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RESEARCH ARTICLE

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Sensory nerve endings in the hard palate and papilla incisiva of the goat

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Abstract The sensory innervation of the papilla incisiva in the hard palate of the domestic goat was studied with light and electron microscopy, supplemented by electrophysiological studies of free nerve endings. The goat lacks incisor teeth. Grass and leaves are not bitten, but pulled off by pressing them between the tongue and papilla incisiva. Thus, the masticatory mucosa is subject to particularly heavy mechanical loads requiring functional specialization of the horny epithelium in the form of thickening, i.e., the papilla incisiva and 12–14 pairs of rugae palatinae. A thin layer of firm connective tissue (lamina propria) attaches the mucosa to the periost of the hard palate. Sensory nerve fibers were found most abundantly in the papilla incisiva. Their number decreased drastically in aboral direction. A section through the first four rugae palatinae contains only about 10% of the number of free nerve endings found in the same area of mucosa from the papilla incisiva. Four types of sensory nerve endings were found. Free nerve endings were seen ubiquitously in the epithelium and superficial layer of the lamina propria. Merkel nerve endings were found in the bases of the epithelial thickenings in the papilla incisiva and rugae palatinae. Few Ruffini corpuscles were found in the deeper layer of the lamina propria, while lamellated corpuscles were seen just below the basement membrane of the epithelial pegs. Thus, a variety of sensory nerve endings were found in the hard palate, especially in those areas that are in close contact with the tongue during chewing of food. This rich innervation suggests an important role in monitoring the mechanical properties of food. Recordings were made from cell bodies supplying these terminals. Classic low-threshold, slowly adapting responses were observed in Aß afferent populations. This activity was probably mediated by Merkel type endings. Alternately, high-threshold and suprathreshold responses obtained from Aδ category afferents were likely to be nociceptive. In support of this, threshold and suprathreshold sensitization was observed following injection of serotonin into the receptive field of Aδ populations. This activity was likely to be derived from the aforementioned free nerve endings.

Key words Mechano-receptors · Nociceptors · Palate · Merkel cell · Ruffini corpuscle · Free nerve ending · Lamellated corpuscle · Serotonin

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Introduction

Unlike carnivores, which usually bite off chunks of meat from their prey, goats and other herbivores pull off grass and leaves pressing them between the tongue and palate. Thus, in these animals, the mucosa of the hard palate needs to be specially designed for this purpose in order to cope with the high mechanical loads. In the goat, incisor and canine teeth are lacking, while the papilla incisiva takes up most of the anterior part of the hard palate, extending over an area of about 25×30 mm (see Fig. 1). Twelve to fourteen pairs of rugae palatinae follow in the posterior part of the hard palate.

The mucosa of these areas is thickened and firmly linked with the underlying connective tissue through epithelial thickenings (pegs), containing a rich supply of sensory nerve fibers (Cooper et al. 1991a, 1991b). Using light and electron microscopy on smaller mammals like the rat, a variety of sensory nerve endings were found in the mucosa of the hard palate (Yeh and Byers 1983; Byers and Yeh 1984; Chan and Byers 1985).

Physiological studies of receptors in this particular location have, so far, concentrated on the response characteristics of free nerve endings, especially the mechano-nociceptors (MN). They are a subgroup of Aδ high-threshold mechanoreceptors (HTM), which were first identified by Perl and coworkers (originally “insensitive

mechanoreceptors"; Burgess and Perl 1967; Perl 1968). Mechano-nociceptors have properties suggestive of an important role in the coding of mechanical pain. The threshold and reactive range of MN transduction parallels pain reports of humans receiving similar stimuli to similar tissues (Cooper 1993; Cooper et al. 1993). Force transduction by MNs is likely to be modified following exposure to algogenic substances that are synthesized and released following trauma and inflammation (Cooper et al. 1991a).

The aim of the present study was to examine the distribution, ultrastructure, and electrophysiology of the different types of mechanoreceptors in the hard palate of the goat and to compare the results with those from other large mammals, like the rhesus monkey (Halata and Baumann 1999). Preliminary reports of a portion of these data have been published in abstract form (Friedman et al. 1988; Schwegmann et al. 1993).

Material and methods

Physiological studies

The physiological studies were carried out in the Department of Oral Surgery of the University of Florida in Gainesville, Florida, USA.

Animals

Twenty six male goats (*Capra hircus*) served as subjects. Goats were housed in pasture or in runs maintained by the University of Florida Veterinary Hospital. Health and care of the goats were supervised by the University of Florida veterinary and animal care staff. All procedures employed in the present study were reviewed and approved by the local committee on animal care.

Exposure of and recording from the trigeminal ganglion

Subjects were anesthetized with a combination of alpha-chloralose and sodium pentobarbital (i.a.). Chloralose was administered via a Ringer drip (7.5 mg/ml). Both substances were administered to effect. The trigeminal ganglion was exposed, from a lateral approach, after an extensive dissection of the vessels and glands caudal to the mandibular ramus and removal of a small piece of temporal bone just caudal to the oval foramen. The ganglion was penetrated with either glass pipettes or tungsten microelectrodes (Micro Probe Inc.) until receptive fields were located on the palate. Neural activity was digitized and stored on a Vetter 3000 and Panasonic VHS unit (Pacer Electronics) and printed on-line via a DASH IV thermal polygraph (Grass-Astromed). Complete descriptions of surgical dissection and recording procedures have been published previously (Cooper et al. 1991a).

Drugs and procedures

Serotonin (12.5 µg or 60 nmol) was dissolved in 5 µl saline (37°C) just prior to injection. Injections were made in the proximity of the receptive field using microsyringes (Fisher Chemical). Control cases were saline injections (n=10) of the same volume. Needles penetrated the papilla at a distance of 10–15 mm from the receptive field. The needle was then brought into the close vicinity of the receptive field (within 5 mm) and the volume of 5 µl of solution was injected over a period of 1–2 s. Repeated tests of neural reactivity were made at 5, 30, and 60 min intervals following individual injections.

Conduction velocity

Conduction time was determined by electrical stimulation of the receptive field. The time between the electrical artifact and the arrival of the action potential at the recording electrode was determined by inspection of printed records of the event. To arrive at the conduction velocity, conduction distance was divided by the conduction time.

