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THE CARDIOVASCULAR RESPONSES ELICITED FROM THE POSTERIOR CEREBELLAR CORTEX IN THE ANAESTHETIZED AND DECEREBRATE RABBIT

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SUMMARY

1. In this study the posterior cerebellar cortex has been electrically stimulated and changes in heart rate, arterial blood pressure, regional blood flows and renal sympathetic nerve discharge have been recorded in both the anaesthetized and the decerebrate unanaesthetized rabbit.

2. Specifically, lobules VII, VIII, IX and X of the posterior cerebellar vermis were stimulated but the only region which elicited cardiovascular changes was lobule IX (the uvula). The responsive area of the uvula was localized to the medial regions of sublobules a, b and c and was identical in both anaesthetized and decerebrate animals.

3. Under urethane anaesthesia, uvula stimulation evoked a small bradycardia, a fall in arterial pressure, a transient inhibition of renal sympathetic nerve activity, with no change in renal vascular conductance, and an increase in femoral vascular conductance.

4. Stimulation of an identical area in the decerebrate rabbit evoked a marked tachycardia, an increase in blood pressure, maintained increase in renal sympathetic nerve discharge, and decreases in both renal and femoral conductances.

5. The response evoked from the decerebrate rabbit could be reversed by a small dose of anaesthetic to a pattern of response which was essentially identical to that seen in the urethane-anaesthetized rabbit.

6. This influence of anaesthetics on the pattern of cardiovascular responses that may be elicited from the cerebellar cortex indicates that caution should be exercised when making physiological inferences on the basis of stimulation experiments in anaesthetized preparations.

7. In the light of the cardiovascular changes that may be evoked from the uvula, and recent neuroanatomical and neurophysiological data concerning afferent and efferent connexions of this cerebellar region, we discuss the possibility that the uvula plays a role in the alerting reaction of the rabbit.

INTRODUCTION

It is well known that the cerebellar cortex can influence the cardiovascular system. The majority of studies, however, have described changes in only arterial blood

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pressure without details of regional circulatory responses or heart rate changes, and even the exact location of the area of the cortex that was activated has not been defined. Furthermore even when the vermal cortex was stimulated contradictory responses were observed when the data from different studies were compared. For example, electrical stimulation of the anterior vermis in the precollicular decerebrate (Moruzzi, 1940) and anaesthetized (Rasheed, Manchanda & Anand, 1970) cat evoked depressor responses. However, Hoffer, Mitra & Snider (1972) also working with anaesthetized cats found rises in arterial pressure associated with a decrease in renal and cutaneous blood flows and a rise in muscle blood flow evoked from the anterior vermis. In contrast, stimulation of the anterior vermis in the unanaesthetized restrained rabbit evoked pressor responses (Ban, Hilliard & Sawyer, 1960; Ramu & Bergmann, 1967) but Nisimaru, Yamamoto & Shimoyama (1984) showed falls in arterial pressure with an inhibition of renal sympathetic nerve activity from lobules I, II and III of the anterior vermal cortex in the anaesthetized rabbit.

Fewer reports exist for arterial pressure changes evoked from the posterior vermis. In the anaesthetized cat, Hoffer *et al.* (1972) found that stimulation of this area produced depressor responses. In the unanaesthetized restrained rabbit, Ramu & Bergmann (1967) reported increases in arterial pressure but Sawyer, Hilliard & Ban (1961) have shown both increases and decreases in arterial pressure (but usually decreases). Recently Nisimaru *et al.* (1984) described falls in arterial pressure and inhibition of renal sympathetic activity during stimulation of lobules VII and VIII of the posterior vermis in the anaesthetized rabbit and, subsequently, similar observations have been made during stimulation of lobule X again in the anaesthetized rabbit (Nisimaru & Watanabe, 1985).

In view of the variability in arterial pressure responses and the absence of data detailing changes in other cardiovascular variables elicited from vermal cortex stimulation, with one exception in the cat (see Hoffer *et al.* 1972), we have made a more detailed study by recording changes in heart rate, arterial pressure, regional blood flows and renal sympathetic nerve discharge during stimulation of the posterior cerebellar vermis in anaesthetized and decerebrate rabbits.

Preliminary reports of part of this work have been published (Bradley, Ghelarducci, Paton & Spyer, 1985, 1986; Bradley & Paton, 1986).

METHODS

Experiments were performed on twenty-three New Zealand white rabbits (2·0–3·25 kg body weight). Eleven were anaesthetized with urethane (Sigma, 1·4 g kg^{-1} I.V.) and twelve with alphaxalone alphadolone (Saffan, Glaxovet Ltd., U.K., 3 mg kg^{-1} I.V. as required). The depth of anaesthesia was judged by testing the withdrawal reflex to pinching a paw.

In all animals the bladder was cannulated and a tracheotomy performed enabling monitoring of end-tidal CO_2 (P. K. Morgan Ltd., U.K.), which was kept at around 4·5 %. The right femoral artery was cannulated for measurement of arterial blood pressure and heart rate was derived from the pulse wave form using a rate-meter. Arterial blood samples were routinely taken during all experiments and pH, arterial oxygen and carbon dioxide pressures (P_{a,O_2} and P_{a,CO_2}) and bicarbonate levels were measured, and corrected, if necessary by appropriate infusions or by varying inspired gas composition. Rectal temperature was maintained at 38 ± 1 °C.

Three out of the eleven urethane-anaesthetized rabbits and all the Saffan-anaesthetized rabbits were paralysed with gallamine triethiodide (Flaxedil, May & Baker Ltd., U.K.), given intravenously (4 mg kg^{-1}) and artificially ventilated. In the Saffan-anaesthetized rabbits both common carotid

arteries were ligated and the animals decerebrated using undercutting and suction techniques leaving the superior colliculi intact. Histological analysis was carried out using standard techniques and showed that the hypothalamus had been removed.

