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RESPONSE CHARACTERISTICS OF PULMOCUTANEOUS ARTERIAL BARORECEPTORS IN THE TOAD, *BUFO MARINUS*

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SUMMARY

1. Response characteristics of baroreceptors with receptive fields in the pulmocutaneous artery (p.c.a.) were determined in pithed toads by applying pressure steps, ramps, sine waves, and volume infusions into the vascularly isolated and perfused p.c.a.

2. The baroreceptors exhibited phasic and tonic discharge thresholds ($30{\cdot}3 \pm 2{\cdot}3$ and $36{\cdot}2 \pm 2{\cdot}8$ mmHg respectively) which were above mean arterial pressure values reported for conscious undisturbed toads. They are comparable, in this respect, to non-myelinated mammalian arterial baroreceptors.

3. The maximum-phasic and minimum-adapted discharge frequencies of the p.c.a. baroreceptors were low (30 and 2–3 spikes s^{-1}, respectively), but resembled those reported for mammalian non-myelinated baroreceptors when an adjustment was made for the difference in the temperature of mammalian and amphibian preparations.

4. The sensitivity of the baroreceptor discharge frequency to pressure ($\Delta F/\Delta P$) was estimated from pressure-step and pressure-ramp stimuli. Both estimates were greater than those reported for mammalian systemic arterial baroreceptors after the values were normalized to the maximum discharge frequency of the receptors. $\Delta F/\Delta P$ and saturation discharge frequency values estimated from ramp stimuli increased with the dP/dt of pressure ramps.

5. The diameter of the p.c.a. was measured by sonomicrometry in toads anaesthetized with urethane. The diameter pulsation was $7{\cdot}7 \pm 0{\cdot}3$ % of the mean diameter ($3{\cdot}5 \pm 0{\cdot}1$ mm) at a mean pulse pressure of 22 ± 1 mmHg, and Peterson's pressure–strain modulus was calculated to be $4{\cdot}0 \times 10^5 \pm 0{\cdot}3 \times 10^5$ dyn cm^{-2}, which suggests that the p.c.a. is highly compliant, and in this respect is comparable to the pulmonary artery, but not to systemic arteries, in mammals. Baroreceptor discharge began near the point of peak dynamic compliance (dV/dP) and continued as dV/dP decreased. Increasing the rate of infusion reduced the peak dV/dP, but increased the baroreceptor discharge frequency.

6. The response to sinusoidal oscillating pressure stimuli was distorted by rectification. Increasing the frequency of sinusoidal stimulation over the range 0·05–1·0 cycles s^{-1} reduced the number of spikes per cycle, but increased the mean discharge frequency.

INTRODUCTION

Arterial baroreceptor endings are distributed among each of the three central arterial arches in anuran amphibians (Neil, Strom & Zotterman, 1950; Ishii, Honda & Ishii, 1966; Ishii & Ishii, 1978; Ishii, Ishii & Kusakabe, 1985*a*; Van Vliet & West, 1987). The distribution is similar to that found in mammals (Van Vliet & West, 1987), and is consistent with the suggestion that baroreceptors are restricted to the vascular remnants of the embryonic branchial circulation (Koch, cited by Heymans & Neil, 1958; Adams, 1958). In terms of their demonstrated effects on heart rate, the dominant baroreceptor population in the toad appears to be that located in the pulmocutaneous artery (p.c.a.) (Smith, Berger & Evans, 1981; West & Van Vliet, 1983). This population may be considered to be homologous with the pulmonary arterial baroreceptor population in mammals (Van Vliet & West, 1987).

Toad p.c.a. baroreceptors are active within the physiological range of arterial pressures though their discharge is sparse at pressures approaching those found in resting conscious toads (Ishii & Ishii, 1978; Van Vliet & West, 1987). Recently we reported that p.c.a. baroreceptors were connected to slowly conducting afferents which exhibited conduction velocities typical of non-myelinated fibres (Van Vliet & West, 1987). The presence or absence of myelination in mammalian baroreceptors is associated with marked differences in the structure of the baroreceptive endings, the response characteristics of the receptors, and the baroreflexes which they mediate (Kirchheim, 1976; Thoren, 1981). Whether this association between baroreceptor structure and function exists in other vertebrates cannot be assessed since, with the exception of the properties discussed above, the response characteristics of baroreceptors in ectothermic vertebrates have not been described.

In this paper we describe the response characteristics of p.c.a. baroreceptors in the toad, and compare their characteristics to those of myelinated and non-myelinated mammalian baroreceptors. In order to facilitate comparisons between baroreceptor populations in different circulations and species, we used several stimulating pressure wave forms (steps, ramps, sine waves), and have attempted to derive objective methods of analysis by which baroreceptor response characteristics may be measured and compared.

METHODS

The results described in the present study were obtained from recordings of p.c.a. baroreceptor activity from the recurrent laryngeal branch of the vagus nerve of pithed, unidirectional ventilated, female toads (*Bufo marinus*), following cannulation and vascular isolation of the p.c.a. and the p.c.a. division of the truncus. Experiments were performed year round at room temperature (19–21 °C). The detailed methodology and results for the initial preparation have been described previously (Van Vliet & West, 1987).

Preparation and protocol for applying pressure wave forms to the p.c.a. In preparations in which a single unit, or two clearly distinguishable p.c.a. baroreceptor units were recorded, the extrinsic pulmonary artery was ligated, and the p.c.a. region of the truncus was cannulated with polyethylene tubing. Infusions and pressure wave forms were applied via the truncal cannula, and were monitored via a cannula (PE50, Intramedic) which had been previously implanted in the cutaneous artery and connected to a Beckman 4-327-0 pressure transducer. In preliminary experiments it was found that the resistance of the truncal cannula (PE50, 0·58 mm i.d.) limited the rate of pressure development within the p.c.a. In the experiments which are reported here, we used truncal cannulae of the largest inner diameter possible (up to 1·6 mm i.d., PE205). The isolated p.c.a. was per-

fused with a physiological saline solution of the following composition (mM): Na^+, 110·8; K^+, 2·4; Ca^{2+}, 4·0; Mg^{2+}, 0·9; Cl^-, 109·6; SO_4^{2-}, 0·9; HCO_3^-, 11·5; and $H_2PO_4^-$, 0·1. The solution was aerated with a mixture of 98% oxygen and 2% carbon dioxide (P_{CO_2} = 14 mmHg), adjusted to pH 7·80±0·01 with HCl or NaOH, and 1·8 g glucose l^{-1} was added immediately before use.