Statistics

Nociceptors were characterized with respect to their capacity to encode intense mechanical stimuli. Ramped or stepped stimulus presentations of force were made in either displacement or force-servo mode using a 2 mm diameter, spherically tipped probe mounted on a precision stimulator (Cooper and Hargens 1993). The instantaneous relationship between force and interspike interval formed data pairs that were pooled, logarithmically transformed, and fit to power functions using simple linear regression (Statistical Analysis System). We refer to these as transduction or coding functions. Separate regression lines were determined for dynamic or static reactivity, depending upon the preferred response form of the afferent being tested (Cooper et al. 1991a). Functions were accepted only when significant. An F test was used to determine the significance of the fit. With the HC stimulator, the physical relationship between the probe and the receptive field was maintained within 1.5 µm resolution. The spatial and vectorial relationship between the probe tip and the tissue was maintained over the entire testing period with substantial precision. A more complete description of the stimulation and quantification procedures is given in previous reports (Cooper et al. 1991a; Cooper and Hargens 1993).

Features of transduction curves were used to quantify coding. These features included activation threshold (instantaneous pressure corresponding to the first action potential) and mean dynamic range, defined as mean force range (minima to maxima) of the coding function.

To evaluate sensitization of MNs, each MN feature was pooled according to condition (control or serotonin injected), and change scores were computed for pre- and post-injection cases. The Walsh test was used to determine whether changes in dynamic range had occurred in related samples (pre-injection versus post-injection). The Mann-Whitney U test was used to determine significance of independent samples.

Morphological studies

The morphological studies were mainly carried out in the Department of Functional Anatomy of the University of Hamburg, Germany. Two adult goats (*Capra hircus*) were killed with an overdose of pentobarbital and perfused via the ascending aorta with 6% glutardialdehyde in 0.05 M phosphate buffer. The mucosa of the hard palate, including the entire papilla incisiva, was carefully removed from the animals and cut longitudinally into four strips of similar thickness on either side. Each of these strips was then cut into smaller tissue blocks of about 1.5 mm side length. These were then postfixed in 1% OsO_4 in 0.1 M sodium phosphate buffer with 1% sucrose at pH 7.4 for 2 h before embedding in Epon 812 (Luft 1961).

Serial semithin sections obtained from these blocks were stained according to Laczko and Levai (1975) and examined with light microscopy. Selected semithin sections were re-embedded, cut into ultrathin sections, and contrasted with 1% uranyl acetate and 1% lead citrate (Reynolds 1963) for electron microscopy (Philips 300).

A third goat was perfused with Bouin solution and the entire hard palate removed, including the bone. Following storage in ethanol and EDTA for 6 months, the palate (bone and mucosa) was cut into strips as described above. These were divided into blocks of 25 mm length for embedding in paraffin. Sections of 10 µm

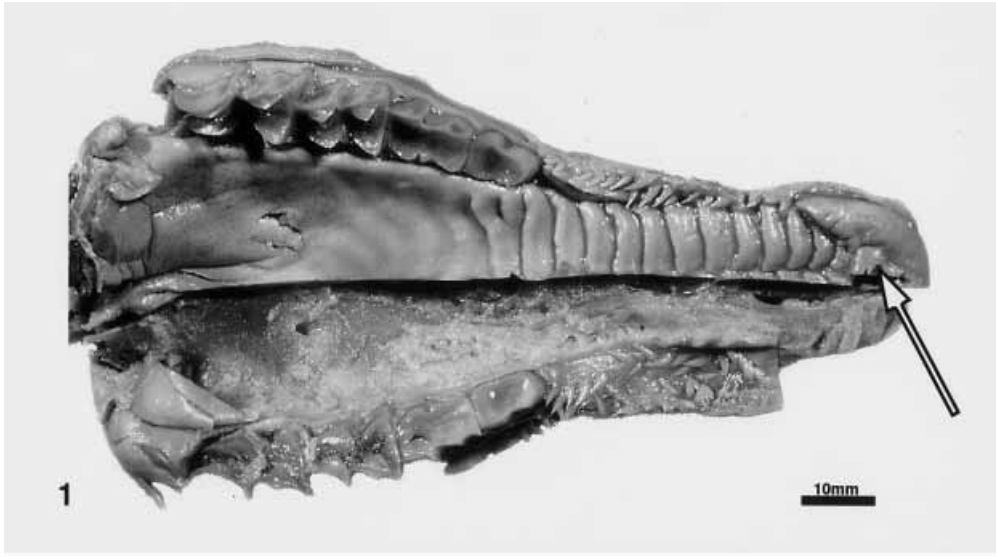
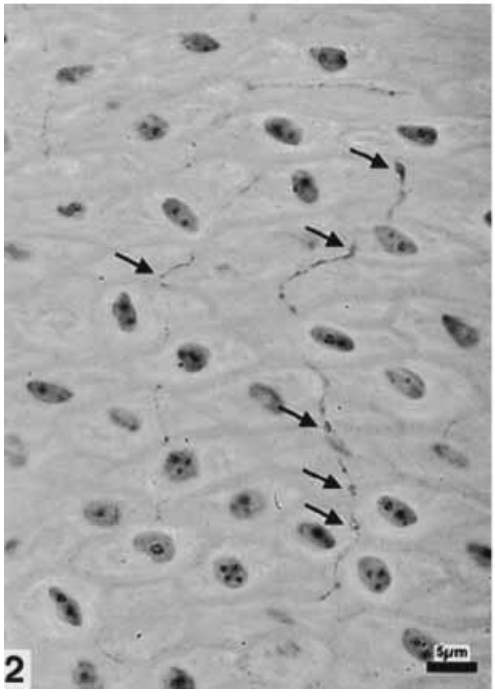


Fig. 1 Photograph of the goat palate with papilla incisiva (*arrow*) and 12 rugae palatinae. The mucosa of the *left half* has been removed. The goat lacks incisor and canine teeth in the upper jaw. The rugae palatinae extend to the beginning of the premolars (P1 and P2)



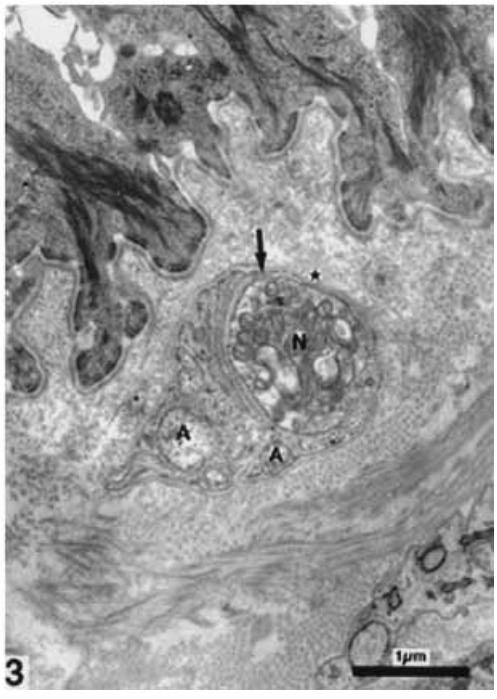


Fig. 2 Light micrograph of an unmyelinated nerve fiber with intermittent enlargements (*arrows*) just below the stratum corneum in the goat papilla incisiva. Silver-stained paraffin section

