observations suggest that the site or mechanism for the increased latency of pupillary light reflex and reduced visual acuity may be different. In addition, the delay of reaction times by psychophysical experiments was greater than that of the reflexes of pupil. Thus, the visual system in amblyopia has abnormal processing of higher integration centers as well as retinal macular region.

Key words: pupillary light reflex, functional amblyopia, strabismic amblyopia, anisometropic amblyopia, infrared electropupillogram, long latency

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References


Palisade Endings in Human Extraocular Muscles

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The presence of nerve terminals in the tendinous insertions of human eye muscles was investigated histologically in adult human eye muscles obtained from donor eyes and in muscle pieces resected from juvenile patients undergoing surgical correction for strabismus. Lateral and medial recti, superior and inferior oblique muscles from adults, were stained "en bloc" using a silver impregnation method. Numbers of nerve terminals were isolated that resembled "palisade endings" or "musculotendinous cylinders" previously described in other species. A single palisade ending consists of nerve terminals at the distal musculotendinous interface of juvenile muscle also was observed when some resected specimens of lateral and medial recti were sectioned and stained using Holmes' silver method with a picrofuchsin counterstain. No conventional Golgi tendon organs were seen. Invest Ophthalmol Vis Sci 25:471–476, 1984

Much emphasis has been placed in the past 100 years on a preeminent role for corollary discharge in the perception of eye position. However, some experimental findings do not support the view that corollary discharge is the only element essential for eye position sense. Recently, Steinbach and Smith have shown that patients who have undergone repeated extraocular muscle surgery have an altered ability to recognize their eye position. Since the surgery removed only small amounts of tissue near the global insertions of eye muscles, the suggestion was made that sensory receptors in the tendon might play a previously unsuspected role in proprioceptive processes.

Little is known about the sensory innervation at the musculotendinous interface of human eye muscles. In many mammals, a rich supply of specialized terminals called "palisade endings" or "musculotendinous cylinders" is present at tendinous attachments of extraocular muscles.
suggested that human muscles might also contain a similar type of receptor, but the structure and distribution of these endings in the human have never been reported specifically. In light of the recent evidence suggesting a proprioceptive role for receptors near eye muscle insertions, the present study was conducted to identify and describe receptors that are present near eye muscle attachments and that might be removed by surgical resections.

Materials and Methods. "En Bloc" Silver Staining of Extraocular Muscles: Lateral and medial recti, superior and inferior oblique muscles, were obtained postmortem from four men and one woman, aged 53–66 years. Recti and oblique muscles also were removed from two cats (2.5 and 3.2 kg) that were killed with an overdose of sodium pentobarbital. Muscles were suspended by nylon thread in de Castro’s fixative for at least 5 days and stained using a silver impregnation method as modified by Boddy and Diwan (personal communication). Initial muscle microdissections were carried out in glycerol at X80 magnification using a stereomicroscope. Regions of tissue near the musculotendinous junction that contained several nerve axons were excised and placed in glycerol on glass slides. This small muscle specimen was compressed firmly under a glass coverslip and inspected at X400 for the presence of nerve terminals. Well-stained terminals were microdissected further and preserved in glycerol on glass slides. Terminals were drawn using a camera lucida attachment on a binocular microscope.

Serial Section Analysis of Resected Human Muscles: Extraocular muscle specimens were obtained from 12 children aged 9 months to 10 years who underwent a routine procedure for the surgical correction of strabismus. Resected tissues were placed in 10% formal saline for 7 days. Tissues were dehydrated through graded alcohols and toluene and embedded in a mixture of paraffin and plastic polymers (Paraplast, Sherwood). Tissues were cut serially in 10 μm sections. Sections were stained with Holmes’ silver method and counterstained with picrofuscin.

Results. Teased Muscle Specimens: The musculotendinous junction of human extraocular muscle contained many nerve endings that closely resembled palisade endings of the cat. Each ending appeared as a network of thin nerve strands that invested the inserting tip of a single extrafusal fiber (Fig. 1). The nerve terminals composing a single ending usually originated from an axon branch measuring 1–3 μm in diameter that approached its target muscle fiber through the tendon and divided 1–4 times closer to the point of muscle fiber insertion. These preterminal branches often split into additional fine filaments that ramified around the inserting tip of the muscle fiber. Rarely, one or more nerve filaments also arborized in the collagenous tissue close to the extrafusal fiber insertion. Most terminal filaments appeared as simple threads, but some filaments had swellings or ringlike structures close to their points of termination (Fig. 1d,e; Fig. 2). A few endings had longer filaments that coursed along the shaft of the muscle fiber (Fig. 2). Cat palisade endings had similar morphological features to those in humans. However, they were often more elaborate and formed a dense feltwork at the end of the muscle fiber as previously described.