Baroreceptor neurograms were recorded during the application of pressure steps, pressure ramps, volume infusions and pressure sinusoids. Pressure steps were generated by opening the truncal catheter to a hydrostatic pressure head (West & Van Vliet, 1983). Since the p.c.a. baroreceptors often discharged when the vessel collapsed at low pressures, pressure steps were superimposed on sub-threshold pressures of 10–25 mmHg. Volume infusions were generated by infusing physiological saline into the truncal cannula at a calibrated rate. Pressure ramps were generated by infusing physiological saline into a mercury column connected in parallel with the p.c.a. catheter. A Harvard Apparatus model 940 pump was used for infusions. At least a 1 min perfusion of physiological saline was given between steps, ramps, or infusions, and the p.c.a. was perfused for 10 min when switching between step, ramp, or infusion protocols. Pressure sinusoids were generated by connecting the truncal cannula in series with a syringe attached to the eccentric cam of a d.c. motor, or to a rubber hose placed within a Harvard Apparatus 1203 peristaltic pump. The p.c.a. pressures were monitored from the cutaneous arterial cannula, and were usually not allowed to exceed 80 mmHg.

Measurement of p.c.a. diameter. Three toads were anaesthetized with urethane (2 g kg^{-1}, I.P.), and were prepared for unidirectional ventilation with a humidified mixture of oxygen (98%) and carbon dioxide (2%). The right p.c.a. was exposed by removal of the foreleg and pectoral girdle on the right side, and the cutaneous artery was cannulated for blood-pressure monitoring. Two epoxy-coated piezoelectric crystals (1·0 mm) were placed on opposing sides of the p.c.a., with their lenses facing each other. The crystals were attached to the arterial wall with cyanoacrylate cement. The crystals' leads were anchored 5 cm from the p.c.a., so that the crystals and their leads floated, and did not influence the position or movement of the p.c.a. The crystals were connected to a piezoelectric sonomicrometer (Tritron Tech Inc.). The output of the sonomicrometer was recorded on a pen recorder together with the p.c.a. pressure trace. The distance between crystals was determined by comparing the sonomicrometer output to calibration signals.

The p.c.a. diameter was recorded at p.c.a. pressures which were varied by occluding the contralateral truncus. For each measurement, the mean p.c.a. pressure and diameter were also determined using a low-pass filter (< 0·08–0·3 Hz). Peterson's pressure–strain modulus (E_p) was calculated as the product of the p.c.a. pulse pressure and mean p.c.a. diameter, divided by the magnitude of the p.c.a. diameter pulse (Milnor, 1982).

Recording and analysis of data. Results presented are based upon the following number of preparations: pressure steps, fourteen; pressure ramps, eleven; volume infusions, eleven; and sine waves, seven. In most cases, several of the pressure stimuli were applied to the same preparation. Some data sets were excluded from grouped-data analysis because of inconsistencies in protocol or stimulating-pressure functions.

All signals were displayed on a Beckman 511A four-channel pen recorder, and were recorded on a Hewlett Packard 3964A four-channel FM tape recorder. Pressures and their first derivative were obtained using Beckman 9853A and 9879 couplers respectively. Neurograms were reproduced on the pen recorder at $\frac{1}{2}$ to $\frac{1}{16}$ of the original recording speed. Spikes were detected based on their amplitude using a Frederick Haer & Co. amplitude analyser. Instantaneous spike frequency was determined using a Beckman 9857B cardiotachometer, or by measuring the spike–spike interval from high-speed pen-recorder tracings.

All reported statistics are expressed as the mean ±the standard error (S.E.) of the mean of n observations on N animals. Linear regressions of raw and transformed data were computed using Curvefit (Johnson, 1984), and where referred to in the text, the variables m and b represent the constants of the regression equation: $Y = mX + b$. In order to describe the adaptation of baroreceptor discharge frequency in response to a step increase in pressure, the mean discharge frequency was determined over 2 s intervals from 0–10 s, and over 5 s intervals from 10–60 s. A power function of the form:

$$F(t) = Bt^{-k}, \text{ for } t > 0, \tag{1}$$

was fitted to the data by performing a regression of $\ln(F)$ against $\ln(t)$, where F is the mean discharge frequency at time t, $B = \exp(b)$, and $k = -m$. A two-term exponential function of the form:

$$F(t) = A \exp(-t/\tau) + F_\infty, \text{ for } t > 0, \tag{2}$$

was also fitted to the data by performing regressions of F against $\exp(-t/\tau)$, where A and F_∞ represent the regression slope and y-intercept, respectively. Multiples of 0·1 starting at 0·0 were used for the value of τ. The final value of τ was considered to be the value which produced the maximum-regression F statistic. Solution of the exponential equation and plotting of three-dimensional graphs of raw and fitted data were performed using an IBM personal computer and programs written in BASICA (Microsoft Corp.).

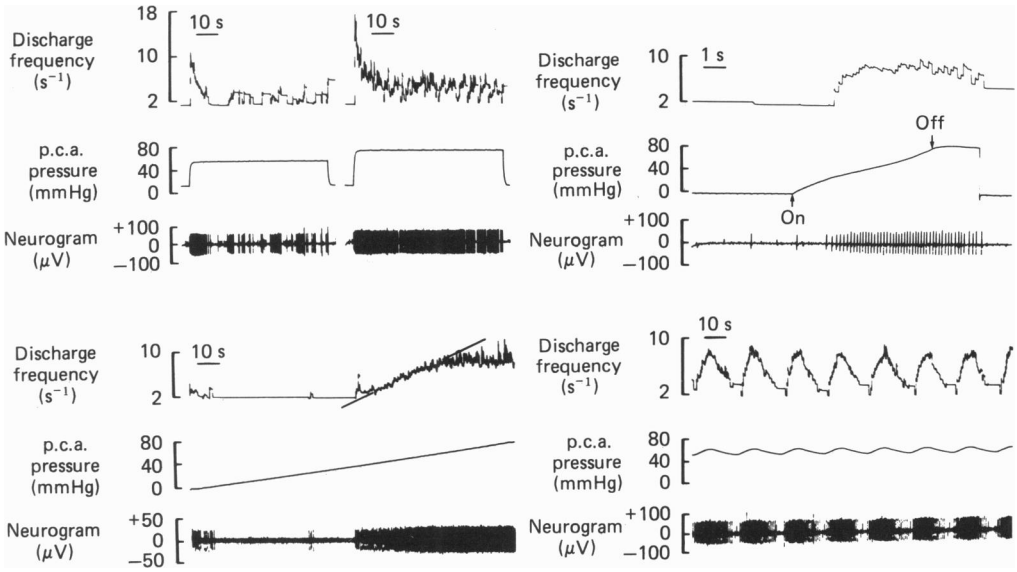

Fig. 1. Response of p.c.a. baroreceptors to the four pressure wave forms used in the present study. Upper left: response to two 60 s pressure steps. Lower left: response to slow pressure ramp (0·6 mmHg s^{-1}). Line drawn on discharge-frequency trace illustrates graphical estimation of rate of change of discharge frequency with time used in calculating pressure sensitivity (dF/dP). Upper right: response to infusion of physiological saline at constant rate (32 μl s^{-1}). Arrows indicate when infusion began and ended. Lower right: response to sinusoidal pressure stimuli. Mean and pulse pressures were 55 and 10 mmHg respectively. Frequency was 0·05 s^{-1}. All tracings are from different units. Time bars are given in upper-left-hand corner of each trace.