Fig. 3 Detail view of a free nerve ending (*N*) located in the stratum papillare of the lamina propria below the basement membrane of the epithelium. The nerve terminal is filled with mitochondria and partially wrapped by cytoplasmic lamellae of the terminal glial cell. In the area marked with an *asterisk*, the nerve terminal is only covered by the basal lamina. Smaller axon-terminals (*A*) are incompletely covered by the terminal glial cell

were placed on gelatine-coated glass slides for silver staining according to Spaethe (1984). This method has been standardized for quantitative studies of unmyelinated nerve fibers in epithelia (Spaethe 1991).

Results

Morphology

The goat lacks incisors and canine teeth in the upper jaw. The hard palate is covered by a multilayered, horny, flat epithelium firmly connected with the periost through the lamina propria. The epithelium is between 200 and 400 µm thick and consists of three layers: (1) stratum basale, (2) stratum spinosum, and (3) stratum corneum. The front part of the palatal mucosa is thickened to form the papilla incisiva (measuring about 25×30 mm) behind which twelve to fourteen rugae palatinae are located (Fig. 1).

At the junction between epithelium and lamina propria are epithelial thickenings (pegs) of different height, interlocking the two layers. In the papilla incisiva and rugae palatinae, these pegs are especially thick and well developed. The lamina propria consists of a superficial layer facing the epithelium. This layer forms a negative of the epithelial thickenings: thinner below epithelial pegs and protruding between them. In analogy to the nomenclature of the skin, this could be called the papillary layer. The deeper layer consists of dense connective tissue with some seromucous salivary glands. This layer is firmly attached to the periost of the hard palate allowing minimal movement of the mucosa against the bone.

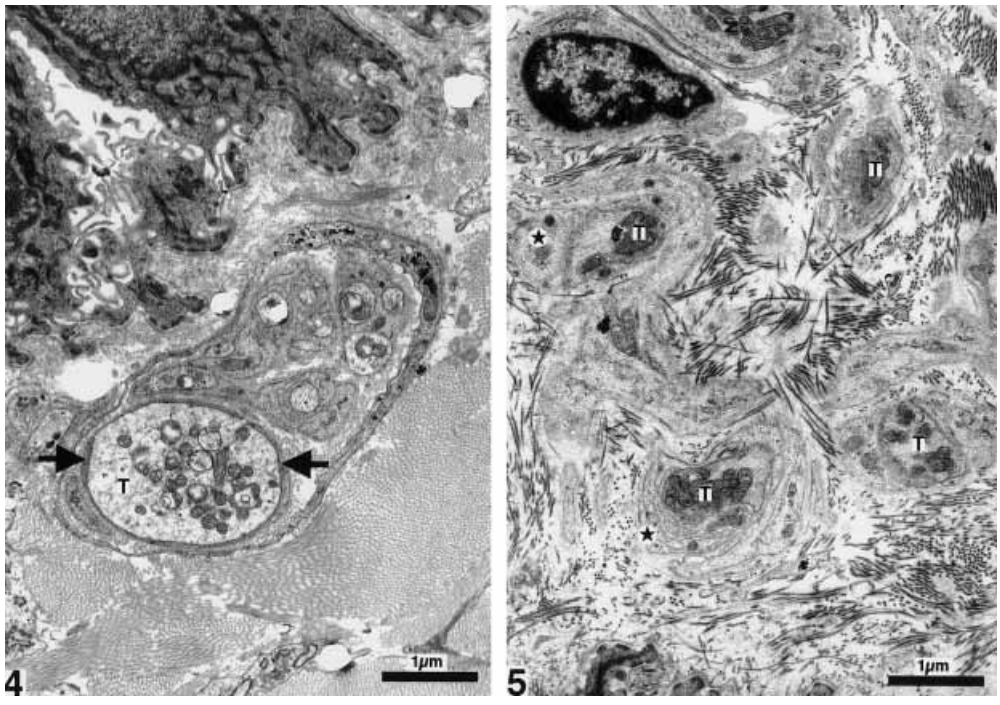


Fig. 4 Free nerve ending (*T*) in the stratum papillare of the lamina propria in the goat papilla incisiva. The terminal is incompletely surrounded by a cytoplasmic lamella of the terminal glial cell (*arrows*). Collagen fibers partially bundled by thin processes of fibroblasts are seen next to the nerve terminal

Fig. 5 Branches of free nerve endings (*T*) in the stratum papillare of the lamina propria in the papilla incisiva. Pinocytotic vesicles can be seen in the lamellae of the terminal glial cells (*stars*)

Four types of sensory nerve endings were found:

- free nerve endings within the epithelium and the superficial layer of the lamina propria (see Figs. 2, 3, 4, and 5)
- Merkel nerve endings in the bases of epithelial thickenings (see Figs. 6, 7, and 8)
- Ruffini corpuscles in the deeper layer of connective tissue, about 250–400 µm below the basement membrane of the epithelium (see Fig. 10)
- small lamellated corpuscles below the epithelial thickenings (see Figs. 11 and 12)

Free nerve endings

During light microscopy of silver stained sections, thinly myelinated (Aδ) or unmyelinated (C) axons, with intermittent enlargements resembling a chain of pearls, were found throughout the epithelium (Fig. 2). Their number was highest in the papilla incisiva and decreased drastically in dorsal direction. In the papilla incisiva, we found in a 10 µm section of 25 mm length between 200 and 250 free nerve endings. In contrast, in a section through the first four rugae palatinae of about the same length, we counted only 20–30 free nerve endings.

Also, in the lamina propria, a rich supply with thinly myelinated or unmyelinated nerve fibers was found. The axons showed intensive terminal branching (as observed in serial sections not shown here) before forming terminals (Fig. 5). Electron microscopically, the terminals were filled with accumulations of mitochondria and only partly covered by glial cells (Figs. 3 and 4). The axolemma has areas of direct contact with the basal lamina. In those areas of the terminals covered by terminal glial cells, large numbers of pinocytotic vesicles were seen within the lamellae of glial cells (Fig. 5).