In both anaesthetized and unanaesthetized decerebrate animals the posterior vermis (lobules VII, VIII and IX) was exposed by retraction of nuchal muscles and removal of the overlying occipital bone and stimulated using constant current via either a unipolar silver ball electrode (diameter 0·5 mm, surface negative) or intracortically (< 1·0 mm depth) with a metal-filled micro-electrode with a 6 s stimulus train (0·2 ms, 100 Hz) and 0·1 to 0·4 mA intensity in the unanaesthetized decerebrate rabbits and 0·5 to 0·8 mA intensity in the anaesthetized animals. Lobule X was stimulated using the metal-filled micro-electrode and penetrations were histologically identified.

Changes in vascular conductance and resistance in the renal and femoral beds have been studied using cuff-type electromagnetic flowmeters (Devices Ltd., U.K.) and pump perfusion at constant flow using a roller pump (Watson-Marlow Ltd., U.K.). The electromagnetic flowmeters were calibrated *in vitro* using constant-flow perfusion of a length of freshly obtained artery, and during the experiments a zero-flow signal was obtained at regular intervals. In all the hind-limb blood flow studies, the femoral artery was approached from a medial aspect and the profunda artery ligated and the limb kept warm by wrapping in cotton wool. In all the renal blood flow and renal nerve recording studies, the left kidney was exposed retroperitoneally and the renal nerves carefully dissected from the artery to prevent damage by subsequent experimental procedures. The flow probes were placed distal to the profunda branch in the femoral bed and close to the aorta in the renal studies of arterial flow. During a renal blood flow experiment half-hourly urine samples were taken from both ureters allowing sodium and potassium concentrations, volume and osmolarity measurements to be compared for the operated and unoperated kidneys.

Constant-flow studies in all animals involved taking blood from the right common carotid artery and pumping it via a heat-exchanging coil into either the left femoral artery and/or in some of the anaesthetized rabbits to the left renal artery while perfusion pressure was monitored. The femoral bed was vascularly isolated by ligating all collateral supplies to surrounding musculature and the output cannula carrying blood from the pump was inserted into the femoral artery distal to its profunda branch. In the renal bed, the input cannula was inserted into the renal artery as near to the dorsal aorta as possible and the kidney was never without blood for more than 30 s. Vascular isolation was confirmed at the end of the experiment by turning off the pump and recording < 7 mmHg perfusion pressure in both vascular beds. The flow rate of the pump was calibrated at the end of each experiment by collecting blood over a timed period. Central venous pressure was recorded in all constant-flow experiments via a cannula inserted via the right femoral vein into the inferior vena cava. Vascular conductance was calculated from the electromagnetic blood flow and pump perfusion records by measuring the peak response values of mean arterial pressure and mean blood flow or mean perfusion pressure and the pump flow rate respectively.

Renal sympathetic discharge was recorded from the renal nerves of the left kidney using a bipolar silver-wire electrode and stored on tape with the arterial pressure signal (using an R-61 tape recorder, Teac Corp., Japan).

In some experiments one-eighth of the full anaesthetic dose of either α-chloralose (10 mg kg^{-1}), sodium pentobarbitone (5 mg kg^{-1}) or urethane (190 mg kg^{-1}) was administered intravenously to the unanaesthetized decerebrate rabbits to observe the effects of anaesthesia on the cardiovascular responses evoked from the uvula.

The statistical significance of the data is based on a two-sample t test carried out by a minitab computer program.

RESULTS

Localization of the responsive area

The responsive area of the cerebellar cortex was assessed by measuring the changes in mean arterial pressure (M.A.P.) with respect to control levels, on stimulating with either a silver ball-type electrode or micro-electrode. Fig. 1 compares data obtained from the urethane-anaesthetized animals in which 0·7 mA stimulus intensity was

required to induce a depressor response and from the decerebrate animals using 0·2 mA stimulus intensity which was necessary to evoke a pressor response. The responsive area in both groups of animals was essentially identical in that the cardiovascular changes were evoked consistently from a localized area restricted to the mid line and intermediate region of sublobules IXa, IXb and IXc of the posterior

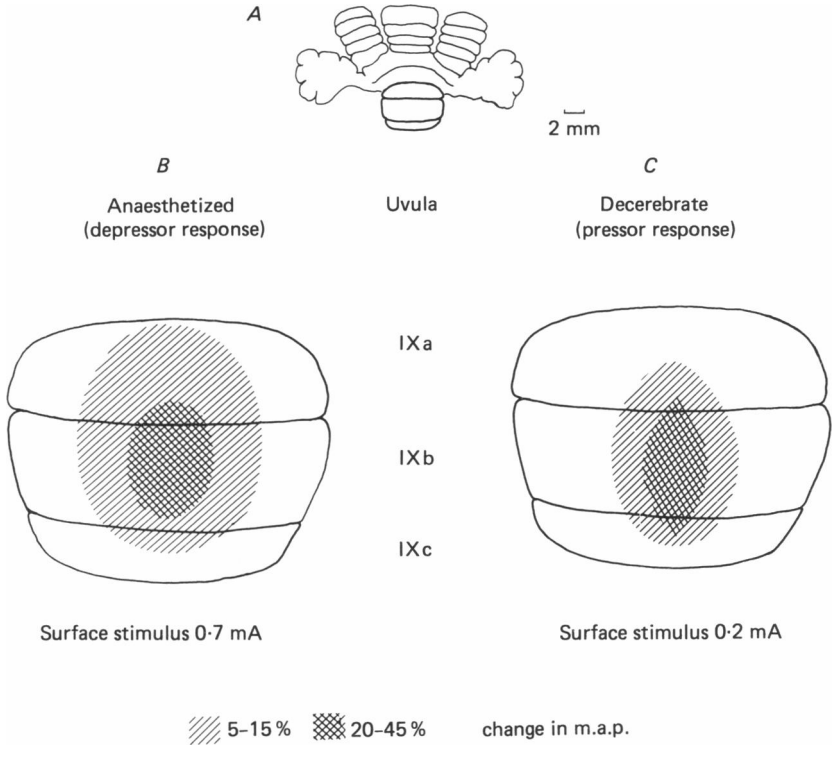

Fig. 1. *A*, posterior view of the rabbit cerebellum. *B* and *C* compare the percentage change in mean arterial pressure in the urethane-anaesthetized and decerebrate rabbits respectively evoked by stimulation of sublobules a, b and c of the uvula (lobule IX).

vermis. Stimulation here produced a 5–15 % change in M.A.P. but a 20–45 % change was elicited from a more localized region spanning the mid line aspects of sublobules IXa and IXb.