RESULTS

Response of p.c.a. baroreceptors to pressure steps

Step increases in p.c.a. pressure elicited a rapid burst of firing which then decreased with time (Fig. 1). Unless the pressure was held well above threshold values, the discharge subsided and was replaced by infrequent bursts of activity. Increasing the height of the pressure step elicited a tonic discharge, but even at high pressures the tonic discharge was often irregular. In general, the discharge became intermittent if the frequency fell below 2–4 spikes s^{-1}.

Phasic (maximum-instantaneous) and mean-adapted (45–60 s) baroreceptor discharge frequencies increased as a non-linear function of the height of pressure steps, but the relationship could be linearized by using a logarithmic pressure scale (Fig. 2). Regressions of the discharge frequency against the natural logarithm of the pressure-step height were highly significant (regression correlation coefficient,

$R = 0{\cdot}946$, $N = 8$, $n = 16$; Fig. 3), and were marginally more significant then regressions of discharge frequency against the inverse or power functions of the pressure-step height ($R = 0{\cdot}943$ and $0{\cdot}941$ respectively). Pressure thresholds, estimated as the x-intercept of the regression lines (i.e. $P = \exp(-b/m)$), were $30{\cdot}3 \pm 2{\cdot}3$ and $36{\cdot}2 \pm 2{\cdot}8$ mmHg for phasic and adapted discharge respectively (Fig. 3). The

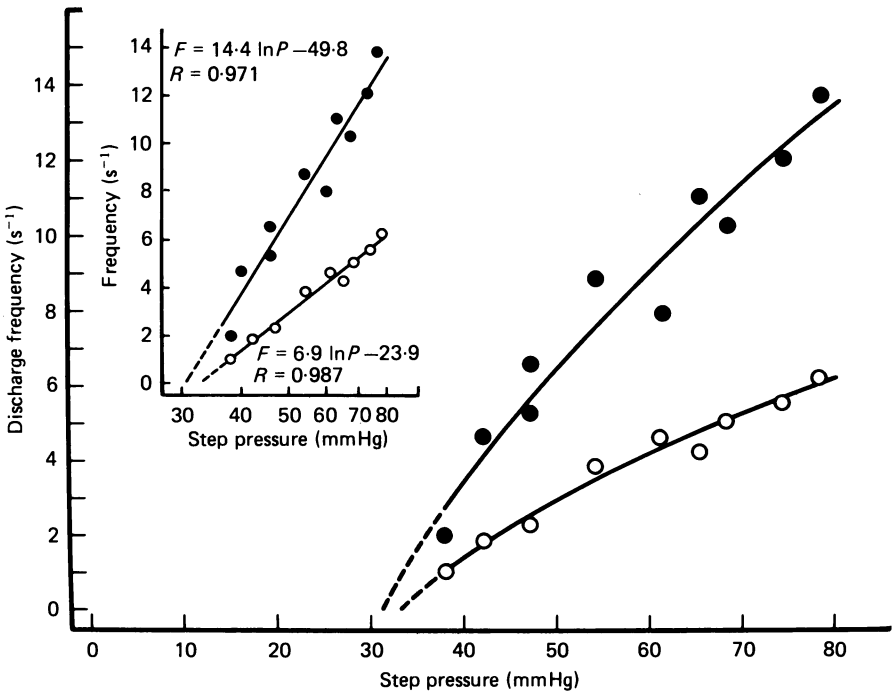

Fig. 2. Relationship between pressure-step height and phasic (maximum-initial, filled circles) and adapted (45–60 s, open circles) baroreceptor discharge frequency. Linear relationship between discharge frequency and the natural logarithm of pressure-step height is shown for the same receptor in the inset (upper left). The regression equation for the linearized relationship was $F = m \ln P + b$, where F is the mean discharge frequency, and P is the pressure-step height. Data were obtained from the response of a single p.c.a. baroreceptor unit to ten pressure steps. The dashed lines in the inset represent the extrapolated region of the regression lines.

maximum phasic discharge frequency of the receptors was $13{\cdot}7 \pm 2{\cdot}6$ spikes s^{-1} at step pressures of $75{\cdot}5 \pm 1{\cdot}7$ mmHg ($N = n = 8$), but frequencies up to 30 spikes s^{-1} were observed in some units. The slope (m) of the linearized relationship ranged from 7·0 to 35·1 spikes s^{-1}, and from 4·1 to 8·6 spikes s^{-1} for phasic and adapted firing respectively (Figs. 2 and 3). The slope represents the increase in discharge frequency for each e-fold (2·72) increase in pressure, and was used to calculate pressure sensitivity of the baroreceptor discharge ($\Delta F/\Delta P$), since for the regression equation used in Figs. 2 and 3:

$$\Delta F/\Delta P = m/P, \text{ for } P \geqslant \text{threshold}. \quad (3)$$

Sensitivity values predicted by eqn. (3) for phasic and adapted discharge at threshold pressures were $0{\cdot}51 \pm 0{\cdot}09$ spikes s^{-1} $mmHg^{-1}$ and 0·19 spikes s^{-1} $mmHg^{-1}$, respectively ($N = n = 8$).

Adaptation rates estimated as the mean fractional exponent of the power function in eqn. (1) for each baroreceptor ranged from $0{\cdot}134 \pm 0{\cdot}01$ to $0{\cdot}512 \pm 0{\cdot}08$ ($N = 9$, $n = 64$; mean $= 0{\cdot}245 \pm 0{\cdot}04$, $N = n = 9$). The time constant of adaptation determined by exponential fitting (eqn. (2)) ranged from $3{\cdot}7 \pm 0{\cdot}3$ to $20{\cdot}1 \pm 7{\cdot}5$ s ($N = 9$, $n = 67$; mean $= 10{\cdot}3 \pm 1{\cdot}9$ s, $N = n = 9$). The result of exponential modelling