Merkel nerve endings

The basal layer of the epithelial thickenings contained groups of Merkel cells, with their nerve endings supplied by one or two myelinated axons with diameters of 4–5 µm (Figs. 6 and 7). Their number depended on the thickness of the epithelial pegs. In larger pegs, up to eight Merkel nerve endings were found, while smaller ones had only individual Merkel nerve endings. The number of Merkel nerve endings was highest in the incisive papilla, where they were found in almost every epithelial peg. In the dorsal parts of the palate, the number of Merkel nerve endings decreased in much the same way as described for the free nerve endings. Also, the number and height of epithelial pegs decreased in aboral direction.

Each Merkel nerve ending consisted of a Merkel cell and discoid nerve terminal. The Merkel cells were oval in shape, with the long axis oriented in parallel to the mucosal surface. The corresponding nerve terminals were also elongated and positioned below the Merkel cells towards the basement membrane (Fig. 7). The Merkel cells had lobulated nuclei and contained typical dense core granules in that part of the cytoplasm facing the nerve terminal (Fig. 8). Desmosomal contacts with the surrounding keratinocytes were often seen. Between these contact sites, protoplasmic protrusions extended either between or were invaginated into neighboring keratinocytes (Fig. 8). The discoid nerve terminals were characterized by accumulation of mitochondria and electron-microscopically clear vesicles. Before reach-

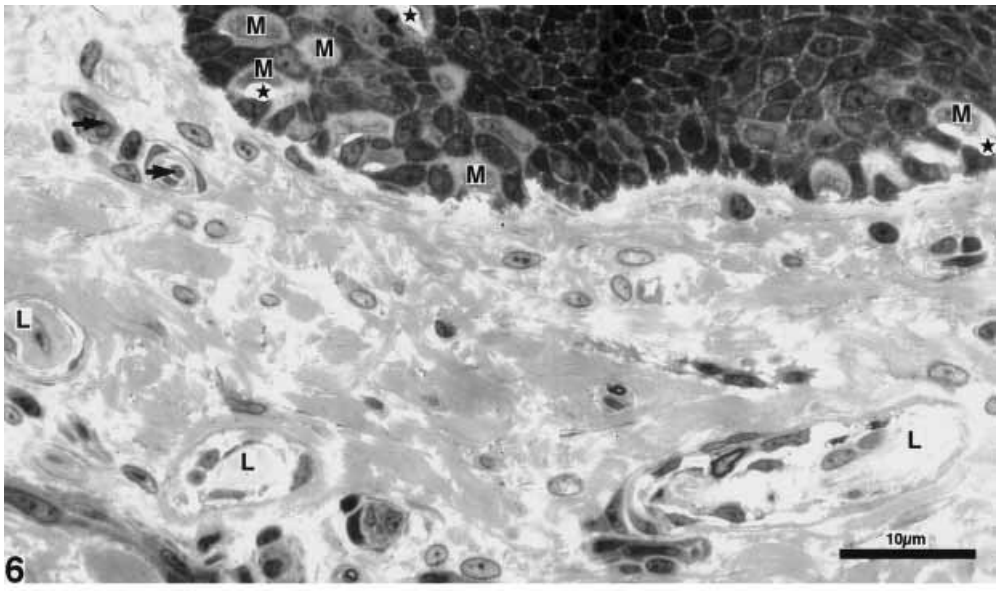


Fig. 6 Light micrograph of a group of Merkel cells (*M*) at the base of an epithelial peg in the papilla incisiva. The corresponding nerve terminals are seen as empty spaces and marked with (*). Myelinated axons (*arrows*) run through the lamina propria towards the Merkel cells. Lamellated corpuscles (*L*) are seen in deeper parts of the lamina propria below the Merkel cells

Fig. 7 Merkel cells (*M*) with nerve terminals (*T*) at the base of an epithelial peg in the papilla incisiva. The Merkel cells are elongated and their long axes run parallel to the mucosal surface. On the side of the Merkel cells facing the basement membrane, the associated nerve terminals (*T*) can be seen. Free nerve endings in the lamina propria are indicated by *arrows*

ing the terminal, the afferent axon lost its myelin sheath and the basal lamina of the axon could merge with the basement membrane of the epithelium (Fig. 9).

Ruffini corpuscles

Ruffini corpuscles were found in very small numbers (one or two) in the lamina propria of the papilla incisiva (Fig. 10). Similar to those found in other locations, they were cylindrical in shape with a diameter of about 50 µm and up to 300 µm long, oriented in parallel to the direction of the collagen fibers. Up to four layers of flat perineural cells formed an incomplete capsule of the cylinder, leaving gaps allowing collagen fibers to enter the corpuscle. Thin lamellar cells separated compartments of collagen fibers (Fig. 10). The afferent axons were thick (3–5 µm), myelinated fibers (Aß). Within the cylinder, the axon lost the myelin sheath and branched intensively into numerous terminals. Each terminal was partly sandwiched between thin lamellae of terminal glial cells (Fig. 10).

Lamellated corpuscles

Lamellated corpuscles were found in the papillary layer of the lamina propria. Their number was largest in the papilla incisiva. Within a 10 µm section of 25 mm length, up to 40

