*Journal of Physiology* (1990), **428**, *pp.* 693–705
*With 6 figures*
*Printed in Great Britain*



# NUCLEUS TRACTUS SOLITARIUS AS MEDIATOR OF EVOKED PARABRACHIAL CARDIOVASCULAR RESPONSES IN THE DECEREBRATE RABBIT

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(*Received 11 January 1990*)

SUMMARY

1. The present study has assessed the importance of neurones within the nucleus tractus solitarius (NTS) in mediating the cardiovascular response evoked from the parabrachial nucleus (PBN) in the decerebrate rabbit. Microinjection techniques were employed so that the magnitude of the circulatory responses elicited from the PBN could be compared before, and after, kainic acid or bicuculline were microinjected into restricted regions of the NTS.

2. Electrical stimulation of the PBN (both medial and lateral regions) evoked variable changes in heart rate, a pressor response, vasoconstriction in the hindlimb and an increase in renal sympathetic nerve activity. Glutamate injected into these regions of the PBN elicited a similar pattern of response except that a tachycardia was observed consistently.

3. Both electrical and chemical stimulation of restricted regions of the NTS evoked bradycardia and a depressor response together with an increase in femoral vascular conductance and an inhibition of activity in the renal nerve.

4. Chemical lesions placed in these regions of the NTS by microinjecting kainic acid were found to attenuate both the heart rate and arterial blood pressure responses elicited from sites in the medial and lateral PBN using either electrical or chemical stimulation. Equivalent effects were produced on microinjecting the $GABA_a$ receptor antagonist bicuculline into the NTS.

5. These data indicate that NTS neurones play a part in mediating the cardiovascular responses that are evoked from the PBN and suggest that the action of the PBN at the level of the NTS is mediated via a GABAergic mechanism.

## INTRODUCTION

Recent studies in our laboratory have implicated the lateral portion of the parabrachial nucleus (PBN) in the mediation of the cardiovascular responses evoked from the posterior vermis (lobule IXb) of the cerebellum in the decerebrate rabbit (Bradley, Ghelarducci, La Noce, Paton, Sebastiani, Spyer & Sykes, 1989; Paton & Spyer 1989, 1990). This conclusion was based on the fact that the tachycardia/pressor

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response evoked from IXb was attenuated following a microinjection of bicuculline into a caudal region of the lateral PBN (Paton & Spyer, 1990). Although no evidence of a direct projection from lobule IXb to the nucleus tractus solitarius (NTS) has been demonstrated, the integrity of a GABAergic mechanism within this nucleus was essential for the expression of the cardiovascular response evoked from lobule IXb (Paton & Spyer 1989, 1990).

An influence of the PBN in control of circulation has been described in a number of previous investigations. Stimulation at sites within the PBN elicits pronounced increases in arterial blood pressure in the cat (Mravitch, Kumada & Reis, 1982; Hade, Mifflin, Donta & Felder, 1988), rabbit (Hamilton, Ellenberger, Liskowsky & Schniederman, 1981; Paton & Spyer, 1989, 1990) and rat (Ward, 1988). The question arises as to the role of the NTS in mediating these PBN-evoked responses. There is substantial evidence that both the lateral and medial regions of the PBN project to areas of the NTS in the cat (Smith, Morrison, Ellenberger, Otto & Feldman, 1989) and rat (Saper & Loewy, 1980) that are known to receive an innervation from baroreceptor afferents. In addition, Felder & Mifflin (1988) have shown that neurones receiving baroreceptor inputs in the NTS were excited and/or inhibited by electrical stimulation of the lateral and medial regions of the PBN in the cat. In contrast in the rabbit Hamilton *et al.* (1981) reported that NTS neurones receiving excitatory input from the aortic nerve were also excited by electrical stimulation of the lateral PBN. In the present study we have sought to determine the functional significance of the projection from the PBN to the NTS and to investigate the importance of neurones in the NTS in mediating the cardiovascular changes evoked from the lateral PBN.

A preliminary report of this work was communicated to the Physiological Society (Paton, Silva-Carvalho, Spyer & Thompson, 1989).

## METHODS

Experiments were performed on eighteen New Zealand White rabbits (2·3–3·1 kg body weight). All animals were anaesthetized with alphaxalone–alphadolone (Saffan, Glaxovet Ltd, UK, 4 mg $kg^{-1}$ given I.V. and supplemented with 4 mg bolus doses as required). The right femoral vein was cannulated to allow administration of Saffan and other drugs. The right femoral artery was cannulated and connected to a transducer (Gould Statham, USA, P23Db) for measurement of arterial blood pressure, heart rate being derived from the pulse waveform using a rate-meter (Neurolog, Digitimer Ltd, UK, model NL 250).

The trachea was intubated below the larynx and the bladder cannulated and drained in all animals. From a side-arm of the tracheal cannula end-tidal $CO_2$ was sampled and monitored continuously using an infra-red gas analyser (P.K. Morgan Ltd, UK, model 901) and maintained between 4·5 and 5·0% by altering minute volume or by I.V. bolus injection of molar sodium bicarbonate solution when necessary. Rectal temperature was measured using a thermometer and maintained at $38 \pm 0{\cdot}5$ °C with a heating lamp.

