
Abstract: Upper-limb orthotic systems have been designed for restoring the upper-limb functions of individuals with disabilities resulting from spinal cord injury (SCI), stroke and muscular dystrophy. These systems employ either functional electrical stimulation or external power. It is proposed that, instead of time-consuming and complicated monitoring using sensors and motion analysis, a software simulator with both angular displacement and acceleration parameters can facilitate the design of a control strategy for an orthosis. Reaching movements of three cervical SCI subjects are used to verify the simulator. A motion analysis system is used to measure the range of motion and joint angles during hand reaching. Results indicate that quaternion and spline curve techniques are suitable for interpolation of the hand reaching movements. The information needed for good simulation only compress the shoulder and elbow joint angles in a few key postures. Stimulated acceleration signals on the upper-arm segment have a high correlation coefficient (> 0.9) and a small root mean squared error (< 0.11 g) with a real bi-axial accelerometer.


Abstract: It has been proposed that aquaporin-4 (AQP4), a water channel expressed at the plasmalemma of skeletal muscle cells, is important in normal muscle physiology and in the pathophysiology of Duchenne's muscular dystrophy. To test this hypothesis, muscle water permeability and function were compared in wild-type and AQP4 knockout mice. Immunofluorescence and freeze-fracture electron microscopy showed AQP4 protein expression in plasmalemma of fast-twitch skeletal muscle fibers of wild-type mice. Osmotic water permeability was measured in microdissected muscle fibers from the extensor digitorum longus (EDL) and fractionated membrane vesicles from EDL homogenates. With the use of spatial-filtering microscopy to measure osmotically induced volume changes in EDL fibers, half times (t(1/2)) for osmotic equilibration (7.5-8.5 s) were not affected by AQP4 deletion. Stopped-flow light-scattering measurements of osmotically induced volume changes in plasmalemma vesicles also showed no significant differences in water permeability. Similar water permeability, yet approximately 90% decreased AQP4 protein expression was found in EDL from mdx mice that lack dystrophin. Skeletal muscle function was measured by force generation in isolated EDL, treadmill performance time, and in vivo muscle swelling in response to water intoxication. No differences were found in EDL force generation after electrical stimulation [42 +/- 2 (wild-type) vs. 41 +/- 2 (knockout) g/s], treadmill performance time (22 vs. 26 min; 29 m/min, 13 degrees incline), or muscle swelling (2.8 vs. 2.9% increased water content at 90 min after intraperitoneal water infusion). Together these results provide evidence against a significant role of AQP4 in skeletal muscle physiology in mice.


Abstract: The study of the underlying mechanisms by which cells respond to
mechanical stimuli, i.e. the link between the mechanical stimulus and gene expression, represents a new and important area in the morphological sciences. Several cell types (‘mechanocytes’), e.g. osteoblasts and fibroblasts as well as smooth, cardiac and skeletal muscle cells are activated by mechanical strain and there is now mounting evidence that this involves the cytoskeleton. Muscle offers one of the best opportunities for studying this type of mechanotransduction as the mechanical activity generated by and imposed upon muscle tissue can be accurately controlled and measured in both in vitro and in vivo systems. Muscle is highly responsive to changes in functional demands. Overload leads to hypertrophy, whilst decreased load force generation and immobilisation with the muscle in the shortened position leads to atrophy. For instance it has been shown that stretch is an important mechanical signal for the production of more actin and myosin filaments and the addition of new sarcomeres in series and in parallel. This is preceded by upregulation of transcription of the appropriate genes some of which such as the myosin isoforms markedly change the muscle phenotype. Indeed, the switch in the expression induced by mechanical activity of myosin heavy chain genes which encode different molecular motors is a means via which the tissue adapts to a given type of physical activity. As far as increase in mass is concerned, our group have cloned the cDNA of a splice variant of IGF-1 that is produced by active muscle that appears to be the factor that controls local tissue repair, maintenance and remodelling. From its sequence it can be seen that it is derived from the IGF-1 gene by alternative splicing but it has different exons to the liver isoforms. It has a 52 base insert in the E domain which alters the reading frame of the 3’ end. Therefore, this splice variant of IGF-1 is likely to bind to a different binding protein which exists in the interstitial tissue spaces of muscle, neuronal tissue and bone. This would be expected to localise its action as it would be unstable in the unbound form which is important as its production would not disturb the glucose homeostasis unduly. This new growth factor has been called mechano growth factor (MGF) to distinguish it from the liver IGFs which have a systemic mode of action. Although the liver is usually thought of as the source of circulating IGF-1, it has recently been shown that during exercise skeletal muscle not only produces much of the circulating IGF-1 but active musculature also utilises most of the IGF-I produced. We have cloned both an autocrine and endocrine IGF-1, both of which are upregulated in cardiac as well as skeletal muscle when subjected to overload. It has been shown that, in contrast to normal muscle, MGF is not detectable in dystrophic mdx muscles even when subjected to stretch and stretch combined with electrical stimulation. This is true for muscular dystrophies that are due to the lack of dystrophin (X-linked) and due to a laminin deficiency (autosomal), thus indicating that the dystrophin cytoskeletal complex may be involved in the mechanotransduction mechanism. When this complex is defective the necessary systemic as well as autocrine IGF-1 growth factors required for local repair are not produced and the ensuing cell death results in progressive loss of muscle mass. The discovery of the locally produced IGF-1 appears to provide the link between the mechanical stimulus and the activation of gene expression.


