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OBSERVATION ON THE LOCALIZATION OF MECHANORECEPTORS IN THE KIDNEY AND AFFERENT NERVE FIBRES IN THE RENAL NERVES IN THE RABBIT

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SUMMARY

1. The distribution and localization of mechanoreceptors in the kidney were studied by recording afferent impulses from the renal nerve bundle or from single nerve fibres in the isolated kidney preparation in the rabbit.

2. It was observed that mechanoreceptors are distributed in the cranial, central and caudal portions as well as the pelvic portion of the kidney. Diameter range of single nerve fibres from which afferent impulses were recorded was from 2 to 8 μm.

3. Histological studies show that the renal nerve possesses abundant non-myelinated nerve fibres with a relatively small number of myelinated nerve fibres. The myelinated axons had diameters ranging from 0·5 to 13·4 μm and the peak of the unimodal distribution curve was 1·5–2·4 μm.

INTRODUCTION

There are several reports on afferent discharges from mechanoreceptors in the kidney of different animals such as rats (Åström & Crafoord, 1967), cats (Åström & Crafoord, 1968; Beacham & Kunze, 1969), dogs (Ueda, Uchida & Kamisaka, 1967; Uchida, Kamisaka & Ueda, 1971) and rabbits (Niijima, 1971, 1972).

These reports locate the mechanoreceptors mainly in the parenchyma of the kidney, although Åström & Crafoord (1968) suggested that afferent discharges originated from receptors in the pelvis of the kidney. Niijima (1971) also observed a burst of discharge from fine filaments of renal nerves accompanying the manual compression of pelvic area of the kidney.

However, the distribution, the localization, the size of the receptive field and the diameter of the afferent nerve fibres from mechanoreceptors still remained unclear.

This paper is mainly concerned with these features as studied by electrophysiological and histological methods.

METHODS

Experiments were performed on rabbits. Adult animals of either sex were used. The animals were anaesthetized with urethane (1 g/kg) injected s.c. Both kidneys with renal artery, renal vein and renal nerve trunks were isolated. Oxygenated Locke's solution was delivered by catheter from a reservoir to the renal artery. The temperature of the perfusion solution was kept about 25° C. The solution entered through the renal artery, circulated in the kidney, and exited through the renal vein (Niijima, 1971).

Afferent impulse discharges were recorded from filaments of renal nerves or from single afferent nerve fibres which were dissected from the peripheral cut end of renal nerve trunks under a dissection microscope (× 80). All dissected single nerve fibres were examined by a high-power microscope and in some cases photomicrographs were taken to measure the diameters. To localize the receptive fields, a pressure stimulus (nylon hair) was used.

After placing the dissected nerve fibre or renal nerve filament on bipolar silver–silver chloride wire electrodes, discharges were recorded through a condenser-coupled differential amplifier (time constant 0·003 sec) with a kymograph camera.

For histological examination, renal nerve trunks were excised from the animal and immediately immersed in 2 % (w/v) ice-cold OsO_4 buffered to pH 7·4 with veronal acetate. After dehydration the tissues were soaked in propylene oxide, passed into a mixture of epoxiresin and propylene oxide, and embedded in epoxiresin. The block obtained was trimmed and sectioned transversely with a Porter–Blum ultramicrotome at 1 μm in thickness. For observation and taking photomicrographs, sections were mounted on a glass slide and stained by warm 1 % toluidine blue for 5–6 min (Yamamoto, 1963).

RESULTS

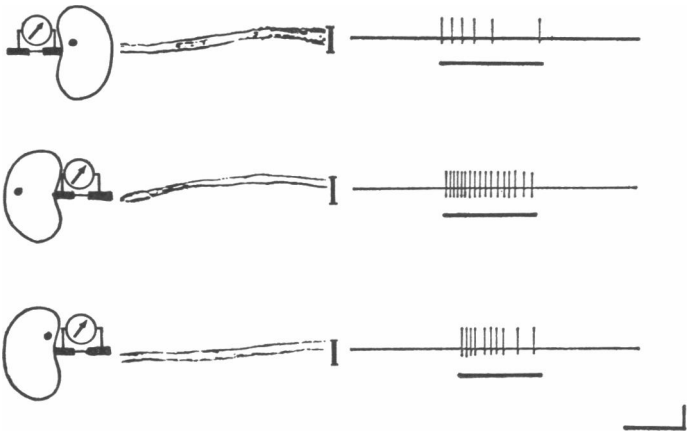
Afferent impulse discharges from the renal nerve trunk. When a renal nerve trunk of an isolated kidney preparation was placed on the recording electrodes and perfusion pressure was kept at 0 mmHg, no resting discharge could be detected. When a pressure stimulus by a nylon hair was applied on the surface of the kidney, a burst discharge was observed.