All animals were paralysed with decamethomium bromide (Sigma Ltd, UK, 0·25 mg $kg^{-1}$ I.V.) and supplemented every 20 min with the same dose. They were ventilated artificially (Harvard Apparatus Co., USA, model 665) with air enriched with oxygen (tidal volume 15–20 ml at 50–60 cycles $min^{-1}$), but only after the depth of anaesthesia had been fully assessed by observing the withdrawal reflex to pinching a paw and stability of arterial blood pressure and heart rate. Once both common carotid arteries were ligated the animal was decerebrated using undercutting and suction techniques leaving the superior colliculi intact.

In some experiments the left femoral artery was prepared for recording blood flow using an electromagnetic flowmeter (Carolina Medical Electronics) which was calibrated as described

previously (Bradley, Ghelarducci, Paton & Spyer, 1987). All small collateral vessels and the profunda artery were ligated and the hindlimb kept warm by wrapping it in a Polythene bag to enhance blood flow. From the blood flow and arterial pressure signals femoral conductance was calculated on-line using a custom-built meter. In addition, the left kidney was approached retroperitoneally and the renal nerves dissected away from surrounding tissue and blood vessels, and cut peripherally. The central end of the renal nerve was placed on a bipolar silver wire hook recording electrode, covered in semi-solid paraffin and the activity differentially amplified and filtered (Neurolog NL 100, 104 and 125 nodules).

The carotid sinus baroreceptors were activated by preparing bilateral blind sacs of the carotid sinuses. The internal and external carotid arteries were ligated and the external maxillary artery cannulated to permit close-arterial injection of saline (0·2–0·3 ml) to inflate the carotid sinus region following occlusion of the common carotid artery.

In all experiments the animal's head was placed in a stereotaxic head holder (Kopf Instruments) such that the difference in height between lambda and bregma was zero. A multi-barrelled microelectrode (tip diameter 25–35 $\mu$m) was orientated into the right or left PBN using stereotaxic co-ordinates (2·3 $\pm$ 0·3 mm rostral to lambda, 3·0 $\pm$ 0·5 mm lateral to midline; 11–13 mm below dura) and a second was positioned into the ipsilateral NTS. One barrel of both electrodes was filled with Woods' metal for electrical stimulation (4 s train, 100 Hz, 0·5 ms, 10–350 $\mu$A), another with glutamate (0·1–0·4 M; pH 7·4 $\pm$ 0·1) since this excites perikarya but not fibres of passage (Crawford & Curtis, 1964; Fries & Zieglgansberger, 1974), and a third with freshly prepared artificial CSF. This was microinjected as a control for volume-related artifacts. The microelectrode positioned into the NTS also contained kainic acid (100 mM; pH 7·4 $\pm$ 0·1), a neurotoxin, and the $GABA_A$ antagonist bicuculline methiodide (5 nM–100 mM; pH 7·4 $\pm$ 0·1). In all experiments the volumes injected ranged from 50 to 100 nl over a 4–8 s period. All drugs were dissolved in artificial CSF except bicuculline which was made up in saline. In some experiments either one or both microelectrodes contained Pontamine Sky Blue dye so that the spread of a 50–100 nl microinjection could be estimated.

Stimulation sites in the lateral PBN were selected where a glutamate microinjection evoked increases in heart rate and arterial blood pressure, whilst for the NTS sites eliciting a qualitatively opposite effect were identified. The magnitude of the cardiovascular response evoked from the lateral PBN using both electrical and chemical stimulation was compared before and after a microinjection of kainic acid or bicuculline into the ipsilateral NTS. All stimulation sites were marked either with dye (see above) or by making a DC lesion with constant current (50 $\mu$A; 40 s) and identified subsequently using standard histological procedures.

All variables were recorded on an eight-channel recorder (Gould Electronics, USA, model 2800S), and from the charts the cardiovascular variables were analysed using the Nanostat statistical package (two-sample $t$ test). In the numerical analysis '$n$' refers to number of animals. All results were the mean $\pm$ S.E.M. and were taken as being significant at the 5% level.

## RESULTS

The cardiovascular responses evoked from the medial and lateral PBN were qualitatively similar to those reported in a previous report using electrical and chemical stimulation (Paton & Spyer, 1990). In this study the intensity used for stimulation of the PBN was always submaximal.

### *Cardiovascular responses evoked from the parabrachial nucleus*

Electrical stimulation of the PBN evoked a pronounced bradycardia of 96·2 $\pm$ 10·68 beats $min^{-1}$ (forty-five tests) in ten rabbits (Fig. 1) but a tachycardia of 33·8 $\pm$ 5·1 beats $min^{-1}$ (eleven tests) in three animals. In three other rabbits there was a biphasic change in heart rate, either a bradycardia–tachycardia or a tachycardia–bradycardia sequence. These heart rate changes were accompanied by increases in arterial blood pressure of 43·2 $\pm$ 1·9 mmHg ($n$ = 16, $P < 0·001$; sixty-one

tests; Fig. 1), a fall in femoral conductance of $0{\cdot}04 \pm 0{\cdot}003$ ml $min^{-1}$ $mmHg^{-1}$ ($n = 7$, $P < 0{\cdot}001$; twenty-nine tests) and a marked increase in renal nerve discharge in seven animals where this was recorded. Following a microinjection of glutamate into the PBN a consistent response was elicited that included a tachycardia of $29{\cdot}6 \pm 7{\cdot}2$