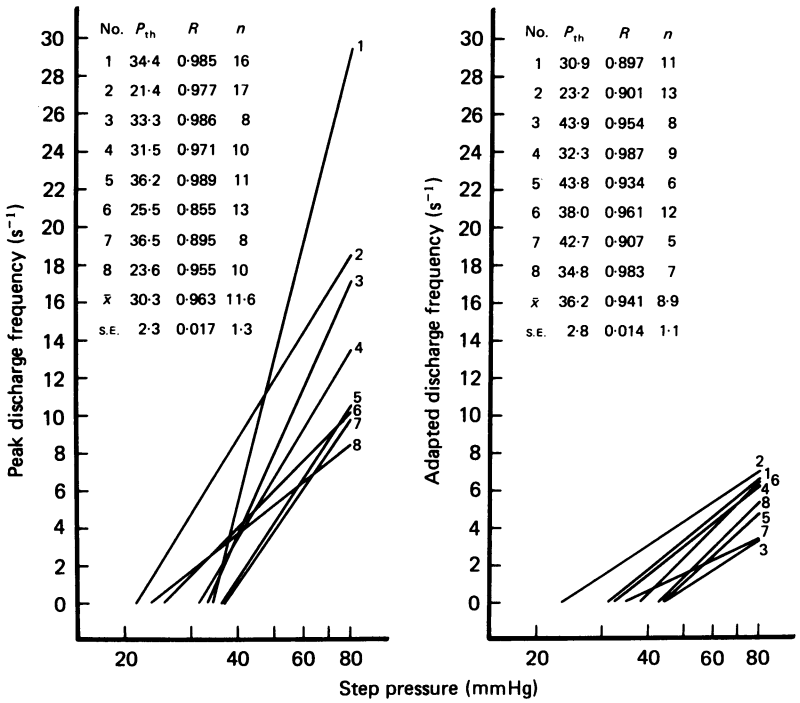

Fig. 3. Relationship between pressure-step height and phasic (left) and tonic (right) discharge frequencies of eight p.c.a. baroreceptors. Regression correlation coefficients (R), number of pressure steps used, and estimated pressure threshold (P_{th}) are shown in the inserted Tables (upper-left-hand corners).

of adaptation is shown in Fig. 4, which illustrates the time course of adaptation for the baroreceptor units exhibiting the longest, median and shortest time constants.

Response of p.c.a. baroreceptors to pressure ramps

Pressure ramps were included in the protocol in order to relate the discharge of the baroreceptors to the first derivative of the p.c.a. pressure (dP/dt). Pressure ramps were delivered at five or six different rates between approximately 0·5 and 30 mmHg s^{-1} over the range 0–80 mmHg. Typical results are shown in Fig. 1. Some baroreceptors discharged continuously at 0 mmHg, but stopped firing as the pressure increased above 10–25 mmHg. Intermittent baroreceptor firing then started at pressures between 30 and 50 mmHg. Continuous firing began at $40{\cdot}7 \pm 0{\cdot}9$ mmHg at discharge frequencies between 2–4 spikes s^{-1} and increased approximately linearly with pressure until a saturation frequency was reached (Fig. 1). The slope of the near-linear portion of the increase in frequency ($\Delta F/\Delta t$) was estimated graphically,

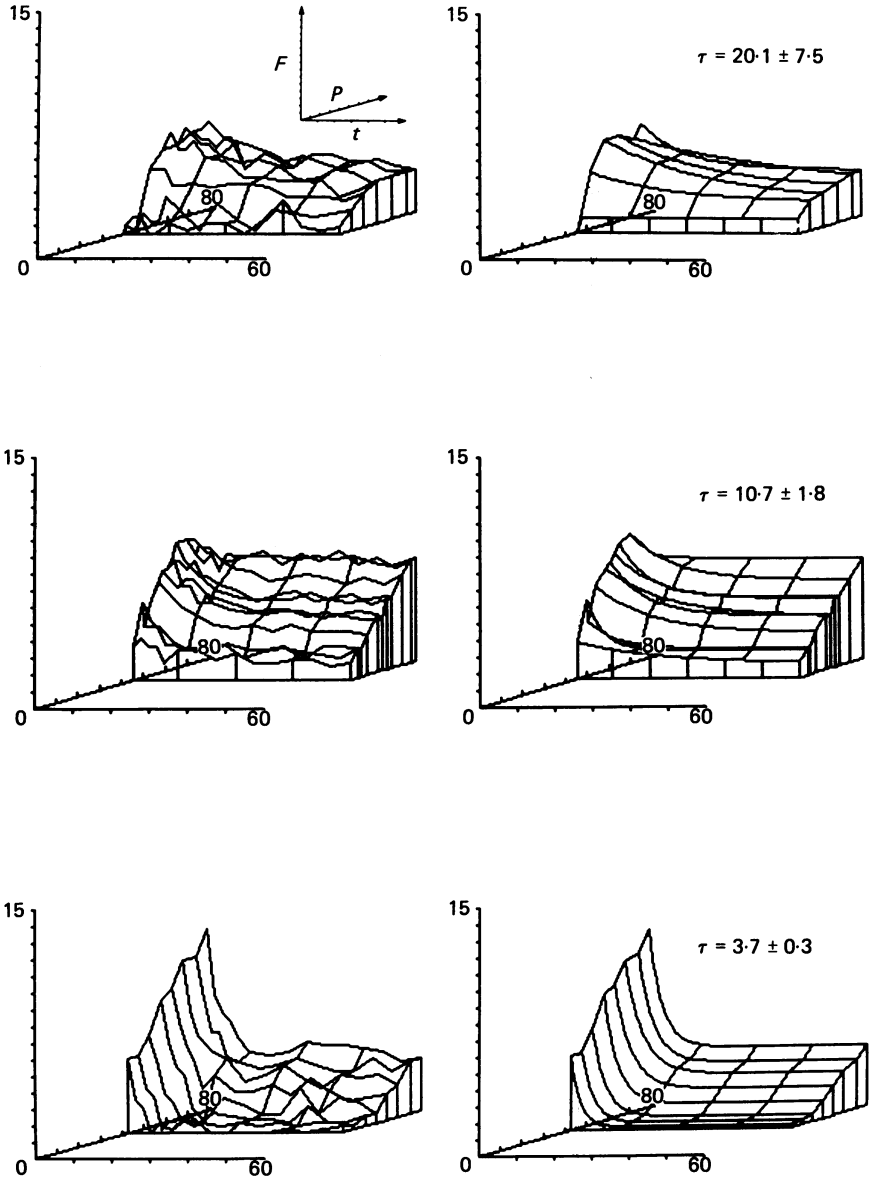

Fig. 4. Three-dimensional representation of the adaptation of p.c.a. baroreceptors to step changes in pressure. Left: graphs for raw data plotted at 2 s intervals from 0 to 10 s and 5 s intervals from 10–60 s. Right: graphs for same data following fitting of the data by the exponential function given in eqn. (2). Discharge frequency (F, s^{-1}), pressure-step height (P, mmHg) and time (t, s) axis are shown in upper-left-hand corner. The examples selected represent the data with the largest (top), median (middle) and smallest (bottom) time constants (τ).

and the receptor sensitivity over the linear range was calculated as the quotient of $\Delta F/\Delta t$ and dP/dt. Sensitivity of individual receptors ranged from $0{\cdot}19 \pm 0{\cdot}03$ to $0{\cdot}52 \pm 0{\cdot}12$ spikes s^{-1} $mmHg^{-1}$ (mean $0{\cdot}27 \pm 0{\cdot}03$ spikes s^{-1} $mmHg^{-1}$, $N = 11$, $n = 58$). Sensitivity increased with dP/dt in ten of eleven preparations, and saturation frequency increased with dP/dt in all preparations. Fig. 5 shows the results for five baroreceptor units for which the dP/dt values of pressure ramps were similar.

