Reports


Effect of Antagonist Weakening on Developed Tension in Cat Extraocular Muscle

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Purpose. In a previous study, the authors found that recession of an extraocular muscle resulted in atrophy of both the recessed muscle and its antagonist. To determine if atrophy, caused by weakening of an extraocular muscle, results in changes in developed tension in the antagonist, the authors studied force development of the cat lateral rectus muscle after adductor weakening.

Methods. Tenotomy of the left inferior, medial, and superior rectus muscles was performed in 18 cats. At 3, 6, and 12 weeks after surgery, the right (control) and left lateral rectus muscles were exposed through a lateral orbitotomy and were attached to isometric force transducers. Length–tension curves were obtained by direct muscle stimulation using bipolar contact electrodes at 0.1 Hz and 50% suprathreshold stimulus intensity. In addition, peak tetanic tension was measured at the optimal resting tension using a 5-second stimulus train at 200 Hz. Pooled data from the operative and control muscles at each postoperative interval were compared.

Results. Three weeks after adductor weakening, a 28% decrease in maximal single-twitch tension was seen in the left lateral rectus muscle when compared with controls. This difference disappeared at 6 weeks. No statistically significant changes in peak tetanic tension occurred at any time interval after surgery.


Patients with strabismus have congenital or acquired misalignment of the ocular axes. If the alignment is stable, we can assume that the elastic forces across the involved extraocular muscles are at equilibrium. These elastic forces consist of the elasticity of orbital tissue other than muscle, the elasticity of the extraocular muscles to passive stretch, and the elasticity associated with muscle contraction. Strabismus surgery alters this equilibrium by changing the rotational position of the globe and by changing the resting tension of the operated muscles. Recession of a horizontal rectus muscle, for example, results in a profound drop in the resting tension of that muscle at the new insertion site.

Studies in limb muscle have shown that long-term changes in resting tension result in changes in muscle fiber morphometry. Decreased tension causes muscle fiber atrophy; increased tension results in compensatory hypertrophy. Our previous studies in extraocular muscle indicated that a similar phenomenon occurs after strabismus surgery. Recession procedures cause atrophy of both the recessed muscle and its antagonist, whereas resection causes hypertrophy of the agonist–antagonist pair. These findings suggest that the change in resting tension caused by the procedure affects both the operated muscle and its antagonist(s). Changes in extraocular muscle morphometry are transient. Fiber diameters returned to normal within 2 to 3 months in recession and resection preparations.

The purpose of the current study was to determine whether the atrophy observed after recession of extraocular muscles results in any changes in developed tension in the antagonist, using the cat as a model.

METHODS. Eighteen cats were premedicated with intramuscular atropine, 0.05 mg/kg, and a mixture of ketamine, 20 mg/kg, and xylazine, 1 mg/kg. After endotracheal intubation, anesthesia was continued with isoflurane. The animals were ventilated continuously, and core body temperature was monitored.

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and maintained within the normal range with a heating pad. Tenotomy of the left inferior, medial, and superior rectus muscles was performed through a conjunctival peritomy. We elected to weaken all the adductors in this fashion because doing so results in a small exotropia of the operated eye immediately after surgery. Tenotomy of the medial rectus alone did not result in any appreciable change in eye alignment. The cat with the largest exotropic shift was photographed 1 week after surgery. The angle of exotropia in this cat was estimated at 15° by comparing the corneal light reflexes in the operated and unoperated eyes. A combination ointment containing 0.3% tobramycin and 0.1% dexamethasone was placed in the operated eye. Buprenorphine (0.05 mg/kg) was administered as needed for analgesia. No evidence of anterior segment ischemia was noted in any of the operated eyes.

The animals were maintained in animal care facilities accredited by the American Association of Laboratory Sciences. The project followed established rules of safe use of laboratory animals, and it was approved by the local Institutional Animal Care and Use Committee. The investigational protocol was in accord with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

At 3-, 6-, and 12-week intervals after surgery, six cats each were reanesthetized and monitored as described above. The cat's head was mounted in a stereotactic head holder and secured to prevent any head movement. The lateral rectus muscles of both orbits were exposed through a lateral orbitotomy, and the insertional tendons were transected from the globe. The tendons were attached to isometric force transducers (Grass FT-03; Astro-Med, West Warwick, RI) with 3-0 silk. The force transducers were mounted on a direct writing polygraph (Gould WindowGraf; Gould, Valley View, OH). This approach was chosen to study the muscles in situ in the live, anesthetized animal, thus maintaining normal temperature and adequate perfusion of the muscles.

The muscles were stimulated directly by bipolar platinum contact electrodes at 0.1 Hz, 50% above threshold voltage (minimum, 5 V), and 0.4-msec impulse duration. Electrodes were positioned on the distal third of the muscle, near the insertional tendon, to avoid indirect stimulation of the muscle by terminal nerves or the endplate region. Isometric length-tension curves were established for each muscle by varying the preload (resting tension) over a range from 0.2 to 60 g. Preload was increased stepwise by adjusting the resting muscle length after developed tension reached a plateau for 10 consecutive single twitches. In addition, tetanic tension development was tested at the resting tension that produced optimal force output (preload of 15 to 20 g) by applying a 5-second, 200-Hz impulse train (Fig. 1). It should be noted that the lack of fade of tetanic tension development and the absence of posttetanic potentiation indicate that indirect (nerve or endplate) stimulation did not occur under the described experimental procedure.