In humans as in cats, a single nerve fiber measuring less than 5 μm entered the tendon from a nerve bundle in the extraocular muscle mass and supplied several palisade endings on neighbouring extrafusal fibers. Palisade endings were found in all four kinds of human extraocular muscles that were stained in this study. However, it was not possible to estimate the density of receptors in a single muscle, for nerves often ceased to impregnate thoroughly as they passed into the dense collagenous tissue of the tendon. The problem was most apparent in human muscles where connective tissues were denser and often penetrated into the muscle mass. Many palisade endings were difficult to discern and others were undoubtedly unstained. In well-stained regions of tissue, palisade endings showed an irregular distribution. Some musculotendinous regions appeared devoid of innervation, but other regions were crowded with palisade endings on many adjacent muscle fibers. We were not able to determine if these endings were only associated with multiply-innervated muscle fibers of the global layer, although this association has been reported previously in the cat. Golgi tendon organs were never identified in well-stained regions of extraocular muscles.

Examinations of Resected Tissues: Resected tissues from juvenile extraocular muscles varied in their composition. Some resected specimens were composed only of tendon and contained few nerve profiles, while other specimens also included part of a musculotendinous junction. In three specimens, fine (<2 μm) nerve filaments invested the tips of many extrafusal fibers in patterns consistent with those of palisade endings. Endings were identified most readily in longitudinal or oblique muscle sections (Fig. 3). Nerve terminals were common in certain parts of the musculotendinous junction but could not be found in other zones of fiber insertion. No Golgi tendon organs or muscle spindles were identified in these small resected specimens.

Discussion. We were led to look for proprioceptors at the insertions of eye muscles because of behavioral data obtained from strabismus patients. The present observation of endings like the palisade endings previously described in other species suggest that this re-
Fig. 1. Human palisade endings (a–e) represented in photomicrographs, left, and corresponding camera lucida drawings, right. Palisade endings in the upper two photomicrographs are restricted to the tip of a single extrafusal fiber. Palisade ending (e) has terminal structure which extends further along the muscle fiber shaft. Bars = 50 μm.
ceptor must be considered as a potential source of afferent feedback which may be removed by strabismus surgery. (We are assuming, along with others, that these are true receptors and have no motor function.) However, the functional role for this ending in proprioceptive processes is difficult to predict from the little information we now have about its sensory behavior. Physiologic studies of extraocular afferent fibers previously have described receptor responses that have a range of tension thresholds and rates of adaptation but the origin of these responses has been difficult to define. Bach-y-Rita and Ito considered all response patterns to originate from a single type of stretch receptor. However, Cooper and Fillenz separated out a grouping of nonspontaneous, rapidly adapting responses with higher tension thresholds, and ascribed these responses to unidentified receptors in tendon. It is tempting to speculate that these responses arise from palisade endings. The other receptor source in tendon usually is considered to be the GTO, but GTOs are rare or absent in most extraocular muscles.

The physiological testing of eye muscle receptors provides some clues about their behavior, but cannot describe the full range of responses that might be generated in a normal behaving subject. The intimate association of the palisade ending with a single muscle fiber may have special functional implications for its capacity to monitor the performance of eye muscles. First, it may ensure a sensitive receptor response to contractions of some motor units, but not others. Second, it may insulate the receptor from moderate passive stretch. Ruskell previously has observed that "many palisade terminals are partly or completely buried in muscle and appear secure from the direct influence of collagen movement." In humans, muscle fibers invested by palisade endings were found to lie in parallel to ribbons of tendon that penetrate into the muscle mass. These stiff tendinous elements may bear much transmitted tension from a passive stretch, so that the palisade ending may be further isolated from the stretch stimulus. As a consequence, the palisade ending might be expected to respond quite differently to eye movements produced by voluntary contractions of eye muscles than to those imposed passively by an external force. It may, therefore, be inappropriate to assess the proprioceptive role of the palisade ending by behavioral studies that rely only on passive eye rotations.