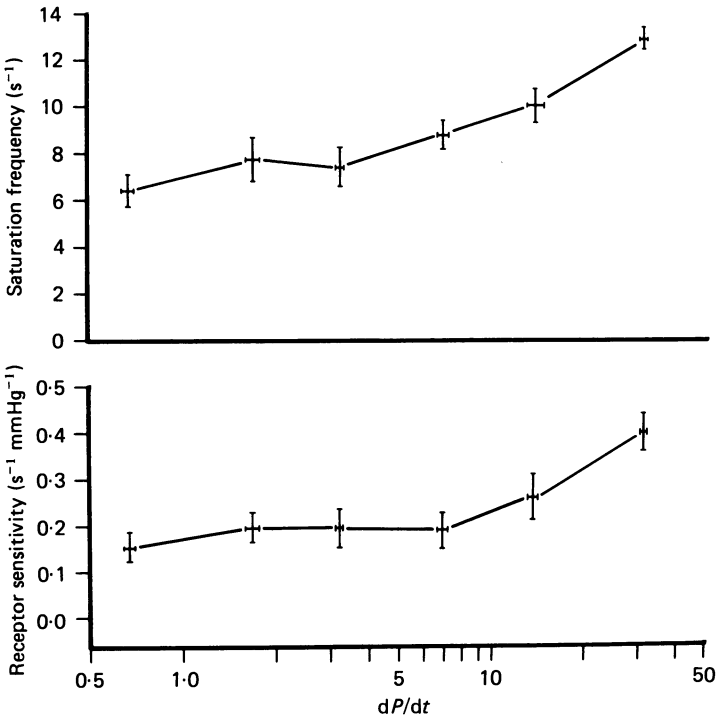

Fig. 5. Effect of the rate of pressure-ramp stimuli (dP/dt, spikes s^{-1} $mmHg^{-1}$) on saturation frequency and sensitivity of p.c.a. baroreceptors. Data points represent the mean values ($\pm$S.E. of mean) from five experiments for which dP/dt values were similar. Saturation frequency was determined as the plateau in discharge frequency (evident in Fig. 1). Receptor sensitivity was determined as the quotient of $\Delta F/dt$ (over an approximately linear range, Fig. 1) and dP/dt.

Response of p.c.a. baroreceptors to volume infusions

The use of volume infusions permitted the dynamic compliance (dV/dP) of the p.c.a. to be determined while simultaneously monitoring the discharge of baroreceptors (Figs. 1 and 6). Pressure–volume curves were sigmoidal; dV/dP initially increased, then decreased, with increasing pressure. Baroreceptor discharge typically began near the point of maximum dV/dP on the pressure–volume curve, and then increased as dV/dP decreased. The dynamic compliance of the p.c.a. was dependent on the rate of infusion: dV/dP was reduced at higher rates of infusion (Fig. 6*B*). Baroreceptor discharge was increasingly sensitive to pressure at higher rates of infusion (Fig. 6*C*), even though the p.c.a. was less distended and dV/dP was less at any given pressure under these conditions (Fig. 6*A* and *B*).

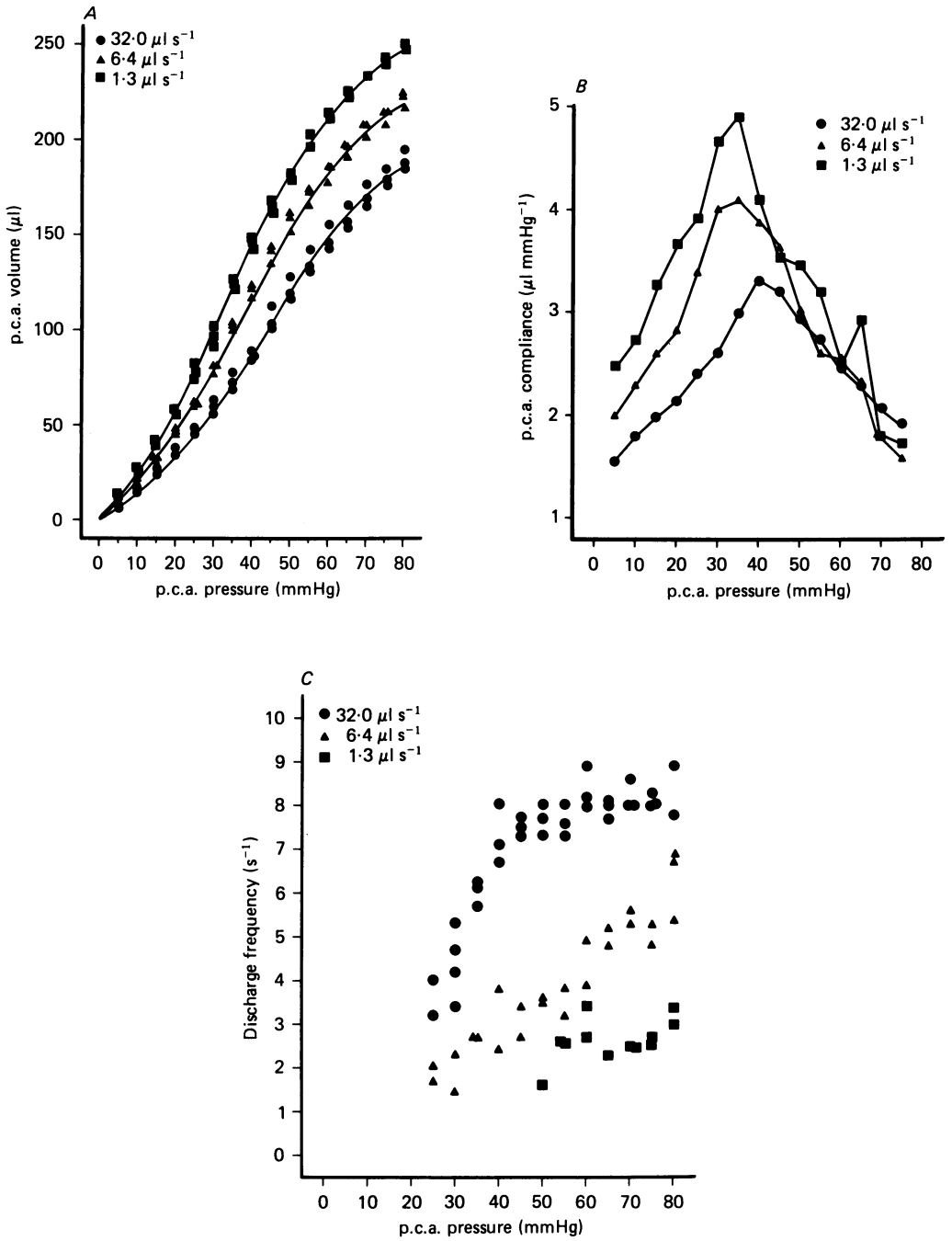

Fig. 6. Effect of the rate of volume infusion on pressure and dynamic compliance of the p.c.a. and p.c.a. baroreceptor discharge frequency. *A*, effect of infusion rate on pressure development within the p.c.a. *B*, effect of infusion rate on dynamic p.c.a. compliance (dV/dP). *C*, effect of infusion rate on the discharge frequency of the p.c.a. baroreceptors. Infusion rate symbols are explained at the top of each graph. Results are based on two to three repeated determinations.

