	-5.3%	205.00	-10.1%	
Mean:	224.67	221.00	-1.6%	210.67	-6.2%	
Standard Dev.:	7.74	10.18		9.50		
MEAN	227.39	220.11		208.28		

Table 14 : Peak torque values (N.m) in the female quadriceps after uphill and downhill running.The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running.

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	161.00	166.00	3.1%	164.00	1.9%	153.17
	148.00	152.00	2.7%	150.00	1.4%	
	156.00	159.00	1.9%	152.00	-2.6%	
	138.00	133.00	-3.6%	130.00	-5.8%	
	165.00	161.00	-2.4%	150.00	-9.1%	
	152.00	162.00	6.6%	158.00	3.9%	
Mean:	153.33	155.50	1.4%	150.67	-1.7%	
Standard Dev.:	9.67	11.95		11.50		
Down-hill 1	175.00	168.00	-4.0%	152.00	-13.1%	149.94
	158.00	147.00	-7.0%	138.00	-12.7%	
	159.00	146.00	-8.2%	133.00	-16.4%	
	147.00	138.00	-6.1%	122.00	-17.0%	
	161.00	151.00	-6.2%	146.00	-9.3%	
	160.00	152.00	-5.0%	146.00	-8.8%	
Mean:	160.00	150.33	-6.1%	139.50	-12.9%	
Standard Dev.:	8.94	9.97		10.88		
Down-hill 2	162.00	159.00	-1.9%	150.00	-7.4%	153.28
	164.00	156.00	-4.9%	152.00	-7.3%	
	148.00	141.00	-4.7%	139.00	-6.1%	
	154.00	156.00	1.3%	146.00	-5.2%	
	158.00	150.00	-5.1%	149.00	-5.7%	
	162.00	157.00	-3.1%	156.00	-3.7%	
Mean:	158.00	153.17	-3.1%	148.67	-5.9%	
Standard Dev.:	6.07	6.68		5.79		
MEAN	157.11	153.00		146.28		

Table 15 : Torque at an angular velocity of 180°/seconds (N.m) in the male hamstrings after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	98.00	110.00	12.2%	115.00	17.3%	109.11
	111.00	108.00	-2.7%	114.00	2.7%	
	90.00	97.00	7.8%	99.00	10.0%	
	119.00	114.00	-4.2%	121.00	1.7%	
	105.00	116.00	10.5%	114.00	8.6%	
	109.00	110.00	0.9%	114.00	4.6%	
Mean:	105.33	109.17	4.1%	112.83	7.5%	
Standard Dev.:	10.21	6.65		7.31		
Down-hill 1	97.00	95.00	-2.1%	82.00	-15.5%	98.17
	114.00	106.00	-7.0%	92.00	-19.3%	
	110.00	96.00	-12.7%	87.00	-20.9%	
	111.00	87.00	-21.6%	74.00	-33.3%	
	108.00	101.00	-6.5%	89.00	-17.6%	
	115.00	108.00	-6.1%	95.00	-17.4%	
Mean:	109.17	98.83	-9.3%	86.50	-20.7%	
Standard Dev.:	6.49	7.78		7.56		
Down-hill 2	109.00	108.00	-0.9%	104.00	-4.6%	105.11
	118.00	114.00	-3.4%	116.00	-1.7%	
	90.00	93.00	3.3%	90.00	0.0%	
	116.00	114.00	-1.7%	112.00	-3.4%	
	104.00	101.00	-2.9%	98.00	-5.8%	
	106.00	100.00	-5.7%	99.00	-6.6%	
Mean:	107.17	105.00	-1.9%	103.17	-3.7%	
Standard Dev.:	10.05	8.44		9.60		
MEAN	107.22	104.33		100.83		