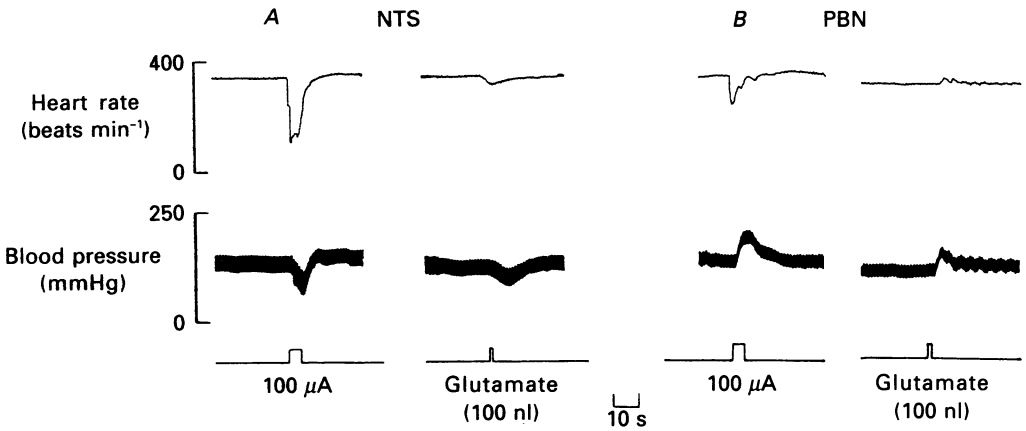


Fig. 1. Effect of electrical (4 s train, 100 Hz, 0·5 ms, 100 μA) and chemical (glutamate 100 nl) stimulation of NTS (*A*) and lateral PBN (*B*) on heart rate and arterial blood pressure in two different animals.

beats $min^{-1}$ ($n = 10$, $P < 0{\cdot}003$; ten tests), a pressor response of $33{\cdot}6 \pm 3{\cdot}8$ mmHg ($n = 15$, $P < 0{\cdot}001$; seventeen tests; Fig. 1) associated with a decrease in femoral conductance of $0{\cdot}03 \pm 0{\cdot}01$ ml $min^{-1}$ ($n = 6$, $P < 0{\cdot}02$; six tests) and an increase in renal nerve activity. The majority of stimulation sites (thirteen animals) were located within the lateral region of the PBN but in five experiments they were within the medial area of the PBN (Fig. 2). In experiments where blue dye was injected a 100 nl microinjection was found to produce a spot of 0·8–1·0 mm diameter which is similar to that observed in other studies (Blessing & Willoughby, 1987; Paton & Spyer, 1990). In all experiments where artificial CSF was microinjected there were no changes in the cardiovascular variables recorded.

*Cardiovascular responses evoked from the nucleus tractus solitarius*

Electrical stimulation of selected sites within the NTS evoked a bradycardia of $85{\cdot}5 \pm 16{\cdot}0$ beats $min^{-1}$ ($n = 16$, $P < 0{\cdot}001$; sixteen tests) and a depressor response of

Fig. 2. Line drawings of standard coronal sections of rabbit medulla (*A*) and pons (*B*). In *A* positions rostrocaudal with regard to the obex are indicated (+1, 0, −1 mm), whilst in *B* the levels rostral to the level of the auditory orifices are shown. Each dot represents the location of an electrolytic lesion made at a site of stimulation. Abbreviations: BCon, brachium conjunctivium; CG, central grey; Coe, locus coeruleus; Cun, cuneate nucleus; Gra, gracilis nucleus; NTS, nucleus tractus solitarius; PBN, parabrachial nucleus; PH, prepositus hypoglossal nucleus; RF, reticular formation; subCoe, sub-nucleus of locus coeruleus; T, tractus; *V*, mesencephalic trigeminal nucleus; X, dorsal vagal motor nucleus; XII, hypoglossal nucleus. Bar = 1 mm.