For convenience, the surface of the kidney was differentiated into four areas – cranial, central, caudal and pelvic portions. The pressure stimuli were applied to these four areas in order to compare the responses. Approximately similar amplitudes of burst discharges were observed from the renal nerve trunk in relation to the pressure stimuli applied to these areas. However, no response could be elicited by a light touch on the surface of the kidney. After peeling off the peritoneal membrane from the kidney, similar responses could still be observed.

After cutting off the ventral half of the kidney in order to permit stimulus presentation directly to the parenchyma, burst discharges were also observed following pressure stimuli to the cortex or to the medulla

of the kidney. In a preparation in which all parts of the kidney were cut off except the pelvis and papilla, a pressure stimulus given to these areas or a stretch of the wall of the pelvis by a pair of forceps evoked burst discharges in the renal nerve trunk. Care was taken in this preparation not to damage the renal nerve.

These results suggest the existence of mechanoreceptors in the kidney not only on the surface, but also in the parenchyma and in the pelvic area. The similarity of the responses observed by stimulation of four different areas also suggests that these mechanoreceptors are distributed with uniform density over the whole kidney.



Text-fig. 1. Afferent impulses recorded from single nerve fibres dissected from renal nerve trunks (rabbit; isolated kidney). Left: schematic illustrations of excised kidney preparations. Filled circles show areas sensitive to pressure stimulation of the surface of the kidney. Middle: photomicrographs of single nerve fibres from which afferent impulses were recorded. Scales at the right side show 10 μm. Right: afferent impulses elicited by pressure stimuli by a nylon hair. Horizontal bars (= 1 sec) below each trace show the time of mechanical stimulation. Vertical bar, 100 μV.

Distribution of renal mechanoreceptors studied by single nerve fibre recording. To detect the receptive field area, single afferent nerve fibres were dissected from renal nerve trunks and recordings were made from them. When a pressure stimulus by a nylon hair was applied within a small area through the surface of the kidney after stopping the perfusion, a train of afferent impulses was observed. When the stimuli were applied to areas other than this receptive field area, no impulses were observed. In this way the distribution of mechanoreceptors and the size of each receptive field area was studied. In some instances, photomicrographs were taken to estimate the diameter of afferent nerve fibres before

recording. It was observed without exception that each receptive field was innervated by one afferent nerve fibre. The size of the receptive field was relatively small and spot-like (1–2 mm in diameter). Text-fig. 1 shows examples of three different receptive fields situated at the pelvic portion (above), central portion (middle) and the border of the pelvic and cranial portions (bottom). These three receptive fields were innervated by three different afferent nerve fibres (photomicrographs). The trains of afferent impulses elicited by pressure stimuli applied to the receptive fields show slow adaptation in these preparations, although there are slight differences in discharge patterns.

TABLE 1. Characteristics of renal afferent nerve fibres and mechanoreceptors in the kidney