The cardiovascular changes produced from the uvula

Urethane-anaesthetized rabbits. Stimulation of the responsive region of the uvula (0·6–0·8 mA intensity) in eleven animals evoked a small bradycardia of $9{\cdot}4 \pm 3{\cdot}0$ beats min^{-1} (mean $\pm$ S.E. of mean; forty tests) from control values of $302{\cdot}7 \pm 6{\cdot}3$ beats min^{-1} and a fall in M.A.P. of $22{\cdot}6 \pm 3{\cdot}1$ mmHg from control values of $90{\cdot}6 \pm 3{\cdot}1$ mmHg (see Table 1 and Fig. 2*A*). There was never a measurable change in pulse pressure. Stimulation in the three paralysed animals evoked qualitatively identical responses but there were small quantitative differences compared to the spontaneously breathing animal.

TABLE 1. Comparison of the cardiovascular changes (mean ± S.E. of mean, n = number of tests, (+) indicates an increase and (−) a decrease in the variable), during uvula stimulation in eleven urethane-anaesthetized and twelve decerebrate rabbits

	Urethane anaesthetized		Decerebrate	
	Control level	Peak response	Control level	Peak response
Heart rate (beats min^{-1})	302·7 ± 6·27	−9·4 ± 2·96 (n = 40)	206·4 ± 5·8	+52·6 ± 5·2 (n = 27)
Mean arterial pressure (mmHg)	90·6 ± 3·12	−22·6 ± 3·11 (n = 40)	105·7 ± 3·6	+45·6 ± 3·2 (n = 27)
Renal conductance (ml min^{-1} $mmHg^{-1}$)	0·262 ± 0·012	+0·002 ± 0·000 (n = 40)	0·205 ± 0·020	−0·093 ± 0·010 (n = 11)
Femoral conductance (ml min^{-1} $mmHg^{-1}$)	0·069 ± 0·077	+0·015 ± 0·002 (n = 30)	0·048 ± 0·004	−0·020 ± 0·002 (n = 16)
Stimulus intensity (mA)		0·7		0·25

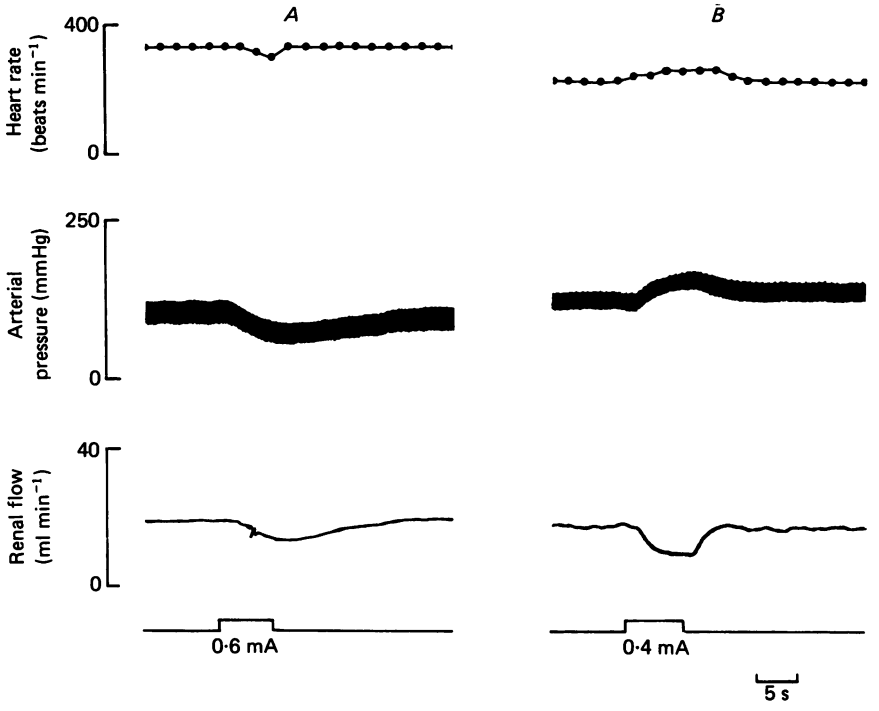

Fig. 2. Comparison of the changes in heart rate, arterial blood pressure and mean renal blood flow during uvula stimulation in the urethane-anaesthetized (*A*) and decerebrate rabbit (*B*). The heart rate values are plotted and calculated from the blood pressure recordings at 2 s intervals.

The fall in M.A.P. was associated with changes in blood flow and vascular conductance in the two vascular beds studied. In four rabbits the renal vascular bed showed significant falls in mean blood flow of $5{\cdot}0 \pm 0{\cdot}4$ ml min^{-1} from control values of $23{\cdot}0 \pm 0{\cdot}8$ ml min^{-1} ($P < 0{\cdot}05$; forty-six tests) during uvula stimulation. This response followed a similar time course to the depressor response and there was no significant change in vascular conductance ($P < 0{\cdot}80$; see Table 1 and Fig. 3*A*). Fig. 4*A* illustrates the typical effect on renal sympathetic nerve activity evoked during uvula stimulation and shows a transient inhibition for the first 2–3 s of the 6 s stimulus period but a return to control levels at a point where the fall in M.A.P. had reached its lowest point. Perfusion of the kidney at constant flow in three rabbits showed no significant change in perfusion pressure from control levels during uvula stimulation ($P > 0{\cdot}30$; twenty-one tests). There was never a change in central venous pressure during uvula stimulation. These data confirmed that the kidney vasculature was playing no role in changing total peripheral resistance and that the fall in renal blood flow was a passive effect secondary to the fall in arterial pressure. In two animals resting M.A.P. was artificially raised by injection of 0·9 % saline and the effects of uvula stimulation on renal blood flow were seen to be unaffected suggesting that the evoked depressor response reduced arterial pressure outside the autoregulatory limits of the kidney. Urine sampling during renal blood flow recording was carried out from the