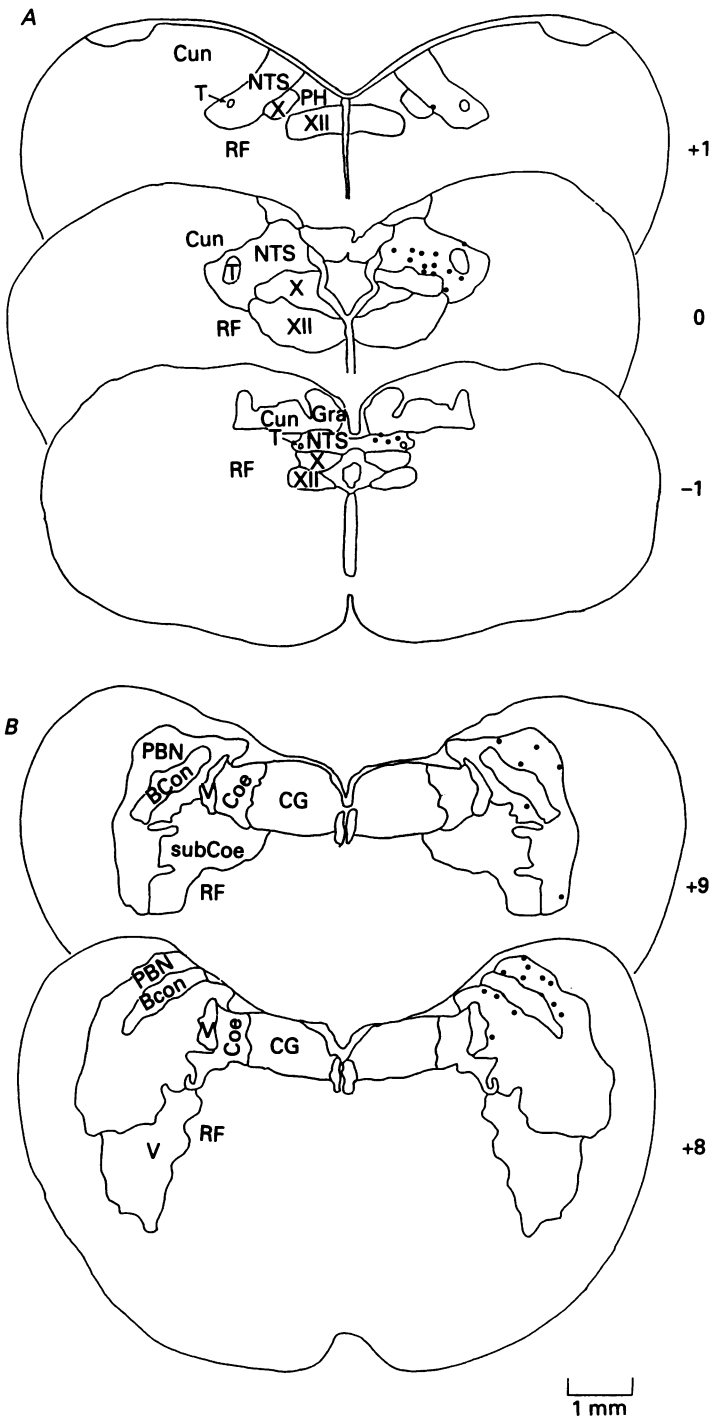


Fig. 2. For legend see facing page.

22·7 ± 2·9 mmHg ($n = 13$, $P < 0·001$; thirteen tests; Fig. 1). In three rabbits there was a cessation of on-going activity in the renal nerve. Activation of neurones within the NTS by microinjecting glutamate at these sites produced a similar pattern of response: falls in both heart rate (26·4 ± 4·8 beats $min^{-1}$; $n = 10$, $P < 0·003$; ten tests) and blood pressure (14·5 ± 2·1 mmHg; $n = 15$, $P < 0·001$; fifteen tests) (Fig. 1) and an inhibition of renal nerve activity. These responses were found to be evoked from regions of the NTS at the level of the obex and approximately 1 mm caudal to it (Fig. 2).

*Effect of the microinjection of kainic acid on the cardiovascular responses evoked from the parabrachial nucleus*

A microinjection of kainic acid into the NTS elicited no obvious change in heart rate in two animals or a bradycardia of 16 ± 4·6 beats $min^{1-}$ (thirteen tests) in three. There were variable changes in arterial blood pressure including increases (15 and

TABLE 1. A comparison of the baseline heart rate and arterial blood pressure levels before and after a microinjection of kainic acid or bicuculline (where values for femoral arterial conductance are shown) into the NTS. There was no significant difference in the pre- and post-injection levels of the cardiovascular variables monitored. $n$ is the number of tests

| | Control | Post kainic acid | | |
|---|---|---|---|---|
| Heart rate (beats $min^{-1}$) | 314·66 ± 6·53 | 337·77 ± 13·96 | $n = 9$ | ($P < 0·025$) |
| Blood pressure (mmHg) | 115·00 ± 3·37 | 117·38 ± 6·67 | $n = 18$ | (n.s.) |
| | Control | Post bicuculline | | |
| Heart rate (beats $min^{-1}$) | 278·66 ± 10·13 | 294·07 ± 11·54 | $n = 27$ | (n.s.) |
| Blood pressure (mmHg) | 104·40 ± 3·69 | 94·29 ± 4·79 | $n = 27$ | (n.s.) |
| Conductance (ml $min^{-1}$ $mmHg^{-1}$) | 0·105 ± 0·013 | 0·101 ± 0·011 | $n = 19$ | (n.s.) |

28 mmHg; two tests) in two rabbits, a decrease (6 mmHg) in one and no obvious change in another. A period of 10 min was allowed to elapse following the injection of kainic acid into the NTS before assessing the effect of the neurotoxin on the magnitude of the cardiovascular response evoked from the PBN. At this time baseline values of arterial blood pressure and heart rate were the same as prior to the injection of kainic acid (Table 1). Following kainic acid injection into the ipsilateral NTS the bradycardia evoked by electrical stimulation of PBN was reduced significantly by 36·7% in four rabbits (from 48·0 ± 9·08 to 30·4 ± 5·94 beats $min^{-1}$; $n = 4$, $P < 0·028$; ten tests) and the tachycardia reversed to a bradycardia in others (9·33 ± 2·5 to −7·00 ± 5·89 beats $min^{-1}$; $n = 5$, $P < 0·001$; twelve tests). The pressor response evoked by electrical stimulation of the PBN was abolished in one animal (Fig. 3) or the magnitude decreased in four animals by 45·9% (from 45·38 ± 3·11 to 20·83 ± 3·51 mmHg; $n = 4$, $P < 0·001$; eighteen tests) (Fig. 4).