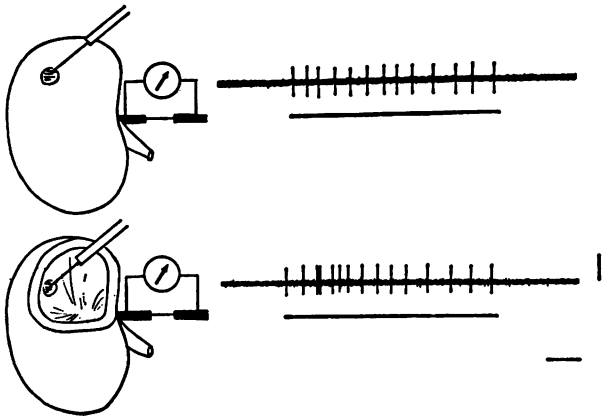
Fibre no.	Diameter (μm)	Adaptation of receptor	Situation of receptor
1	4	Slow	Caudal portion
2	4	Slow	Caudal portion
3	3	Slow	Caudal portion
4	8	Slow	Caudal portion
5	6	Slow	Cranial portion
6	2	Slow	Caudal portion
7	5	Slow	Pelvic portion
8	4	Slow	Central portion
9	4	Slow	Pelvic portion
10	3	Slow	Central portion
Average	4·3		

On ten different single afferent nerve fibres, the fibre diameter and the location and rate of adaptation of the corresponding receptors were studied (Table 1). All of these studies were made by pressure stimuli applied through the surface of the kidney. These receptive fields were found throughout the kidney.

Localization of renal mechanoreceptors. From the experimental results described above, it is suggested that there are two main locations of receptors in the kidney – in the parenchyma and in the wall of the pelvis.

Text-fig. 2 shows the localization of a receptor in the parenchyma of the kidney. A pressure stimulus applied on the surface elicited a train of afferent impulses in the single nerve fibre when it was applied on the receptive field area at the cranial portion of the kidney. The effective stimulus is not a light touch on the surface but a pressure, suggesting the localization of the receptor inside the kidney (Text-fig. 2, above). Small pieces of the kidney parenchyma were then taken off step by step in order to localize the receptor. It was localized in the medulla near the cortex

at the cranial portion of the kidney. A train of discharges was observed when a pressure stimulus was applied on this area (Text-fig. 2, below). The discharge pattern shows that the receptor belongs to the slowly adapting type.

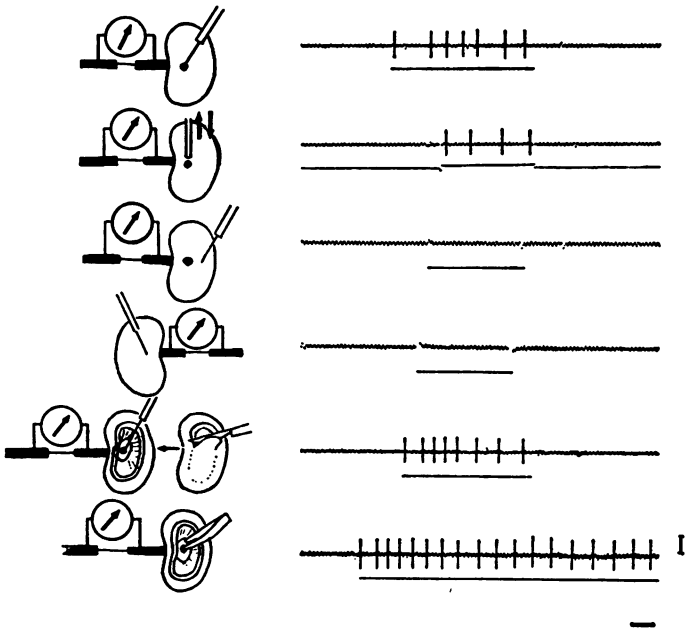


Text-fig. 2. Location of mechanoreceptors in the parenchyma of the kidney (rabbit, isolated kidney). Left: schematic illustrations of kidney preparation. Shaded circles show areas sensitive to pressure stimulation. Right: afferent impulses recorded from a single nerve fibre. Above, mechanical stimulation to the surface of the kidney. Below, mechanical stimulation to the parenchyma of the kidney after resection of part of the parenchyma. No afferent impulses could be observed after resection of shaded area. Horizontal bar, 1 sec. Vertical bar, 100 μV.