Response of p.c.a. baroreceptors to sine waves

Seven baroreceptor units were subjected to approximately sinusoidal pressure oscillations at a mean pressure of 40 mmHg, a peak-to-peak amplitude of 10 or 15 mmHg, and at frequencies between 0·05 and 1 cycles s^{-1}. The response of the baroreceptors to sinusoidal stimulation was rectified, or 'clipped', since baroreceptor

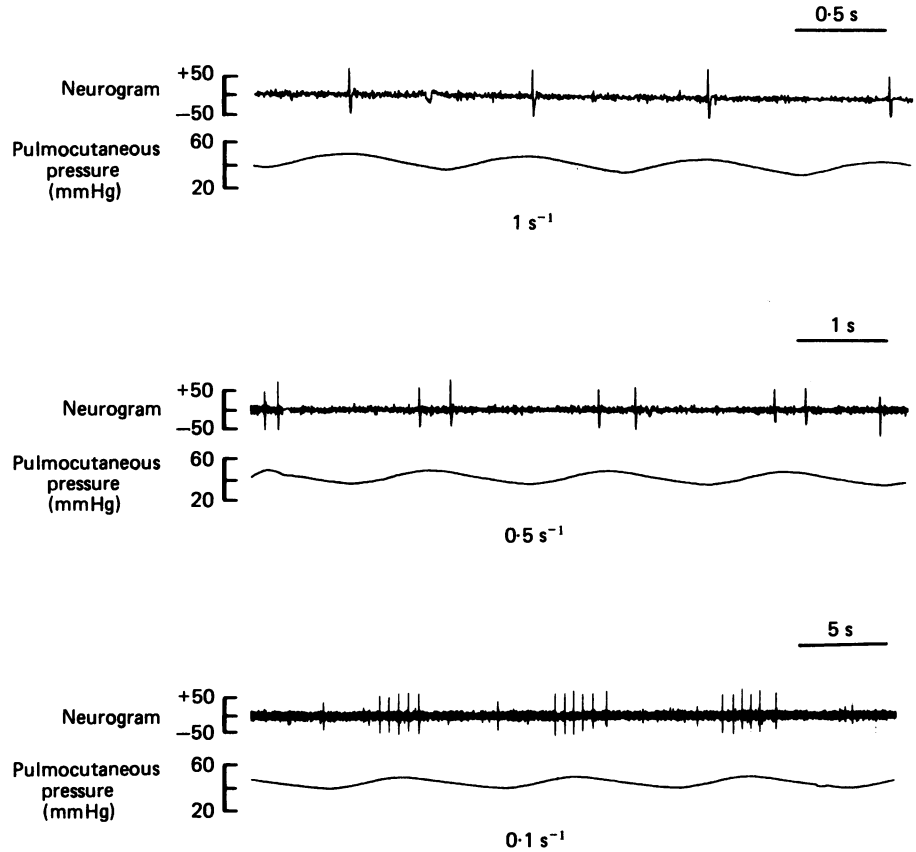

Fig. 7. Tracings showing the effect of sinusoidal pressure stimulus frequency on the discharge of a p.c.a. baroreceptor unit. The mean and peak-to-peak amplitude of the stimulus were 40 and 10 mmHg respectively. The baroreceptor unit shown in the tracing corresponds to the data represented by the open circle symbol in Fig. 8. Time bars and stimulus frequencies are indicated on each trace.

firing was not continuous during the falling and initial rising phases of the stimulus (Figs. 1 and 7), even in one preparation in which the mean pressure was increased to 120 mmHg. Figs. 7 and 8 show the relationship between stimulus frequency and the number of spikes per cardiac cycle. In five of the six units, the number of spikes per cycle fell with increasing stimulus frequency (Figs. 7 and 8). However, the average discharge frequency increased with stimulus frequency in these units (Fig. 8). At higher mean stimulus pressures (55–60 mmHg), baroreceptor discharge frequencies were increased, but the relationships to stimulus frequency were similar to those obtained at 40 mmHg.

Measurement of p.c.a. diameter

The p.c.a. diameter was measured by sonomicrometry in three toads anaesthetized with urethane, and a summary of the results is presented in Table 1. During pressure cycles, the profile of p.c.a. diameter was similar to that of the arterial pressure pulse

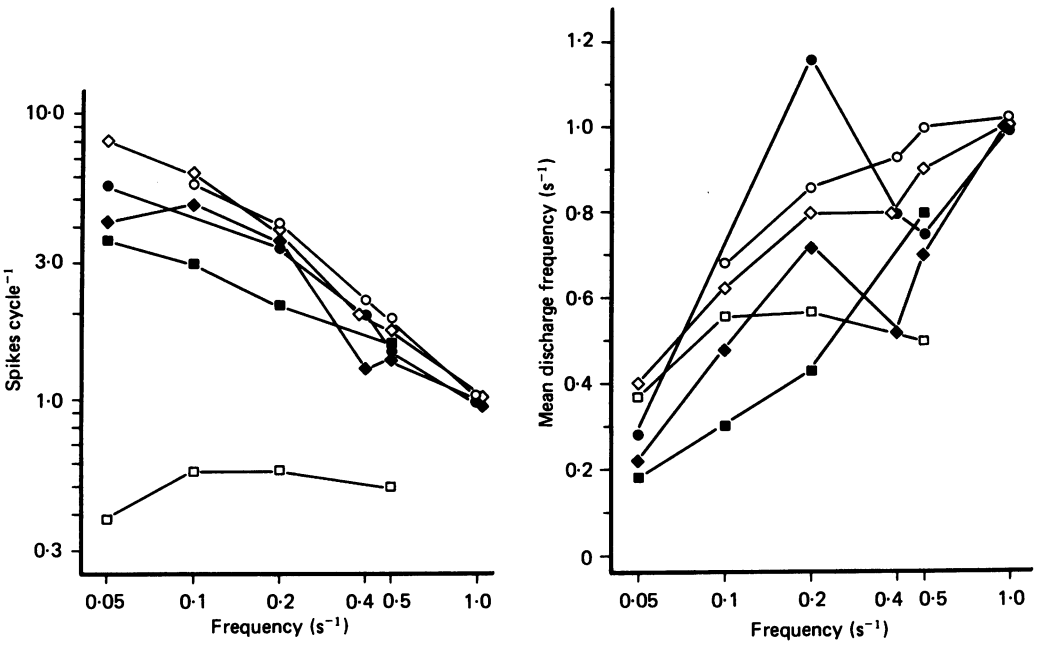

Fig. 8. Effects of the frequency of sinusoidal pressure stimuli on the discharge of p.c.a. baroreceptors. The number of spikes per pressure-cycle decreases but the mean discharge frequency increases with increasing frequency of sinusoidal stimulation. Based on results from six baroreceptor units which have equivalent symbols in both graphs.