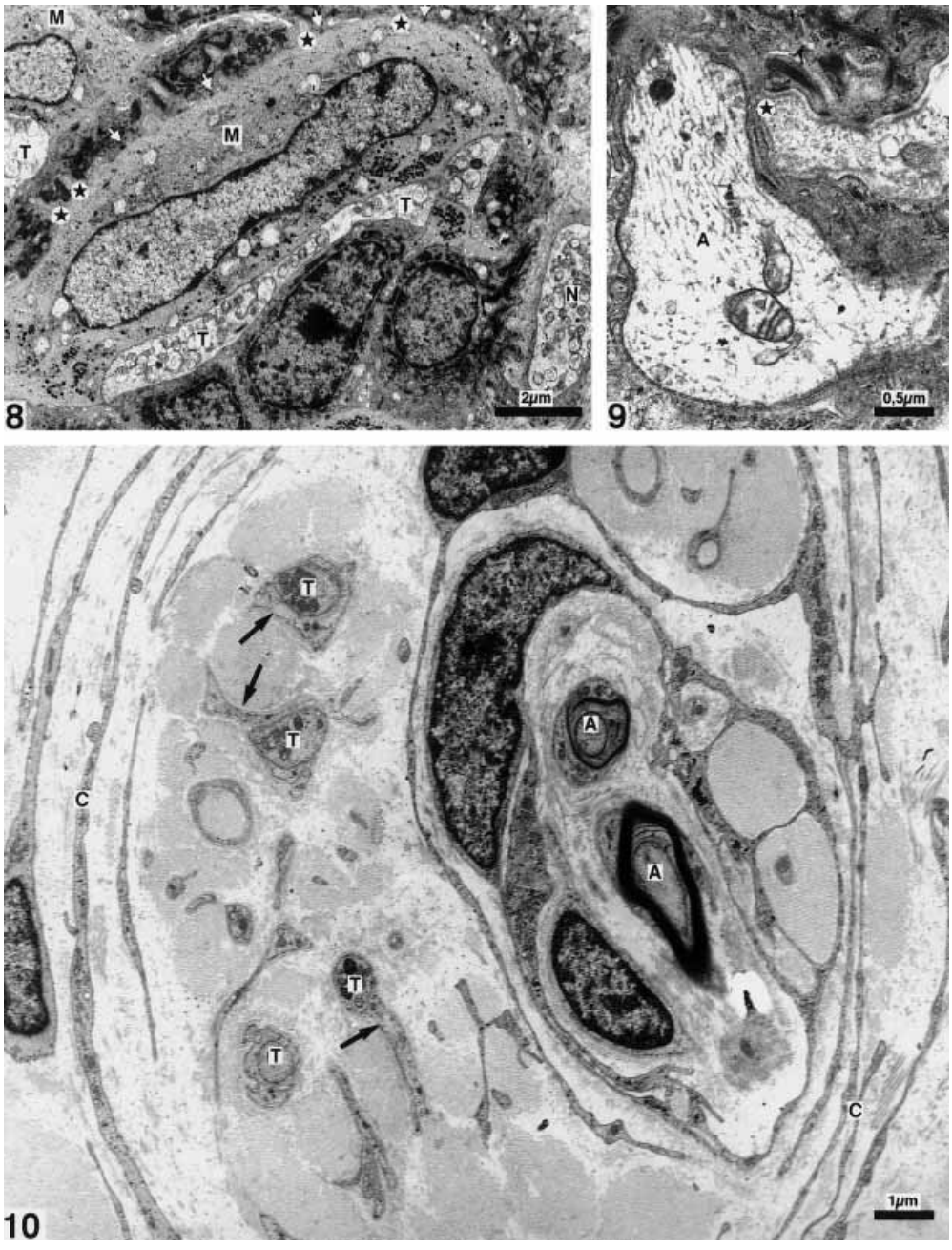


Fig. 8 Close-up of Merkel cells (*M*) showing the typical elongated shape with osmiophilic granules, particularly in that part of the cytoplasm facing the nerve terminal (*T*). On the opposite side, numerous cytoplasmic protrusions (*stars*) extending between keratinocytes are found. Desmosomal contacts between Merkel cell and keratinocytes are marked by *arrows*

Fig. 9 Afferent axon (*A*) of a Merkel cell from the papilla incisiva. The basal lamina of the terminal glial cell merges with the basement membrane (*stars*)

Fig. 10 Cross-section through a Ruffini corpuscle in the lamina propria of the papilla incisiva. The supplying myelinated axon (*A*), with a diameter of about 3 µm, branches and finally forms terminals (*T*), partly covered by cytoplasmic lamellae of terminal glial cells (*arrows*). Bundles of collagen fibers fill the space between nerve terminals and the capsule of the corpuscle (*C*) formed by fibroblasts

lamellated corpuscles could be found, while, in a section through the rugae palatinae of the same size, their number did not exceed 12. They were rarely found in those areas of the mucosa lacking epithelial pegs. Lamellated corpuscles were oval in shape, with diameters of about 40 µm and a length of up to 200 µm. The longitudinal axis of the corpuscles ran parallel to the mucosal surface.

The lamellated corpuscles consisted of a nerve terminal, an “inner core”, and capsule (Fig. 11). The inner core was formed by thin cytoplasmic processes of terminal glial cells covered by basal laminae and contained, in the center, an oval-shaped nerve terminal. The corpuscles were innervated by myelinated afferent axons of 2–4 µm diameter. After losing the myelin sheath, the unmyelinated terminal axon could branch before enlarging to form nerve terminals typically containing mitochondria and electron-empty vesicles (Fig. 12). Finger-like cytoplasmic protrusions extended from the nerve terminal between the layers of the inner core. Desmosome-like structures could often be seen at the tip of such protrusions.

Physiology

Low-threshold mechanoreceptors

Afferents were categorized as low-threshold mechanoreceptors when their von Frey threshold was less than 1 g

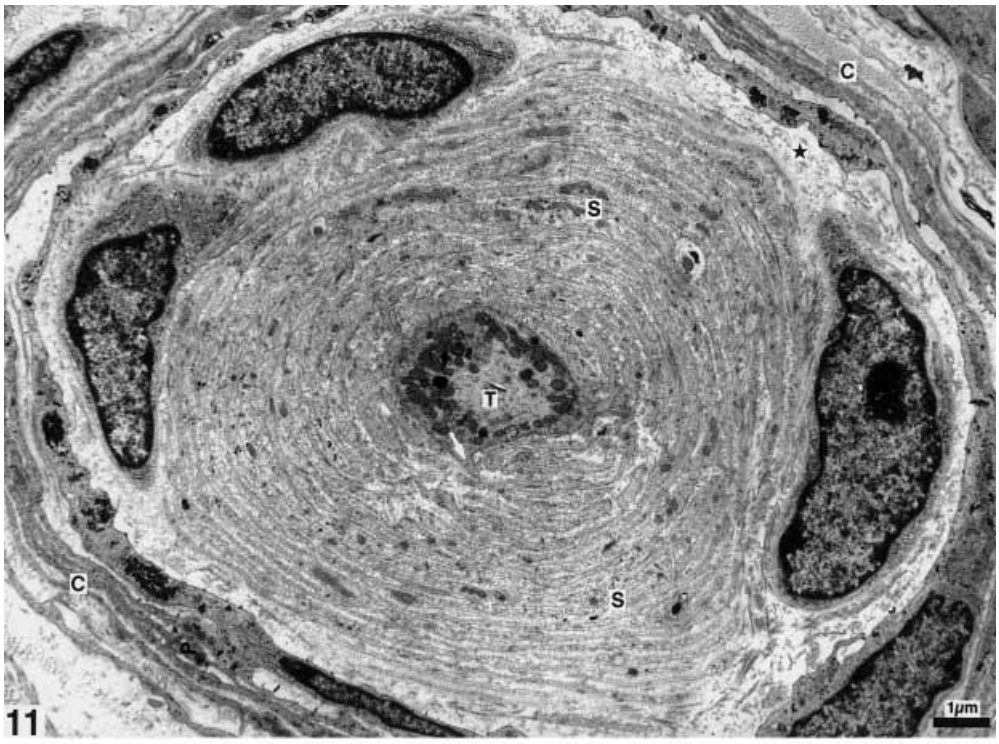


Fig. 11 Inner core of a lamellated corpuscle in the lamina propria of the papilla incisiva. The nerve terminal (*T*) filled with mitochondria is in the center of the inner core, sending a finger-like protrusion (*white arrow*) between the surrounding cytoplasmic lamellae formed by terminal glial cells (*S*). Perineural cells surround the inner core of the corpuscle, forming a thin capsule (*C*)