Table 16 : Torque at an angular velocity of 180°/seconds (N.m) in the female hamstrings after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	59.00	64.00	8.5%	57.00	-3.4%	
	72.00	70.00	-2.8%	58.00	-19.4%	
	68.00	66.00	-2.9%	72.00	5.9%	
	78.00	83.00	6.4%	75.00	-3.8%	64.33
	52.00	59.00	13.5%	42.00	-19.2%	
	63.00	64.00	1.6%	56.00	-11.1%	
Mean:	65.33	67.67	4.0%	60.00	-8.5%	
Standard Dev.:	9.33	8.31		12.02		
Down-hill 1	57.00	52.00	-8.8%	36.00	-36.8%	
	42.00	40.00	-4.8%	32.00	-23.8%	
	58.00	50.00	-13.8%	30.00	-48.3%	
	56.00	58.00	3.6%	49.00	-12.5%	53.00
	78.00	72.00	-7.7%	59.00	-24.4%	
	76.00	63.00	-17.1%	46.00	-39.5%	
Mean:	61.17	55.83	-8.1%	42.00	-30.9%	
Standard Dev.:	13.60	11.11		11.26		
Down-hill 2	59.00	49.00	-16.9%	51.00	-13.6%	
	48.00	40.00	-16.7%	42.00	-12.5%	
	56.00	52.00	-7.1%	55.00	-1.8%	
	76.00	69.00	-9.2%	70.00	-7.9%	54.89
	57.00	49.00	-14.0%	50.00	-12.3%	
	62.00	51.00	-17.7%	52.00	-16.1%	
Mean:	59.67	51.67	-13.6%	53.33	-10.7%	
Standard Dev.:	9.27	9.50		9.24		
MEAN	62.06	58.39		51.78		

Table 17 : Torque at an angular velocity of 180°/seconds (N.m) in the male quadriceps after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	165.00	173.00	4.8%	168.00	1.8%	162.39
	173.00	169.00	-2.3%	159.00	-8.1%	
	164.00	180.00	9.8%	176.00	7.3%	
	152.00	165.00	8.6%	163.00	7.2%	
	179.00	142.00	-20.7%	143.00	-20.1%	
	150.00	152.00	1.3%	150.00	0.0%	
Mean:	163.83	163.50	0.3%	159.83	-2.0%	
Standard Dev.:	11.37	14.07		11.99		
Down-hill 1	172.00	164.00	-4.7%	150.00	-12.8%	154.39
	168.00	156.00	-7.1%	146.00	-13.1%	
	164.00	152.00	-7.3%	129.00	-21.3%	
	175.00	160.00	-8.6%	142.00	-18.9%	
	142.00	131.00	-7.7%	115.00	-19.0%	
	182.00	170.00	-6.6%	161.00	-11.5%	
Mean:	167.17	155.50	-7.0%	140.50	-16.1%	
Standard Dev.:	13.78	13.53		16.28		
Down-hill 2	172.00	169.00	-1.7%	160.00	-7.0%	159.11
	173.00	168.00	-2.9%	159.00	-8.1%	
	136.00	138.00	1.5%	129.00	-5.1%	
	159.00	157.00	-1.3%	152.00	-4.4%	
	169.00	165.00	-2.4%	160.00	-5.3%	
	175.00	170.00	-2.9%	153.00	-12.6%	
Mean:	164.00	161.17	-1.6%	152.17	-7.1%	
Standard Dev.:	14.83	12.29		11.89		
MEAN	165.00	160.06		150.83		

Table 18 : Torque at an angular velocity of 180°/seconds (N.m) in the female quadriceps after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	92.00	89.00	-3.3%	78.00	-15.2%	94.28
	90.00	87.00	-3.3%	72.00	-20.0%	
	115.00	114.00	-0.9%	120.00	4.3%	
	86.00	84.00	-2.3%	78.00	-9.3%	
	99.00	92.00	-7.1%	89.00	-10.1%	
	118.00	103.00	-12.7%	91.00	-22.9%	
Mean:	100.00	94.83	-4.9%	88.00	-12.2%	
Standard Dev.:	13.49	11.44		17.26		
Down-hill 1	110.00	107.00	-2.7%	86.00	-21.8%	94.50
	89.00	82.00	-7.9%	84.00	-5.6%	
	125.00	120.00	-4.0%	92.00	-26.4%	
	94.00	79.00	-16.0%	70.00	-25.5%	
	110.00	92.00	-16.4%	90.00	-18.2%	
	102.00	85.00	-16.7%	84.00	-17.6%	
Mean:	105.00	94.17	-10.6%	84.33	-19.2%	
Standard Dev.:	12.93	16.12		7.74		
Down-hill 2	120.00	112.00	-6.7%	110.00	-8.3%	103.61
	100.00	96.00	-4.0%	94.00	-6.0%	
	113.00	126.00	11.5%	124.00	9.7%	
	92.00	89.00	-3.3%	88.00	-4.3%	
	114.00	97.00	-14.9%	96.00	-15.8%	
	106.00	98.00	-7.5%	90.00	-15.1%	
Mean:	107.50	103.00	-4.1%	100.33	-6.6%	
Standard Dev.:	10.27	13.54		13.94		
MEAN	104.17	97.33		90.89		