TABLE 1. Changes in p.c.a. diameter in urethanized toads (based on thirty-nine observations in three toads)

	Mean diameter (mm)	Diameter pulse (mm)	Diameter pulse (%)	Mean pressure (mmHg)	Pressure pulse (mmHg)	Pressure–strain modulus (10^5 dyn cm^{-2})
Mean	3·54	0·27	7·7	45·7	22·0	4·0
S.E. of mean	0·07	0·009	0·3	0·9	1·1	0·3
Range	(12·9–4·6)	(0·18–0·41)	(4·5–11·6)	(33–60)	(12–37)	(2·2–9·5)

(Fig. 9). The mean magnitude of changes in p.c.a. diameter during pressure cycles was 7·7% of the mean diameter. On average, the p.c.a. diameter changed 12·3 μm mmHg^{-1}. Peterson's pressure–strain modulus (Milnor, 1982) was calculated to be $4{\cdot}0 \times 10^5 \pm 0{\cdot}3 \times 10^5$ dyn cm^{-2} (298·9 mmHg).

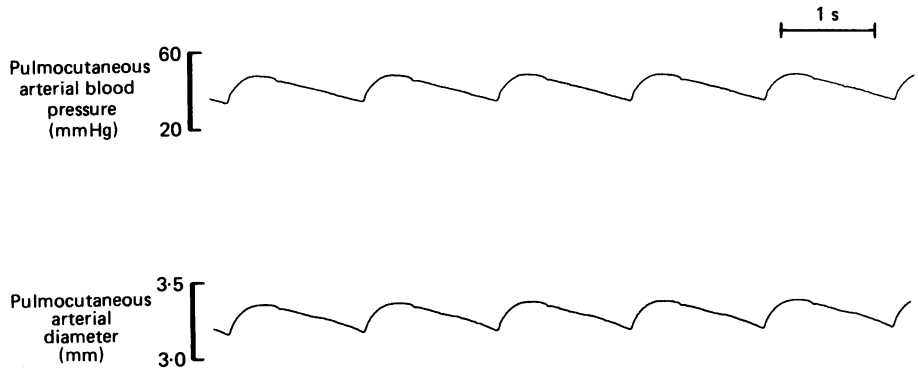

Fig. 9. Simultaneous recording of p.c.a. pressure and diameter in urethanized toad. Diameter was measured by a piezoelectric sonomicrometer. Time bar given in upper-right-hand corner.

DISCUSSION

The present study has characterized the static and dynamic behaviour of the p.c.a. baroreceptors of the toad. In general, previous recordings of arterial baroreceptor activity in ectotherms have served to demonstrate their presence and location in the arterial circulation, and little emphasis has been placed on the characteristics of the receptors and their afferent fibres (Neil *et al.* 1950; Ishii *et al.* 1966; Ishii & Ishii, 1978; Ishii *et al.* 1985*a*, *b*; Van Vliet & West, 1987). Recently however, we have reported that the p.c.a. baroreceptors are connected to slowly conducting afferents which exhibit conduction velocities typical of non-myelinated afferent fibres (Van Vliet & West, 1987). Since functional characteristics have also been reported for myelinated and non-myelinated mammalian systemic arterial baroreceptors, comparisons may now be made between the properties of mammalian and amphibian baroreceptors.

Frequency of p.c.a. baroreceptor discharge

A striking characteristic of the p.c.a. baroreceptors found in the present study and apparent in previous studies is their low discharge frequency (Table 2; Ishii & Ishii, 1978; Van Vliet & West, 1987). The peak-phasic and minimum-adapted instantaneous discharge frequencies in the present study were approximately 30 and 2–4 spikes s^{-1}, respectively, which are considerably less than those observed for mammalian baroreceptors (Table 2). If an adjustment is made for the temperature differences between amphibian and mammalian preparations ($\sim$ 17 °C), the adjusted maximum-phasic and minimum-adapted discharge frequencies of p.c.a. baroreceptors at 37 °C (106–124 and 7·1–12·4 spikes s^{-1}, respectively, assuming a Q_{10} of 2·1–2·3, Diamond, 1955; Gallego, Eyzaquirre & Monti-Bloch, 1979) are found to be similar to those reported for non-myelinated mammalian baroreceptors, but are less than half of the values reported for myelinated mammalian baroreceptors (Table 2).

P.c.a. baroreceptor pressure thresholds

The range of toad p.c.a. baroreceptor thresholds found in the present and previous studies overlap with the lower range of those for mammalian myelinated systemic baroreceptors, and are just above those for mammalian pulmonary arterial baro-

receptors (Table 2). Since the arterial pressures to which baroreceptors are normally exposed differ between both species and systemic and pulmonary circulations, it is probably more meaningful to compare baroreceptor thresholds relative to the normal arterial pressures of the appropriate circulation and species (see Gilmore & Tomomatsu, 1984). Expressed in this manner, p.c.a. baroreceptor thresholds are found to

TABLE 2. Comparison of anuran amphibian and mammalian arterial baroreceptor characteristics

	Toad	Mammal		
Variable	p.c.a. non-myelinated	Systemic myelinated	Systemic non-myelinated	Pulmonary
Conduction velocity ($m\ s^{-1}$)	0·3–0·7 (a)	4–53 (b,c)	0·3–2·0 (c-g)	—
Threshold pressure (mmHg)	21–37 (phasic) 23–44 (adapted)	20–100* (c,h)	65–140* (c,d)	16–25/7–13†
Threshold as percentage of arterial pressure	75–157‡	22–111§	72–156§	~ 100 (l)
Maximum discharge frequency (s^{-1})	30	250–350 (j)	50–150 ‖ (j,) 120(f) 132(k)	200–300 (i)
Minimum adapted discharge frequency (s^{-1})	2–3	20–40 (l)	< 10 (f)	—
Pressure sensitivity ($s^{-1}\ mmHg^{-1}$)	0·2–0·5	0·2–1·8 (c,l,m)	0·1–0·2 (c,l)	—
Normalized sensitivity (% $mmHg^{-1}$)	0·7–1·7	0·04–0·5	0·05–0·1	—