In all five animals in which the test was undertaken, a microinjection of glutamate into the lateral PBN failed to elicit a measurable change in heart rate or arterial blood pressure after delivery of kainic acid into the ipsilateral NTS. A possible explanation for this observation might be the long-term effect of the first microinjection of glutamate producing depolarization block (see Lipski, Bellingham, West & Pilowsky, 1988) thus preventing further glutamate injections from exciting neurones within the PBN. This is unlikely on two accounts. First, periods of 1–1·5 h

were allowed to elapse between subsequent microinjections of glutamate into the PBN which is far in excess of the time suggested by Lipski *et al.* (1988) to avoid problems of depolarization block. Second, in some experiments glutamate was microinjected into the PBN repeatedly at intervals of 15–20 min and produced a

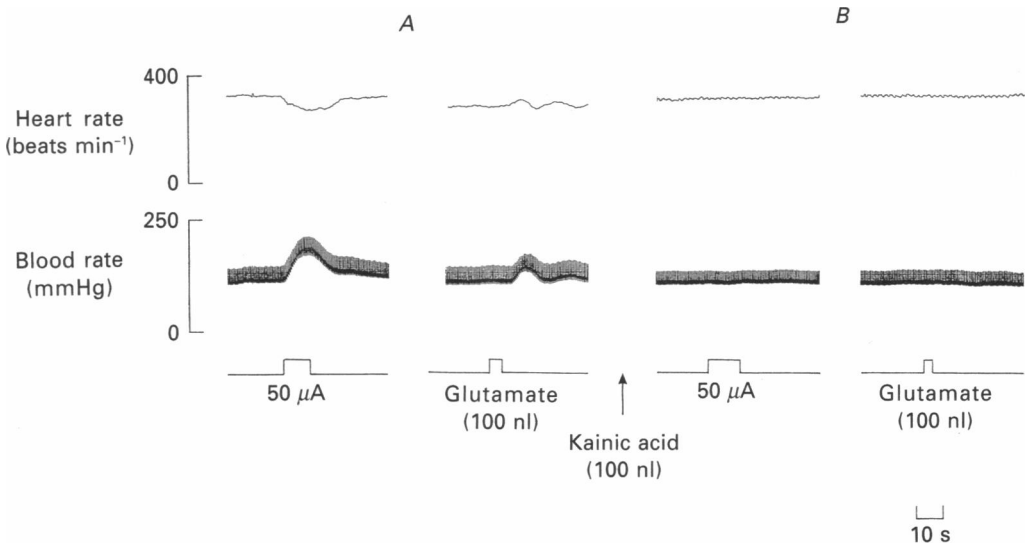


Fig. 3. Effect of a kainic acid microinjection (100 nl) into the NTS on the cardiovascular response evoked from the PBN with electrical and chemical stimulation. *A*, changes in heart rate and arterial blood pressure evoked by stimulation of the lateral parabrachial nucleus with electrical stimulation (50 $\mu$A) and glutamate (100 nl). *B*, effect of the same stimuli given 10 min after the microinjection of kainic acid into the NTS.

response of similar magnitude on successive injection. Comparison of the baroreflex elicited by inflation of the blind sac of the ipsilateral carotid sinus before, and after, the microinjection of kainate into the NTS showed a significant decrease of the evoked changes in heart rate (from $24{\cdot}57 \pm 11{\cdot}28$ to $3{\cdot}42 \pm 3{\cdot}3$ beats min$^{-1}$; $n = 7$, $P < 0{\cdot}041$; seven tests) and blood pressure (from $18{\cdot}71 \pm 6{\cdot}79$ to $1{\cdot}28 \pm 0{\cdot}83$ mmHg; $n = 7$, $P < 0{\cdot}027$; seven tests).

*Effect of the microinjection of bicuculline into the nucleus tractus solitarius on the cardiovascular response evoked from the lateral parabrachial nucleus*

A microinjection of bicuculline into the NTS produced either no change in the cardiovascular variables recorded or a similar but smaller pattern of response to that evoked with glutamate (see above). In one animal a bradycardia was observed (24 beats min$^{-1}$) and in four rabbits a depressor response of $7{\cdot}0 \pm 2{\cdot}7$ mmHg (four tests) associated with inconsistent changes in femoral vascular conductance and a reduction in renal nerve activity. Once the cardiovascular variables had returned to control levels (2–10 min; see Table 1) the PBN was re-stimulated. The bradycardia evoked with electrical stimulation from the PBN was attenuated significantly (from $105{\cdot}83 \pm 12{\cdot}87$ to $42{\cdot}83 \pm 12{\cdot}19$ beats min$^{-1}$; $n = 9$, $P < 0{\cdot}001$; twenty-four tests (see Figs 5 and 6).