Text-fig. 3 shows the localization of a receptor in the wall of the pelvis. The receptive field area was detected at the pelvic portion of the kidney by means of the pressure stimulus applied to the surface of the kidney (Text-fig. 3, top). The receptor showed a slowly adapting response to a constant pressure stimulus (Niijima, 1970) given by a magnet device (Text-fig. 3, second trace). A stimulus applied outside the receptive field area caused no response (Text-fig. 3, third and fourth trace). After cutting off the ventral half of the kidney, a sensitive spot to pressure stimulus was found on the wall of the pelvis. A train of afferent impulses was observed when a pressure stimulus by a nylon hair or a slight pinch by a pair of forceps was applied on the sensitive spot of the pelvis. The same response was observed by a stretch of the wall of the pelvis with a pair of forceps (Text-fig. 3, fifth and sixth trace).

Histological studies

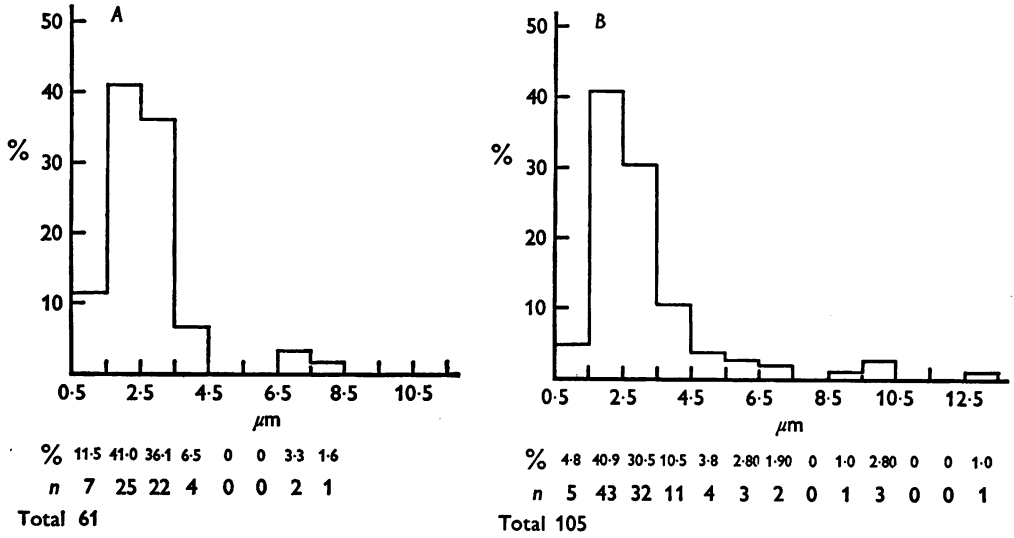
Observations were made to study the fibre content of the renal nerve. Results presented below show that the renal nerve possesses numerous non-myelinated fibres besides a rather small number of myelinated axons.



Text-fig. 3. Location of mechanoreceptor in the pelvis of the kidney (rabbit, isolated kidney). Left: schematic illustrations of the kidney. Filled circles show receptive field area. Right: afferent impulses recorded from a single nerve fibre. Top trace, mechanical stimulation to receptive field on the surface of the kidney by a nylon hair. Second trace, mechanical stimulation with constant pressure by a magnetic device. Third trace, mechanical stimulation applied outside the receptive field. Fourth trace, mechanical stimulation applied to dorsal surface of the kidney. Fifth trace, mechanical stimulation applied to the receptive field on the pelvis after cutting off the ventral half of the kidney. Sixth trace, distension of the wall of the pelvis by a pair of forceps. Horizontal bars below each trace show the time of stimulation. Horizontal bar, 1 sec. Vertical bar, 100 μV.

Pl. 1 illustrates a cross-section of a renal nerve trunk. The abundance of non-myelinated fibres is evident. The myelinated nerve fibres are scattered in the bed of non-myelinated nerve fibres (low-power magnification). In a photomicrograph taken with high-power magnification, the Schwann-cell nucleus can be seen surrounded by a number of non-myelinated nerve fibres.

The diameter distribution curve of myelinated nerve fibres in this nerve bundle is shown in Text-fig. 4*A*. A total of sixty-one myelinated nerve fibres observed in this nerve bundle were divided into eight classes at 1 μm intervals. The fibre diameter shows a unimodal distribution range from 0·5 to 8·4 μm, with a peak at 1·5–2·4 μm. Text-fig. 4*B* shows the diameter distribution of total myelinated nerve fibres in a renal nerve consisting of three nerve bundles. These three nerve bundles were about the same size in diameter (0·1 mm). One bundle contained numerous non-myelinated nerve fibres with a small number (9) of myelinated fibres.