Abstract: Persistent atrial standstill is an uncommon clinical finding, this condition has no atrial electrical activity and do not respond to electrical stimulation. Electrophysiologic mapping of the heart, demonstrates two types of standstill: total
and partial. There are three types of patients with this condition: patients with chronic cardiopathy, patients with muscular dystrophy and the third idiopathic group. In this article, we present two clinical cases, the first one with dilated cardiomiopathy, in which we demonstrated total atrial standstill. The second patient with rheumatic heart disease, in which we demonstrated partial standstill that included the apical portion of the right atrium. We discuss the clinical and electrophysiological finding of both cases and we review the literature.


Abstract: We present an in vitro model in which mouse skeletal muscle fibers undergo degeneration by increasing the current strength of tetanic stimulation. To understand the mechanisms of muscle fiber necrosis in Duchenne muscular dystrophy patients, the process of fiber degeneration was compared between mdx and control mice. The process consisted of four steps, beginning with muscle fiber contraction and extending to onset of myofibril disruption. The four processes were not observed in fibers in Krebs-HEPES (-Ca2+) buffer, nor in the presence of L-type Ca2+ channel blockers. These results suggest that this degenerative phenomenon is regulated by intracellular Ca2+, which moved into fibers mainly through voltage-dependent L-type Ca2+ channels. With the exception of myofibril disruption, mdx mice also exhibited the three other steps, but at a significantly lower current strength than in the fibers in the control mice. We postulate that excess Ca2+ flux occurs in fibers, mainly through abnormal L-type Ca2+ channels, and that the excessively accumulated calcium results in premature degeneration of the fibers by tetanic contraction. This study would provide a clue to investigate and prevent the degeneration processes in Duchenne muscular dystrophy.


Abstract: Twelve children with progressive muscular dystrophy (10 Duchenne and 2 Becker type) were included in a low-frequency electrical stimulation (LFES) program of the right tibialis anterior (TA) muscle for three months. Muscle strength was estimated by measuring torques in the ankle during short attempts of maximal voluntary isometric contraction (MVIC) in the direction of dorsal flexion of the foot. Muscle fatigue was assessed by the decrease of force during sustained (1-minute) voluntary contraction. The measurements were carried out before the beginning of the stimulation program and immediately after its conclusion. At the end of the stimulation program there were higher torques in 10 out of 12 children in the stimulated leg. The increase in torques in the stimulated leg was statistically significant (p < 0.01). Regarding the fatigue of the stimulated muscle there was no change after the conclusion of stimulation.