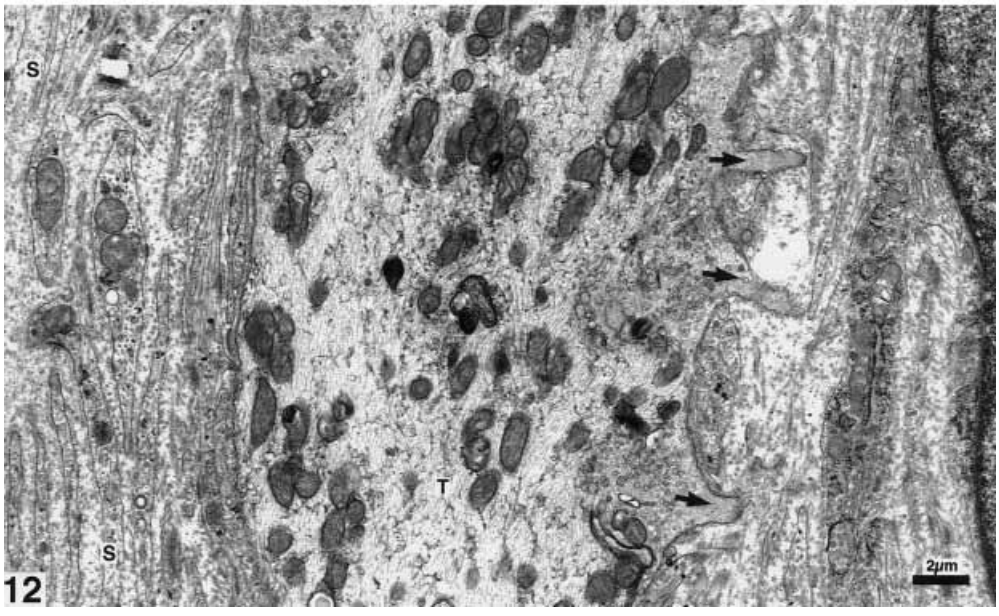


Fig. 12 Close up of a nerve terminal from the inner core of a lamellated corpuscle in oblique section. The nerve terminal (*T*), containing mitochondria and clear vesicles, sends finger-like cytoplasmic protrusions (*arrows*) between the lamellae of terminal glial cells (*S*). At the end of some protrusions, desmosome-like structures can be seen

(=10 mN). Slowly adapting afferents of this kind were frequently encountered on the papilla incisiva (*n*=11). We observed that such endings were very sensitive to light pressure and responded briskly to any maintained application of slight pressure (see Fig. 13). Increases in response frequency could not be maintained when intense pressure was applied (see below). Due to their classic low threshold (<0.5 g), slow adaptation with irregular firing pattern, rapid conduction velocity (47.9±2.4 m/s), and the scarcity of Ruffini endings in the papilla (see above), it is likely that these responses were representative of the many Merkel-type endings that were located here. However, a definitive attribution was not possible. We also encountered rapidly adapting, fast-conducting low-threshold afferents (data not shown). Surprisingly, these were relatively rare in our recordings. This form of activity may have been representative of the myelinated axons from the Pacinian or small lamellated corpuscles we observed histologically (see above).

High-threshold mechanoreceptors

Afferents were categorized as Aδ mechanonociceptors based upon their conduction velocity (22.3±10.9 m/s;

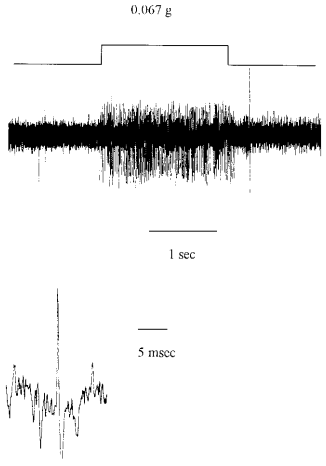
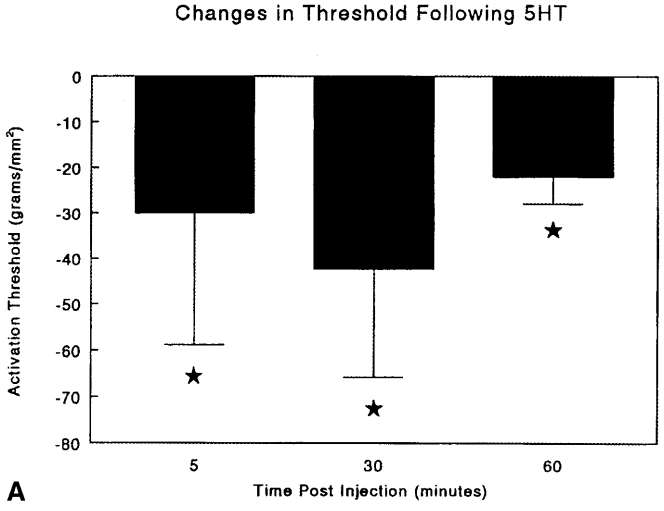


Fig. 13 Response of a low-threshold mechanoreceptor with a receptive field on the papilla incisiva. Application of a von Frey monofilament (0.067 g) produced a slowly adapting response for the duration of the application. An enlarged action potential is shown below. The conduction velocity was 52 m/s