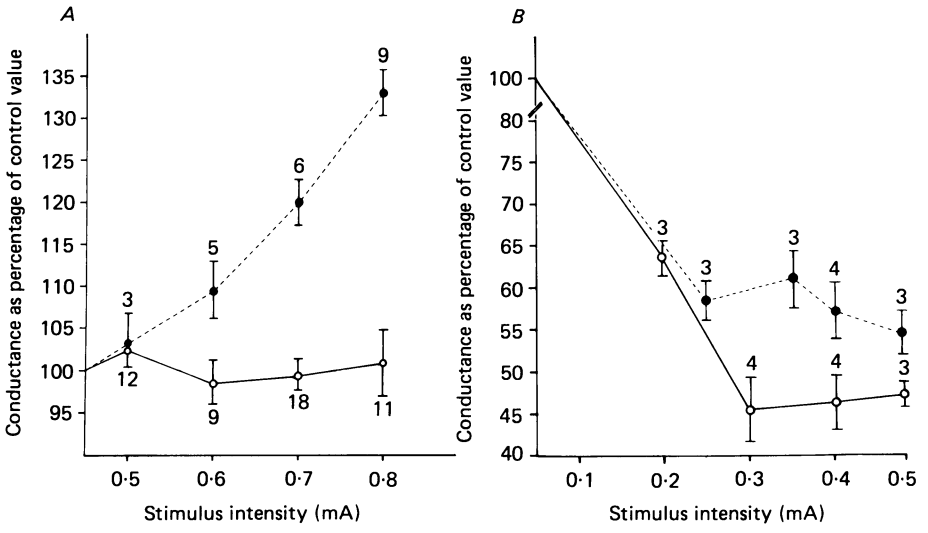

Fig. 3. Comparison of the conductance changes during increased stimulus intensities in the renal and femoral vascular beds in four urethane-anaesthetized (*A*) and three decerebrate rabbits (*B*) during uvula stimulation. *n* refers to the number of tests and is the number shown with each point. Filled circles, femoral bed; open circles, renal bed.

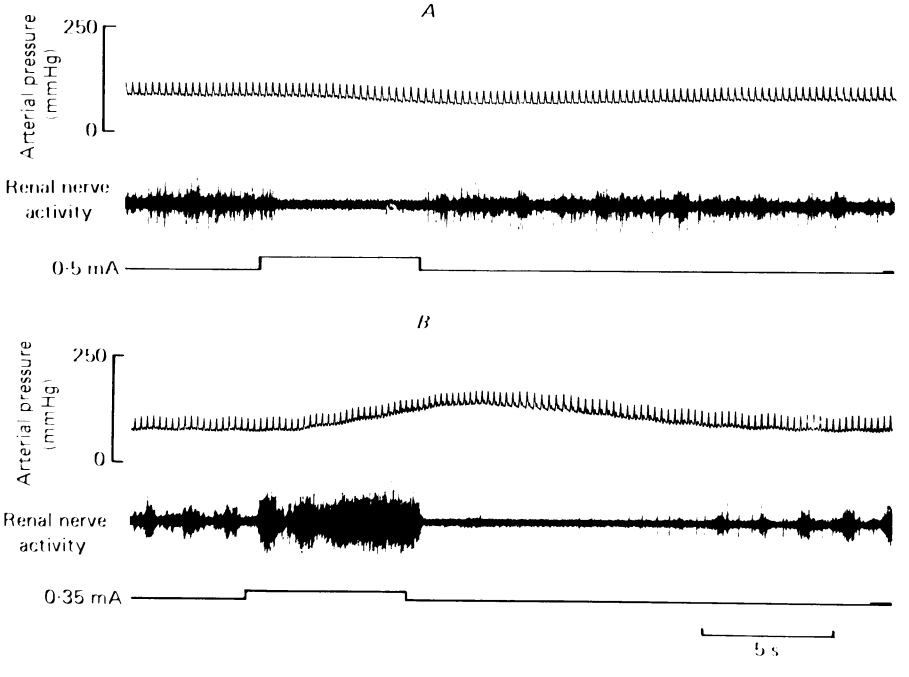

Fig. 4. Comparison of changes in arterial blood pressure and renal sympathetic nerve discharge in the urethane-anaesthetized (*A*) and decerebrate rabbit (*B*) during uvula stimulation.

cannulated ureters of operated and unoperated kidneys and the data indicated that under the experimental conditions the test kidney was filtering at an equivalent rate to the control kidney, implying that surgical intervention had not elicited a deleterious deterioration in renal function. In three rabbits the femoral vascular bed showed no significant change in mean flow ($P > 0{\cdot}67$; thirty tests) during uvula stimulation and, as a result of this, conductance increased significantly by $0{\cdot}015 \pm 0{\cdot}002$ ml min^{-1} mmHg^{-1} from control levels of $0{\cdot}069 \pm 0{\cdot}007$ ml min^{-1} mmHg^{-1} ($P < 0{\cdot}02$) (see Fig. 3*A* and Table 1). This was confirmed by perfusion of the hind limb at constant flow in four rabbits where vasodilatation was indicated by significant falls in perfusion pressure of $10{\cdot}2 \pm 0{\cdot}6$ mmHg from control levels of $85{\cdot}4 \pm 2{\cdot}6$ mmHg ($P < 0{\cdot}001$; fifty tests) during uvula stimulation (see Fig. 5*A*).