Abstract: Nine children suffering from progressive muscular dystrophy (7 Duchenne and 2 Becker) were included in a program of low-frequency electrical stimulation (LFES) of the right tibialis anterior (TA) muscle. Muscle strength and muscle fatigue were estimated by measuring torques in the ankle during attempts of maximal voluntary contraction (MVC) in the direction of dorsal flexion of the foot and during
electrically evoked contractions (EEC). No important increase in the strength of the stimulated muscles was noticed in 4 boys whose muscles were stimulated for 3 months. The muscles of 5 boys who were subjected to electrical stimulation for 9 months showed an improvement; 6 measurements made during the stimulation program revealed that changes of torques in the ankle of the right stimulated extremity were significantly different (P less than 0.001) from the changes of torques in the ankle of the left nonstimulated extremity.


Abstract: Duchenne muscular dystrophy (DMD) is an X-linked disease characterized by progressive muscle weakness and degeneration. Dystrophin is the product of the missing gene in this disorder. However, the cause of the dystrophic process is not understood. Transient muscle injury is normally seen after muscle exercise, and may be a necessary process in muscle growth and preservation. We, therefore, chose to evaluate the role of exercise in Duchenne dystrophy by studying the canine X-linked animal model (CXMD). These dogs also lack dystrophin and have clinical signs similar to humans. Exercise was initiated by electrical stimulation, and muscle metabolism was monitored with phosphorus magnetic resonance spectroscopy (P-MRS). Dogs with CXMD had abnormal muscle pathology and markedly elevated serum CK. The inorganic phosphate (Pi) to phosphocreatine (PCr) ratio was increased in CXMD dogs at rest compared with normal dogs (Pi/(Pi + PCr) = 0.166 +/- 0.054 for CXMD and 0.073 +/- 0.017 for normals, mean +/- SE). No changes in resting ATP, pH, phosphomonoesters (PME), and phosphodiesters (PDE) were seen. The mean Pi/(Pi + PCr) and pH values during stimulation were normal in the CXMD dogs. Two to three days after electrical stimulation, resting Pi/(Pi + PCr) ratios were significantly increased in the CXMD dogs (0.127 +/- 0.029 compared with 0.172 +/- 0.054, mean +/- SD). Normal dogs showed no increase in Pi/(Pi + PCr) following stimulation. There was a 50-fold greater increase in serum CK in CXMD compared with normal dogs following exercise. These results indicate greater muscle injury in CXMD muscle, and suggest that in the absence of dystrophin, exercise-induced muscle injury may play a role in the dystrophic process.


Abstract: Direct electrical stimulation with paired pulses at varied intervals was used to study the propagation velocity and action potential amplitude recovery functions (VRF and ARF) of single muscle fibers. Following a subnormal period with slowed conduction, most of the muscle fibers tested in healthy subjects showed a period of supernormal propagation velocity starting at 3 to 12 ms, with a peak between about 5 and 15 ms, a mean increase of 7%, and an approximately logarithmic decay toward 1 second. The onset of supernormality was earlier in muscle fibers from patients with muscular dystrophy and significantly delayed in those from denervated muscles. Denervated muscle fibers also had a significantly longer refractory period.


Abstract: To evaluate the therapeutic possibilities of chronic electrical stimulation, muscle function studies and quantitative tests of physical assessment were used to
monitor the response of quadriceps femoris to prolonged low frequency stimulation. Comparative studies of the maximum voluntary and electrically elicited responses of muscles of young ambulant children with Duchenne muscular dystrophy, when compared to those of normal children's muscles, revealed lower values of maximum voluntary contraction, significant slowing (P less than 0.001) of mean relaxation times and a higher resistance to fatigue testing. Intermittent chronic low frequency stimulation resulted in a significant (P less than 0.01) increase in mean maximum voluntary contraction of the stimulated muscles compared with the mean force exerted by the unstimulated control muscles. There are clear therapeutic possibilities for the use of chronic low frequency stimulation in these children.