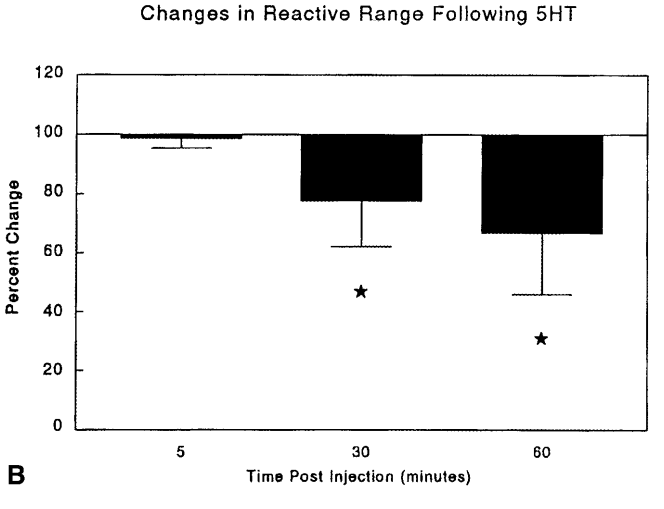
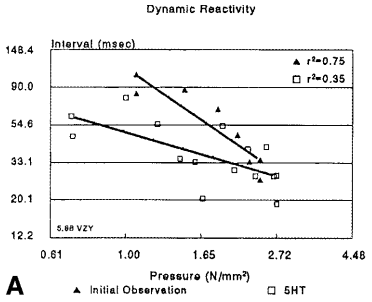
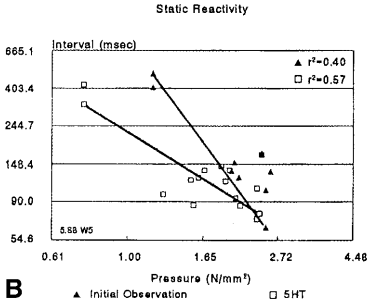


Fig. 14A, B Serotonin-sensitized, Aδ high-threshold mechanoreceptors. **A** The activation of mechanonociceptors was decreased at 5, 15, and 30 min following injection of 60 nmol serotonin (*5HT*). Significant reductions were observed at all intervals (see text). **B** The response range of mechanonociceptors was significantly decreased at 30 and 60 min following serotonin injection. The response range was defined as the difference between the activation threshold and the force that produced the peak frequency response





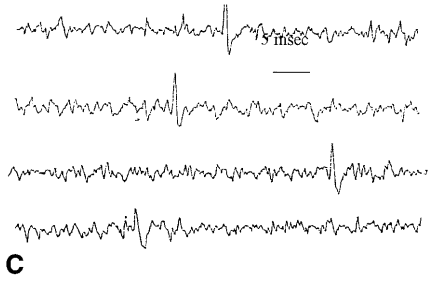


Fig. 15A–C Coding functions were shifted following treatment with serotonin (*5HT*). Power functions were fit to interval data, as described in methods. The resulting functions completely described the threshold and suprathreshold reactivity of these high-threshold mechanoreceptors. In **A** and **B**, there is a shift in minima, which is a reflection of the decrease in activation threshold. Some changes in dynamic range were also apparent (minima-maxima). Functions shown are prior to and 5 min following serotonin injection. **C** Action potentials of an Aδ MN. Coefficients of variation of fitted functions are given in *upper right* of each graph

mean ± standard deviation), high threshold (mean of 92.0 g/mm^2; 9.2 bar), punctate receptive fields and lack of apparent thermal reactivity. Mechanonociceptors were easily distinguished from low-threshold mechanoreceptors (LTMs) by these features. Further evidence that these high-threshold mechanoreceptors were nociceptive was obtained by demonstration of sensitization.

Serotonin modified both threshold and suprathreshold features of nociceptor reactivity. Injection of serotonin (60 nmol in 5 µl) into the receptive field produced rapid shifts in activation thresholds and delayed shifts in transduction range (Fig. 14). Shifts in activation thresholds were apparent within 5 min after injection. Changes persisted throughout all time intervals (5, 30, and 60 min, respectively) and were significantly different from control, saline-injected (5 µl) cases as well as non-injected cases that were tested over the same time intervals (U=23, n=9

and 17, $P<0.002$; $U=22$, $n=10$ and 15, $P<0.002$; $U=5$, $n=4$ and 11, $P<0.05$ at 5, 30, and 60 min intervals, respectively). Threshold decreases were substantial at each test. Threshold decreased rapidly over the first 30 min, but some recovery was apparent thereafter (30.0±28.9, 42.4±23.4, and 22.0±5.9 g/mm^2 at 5, 30, and 60 min, respectively).

Serotonin also produced shifts in the suprathreshold coding range, which were consistent with hyperalgesia. These changes were delayed relative to threshold. Significant shifts in coding range (mean dynamic range) were observed at both the 30-min (77.7±15.5%; $P<0.008$, $n=9$) and 60-min (66.8±20.8%; $P<0.031$, $n=6$) test periods. There was little evidence of sensitization at the 5-min delay (98.7±3.2% of control observations**).** Two individual cases are illustrated in Fig. 15.

Based upon the conduction velocity, threshold, coding range, and capacity for sensitization, it was likely that these high-threshold mechanoreceptors were nociceptive. They may have been representative of the numerous free nerve endings that were present in the epithelium and lamina propria of the papilla incisiva.

Discussion

The present study demonstrates that the goat hard palate is richly supplied with a variety of mechanoreceptors. The papilla incisiva of the goat has a high number of free nerve endings as well as specific mechanoreceptors, such as Merkel cell receptors, lamellated corpuscles, and a few Ruffini corpuscles.

Merkel nerve endings

Merkel cells were found in groups of up to eight in the epithelial pegs of the papilla incisiva and rugae palatinae. In the papilla incisiva, they were seen in almost every single epithelial peg, while they were less widespread in the rugae palatinae, with generally decreasing numbers in aboral direction. Merkel cell receptors are low-threshold mechanoreceptors with slowly adapting responses (SA-I receptors; see Iggo and Muir 1969). Also in the goat palate, responses of Merkel-cell receptors to low-stimulating forces of less than 1 g within a very narrow receptive field showed the characteristic irregular firing pattern (Horch et al. 1974; Baumann et al. 1990). In contrast to "touch domes" in the skin, with up to 50 Merkel cells, or those in the cheek pouch of the hamster, with up to 200 Merkel cells (Tazaki and Iggo 1998), such large accumulations of Merkel cells forming epithelial protrusions (touch domes) were not seen in the goat papilla incisiva. It has been shown that most touch domes are innervated by one myelinated axon irrespective of the number of Merkel cells (Nurse et al. 1984). Thus, in the papilla incisiva, the spatial resolution must be much higher than in touch domes, which may have a lower threshold due to the high convergence of receptors on a single nerve fiber.