Text-fig. 4. *A*, diameter distribution curve of myelinated nerve fibres in a bundle of renal nerve in rabbit. Photomicrographs of this bundle were shown in Pl. 1. *B*, diameter distribution curve of myelinated nerve fibres in a renal nerve which consisted of three nerve bundles.

The other two bundles had about the same number (52 and 44) of myelinated nerve fibres. The total of 105 myelinated nerve fibres were divided at 1 μm intervals into thirteen classes to present a diameter distribution curve (Text-fig. 4*B*). The fibre diameter shows a unimodal distribution ranging from 0·5 to 13·4 μm, with a peak at 1·5–2·4 μm. The percentage distribution of the fibre diameters is presented in detail in Text-fig. 4*B*.

These data show that most of the myelinated nerve fibres in the renal nerve are small in diameter, with over 90% falling in the range 0·5–6·4 μm.

DISCUSSION

The responses recorded from a renal nerve bundle provide evidence that mechanoreceptors are distributed in the cranial, central and caudal portions as well as the pelvic portion of the kidney. Single nerve-fibre recording confirmed that mechanoreceptors exist in these areas, and permitted a more precise localization of mechanoreceptors in the parenchyma and in the wall of the pelvis.

The diameter range of single nerve fibres from which afferent impulses were recorded was from 2 to 8 μm (Table 1) with an average value of 4·3 μm. Conduction velocities calculated from these values (Hursh, 1939) are 12–48 m/sec, with an average of 25·8 m/sec. This is approximately the same value estimated in renal afferent nerve fibres in cats (Beacham & Kunze, 1969). They reported that the average conduction velocity was 23·7 m/sec with a range of 6–45 m/sec.

In the histological studies, the diameter distribution curve (Text-fig. 4*B*) of the myelinated nerve fibres showed tht 93·3 % were from 0·5 to 6·4 μm and 5·7 % from 6·5 to 10·4 μm, with the curve peaking at 1·5–2·4 μm.

It has been assumed that most of the sympathetic nerve fibres in the renal nerve are post-ganglionic non-myelinated axons (Ranson & Clark, 1963). In addition, no vagal innervation has been demonstrated to the kidney through renal nerve (Pitts, 1966). It seems likely, therefore, that the myelinated nerve fibres observed in the renal nerve are afferent in nature.

The diameter distributions of other autonomic nerves, such as the carotid nerve which also contains afferent nerve fibres, are similar to that of the renal nerve. The myelinated nerve fibres in the carotid nerve number from 600 to 700 fibres (de Castro, 1951), and 96·5 % of these fibres had diameters from 1·5 to 5 μm and 3·5 % had diameters of 6–8 μm. Eyzaguirre & Uchizono (1961) obtained a similar diameter distribution in one carotid nerve in the cat.

Concerning the function of the receptors in the parenchyma of the kidney, several suggestions have been presented. Some receptors are considered to be responsive to increases in subcapsular pressure and to venous distension in rat and cat (Åström & Crafoord, 1967, 1968). Beacham & Kunze (1969) suggested that receptors sensitive to change of both ureteral and renal vein pressure are situated deep in the renal medulla. Uchida *et al.* (1971) found receptors in the dog which are responsive to intrarenal pressure and they stated that these are probably situated in the interstitial tissues. Further, Niijima (1971) presented a report that some mechanoreceptors are localized around the arterial walls in the kidney.

With respect to the presence of receptors in the wall of the renal pelvis, Åström & Crafoord (1968) observed in cats that small action potentials were elicited by distension of the pelvis and they stated that these potentials probably originated from so-called visceral pain afferents (non-myelinated C-fibre activity). The present results show that several afferent nerve fibres which have their nerve endings in the pelvis are myelinated. However, the present data also show that there are numerous non-myelinated nerve fibres in the renal nerve, some of which might be afferents from nerve endings in the parenchyma or pelvis of the kidney.