Abstract: Low frequency chronic electrical stimulation can have a beneficial effect on dystrophic muscles. The present study was undertaken to assess the long term effect of such stimulation on the fast hind limb muscles of dystrophic mice. The relationship between the changes induced by stimulation and the initial condition of the dystrophic muscles, as well as other factors which might contribute to this relationship, were examined. The stimulation induced an increase in the force output of weak dystrophic muscles and a speeding of their time course of contraction and relaxation, as well as an increase in their fatigue resistance. In relatively strong dystrophic muscles, the stimulation induced similar changes in contractile speed and fatigue characteristics, but it led to a slight decrease in force output. Our results suggest that the stimulation promotes the growth and differentiation of the small regenerating fibres known to be present in the diseased muscles and, in addition, induces an increase in the mitochondrial content of the muscle fibres. Our results indicate that these effects are not permanent.


Abstract: We have previously reported that, in dystrophic mice, functional overload has a damaging effect on the tibialis anterior (TA) muscle. In the present study, we have examined the effect of a load reduction on the TA and extensor digitorum longus (EDL) muscles. Our results show that reducing the passive load to which these muscles are subjected in dystrophic mice by resecting the Achilles tendon has a beneficial effect. The force output of the "released" EDL muscle improved, while the time course of contraction and relaxation of the "released" TA muscle became faster. Also in this muscle, resistance to fatigue became significantly greater. Low frequency electrical stimulation of the "released" muscles via implanted electrodes had little effect on their force output. It led, however, to a relative speeding of their time course of contraction and relaxation and to a further increase in their resistance to fatigue. Taken together, our results suggest that the beneficial effect of low frequency electrical stimulation on the force output of weak dystrophic muscles, described in the preceding paper, might be conditioned by the load to which these muscles are subjected.


Abstract: In children isometric muscle force can be measured with acceptable...
reproducibility by using a simple hand-held dynamometer. Reference values for 10 different muscle groups are given for children aged 3.5-15 years. If age and weight are known, the force can be predicted. The most pronounced differences between the dominant and the non-dominant side were found in the elbow flexors, 3 of the 6 age groups showing greater force on the dominant side, and in the wrist extensors, the 2 oldest age groups being stronger on the dominant side. Sex differences were present as early as 9.5-11 years of age, boys being stronger than girls. Isokinetic muscle torque of the dorsiflexors of the ankle increased with age. Reference values are given for peak torque in children 6, 9, 12, and 15 years of age. The most intense force development occurs between 12 and 15 years of age in boys, and earlier in girls. Sex differences appear in early puberty. In young children the dominant leg was the stronger at the highest velocities. In the older children the non-dominant leg was the stronger at low velocities. Isokinetic measurements are time-consuming and require experience, and should be regarded as complementary to isometric testing. In muscle groups that are too weak to overcome gravity isometric and isokinetic methods cannot be used. Functional tests of motor ability are especially useful in patients with severely impaired muscle function when other test methods are inadequate or difficult to evaluate. The natural course of Duchenne muscular dystrophy was followed in 16 boys by means of functional tests, isometric tests, isokinetic tests of concentric muscle contraction, and manual tests. Of these only the isokinetic method proved unreliable, possibly because of difficulty in activating the muscles at different speeds. The function of adductor pollicis was studied by supramaximal electrical stimulation of the ulnar nerve. Force-frequency curves and reference values for relaxation rate and half contraction time to tetanus for children aged 9, 12, and 15 years are presented. The half contraction time to tetanus was briefer in the older children than in the younger. The relative force developed at a stimulation of 10 Hz increased with age. Apart for the increase in muscle force with increasing age, no other differences emerged between the different age groups. No sex differences were found. The electrical stimulation test is rather painful, and only about 60% of the children persevered to the end of the test.(ABSTRACT TRUNCATED AT 400 WORDS)