On the other hand, the position and orientation of Merkel cells and corresponding nerve terminals is well comparable with the situation in the skin: the nerve terminal was on the side of the Merkel cell facing the basement membrane. This is in clear contrast to the orientation of Merkel cells and nerve terminals in the monkey papilla incisiva, where they are oriented perpendicular rather than parallel to the epithelial surface (Halata and Baumann 1999). This suggests that the Merkel cell is located on that side of the nerve terminal which is exposed to the mechanical stimulus. Although the role of the Merkel cell in these receptors is still controversial (Mills and Diamond 1995), the location of the Merkel cell towards the mechanical stimulus would be in line with the assumption that the mechanoelectric transduction process takes place in the Merkel cell rather than the nerve terminal (Iggo and Findlater 1984; Ogawa 1996; Senok et al. 1996; Senok and Baumann 1997). In the monkey, the papilla incisiva is hidden behind the alveolar process of the incisors and, thus, exposed to pressure applied by the tongue. In this way, the food can be checked while pushed against the hard palate. In contrast, in the goat, the upper incisors are missing and the food is checked before being pulled off by squeezing between lips, tongue, and papilla incisiva. In this study, we did not observe any Merkel cells without contact to nerve terminals. Nor did we find any "dendritic" Merkel cells (Tachibana 1995; Tachibana et al. 1997).

Ruffini corpuscles

Only very few Ruffini corpuscles were found in the goat papilla incisiva (one or two), which were of simple structure in contrast to those in the locomotion apparatus (Halata 1988). Here, they were located in the deep layers of the connective tissue and closely linked to the collagen fibers of the lamina propria. The capsule of the Ruffini corpuscles was developed only in fragments. Through these gaps in the capsule, bundles of collagen fibers entered the corpuscle to contact the terminal branches of the myelinated nerve fiber. In the skin and joint capsules, Ruffini corpuscles are known to have large receptive fields, responding with slowly adapting responses to tissue stretch (Chambers et al. 1972). Thus, a small number of Ruffini corpuscles should be sufficient to monitor the entire papilla incisiva. Their presence suggests that shear forces in the rather dense connective tissue of the papilla incisiva can occur at high mechanical loads.

Lamellated corpuscles

Lamellated corpuscles are found frequently as small Pacinian corpuscles in the mammalian glabrous skin of lips, nose, and finger tips (Halata 1975; Chouchkov 1978). Within the hard palate, two types of lamellated corpuscles have been described: (1) Meissner corpuscles, and (2) small, encapsulated lamellated corpuscles (small Pacinian corpuscles). Meissner corpuscles are mainly found in hu-

man and primates (Munger 1975). In the masticatory mucosa, they can be found in various mammals (Chan and Byers 1985; Tachibana et al. 1989), especially in those parts of the skin and mucosa with pronounced rete pegs linking the epithelium with the underlying connective tissue (Halata and Baumann 1999). The typical example for this arrangement is the ridged skin in the finger tips (Halata 1975). The connective tissue between the epithelial pegs is relatively loose, while the tissue below the pegs is fairly dense, allowing only little movement of the mucosa against the bone of the hard palate. Meissner corpuscles are rapidly adapting mechanoreceptors with small receptive fields (Lindblom and Tapper 1967).

Small lamellated corpuscles are usually found in the dense connective tissue both in skin (Halata, 1975) and locomotion system (Strasmann et al. 1990), while large Pacinian corpuscles are usually located deeper in loose connective tissue of the skin and joint capsules (Halata 1993). Pacinian corpuscles are known to function as rapidly adapting mechanoreceptors (Bolanowski 1988). For this purpose, the lamellae are likely to transmit the mechanical stimulus to the nerve terminal in the center of the inner core, where finger-like cytoplasmic protrusions (see Figure 12) may act as mechanoelectric transducers (Andres and von Düring 1973).

Free nerve endings

Microscopically, two types of free nerve endings could be clearly differentiated: Those reaching the epithelium had a different appearance from those in the lamina propria. As shown in Fig. 2, the terminals of C-fibers did not branch within the epithelium. They resembled “pearl chains” with small thickenings along the terminal part of the axon. Their absolute number was highest in the papilla incisiva, decreasing in dorsal direction, but still relatively small and, thus, they are not easily found during electron microscopy. In contrast, free nerve endings in the lamina propria were mainly supplied by Aδ-fibers. Approaching the papillary layer, these nerve fibers lost their myelin sheath and branched intensively. Unfortunately, the present study does not allow specific identification of those MN-units, which had been examined physiologically. But we believe that those units were free nerve endings of thinly myelinated nerve fibers located in the lamina propria. With normal mean thresholds of 92 g/mm^2, these units are not likely to respond if normal food is pressed against the papilla incisiva.

Sensitization of nociceptors by serotonin

Sensitization of mechanical nociceptors has been observed in a variety of preparations (Friedman et al. 1988; Birrell et al. 1990; Herbert and Schmidt 1992; Rueff and Dray 1992; Cooper et al. 1993). It is well recognized that serotonin (5HT) has the capacity to activate and/or sensitize nociceptive afferents in a variety of species and tissues (Fjallbrandt and Iggo 1961; van Gelder 1962; Beck and Handwerker 1974; Mense and Schmidt 1974; Handwerker 1976; Hiss and Mense 1976; Mense 1981; Heppelmann et al. 1987; Lang et al. 1990). Our observation of rapid and large shifts in activation thresholds and delayed, but substantial shifts in reactive range support and extend observations of a role for 5HT in mechanical allodynia and hyperalgesia (Jensen et al. 1990a, 1990b). These changes in sensation may occur via the sensitization of Aδ MNs by 5HT via the G-protein-coupled 5HT$_4$ receptor. As we have previously reported, it is likely that both the lowered activation threshold and narrowing of the response range are mediated, in part, via the influence of serotonin on TTX-sensitive and TTX-insensitive Na^+ channels (Cardenas et al. 1997).

In conclusion, the goat hard palate is well equipped with sensory nerve endings, which are highly concentrated in the papilla incisiva and decrease in number in aboral direction in the rugae palatinae. This accumulation of both rapidly and slowly adapting mechanoreceptors in the papilla incisiva can be seen as a functional adjustment for the monitoring of food before it enters the mouth. In addition, these receptors may help to control the position of the tongue during chewing and the pressure applied by the tongue. Extensive innervation of superficial layers by free nerve endings provides a means of detecting noxious stimuli and discouraging continued use of inflamed or damaged tissue.

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