Table 19 : Endurance ratio values (%) in the male hamstrings after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	110.00	93.00	-15.5%	114.00	3.6%	100.50
	96.00	84.00	-12.5%	98.00	2.1%	
	105.00	90.00	-14.3%	103.00	-1.9%	
	82.00	79.00	-3.7%	85.00	3.7%	
	128.00	112.00	-12.5%	130.00	1.6%	
	103.00	92.00	-10.7%	105.00	1.9%	
Mean:	104.00	91.67	-11.5%	105.83	1.8%	
Standard Dev.:	15.24	11.29		15.20		
Down-hill 1	94.00	86.00	-8.5%	82.00	-12.8%	90.78
	102.00	95.00	-6.9%	86.00	-15.7%	
	97.00	89.00	-8.2%	82.00	-15.5%	
	82.00	72.00	-12.2%	70.00	-14.6%	
	126.00	110.00	-12.7%	99.00	-21.4%	
	93.00	87.00	-6.5%	82.00	-11.8%	
Mean:	99.00	89.83	-9.2%	83.50	-15.3%	
Standard Dev.:	14.78	12.45		9.33		
Down-hill 2	93.00	89.00	-4.3%	87.00	-6.5%	95.11
	103.00	98.00	-4.9%	96.00	-6.8%	
	98.00	93.00	-5.1%	89.00	-9.2%	
	81.00	79.00	-2.5%	72.00	-11.1%	
	125.00	120.00	-4.0%	113.00	-9.6%	
	94.00	93.00	-1.1%	89.00	-5.3%	
Mean:	99.00	95.33	-3.6%	91.00	-8.1%	
Standard Dev.:	14.68	13.66		13.37		
MEAN	100.67	92.28		93.44		

Table 20 : Endurance ratio values (%) in the female hamstrings after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	85.00	83.00	-2.4%	90.00	5.9%	
	63.00	60.00	-4.8%	62.00	-1.6%	
	74.00	75.00	1.4%	78.00	5.4%	
	72.00	73.00	1.4%	70.00	-2.8%	72.00
	69.00	62.00	-10.1%	71.00	2.9%	
	70.00	66.00	-5.7%	73.00	4.3%	
Mean:	72.17	69.83	-3.4%	74.00	2.4%	
Standard Dev.:	7.31	8.75		9.40		
Down-hill 1	89.00	72.00	-19.1%	63.00	-29.2%	
	73.00	74.00	1.4%	68.00	-6.8%	
	82.00	85.00	3.7%	73.00	-11.0%	
	69.00	69.00	0.0%	65.00	-5.8%	72.50
	76.00	63.00	-17.1%	72.00	-5.3%	
	78.00	65.00	-16.7%	69.00	-11.5%	
Mean:	77.83	71.33	-8.0%	68.33	-11.6%	
Standard Dev.:	7.03	7.87		3.88		
Down-hill 2	94.00	69.00	-26.6%	62.00	-34.0%	
	64.00	63.00	-1.6%	66.00	3.1%	
	73.00	85.00	16.4%	71.00	-2.7%	
	72.00	72.00	0.0%	77.00	6.9%	72.33
	69.00	74.00	7.2%	80.00	15.9%	
	83.00	65.00	-21.7%	63.00	-24.1%	
Mean:	75.83	71.33	-4.4%	69.83	-5.8%	
Standard Dev.:	10.87	7.87		7.47		
MEAN	75.28	70.83		70.72		