Abstract: It is well established that the properties of muscle fibres are influenced by their neurons and that this is at least in part mediated by the pattern of activity. Application of this knowledge has led to the experimental trial of electrical stimulation in diseased muscle, both in the dystrophic mouse and in children with Duchenne muscular dystrophy. This has shown a beneficial effect of slow frequency stimulation. Another route through which muscle properties can be influenced is by changing the load by procedures such as tenotomy. This has been studied by complete tenotomy in normal animals and recently by selective partial procedures in human disease. Y. Rideau has shown that release of early shortening (contractures) of several muscles, a consistent feature in Duchenne muscular dystrophy, has a beneficial effect on muscle function. From personal observations on a number of Rideau's patients who have undergone this procedure the improvement in function seems disproportionate to what could be explained on simple biomechanical grounds alone and suggests some more fundamental change in the contractile properties of the muscle

Abstract: To determine the possible sources of variation in performance indicators used in therapeutic trials, electrical stimulation techniques were used to measure contractile properties of the adductor pollicis and quadriceps muscles in boys with Duchenne muscular dystrophy. As no therapeutic effects were observed, longitudinal data obtained are taken to indicate changes in disease progress. Variance in voluntary contractions was found to be similar to that with electrically stimulated contractions; thus, variation could not be attributed to motivational changes, but rather to physiologic changes. Dystrophic muscle was slower to relax and less fatiguable than normal. However, such changes are of less significance to the overall disability compared to the loss of muscle bulk (cross-sectional area). Important variations in the function of individual muscles essential to complex performance, such as walking or getting up from the floor, could be masked by combining results from several muscle groups.


Abstract: The effect of chronic low frequency stimulation on the tibialis anterior muscle of children with Duchenne muscular dystrophy was investigated. Baseline data from 16 boys established low values of maximum voluntary contraction which did not improve with age. Studies of the contractile properties revealed significant slowing (p less than 0.001) of mean relaxation time compared to that of normal children's muscles. There was no loss of force during fatigue testing, as in normal children, but in contrast to normal children, there was no potentiation at lower frequencies of stimulation. Intermittent chronic low frequency stimulation of muscles in six young ambulant children with Duchenne muscular dystrophy resulted in a significant increase (p less than 0.05) in mean maximum voluntary contraction compared with the mean forces exerted by the unstimulated control muscles of the contralateral leg.


Abstract: The fast-twitch posterior latissimus dorsi muscle of normal and genetically dystrophic chickens was subjected to continuous indirect electrical stimulation at 10 Hz for periods of 4-8 weeks. To sustain this in vivo nerve stimulation an internally implantable miniature stimulator device was designed. This regime of stimulation caused complete fatigue of the normal muscle within 5 min of its initiation. The dystrophic muscles maintained a very small degree of contractile activity during this initial phase. Tangible twitching of the muscle returned in 5 week birds between 3 and 5 days and in 10 week birds between 11 and 16 days after implantation. After 4 weeks of stimulation, no significant change was measured in the time-to-peak of the isometric twitch response, nor in the half-relaxation time. The resistance to fatigue was significantly increased in the stimulated muscles when tested with a series of tetani at 40 Hz. The mean fibre area was decreased, in all muscles stimulated for longer than 3 weeks, in comparison to their contralateral controls, except where fibre splitting in dystrophic birds abnormally reduced the control value. The majority fibre type of the muscle was changed from type IIB to IIA. The histochemical reactions for both NADH-linked oxidation and phosphorylase were distinctly increased in the stimulated muscles. In normal muscle, stimulation increased somewhat the number
of nuclei per unit area and changed their intracellular distribution, so that a greater proportion was found adjacent to the sarcolemma. The normal posterior latissimus dorsi muscle responded to chronic stimulation with increases of 3-6-fold in its acetylcholinesterase (AChE) activity. The maximum change in AChE occurred after 2 weeks stimulation; a steady level, 3 times that of the control unstimulated muscle, persisted at later times. Chronic stimulation suppressed the over-production of AChE that is characteristic of dystrophic chicken fast-twitch muscle, to attain a level comparable to the AChE activity in a stimulated normal muscle. Stimulation exerted a strong normalizing influence on dystrophic muscle, as assessed morphologically. The characteristic fibre rounding, fibre hypertrophy and myonuclear proliferation were reduced. This influence was most marked where the stimulation was initiated before the major pathological changes had occurred, but was also significant when commenced in strongly affected birds of 10-11 weeks.