Data from the operative and control muscles for each postoperative interval were pooled. Statistical analysis of individual groups was done by analysis of variance and the Student's t-test when appropriate. P < 0.05 was considered significant.

RESULTS. At 3 weeks after surgery, a 28% decrease in maximal single-twitch tension was seen in the left lateral rectus muscle compared to the unoperated controls (P < 0.01) (Fig. 2). This difference disappeared at 6 weeks after surgery. By 12 weeks, there was a trend toward greater developed twitch tension in the operated orbit than in the controls. It is unclear from the current data whether this represents a true change because these values showed no statistically significant difference from those obtained in the corresponding control muscles.

The data suggest that maximal single-twitch tension may occur at a lower preload at 6 and 12 weeks (15 g) than at 3 weeks (20 g) in the operated orbit (Fig. 3). However, these differences are not statistically significant. Maximal single-twitch tension developed at a preload of 20 g in the control muscles. No statistically significant changes occurred in tetanic tension development at any interval after surgery (Fig. 4).

DISCUSSION. Adductor weakening in the cat resulted in a transient decrease in peak twitch tension of the antagonist lateral rectus muscle. This pattern of decreasing developed single-twitch tension followed by recovery resembles the pattern of atrophy seen in extraocular muscle after horizontal rectus recession. In a previous study in rabbits, we found that a large recession of extraocular muscle resulted in a 15% to

![FIGURE 1. Tetanic tension development in the left lateral rectus muscle 3 weeks after surgery, stimulated for 5 seconds at 200 Hz, preload 15 g.](image)
20% decrease in mean cross-sectional fiber diameter in both the recessed muscle and its antagonist. Maximum muscle fiber atrophy was seen 4 weeks after muscle recession. These findings, together with those of the current study, indicate that decreased extraocular muscle resting tension, brought about by antagonist weakening, results in muscle fiber atrophy and a reduction in generated tension early, followed by gradual recovery. Recovery of peak twitch tension is complete by 6 weeks after surgery. Recovery from the atrophy, however, appears to take more than 16 weeks.

The decrease in peak twitch tension, demonstrated in this study, may not necessarily be correlated with muscle fiber atrophy. In those muscles that showed reduced single-twitch tension 3 weeks after surgery, the maximal tetanic force development was equal to that of the controls. One might expect to see a decrease in tetanic tension if muscle fiber atrophy were present. In this model, the mechanism for preservation of peak tetanic tension is unknown. Possible reasons for this include changes in transmembrane calcium movement and calcium release and changes in excitation–contraction coupling mechanisms. The current data, however, do not allow an analysis of the cause.

The basis for recovery of generated tension and normal morphometry after a weakening procedure is also uncertain. Studies of limb muscle immobilized in a shortened position have demonstrated sarcomere loss, presumably to reoptimize actin–myosin overlap. A recent study by Scott demonstrated that sarcomere regulation also occurs in extraocular muscle after a sustained change in the rotational position of the globe. When the resting tension on a muscle is decreased, sarcomere overlap is excessive. Loss of sarcomeres from the ends of the muscle readjusts the
null length for optimum myofilament overlap, and generated tension and fiber diameters normalize.

Conditions that would be expected to decrease the resting tension of an extraocular muscle include cranial nerve palsies, botulinum toxin injection, and surgical or traumatic recession of a muscle. Our results suggest that a transient decrease in peak single-twitch tension might occur in the antagonist of the affected muscle under any of these conditions.

The clinical effects of this phenomenon are unknown. For example, recession of an extraocular muscle should decrease the resting tension across agonist and antagonist muscles so that any change in developed tension in one muscle is mirrored in the other. In the case of extraocular muscle palsy, any transient weakness of the antagonist probably would be overshadowed by the palsy of the agonist. Although the clinical effects may be negligible, these changes in developed tension represent an example of extraocular muscle plasticity and should be considered in ocular motility modeling.

Key Words
cat, extraocular muscle, eye muscle surgery, length–tension, muscle plasticity

Inhibition of Lens Opacification During the Early Stages of Cataract Formation
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Purpose. To characterize the time period during cataract formation in which administration of pantethine inhibits lens cell opacification in the selenite model for cataract.

Methods. Pantethine was administered to neonatal rat pups at selected time points from −0.5 to 17 hours with respect to injection of selenite at time = 0. The injection dose of pantethine was 820 mg/kg (1.5 mmol/kg) diluted in water at 410 mg/ml concentration. The injection dose of selenite was 3.28 mg/kg (19 μmol/kg) diluted in saline at 1.8 mg/ml concentration. Opacification was observed using a slit lamp microscope at selected time points over a 14-day period. Cataracts were staged using a classification of opacity from 0 (normal) to 6 (mature).

Results. The effect of pantethine was characterized by three different time periods: administration −0.5 to 6 hours with respect to selenite injection provided highly significant protection, *P < 0.001; administration 8 hours after selenite provided significant protection, * *P < 0.005; administration 10 to 17 hours after selenite was not protective.

Conclusions. The metabolite pantethine inhibited lens opacification during cataract formation in the selenite model. Even when pantethine was injected several hours after the administration of selenite, opacification was inhibited. Advanced stages of opacification were unresponsive to the administration of pantethine. The inhibitory effect of pantethine was statistically significant when administered during the earliest stage of opacification in the selenite model for cataract. Invest Ophthalmol Vis Sci. 1995;36:2550–2555.

Lens cell transparency is the result of short-range order in the organization of cytoplasmic proteins.