Decerebrate rabbits. Stimulation of the uvula (0·1–0·5 mA) in twelve rabbits consistently evoked a tachycardia of $52{\cdot}6 \pm 5{\cdot}2$ beats min^{-1} from control levels of $206{\cdot}4 \pm 5{\cdot}8$ beats min^{-1} in twenty-seven tests, which was followed by a marked post-stimulus bradycardia (heart rate typically falling to 128 beats min^{-1}). This latter effect was abolished by sectioning both aortic nerves.

The tachycardia was accompanied by a large increase in M.A.P. of $45{\cdot}6 \pm 3{\cdot}2$ mmHg from control levels of $105{\cdot}7 \pm 3{\cdot}6$ mmHg in twelve animals and twenty-seven tests. A narrowing of pulse pressure at the peak of the response was observed, but then a widening of pulse pressure as M.A.P. returned to control levels at the end of the stimulus period suggesting a release of catecholamines from the adrenal medulla. Stimulation with intensities similar to those used in the anaesthetized animal caused an increase in the magnitude of the response although the pattern of response remained qualitatively identical (i.e. it was not converted to a bradycardia–depressor response).

The level of mean renal blood flow (see Fig. 2*B*) in three rabbits during uvula stimulation showed significant falls of $6{\cdot}4 \pm 0{\cdot}6$ ml min^{-1} from control levels of $23{\cdot}7 \pm 1{\cdot}6$ ml min^{-1} ($P < 0{\cdot}03$; eleven tests) suggesting vasoconstriction. This reduction in flow was abolished after renal nerve section. Renal conductance showed a significant decrease of $0{\cdot}093 \pm 0{\cdot}010$ ml min^{-1} mmHg^{-1} from control levels of $0{\cdot}205 \pm 0{\cdot}020$ ml min^{-1} mmHg^{-1} ($P < 0{\cdot}001$). Renal sympathetic discharge in four rabbits typically showed an increase in activity (see Fig. 1*B*) which was maintained throughout the stimulus period. This increase was followed by a decline in activity until M.A.P. had returned to control levels.

The femoral bed of three rabbits was perfused at constant flow and showed a transient yet significant increase in perfusion pressure (indicating vasoconstriction) of $65{\cdot}8 \pm 4{\cdot}2$ mmHg from control values of $98{\cdot}9 \pm 4{\cdot}2$ mmHg ($P < 0{\cdot}001$; sixteen tests) during uvula stimulation. Conductance showed a significant decrease of $0{\cdot}020 \pm 0{\cdot}002$ ml min^{-1} mmHg^{-1} from control levels of $0{\cdot}048 \pm 0{\cdot}004$ ml min^{-1} mmHg^{-1} ($P < 0{\cdot}04$). The increase in perfusion pressure was followed by a rapid return to control levels before the end of the stimulus period (see Fig. 5*B*), although this recovery was delayed following aortic nerve section. There was never a change in central venous pressure in response to uvula stimulation.

The effect of a small dose of anaesthetic

Administration of one-eighth of a normal anaesthetic dose of either urethane, sodium pentobarbitone or α-chloralose to the decerebrate rabbit reversed the

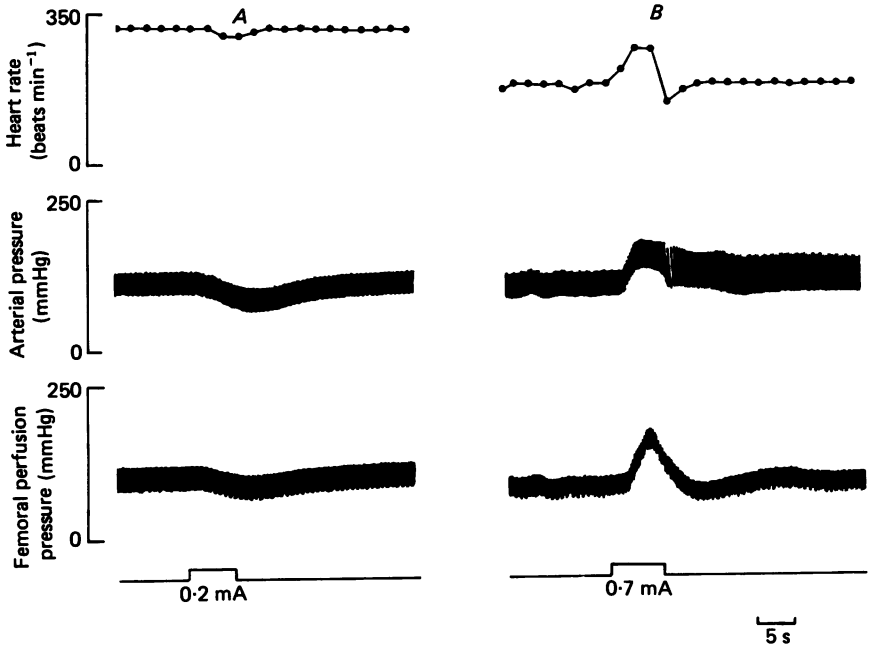

Fig. 5. Comparison of changes in heart rate, arterial blood pressure and femoral perfusion pressure during uvula stimulation in the urethane-anaesthetized (*A*) and decerebrate rabbit (*B*).

