Hypothesis for a Pressure-Sensitive Mechanism in Muscle Spindles

Abstract. *The suggestion is made that the mammalian muscle spindle may serve in part as a pressure sensor. Pressure acting nonuniformly on the spindle would express the intracapsular fluid distad, thus elongating the capsule. "Intracapsular fibers," those intrafusal muscle fibers inserting into the capsule, would be lengthened, whereas "percapsular fibers" passing beyond the capsule would be relatively unaffected. Since "flower-spray" terminals are preferentially associated with the smaller intrafusal fibers, they would chiefly be concerned with the pressure sensing mechanism. Observations in support of this hypothesis are given.*

The contractile status of a muscle is monitored by its tendon and spindle organs. The tendon organ lies "in series" with the contractile fibers and is affected by the total tension developed at the muscle attachments in its vicinity. A given rate of discharge from the tendon organ might be attained at various lengths of the gross muscle, depending upon the degree of active contraction present. Spindle receptors, on the other hand, lie "in parallel" with the contractile fibers and should gauge directly the length of the muscle, or rather the extrafusal fibers, and be relatively independent of tension change. Spindles in a muscle contracting isometrically, for instance, would not signal the activated condition of the muscle.

A third measure of muscle status, intramuscular pressure, might also be monitored by muscle spindles. The spindle capsule with its characteristic fusiform outline enclosing an ample fluid-filled space suggests a double-ended squeeze bulb for mediating some pressure mechanism. Indeed, pressure applied locally to the surface of a muscle may induce a prominent increase in discharge from a spindle, and sites eliciting maximum acceleration are restricted to an area comparable to that of the spindle capsule (Fig. 1). The following is a hypothesis of how such a pressure-sensitive mechanism might operate (*1*).

Pressure exerted by shortening and thickening extrafusal fibers undergoing contraction may impinge upon the expanded equatorial region of the capsule, displacing the intracapsular fluid toward the poles and thus elongating the capsule. Those intrafusal muscle fibers of short length which insert into the capsule itself are stretched by the elongation of the capsule, and sensory endings wrapped around the short fibers undergo stretch and membrane depolarization, setting up an enhanced afferent discharge. The "flower-spray" terminals are associated primarily with the short intrafusal fibers (*2*) and would be chiefly affected by the change in capsule length. The annulospiral endings are associated largely with long intrafusal fibers. These fibers are assumed to slide freely through the sleeve-like ends of the capsule to attach at a distance to muscle fascia or tendons, so that the annulospiral endings would be primarily sensitive to changes in length of the muscle.

The hypothesis has three requirements. (i) Pressure gradients must occur in contracting muscle. If the muscle acted simply as a fluid-filled bag, pressure changes on the spindle would be uniform and no deformation would result. (ii) The gradient must favor compression of the spindles' equatorial region where most of the intracapsular fluid is stored, and there must be free tissue space about the ends of the capsule to allow for its extension. (iii) The ends of the smaller intrafusal fibers must attach into the capsule.

1) The presence of pressure gradients during contractions of the gastrocnemius was monitored during exploration with a 23-gauge needle connected by tubing filled with silicon oil of low viscosity, to a fluid pressure transducer having low-volume displacement. Small pressure gradients could be detected during total contractions, but stronger gradients were seen in subtotal contractions. When a single motor unit was caused to contract in response to