Table 21 : Endurance ratio values (%) in the male quadriceps after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	114.00	102.00	-10.5%	109.00	-4.4%	
	96.00	92.00	-4.2%	94.00	-2.1%	
	84.00	90.00	7.1%	98.00	16.7%	
	106.00	92.00	-13.2%	102.00	-3.8%	98.78
	109.00	101.00	-7.3%	101.00	-7.3%	
	101.00	89.00	-11.9%	98.00	-3.0%	
Mean:	101.67	94.33	-6.7%	100.33	-0.6%	
Standard Dev.:	10.67	5.68		5.09		
Down-hill 1	108.00	104.00	-3.7%	93.00	-13.9%	
	98.00	80.00	-18.4%	70.00	-28.6%	
	94.00	82.00	-12.8%	72.00	-23.4%	
	102.00	92.00	-9.8%	82.00	-19.6%	90.33
	98.00	94.00	-4.1%	84.00	-14.3%	
	102.00	93.00	-8.8%	78.00	-23.5%	
Mean:	100.33	90.83	-9.6%	79.83	-20.5%	
Standard Dev.:	4.80	8.77		8.45		
Down-hill 2	120.00	115.00	-4.2%	98.00	-18.3%	
	92.00	89.00	-3.3%	78.00	-15.2%	
	93.00	87.00	-6.5%	80.00	-14.0%	
	112.00	106.00	-5.4%	94.00	-16.1%	97.50
	99.00	89.00	-10.1%	90.00	-9.1%	
	104.00	102.00	-1.9%	107.00	2.9%	
Mean:	103.33	98.00	-5.2%	91.17	-11.6%	
Standard Dev.:	11.02	11.42		11.00		
MEAN	101.78	94.39		90.44		

Table 22 : Endurance ratio values (%) in the female quadriceps after uphill and downhill running. The data is given as individual absolute values, as well as mean, standard deviation, and percent change after uphill and downhill running

	Pre-Exercise	Post-Exercise		24 Hour Post-Exercise		
	Measured Values	Measured Values	Percentage Change	Measured Values	Percentage Change	MEAN
Up-hill	98.00	83.00	-15.3%	96.00	-2.0%	88.33
	92.00	84.00	-8.7%	94.00	2.2%	
	102.00	96.00	-5.9%	104.00	2.0%	
	78.00	83.00	6.4%	80.00	2.6%	
	86.00	78.00	-9.3%	83.00	-3.5%	
	85.00	80.00	-5.9%	88.00	3.5%	
Mean:	90.17	84.00	-6.4%	90.83	0.8%	
Standard Dev.:	8.91	6.29		8.91		
Down-hill 1	103.00	92.00	-10.7%	79.00	-23.3%	84.83
	92.00	84.00	-8.7%	78.00	-15.2%	
	98.00	83.00	-15.3%	68.00	-30.6%	
	85.00	82.00	-3.5%	69.00	-18.8%	
	96.00	85.00	-11.5%	78.00	-18.8%	
	89.00	90.00	1.1%	76.00	-14.6%	
Mean:	93.83	86.00	-8.1%	74.67	-20.2%	
Standard Dev.:	6.49	4.05		4.89		
Down-hill 2	94.00	85.00	-9.6%	82.00	-12.8%	89.11
	80.00	98.00	22.5%	87.00	8.8%	
	91.00	78.00	-14.3%	95.00	4.4%	
	89.00	86.00	-3.4%	84.00	-5.6%	
	104.00	102.00	-1.9%	82.00	-21.2%	
	96.00	92.00	-4.2%	79.00	-17.7%	
Mean:	92.33	90.17	-1.8%	84.83	-7.4%	
Standard Dev.:	7.97	8.91		5.64		
MEAN	92.11	86.72		83.44		

Table 23 Perceived muscle soreness questionnaire responses after uphill and downhill running

	Pre-Exercise		Post-Exercise		24 Hour Post-Exercise	
	0	0	0	0	0	0
	0	0	0	0	0	0
Up-hill	0	0	0	0	2	2
	0	0	2	2	0	0
	0	0	0	0	0	2
	0	0	2	2	0	2
	0	0	0	2	4	6
	0	0	2	2	2	4
Downhill 1	0	0	4	2	4	2
	0	0	2	4	4	6
	0	0	2	4	4	6
	0	0	2	4	2	2
	0	0	0	2	2	2
	0	0	0	0	2	2
Downhill 2	0	0	2	0	4	2
	0	0	2	2	4	2
	0	0	0	2	2	2
	0	0	0	2	4	2

0 = complete absence of soreness

2 = light pain felt only on palpation

4 = moderate pain , some stiffness and/or weakness during movement

6 = severe pain that limits the range of motion