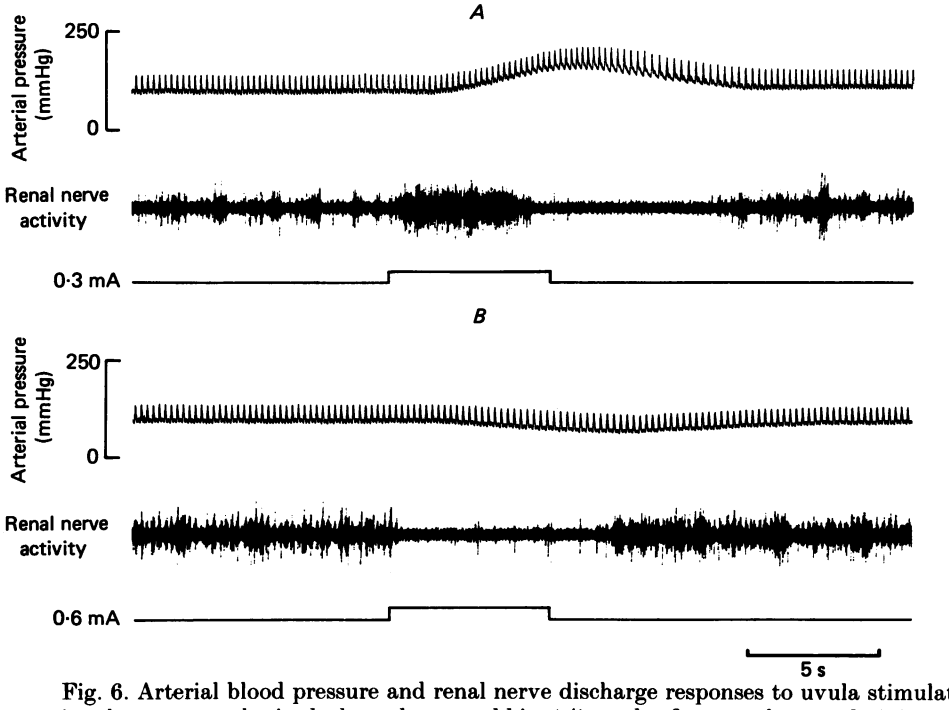

Fig. 6. Arterial blood pressure and renal nerve discharge responses to uvula stimulation in the unanaesthetized decerebrate rabbit (*A*) and after urethane administration (190 mg kg^{-1}, one-eighth the full dose, I.V.) (*B*).

cardiovascular responses to uvula stimulation towards the pattern seen in the urethane-anaesthetized rabbits. The stimulus intensity required to evoke a cardiovascular response had to be increased from 0·2 to 0·7 mA intensity (see Fig. 6). Stimulation of the uvula in seven rabbits now produced a bradycardia of $28{\cdot}1 \pm 3{\cdot}4$ beats min^{-1} from control levels of $256{\cdot}4 \pm 8{\cdot}0$ beats min^{-1} and a fall in arterial pressure of $23{\cdot}2 \pm 2{\cdot}8$ mmHg from basal levels of $83{\cdot}6 \pm 3{\cdot}4$ mmHg. There were falls in femoral perfusion pressure of $20{\cdot}2 \pm 1{\cdot}8$ mmHg from control levels of $73{\cdot}1 \pm 3{\cdot}7$ mmHg in three animals (see Fig. 7). Renal sympathetic nerve activity was

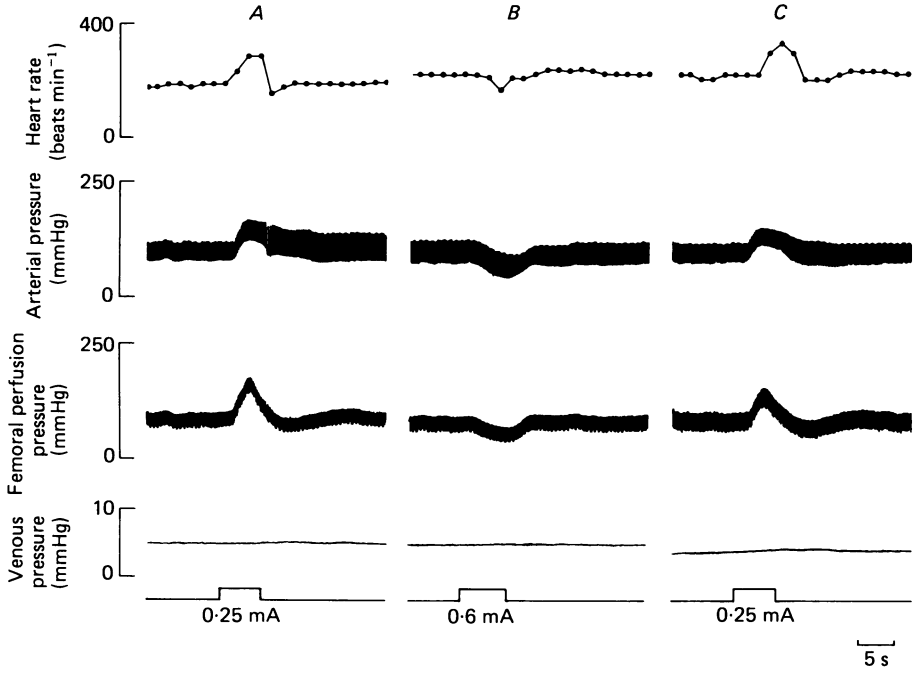

Fig. 7. Comparison of changes in heart rate, arterial blood pressure, femoral perfusion pressure and central venous pressure during uvula stimulation in the unanaesthetized decerebrate rabbit (*A*), after 10 mg α-chloralose kg^{-1} (*B*) and after a 90 min period since the dose of anaesthetic (*C*).

usually inhibited throughout the stimulus period. 2–2·5 h after the administration of the anaesthetic dose, the tachycardia and pressor response had returned. After administration of the short-acting anaesthetic Saffan (3 mg kg^{-1}) stimulation of the uvula in most rabbits failed to elicit any cardiovascular changes even at high stimulus strengths. 20 min after the Saffan was administered, uvula stimulation produced both tachycardia and a pressor effect.