In summary, the present study shows that some afferent fibres originate from mechanoreceptors in the various parts of the kidney. However, it is possible that other types of receptors such as chemoreceptors, osmoreceptors, thermoreceptors and pain receptors are also located in the kidney.

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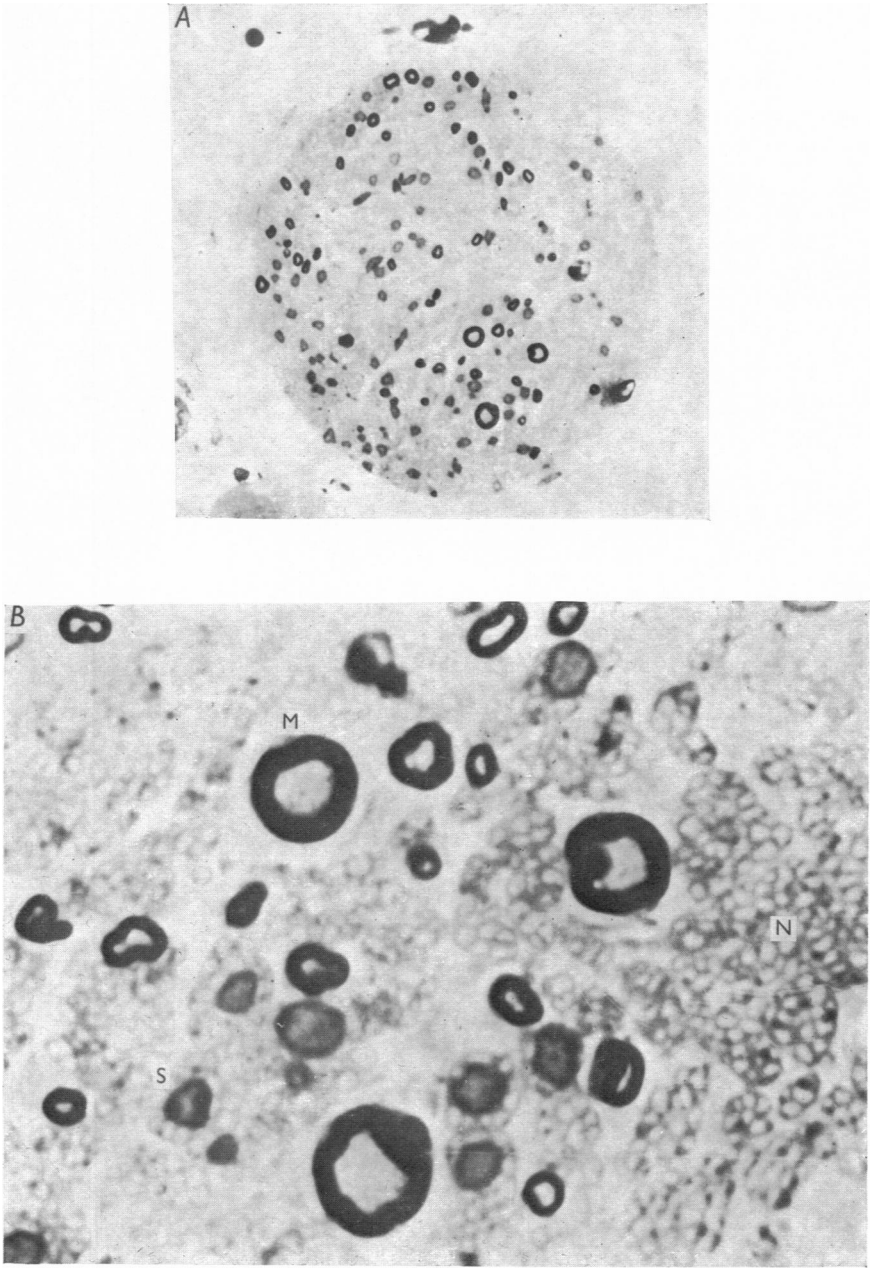
EXPLANATION OF PLATE

Photomicrograph of renal nerve in the rabbit. Upper figure, low-power magnification. Lower figure, high-power magnification. Scales show 10 μm. M, myelinated nerve fibre. N, non-myelinated nerve fibre. S, nucleus of Schwann cell.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