In all animals the pressor response was reduced by 74·5% (from 44·25±3·42 to 11·25±2·3 mmHg; $n = 11$, $P < 0.001$; twenty-eight tests), the decrease in femoral vascular conductance attenuated by 77·4% (from 0·042±0·004 to 0·0095± 0·004 ml $min^{-1}$ $mmHg^{-1}$; $n = 7$, $P < 0.001$; twenty tests) (Fig. 6) and there was

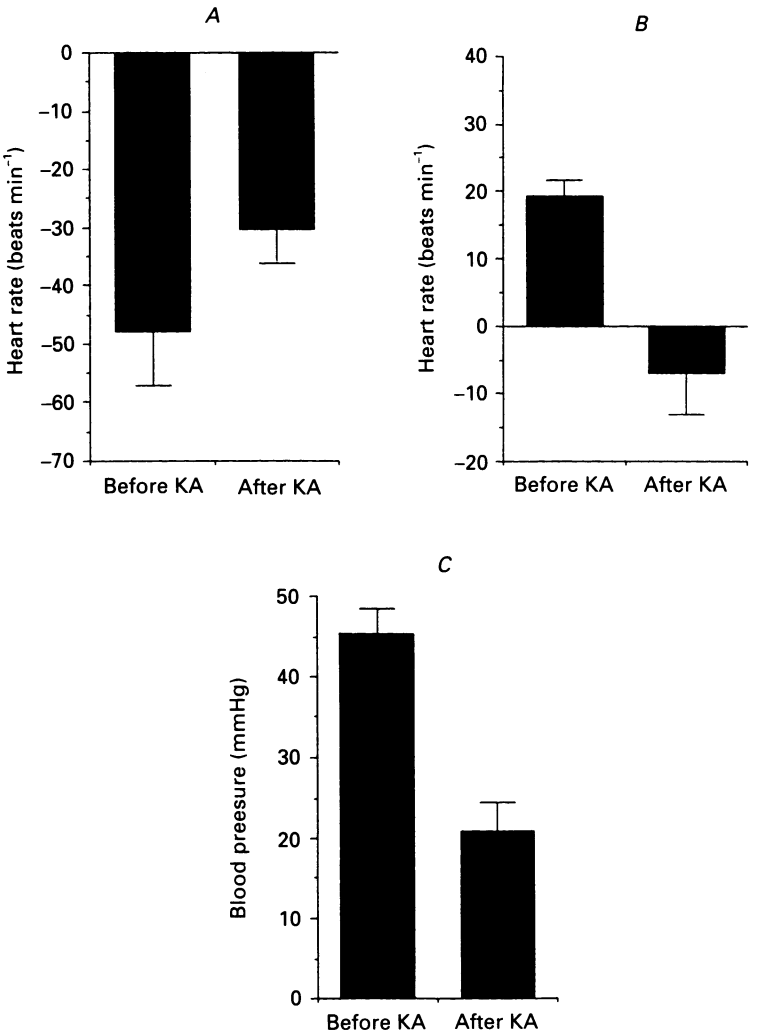


Fig. 4. Effect of a chemical lesion made within the NTS with kainic acid (KA) on heart rate and blood pressure changes evoked by electrical stimulation of the lateral parabrachial nucleus. *A*, tests in which a bradycardia was observed. *B*, test in which the original tachycardia was reversed to a bradycardia after kainic acid. *C*, attenuation of the pressor effect seen in *A* and *B*. Further details in text.

little or no obvious change in on-going activity in the renal neurogram. There was no significant difference in the magnitude of the attenuation of the pressor response to PBN stimulation produced between twenty-two tests where a dose of 100 mM-bicuculline was injected into the NTS (25·83±10·54 mmHg) and six tests

where the dose of bicuculline was 5 nM (34·4 ± 7·33 mmHg). Chemical activation of the PBN following a bicuculline microinjection into the NTS failed to produce the changes described above in the cardiovascular responses recorded (Fig. 5), except in one case where a small bradycardia and depressor response were elicited. (In two