DISCUSSION

This study has shown that stimulation of a highly localized region within the uvula, Larsell's, lobule IX of the posterior cerebellar vermis, can exert a powerful influence on the cardiovascular system. Uvula stimulation in rabbits anaesthetized with

urethane consistently evoked a small bradycardia and a fall in arterial pressure associated with a transient inhibition of renal sympathetic nerve activity and vasodilatation in the hind limb. In comparison the pattern of cardiovascular responses to stimulation of the same area in the decerebrate rabbit was essentially the opposite: a marked tachycardia, a pressor response, a maintained increase in renal sympathetic discharge and vasoconstriction in the hind limb. The responses seen in the decerebrate rabbit were reversed by a small dose of anaesthetic suggesting that the absence of anaesthetic rather than the decerebration itself was responsible for this complete alteration of evoked cardiovascular responses between anaesthetized and decerebrate preparations. Despite stimulation of lobules VII, VIII and X in both anaesthetized and decerebrate rabbits no cardiovascular effects could be evoked at the stimulus strengths that were effective for the uvula.

Previous reports show considerable variation in cardiovascular responses elicited from the cerebellar cortex not only between studies but also in any one study. One possible explanation for this might be depth and/or type of anaesthesia. In the conscious rabbit, for example, Ramu & Bergmann (1967) reported pressor responses from all areas of the cerebellar cortex which could be inhibited by 5–10 mg sodium pentobarbitone kg^{-1}. Hoffer *et al.* (1972) reported that the cardiovascular changes elicited from the posterior lobulus simplex in the α-chloralose-anaesthetized cat, which included a depressor response associated with vasodilatation in the skeletal muscle vascular beds, were suppressed when barbiturate or urethane anaesthesia were used.

More recently, Nisimaru *et al.* (1984) using anaesthetized, paralysed, debuffered and vagotomized rabbits reported a transient inhibition of renal nerve activity associated with a depressor response, but in some animals found a maintained increase in discharge from the renal sympathetic nerves with a pressor response from stimulation of lobules VIIa and VIIIa of the posterior vermis. Their results have a striking resemblance to the present data, in that we found a transient inhibition of renal discharge associated with a depressor response in the anaesthetized animal but could evoke increases in renal nerve activity associated with pressor responses in the unanaesthetized decerebrate rabbit. Furthermore the original blood pressure records from the experiments showing the two types of response described by Nisimaru *et al.* (1984) have different mean resting levels of 80 mmHg (in which a depressor response was evoked) and 150 mmHg where stimulation produced a pressor response. As no indication is given of how the depth of anaesthesia was maintained or assessed for these two animals, this might suggest a major difference in the level of the anaesthesia with the lower basal arterial pressure and depressor response associated with a deeper level of anaesthesia. In addition, the anaesthetic dose quoted by Nisimaru *et al.* (1984) is, in our experience, very low and their quoted stimulus intensities were not sufficient to evoke cardiovascular changes in our anaesthetized rabbits.

In the present study it is quite clear that it is the anaesthetic agent that causes the reversal of the cardiovascular responses between the unanaesthetized and anaesthetized decerebrate rabbit and not the decerebration itself as the responses in the decerebrate rabbit could be reversed by small doses of anaesthetic. In addition, the present study used relatively low constant-current stimuli while in earlier studies

higher current and voltages were used and stimulus spread to the brain stem may explain the inconsistency in the data previously reported. The reversal of the cardiovascular pattern of response may be attributed to cortical stimulation activating either, or both, the efferent pathway from the cortex or antidromically activating the mossy- and climbing-fibre input. If the efferent pathway, and therefore Purkinje cells, are excited the responses will be mediated mainly via an inhibitory action of Purkinje axons on the caudal fastigial nucleus (f.n.) (see Brodal, Pompeiano & Walberg, 1962; Barrett, Bradley, Paton & Spyer, 1985). It is also possible that the f.n. may be activated by antidromic activation of mossy and climbing fibres whose excitatory collaterals innervate the f.n. The mechanisms for the reversal could result from the anaesthetic agent acting to block either the efferent pathway or the antidromic excitation of the afferent fibres. Alternatively, the cortical outflow in the anaesthetized and decerebrate rabbits during uvula stimulation may follow the same descending pathway to the brain stem but the nuclei responsible for mediating the tachycardia–pressor response seen in the decerebrate rabbit may be blocked by the presence of the anaesthetic agents so revealing the bradycardia–depressor response. Finally, the uvula cortex may have both pressor and depressor sites and the anaesthetic agents might be acting to block the pressor pathways. Preliminary evidence from this laboratory using micro-injections of DL-homocysteic acid into the cortex of the uvula in both anaesthetized and decerebrate rabbits has resulted in blood pressure and heart rate changes similar to those obtained with electrical stimulation, suggesting that the electrical stimulus is activating Purkinje cells whose axons descend to the caudal f.n. This would imply that the reversal of our responses is due to the effect of the anaesthetic at the level of the brain stem and not within the neural circuitry of the cerebellar cortex.

It is well established that the posterior vermis projects to the caudal f.n. and the anterior vermis projects to the rostral f.n. (Brodal *et al.* 1962). The fastigial pressor response has been reported in the dog (Dormer & Stone, 1976) and cat (Achari & Downman, 1970) to be mediated by the rostral part of this nucleus. Cardiovascular changes can also be evoked from the caudal f.n. in the rabbit (Bradley, Paton & Spyer, 1986) and the direction of the response is qualitatively identical to those evoked from the uvula cortex in both the anaesthetized and decerebrate rabbits. The pressor response evoked from the rostral area of the f.n. in the rabbit is similar to that reported in other species and the direction of the response is identical in both anaesthetized and unanaesthetized decerebrate rabbits (Bradley *et al.* 1986). This therefore suggests that the cardiovascular responses elicited from the rostral and caudal f.n. are mediated via two separate pathways and may indicate two functional roles for the f.n. Some authors have suggested that cardiovascular responses to stimulation of the cerebellum are abolished by precollicular decerebration (Zanchetti & Zoccolini, 1954; Ban *et al.* 1960; Sawyer *et al.* 1961). From this study, and evidence from the work of Moruzzi (1940) and Hoffer *et al.* (1972), this cannot be the case, as changes in blood pressure have been found in decerebrate preparations even though there is good neurophysiological evidence for pathways from the anterior cortex and f.n. passing to the ventromedial and preoptic areas of the hypothalamus in the rabbit (Ban, Inoue, Ozaki & Kurotsu, 1956; Arikuni & Ban, 1974).