Abstract: It has been reported that chronic electrical stimulation at low frequency applied to dystrophic muscles has a beneficial effect. In this study, the effect of this treatment on the passive membrane properties of muscle fibers from dystrophic mice was followed. Cable properties were assessed by the two-microelectrodes DC method and spatial decay analysis. Earlier results showing a decrease in resting potential, an increase in input resistance and in specific membrane resistance in muscle fibers from dystrophic mice were confirmed. In addition, the specific membrane capacitance of these muscle fibers was found to be lower than normal. This suggests that the membrane properties of fibers from dystrophic muscles are similar to those of immature muscle fibers. Muscle fibers from dystrophic animals that were stimulated for 2 to 4 weeks had membrane properties similar to those from normal muscles. This indicates that electrical stimulation at low frequency for 2 to 4 weeks restores membrane properties of dystrophic muscle fibers to normal and we suggest that an appropriate pattern of stimulation induces the maturation of dystrophic muscle fibers.


Abstract: Muscular potentials were evoked by electrical stimulation of sciatic nerves and recorded from gastrocnemius muscles in dystrophic and normal mice. When frequency of stimulation was accelerated from 0.5 to 5 per sec and continued, the potentials were depressed to a notable extent in normal mice, whereas only a slight decrease or even an increase in them was observed in dystrophic mice. Thus, a simple method has been developed to differentiate pre- and/or postjunctional properties for impulse transmission in dystrophic mice from those in normal mice.


Abstract: Energy liberation and isometric force generation were compared at 25 degrees C in isolated normal (n = 15) and dystrophic (n = 18) posterior latissimus dorsi muscles (PLD) from 16- to 33-day-old chickens. Twitch-energy liberation in dystrophic muscle decreased by 27 +/- 6%, and force per cross-sectional area decreased by 26 +/- 11%. Tetanic energy liberation in dystrophic PLD was
depressed by 32 +/- 10% compared with a 22 +/- 9% reduction in peak force per cross-sectional area plus a 26 +/- 3% reduction in ability to maintain force. Normalizing results using the force-time integral demonstrates an unaltered force generation per unit energy liberation in dystrophic PLD (7 +/- 11% difference from normal). Kinetic properties of the mechanical responses were not significantly different in normal compared with dystrophic PLD. Dystrophic PLD demonstrated hyperexcitability to nerve transection and electrical stimulation. Although force-generating capacity is reduced in dystrophic PLD, coupling of force production to energy utilization appears unaltered.


Abstract: The deterioration of tibialis anterior (TA) and extensor digitorum longus (EDL) muscles in dystrophic mice (C 57 BL dy/dy) was compared. The effects of chronic electrical stimulation on various characteristic properties of these muscles were also studied. The results indicate that EDL muscles are less affected by the disease than TA. This "selectivity" is difficult to explain since both muscles have similar fibre type composition. TA and EDL muscles that were stimulated for 10-28 days developed greater tetanic tensions than the contralateral muscles, but this effect was apparent only when the muscles were severely affected by the disease, that is the contralateral TA or EDL muscles developed less than 50% of the tension produced by muscles from normal animals. In all EDL muscles, stimulation increased the fatigue resistance. The time course of contraction and relaxation of dystrophic muscles is usually slower than that of normal muscles. The stimulation reduced this slowing effect, so that the stimulated muscles became similar to homologous muscles from normal littermates.


Abstract: The hind leg muscles of dystrophic mice (C57 BL dy2J/dy2J) were chronically stimulated at 10 Hz for 30 minutes six times a day. After 14 days of such activity a clinical improvement in the use of the stimulated leg was noticed. The twitch and tetanic tensions developed by the stimulated tibialis anterior and extensor digitorum longus muscles were higher than those developed by the control, unstimulated muscles on the contralateral side. Histochemically visualised activity of the oxidative enzyme succinic dehydrogenase was greater in fibres of the stimulated muscles. The stimulated muscles contained more muscle fibres than unstimulated controls. It is concluded that slow frequency activity has a beneficial effect on muscles of dystrophic mice.