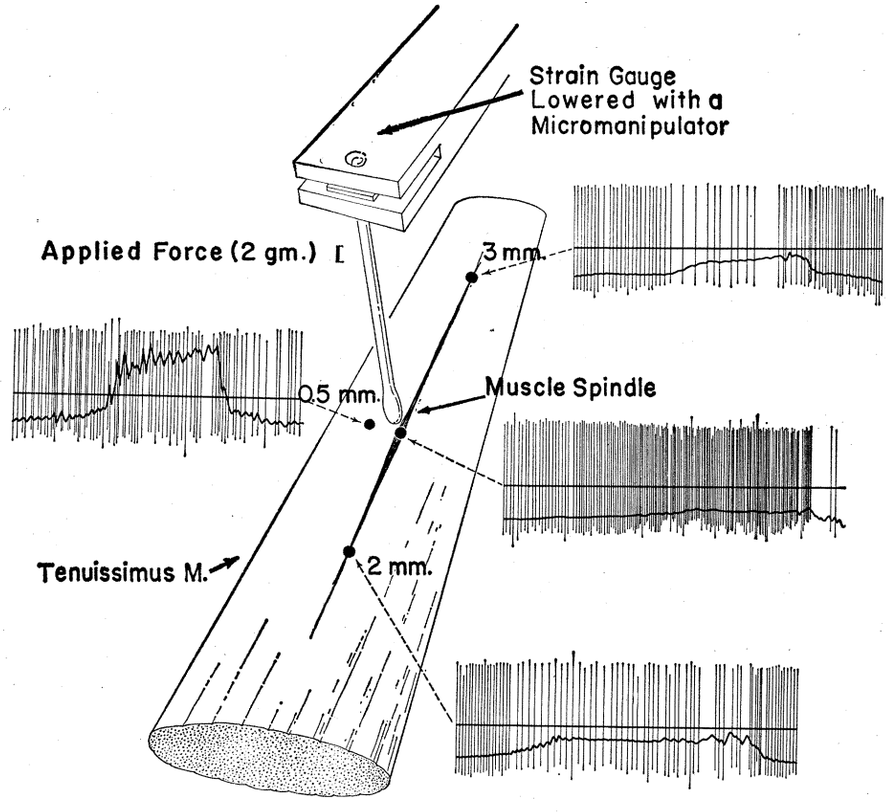

Fig. 1. Effects of gentle probing of the cat's tenuissimus muscle on discharge of a pressure-sensitive unit monitored from an S_1 dorsal root filament. Irregular solid line represents applied pressure as measured by a strain gauge. Very light pressure at the central site caused marked acceleration. Only slight acceleration was obtained from a point 0.5 mm lateral to the sensitive focus, even though higher pressures were employed. Decreases in discharge were produced at sites 2 or 3 mm toward the distal ends. A spindle was subsequently isolated from this area of the muscle by teasing after maceration by Sihler's method.

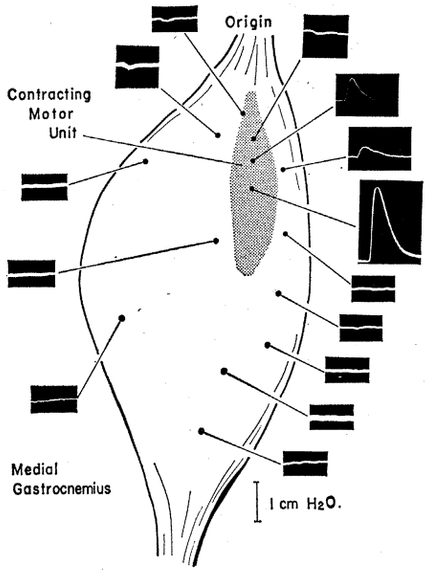

Fig. 2. Pressure changes in the cat's medial gastrocnemius occurring with twitch contractions of a motor unit producing dimpling of the shaded area. Unit was caused to contract by stimulation of a ventral root filament. Sharp increases in pressure were recorded within the motor unit territory; slight decreases in pressure appeared at some neighboring sites; and more distant sites showed no effect.

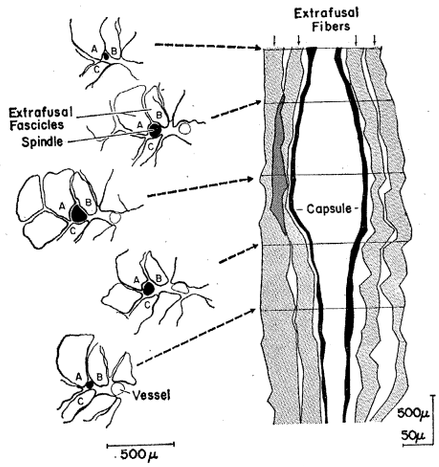

Fig. 3. The five projections at the left represent selected views of cross-sections of a tenuissimus spindle and adjacent muscle fascicles. Where the section passes through the spindle equator, distortion of fascicles *A* and *B* by the impinging capsule is shown. At the right is a longitudinal sectional view of the same spindle as reconstructed from the serial cross sections. The horizontal scale of the representation is expanded six times the vertical scale. Two extrafusal fibers of fascicle *A*, and two from *B* are shown. Their course is seen to bow around the capsular bulge.

stimulation of a ventral root filament, abrupt rises in pressure were obtained in a restricted area at the center of the dimple marking the contraction; at some marginal sites slight drops in pressure were detected; and through most of the muscle no changes were detected (Fig. 2).