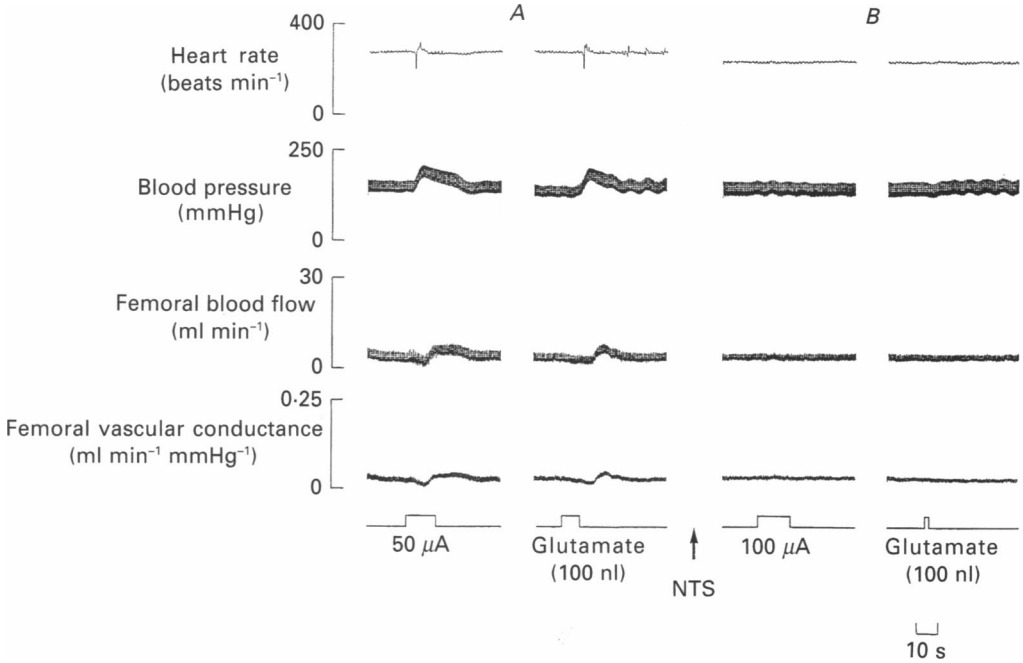


Fig. 5. Effect of a microinjection of bicuculline into a restricted region of the NTS on the cardiovascular response evoked from the PBN with electrical stimulation and glutamate.

cases, a depressor response was observed on electrical stimulation of the PBN following bicuculline injection into the NTS.)

## DISCUSSION

The present series of experiments indicate that the integrity of neurones within the NTS is important in mediating the cardiovascular responses evoked from the PBN in the decerebrate rabbit. Activation of neurones within the lateral PBN with glutamate evoked a tachycardia and pressor response associated with an increase in renal sympathetic nerve discharge and vasoconstriction in the femoral vascular bed. This response was attenuated, or abolished, following a chemical lesion of restricted regions of the NTS with kainic acid. Similarly, the injection of bicuculline into the NTS reduced the magnitude of the cardiovascular response elicited from the PBN. This suggests that the cardiovascular response elicited by stimulation of the lateral PBN is mediated, in part, via a GABAergic mechanism at the level of the NTS.

These conclusions are dependent on the results of studies involving the microinjection of an excitant amino acid (glutamate), a $GABA_a$ antagonist (bicuculline) or the neurotoxin kainic acid into the NTS. The limitations of the microinjection technique have been outlined earlier (and see Nicholson, 1985; Lipski

*et al.* 1988). In the present experiments certain precautions have been taken to control for many of the problems associated with these such as diffusion and specificity. Two different concentrations of bicuculline when injected into the NTS produced the same effect upon the cardiovascular changes elicited by PBN

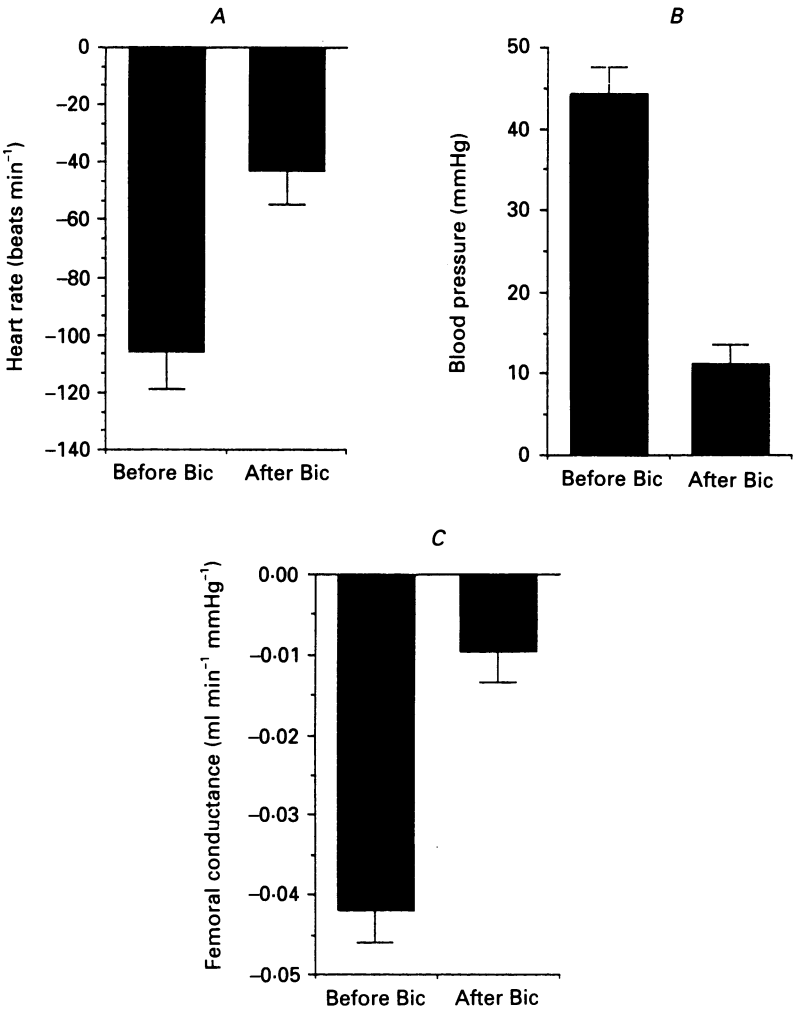


Fig. 6. Effect of the injection of bicuculline (Bic) into the NTS on the bradycardia (*A*), the pressor response (*B*) and the decrease in femoral conductance provoked by electrical stimulation of the lateral parabrachial nucleus (*C*).