Although the functional significance of the uvula at this stage remains speculative,

micro-injections of horseradish peroxidase into the uvula cortex have revealed auditory, vestibular, somato-sensory, proprioceptive and trigeminal inputs (Barrett *et al.* 1985) which have been verified neurophysiologically (Ghelarducci & La Noce, 1985). This suggests that the uvula is not restricted to an involvement in orthostatic reflexes, which only require vestibular information and are partly under rostral f.n. control (Doba & Reis, 1972). We suggest that in view of the widespread sensory input and the pattern of cardiovascular responses the uvula may be involved in the alerting response in the rabbit. Confirmation of this can come only from experiments on conscious animals where cardiovascular changes can be assessed in relationship to any affective behavioural changes. Interestingly, it has already been shown that vermal stimulation can elicit or quieten an outburst of sham rage in the thalamic cat (Zanchetti & Zoccolini, 1952) and will suppress the autonomic components of the defence reaction in anaesthetized cats (Lisander & Martner, 1971).

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REFERENCES

ACHARI, N. K. & DOWNMAN, C. B. B. (1970). Autonomic effector responses to stimulation of nucleus fastigius. *Journal of Physiology* **210**, 637–650.

ARIKUNI, T. & BAN, T. (1974). Excitation and inhibition of hypothalamic neurons by cerebellar stimulation in rabbits. *Experientia* **30**, 504–505.

BAN, T., HILLIARD, J. & SAWYER, C. H. (1960). Autonomic and electroencephalographic responses to stimulation of the rabbit cerebellum. *Anatomical Record* **136**, 309.

BAN, T., INOUE, K., OZAKI, S. & KUROTSU, I. (1956). Interrelation between anterior lobe of cerebellum and hypothalamus in the rabbit. *Medical Journal of the Osaka University* **7**, 101–115.

BARRETT, D. J., BRADLEY, D. J., PATON, J. F. R. & SPYER, K. M. (1985). Afferent and efferent connexions of the uvula in the rabbit. *Journal of Physiology* **369**, 178*P*.

BRADLEY, D. J., GHELARDUCCI, B., PATON, J. F. R. & SPYER, K. M. (1985). Cardiovascular responses to stimulation of the posterior cerebellum in anaesthetized rabbits. *Journal of Physiology* **369**, 130*P*.

BRADLEY, D. J., GHELARDUCCI, B., PATON, J. F. R. & SPYER, K. M. (1986). Cardiovascular responses to stimulation of the posterior cerebellum in the decerebrate rabbit. *Journal of Physiology* **373**, 57*P*.

BRADLEY, D. J. & PATON, J. F. R. (1986). Effect of small doses of anaesthetics on cardiovascular changes evoked from the posterior cerebellum in the decerebrate rabbit. *Journal of Physiology* **376**, 31*P*.

BRADLEY, D. J., PATON, J. F. R. & SPYER, K. M. (1986). Cardiovascular responses elicited from the fastigial nucleus in the anaesthetized and decerebrate rabbit. *Journal of Physiology* **378**, 51*P*.

BRODAL, A., POMPEIANO, O. & WALBERG, F. (1962). Afferent connections of the vestibular nuclei. In *The Vestibular Nuclei and their Connections, Anatomy and Functional Correlations*, chap. 5, pp. 54–86. London: Oliver and Boyd.

DOBA, N. & REIS, D. J. (1972). Changes in regional blood flow and cardiodynamics evoked by electrical stimulation of the fastigial nucleus in the cat and their similarity to orthostatic reflexes. *Journal of Physiology* **227**, 729–747.

DORMER, K. J. & STONE, H. L. (1976). Cerebellar pressor response in the dog. *Journal of Applied Physiology* **41**, 574–580.

GHELARDUCCI, B. & LA NOCE, A. (1985). Convergenza multisensoriale su aree dell'uvula cerebellare con azioni cardiovascolari nel coniglio. *Proc. XXXVII Congresso Nazionale, Societa Italiana di Fisiologia*, Ab. 19.

HOFFER, B. J., MITRA, J. & SNIDER, R. S. (1972). Cerebellar influences on the cardiovascular system. In *Limbic System Mechanisms and Autonomic Function*, ed. HOCKMAN, C. H., pp. 91–112. Springfield, Illinois: Thomas.

LISANDER, B. & MARTNER, J. (1971). Cerebellar suppression of the autonomic components of the defence reaction. *Acta physiologica scandinavica* **81**, 84–95.

MORUZZI, G. (1940). Paleocerebellar inhibition of vasomotor and respiratory carotid sinus reflexes. *Journal of Neurophysiology* **3**, 20–32.

NISIMARU, N. & WATANABE, Y. (1985). Inhibitory effects of cerebellar nodulus (lobule X) stimulation on sympathetic nerve activity and systemic blood pressure in rabbit. *Journal of the Physiological Society of Japan* **47**, 447.

NISIMARU, N., YAMAMOTO, M. & SHIMOYAMA, I. (1984). Inhibitory effects of cerebellar cortical stimulation on sympathetic nerve activity in rabbits. *Japanese Journal of Physiology* **34**, 539–551.

RAMU, A. & BERGMANN, F. (1967). The role of the cerebellum in blood pressure regulation. *Experientia* **23**, 383–384.

RASHEED, B. M. A., MANCHANDA, S. K. & ANAND, B. K. (1970). Effects of stimulation of paleocerebellum on certain vegetative functions in the cat. *Brain Research* **20**, 293–308.

SAWYER, C. H., HILLIARD, J. & BAN, T. (1961). Autonomic and EEG responses to cerebellar stimulation in rabbits. *American Journal of Physiology* **200**, 405–412.

ZANCHETTI, A. & ZOCCOLINI, A. (1954). Autonomic hypothalamic outbursts elicited by cerebellar stimulation. *Journal of Neurophysiology* **17**, 475–483.