2) Reconstruction from serial sections of capsules of various shapes, and relation of the capsules to adjacent muscle, strongly suggest that the equatorial region of the spindle is subjected to pressure during contraction of neighboring extrafusal fibers. Spindles lie in interfascicular clefts where they appear, at least after histological fixation, to be freely suspended in extracellular space. However, the swollen equatorial region presses outward against adjacent fascicles to a degree sufficient to cause deformation of the fascicles (Fig. 3, fascicles *A* and *B*). The course of individual extrafusal fibers is warped from a direct course by the equatorial swelling. Pressure upon the equator thus may derive not only from thickening of extrafusal fibers during contraction, but also from that force vector exerted normal to the line of tension along the shortening extrafusal fiber.

3) Teasing of spindles following maceration and reconstructions from serial sections show that the motor poles of many intrafusal fibers insert into the capsule. Systematic examination of 128 intrafusal fibers from the proximal ends of 25 extensor digitorum brevis and tenuissimus spindles of the cat shows that 60 percent of the intrafusal fibers are clearly "intracapsular," and only 32 percent extend distinctly beyond the capsule as "percapsular fibers." The latter fibers usually have their equatorial nuclei in a bag arrangement, while "intracapsular fiber" nuclei are in single file.

The "intracapsular fibers" in this pressure-sensing mechanism would function, presumably, by causing sustained stretching of the sensory endings, thus altering their sensitivity to changes in pressure (Fig. 4). Since separate motor systems for innervation of small and large intrafusal fibers probably exist (*2*), the length sensing mechanism associated with the large "percapsular fibers" could be independently adjustable. Each system would be expected to have distinct reflex connections centrally. The pressure sensing mechanism might serve to monitor contractile activity in different parts of the muscle

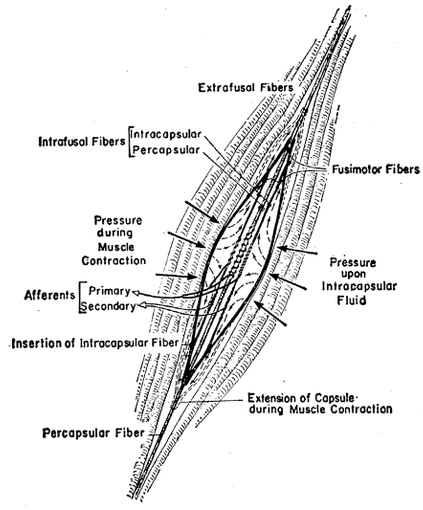

Fig. 4. Schematic diagram of a mechanism in the muscle spindle for converting alterations in intramuscular pressure into changes in sensory discharge.

and play a part in balancing participation by the surrounding motor units. The state of the muscle would thus be gauged by three sensory modalities: (i) tendon organs for total tension developed; (ii) annulospiral endings, for length of the muscle; and (iii) "flower-spray" terminals, for pressure gradients.

CHARLES F. BRIDGMAN
EARL ELDRED

Department of Anatomy, University of California Medical Center, Los Angeles 24

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Cystinuria: In vitro Demonstration of an Intestinal Transport Defect

Abstract. *A defect in the transport of* L-*cystine and* L-*lysine has been found in the intestinal mucosa of patients with cystinuria. Transport studies in normal intestinal mucosa, in contrast to similar studies in the kidney, show that cystine and lysine are mutually inhibitory.*

Cystinuria, a hereditary disease of man, is characterized by formation of cystine renal calculi and by excessive excretion in urine of cystine and the dibasic amino acids, lysine, arginine,