The palisade ending is not the only receptor that may be capable of providing proprioceptive input from the eye. It must be viewed as only one poorly understood element in a complex system that appears available for extracting position information from a range of extraocular and periorbital receptors, as well as efferent signals via corollary discharge.
Fig. 3. Photomicrograph, left, and camera lucida drawings, right, of nerve terminals at the tips of inserting muscle fibres in a serially sectioned specimen of medial rectus obtained by muscle resection. The array of nerve terminals around each fiber has a distribution like that of a palisade ending. However, only part of the neural apparatus is contained in a single 10 μm section, so that the density of terminals appears sparse. In two examples, part of the nerve branch that supplies the nerve network is shown by an arrow. Note the bands of connective tissue that run in parallel to extrafusal fibers as they penetrate into the muscle mass. Bar = 50 μm.

Key words: extraocular muscle, palisade endings, musculotendinous junction, human, proprioceptors

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References

The Minimum Precorneal Oxygen Tension to Avoid Corneal Edema

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One eye of each of eight subjects was exposed to gases containing oxygen concentrations of 1.0%, 2.5%, 4.9%, 7.5%, 10.1%, and 21.4% (oxygen partial pressures ranging from 8 to 158 mmHg) for 8 hr. The precorneal oxygen concentration required to avoid corneal edema for the group as a whole was 10.1% (an oxygen tension of 74 mmHg). There was considerable individual variation both in the corneal swelling response with each of the various oxygen concentrations and in the atmospheric oxygen concentration required to avoid edema: one subject required 7.5%, four subjects required 10.1%, and three subjects required 21.4% oxygen concentration. The results of this study suggest that the cornea requires higher levels of atmospheric oxygen than previously considered necessary for normal function. Invest Ophthalmol Vis Sci 25:476–480, 1984

Since Smelser and Ozanics discovered that atmospheric oxygen was necessary to maintain a normal level of corneal hydration, several attempts have been made to determine the minimum oxygen tension required to avoid corneal edema.1–4

Polse and Mandell in 1970, found that an oxygen partial pressure of 11 to 19 mmHg (oxygen concentration of 1.5 to 2.5%) was required to prevent swelling of the cornea. However, their conclusion was based on results from three subjects exposed to a narrow range of hypoxic conditions (0 to 2.5%) for 3.5 hr. A study by Carney of four eyes exposed to 2% oxygen for 2 hr supported the Polse-Mandell criterion.

Mandell and Farrell in 1980 used gases with oxygen partial pressures of 6.9, 17.1, and 20.2 mmHg (oxygen concentrations of 0.95%, 2.34%, and 2.77%, respectively) to try to determine the minimum oxygen level to avoid edema. Because most of their 28 subjects were available for measurements with only one gas mixture, their results for each gas mixture were obtained on different populations. Another problem experienced by Mandell and Farrell was that they had to extrapolate beyond their data to predict the minimum oxygen tension, as they obtained statistically significant swelling with all three gas mixtures. Nevertheless, using 4-hr exposure to the various gases, they concluded that the minimum oxygen tension needed to avoid edema lay between 23 and 37 mmHg (3.3 to 5.5%). They also reported that there was individual variation of ±8.7 mmHg in this threshold.

We were concerned about two aspects of previous studies: first, the short exposure periods used in these experiments; and second, the limited range of oxygen concentrations used. Indeed, the longest exposure used in any published study was 4 hr and the highest oxygen partial pressure was 20.2 mmHg (2.77%).

In the present study, we examined the nature of the relationship between corneal swelling and precorneal oxygen tension by monitoring corneal thickness,5 while one eye of each subject was exposed for 8 hr to gases with oxygen concentrations of approximately 1%, 2.5%, 5%, 7.5%, 10%, and 21%. This allowed us to derive a more precise estimate of the minimum oxygen tension required to avoid corneal edema.

Materials and Methods. Subjects: Eight subjects (five women and 3 men, ranging in age from 18 to 21 years), from whom informed consent had been obtained, were used in the study. All subjects were free from any ocular disease and were not contact lens wearers.

Materials: Gases of six different concentrations of oxygen (balance nitrogen) were used: 1.0%, 2.5%, 4.9%, 7.5%, 10.1%, and 21.4%. The gases were medical quality and certified by the supplying company (CIG Australia) to a tolerance of ±0.1%.