* Values for rabbit. † Values for dog. ‡ Normal pressure 28 mmHg (n). § Normal pressure 90 mmHg (o). ‖ Presumed non-myelinated (l).

a, Van Vliet & West (1987). b, Paintal (1972). c, Yao & Thoren (1983). d, Thoren & Jones (1977). e, Brown *et al.* (1978). f, Thoren *et al.* (1977). g, Thoren *et al.* (1982). h, Holmes & Ledsome (1984). i, Coleridge & Kidd (1961). j, Landgren (1952). k, Brown, Saum & Tuley (1976). l, Kirchheim (1976). m, Franz, Scher & Ito (1971). n, Wilson *et al.* 1984. o, Korner (1965).

range from near to well above the mean arterial pressure values determined in relatively undisturbed conscious toads (28 mmHg or less, Wilson, Van Vliet & West, 1984; Van Vliet & West, unpublished observations; Table 2). This is also a consistant finding for non-myelinated mammalian baroreceptors and appears to also be the case for mammalian pulmonary arterial receptors with unknown fibre types (Table 2; Coleridge & Kidd, 1961; Thoren, Saum & Brown, 1977; Thoren & Jones, 1977; Thoren, Andresen & Brown, 1982; Yao & Thoren, 1983). In contrast, the range of thresholds for myelinated mammalian systemic arterial baroreceptors extends down to a small fraction of normal arterial pressure, so that their discharge is well developed at normal pressures (Table 2; Kirchheim, 1976). The functional implication of the relatively high threshold of non-myelinated baroreceptors in toads and mammals is that they are more capable of reporting increases in arterial pressure above resting values, than decreases in pressure below normal (Thoren, 1981; Yao & Thoren, 1983; Van Vliet & West, 1987). The high threshold of p.c.a. baroreceptors probably accounts for the relatively high pressures (30–45 mmHg) required to achieve the

maximum open-loop gain of the p.c.a. baroreflex in conscious toads (West & Van Vliet, 1983).

P.c.a. baroreceptor sensitivity

Although the p.c.a. baroreceptors resemble mammalian non-myelinated baroreceptors in terms of their discharge frequencies and relative pressure thresholds, their sensitivity to pressure is higher than that for non-myelinated baroreceptors, and is in the range for that of myelinated baroreceptors, in mammals (Table 2). However, if the values of sensitivity are normalized to the maximum discharge frequency of the receptor, the p.c.a. baroreceptors are found to develop up to 1·7% of their maximum discharge frequency for each 1 mmHg increment in pressure, whereas the normalized sensitivity of mammalian baroreceptors is much lower (Table 2). A relatively high sensitivity is appropriate for amphibian baroreceptors since they operate over a narrower range of absolute arterial pressures than mammalian systemic arterial baroreceptors, and may be related to the relatively high distensibility of the p.c.a. In anaesthetized toads, the pulsation of the p.c.a. diameter was 7·7% of the mean diameter at 22 mmHg pulse pressure (Table 1). Both this relatively large value for diameter pulse and the low value of Peterson's pressure–strain modulus suggest that the p.c.a. is a highly compliant vessel which is much more comparable in its distensibility to mammalian pulmonary than systemic arteries (Milnor, 1982). In addition to the highly compliant nature of the arterial wall, the present study has also shown that the threshold of the p.c.a. baroreceptors lies near the point of maximum dynamic compliance, and both the compliance and pressure sensitivity of the receptors fall off at pressures above threshold. The high distensibility of the p.c.a. suggests that it is exceptionally capable of transducing wall stress imparted by arterial pressure to circumferential strain, which may be of importance either in the direct deformation of baroreceptor endings (Kirchheim, 1976), or in inducing stress in viscoelastic elements of the p.c.a. wall to which they may be coupled.

Adaptation and rate sensitivity of p.c.a. baroreceptors

The adaptation of p.c.a. baroreceptors in the present study was most evident in the response to a step change in pressure (Fig. 1). Since adaptation required several seconds, and a tonic discharge was maintained at high pressure-step values, the receptors may be classified as slowly adapting mechanoreceptors, as are mammalian baroreceptors (Kirchheim, 1976). This is in contrast to other rapidly adapting mechanoreceptors which may show only a brief discharge or a single impulse in response to sustained stimulation (Catton, 1970).

Since the p.c.a. baroreceptors exhibited adaptation in response to a step increase in pressure, it is expected that the adaptation process will also be evident in the form of a rate sensitivity of the receptors to dynamic pressure stimuli. That the p.c.a. baroreceptors are rate sensitive was apparent from (1) the greater dF/dP values calculated for initial than for adapted responses to step increases in pressure, (2) the increase in $\Delta F/\Delta P$ with increases in the dP/dt of pressure-ramp stimulation, and (3) the increase in their mean discharge frequency with increasing frequency of sinusoidal pressure stimuli. In our volume-infusion experiments, increasing the infusion rate

increased the baroreceptor discharge despite a concomitant reduction in dynamic compliance of the p.c.a. The reduction in dynamic compliance at faster infusion rates can be explained by viscoelastic properties of the arterial wall: arteries require time to stretch to their full potential when a distending force or stress is imposed upon them (Milnor, 1982). Although for equivalent levels of distension, both baroreceptor discharge and wall stress will increase with the rate of distension, it is unlikely that the rate sensitivity of the baroreceptors may be explained by the mechanics of the entire arterial wall (Brown, Saum & Yasui, 1978). Rather, the rate sensitivity of the baroreceptors probably arises from the viscoelastic coupling of the receptor endings locally within the arterial wall, and/or by the rate-sensitive properties of the receptor endings themselves (Catton, 1970; Brown *et al.* 1978). The demonstrated rate sensitivity of the p.c.a. baroreceptors suggests that heart rate, dP/dt and the size of the pressure pulse will be important determinants of their discharge frequency during natural stimulation.

Conclusion

From the present study it can be concluded that amphibian p.c.a. baroreceptors are slowly adapting mechanoreceptors which exhibit rate-sensitive behaviour. Their characteristics include a pressure-threshold range near or above resting arterial pressures, a high-pressure sensitivity which is maximum at their threshold, and a low maximum discharge frequency. This suggests that *in vivo*, the activity of the p.c.a. baroreceptor population will be sparse at normal arterial pressures, but will rapidly develop as arterial pressures are elevated above normal. Thus, the p.c.a. baroreflex may be more capable of limiting large increases in arterial pressure than regulating arterial pressure around normal resting values. Comparison of the properties of toad p.c.a. and mammalian systemic arterial baroreceptors suggest that low discharge frequencies and high thresholds relative to normal arterial pressures are characteristics which may be common among non-myelinated baroreceptor afferents.

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