stimulation, whilst control injections made into structures surrounding the NTS had no effect. Thus the data presented support the claim that a relatively restricted region of the NTS is important in the expression of the cardiovascular response elicited from the PBN. This region of the NTS is equivalent to areas of the NTS known to receive baroreceptor afferents in the rabbit (Wallach & Loewy, 1980; Higgins & Schwaber, 1981) and is consistent with the observation reported in this

study that following a microinjection of kainic acid into the NTS the decrease in blood pressure evoked by inflation of the blind sac is reduced. In a previous report (Paton & Spyer, 1990) we have shown that the baroreceptor reflex is potentiated after bicuculline microinjection into restricted portions of the NTS equivalent to those investigated in this study.

The PBN has been shown to evoke increases in heart rate and arterial blood pressure when activated with glutamate in a number of species (cat, Hade *et al.* 1988; rabbit, Paton & Spyer, 1990; rat, Ward, 1988). This is consistent with data obtained from previous studies using electrical stimulation in the cat (Mravitch *et al.* 1982). In the rabbit, Hamilton *et al.* (1981) reported that electrical stimulation of the parabrachial region evoked a bradycardia. This was confirmed in the present study and also in an earlier report (Paton & Spyer, 1990) where the PBN was stimulated electrically. Here a bradycardia was evoked on many occasions suggesting that fibres of passage were activated, since glutamate injections always evoked a tachycardia. Alternatively, the bradycardia might also have involved a baroreceptor-mediated response to the evoked rise in arterial blood pressure. The pressure response to electrical stimulation was usually larger than that evoked by glutamate activation.

Recent studies in this laboratory have indicated that the PBN is involved in mediating the cardiovascular responses evoked from lobule IXb of the posterior cerebellar vermis (Paton & Spyer, 1989, 1990). In the decerebrate rabbit stimulation of IXb elicits tachycardia and a pressor response (Bradley *et al.* 1987) and this can be blocked following a microinjection of bicuculline into the caudal region of the lateral PBN (Paton & Spyer, 1990). Similarly, a bicuculline-sensitive mechanism within the NTS was also shown to attenuate the tachycardia–pressor response mediated from IXb (Paton & Spyer, 1989, 1990) and it was suggested that the caudal portion of the lateral PBN might act as a relay for IXb-evoked influences acting at the level of the NTS. In this respect preliminary evidence has confirmed that a microinjection of bicuculline into the NTS not only blocks the tachycardia–pressor response evoked from the PBN but also attenuated the cardiovascular response evoked from lobule IXb of the cerebellum (J. F. R. Paton, L. Silva-Carvalho, K. M. Spyer & C. S. Thompson, unpublished observation). In addition, there is both anatomical and neurophysiological evidence for a projection from the PBN to the NTS.

In the rat (Saper & Loewy, 1980) and cat (Smith *et al.* 1989) it has been demonstrated that efferent fibres course from the lateral and medial PBN to regions of the NTS known to receive baroreceptor afferents. Further, Felder & Mifflin (1988) have shown that electrical stimulation of the PBN in the cat elicits excitation followed by inhibition of neurones receiving baroreceptor inputs in the NTS. In contrast, in the anaesthetized rabbit inputs from the lateral PBN excited NTS neurones synaptically driven by aortic nerve stimulation (Hamilton *et al.* 1981). This latter finding is inconsistent with the present results since an excitatory input onto such NTS neurones would be expected to produce a fall in heart rate and arterial pressure. However, electrical stimulation of the PBN did elicit a bradycardia, and its magnitude was reduced following kainic acid or bicuculline injections into the NTS. In this study the opposite response was seen (tachycardia–pressor) during chemical stimulation of the lateral PBN. Thus, it is plausible that activation of the lateral

PBN inhibits NTS neurones which in part is responsible for mediating the increases in heart rate and arterial blood pressure. The discrepancy between the present study and that of Hamilton *et al.* (1981) might be a consequence of the different types of preparation used. However, it is of interest that in the present series of experiments chemical stimulation of the lateral PBN after bicuculline was injected into the NTS resulted in a small bradycardia and depressor response in an animal indicating the presence of a mixed population of neurones within the lateral PBN. At present it is not known which brain stem region is responsible for mediating this latter response but the data from this study suggest that it is not via a $GABA_a$ mechanism within the NTS, at least for the depressor component.

Equally the present results contrast with the observations of Mravitch *et al.* (1982) who claim that bilateral electrolytic lesions in the intermediate NTS failed to attenuate the heart rate and blood pressure changes evoked by electrical stimulation of the lateral PBN of the cat. This difference in effect of NTS lesions on responses evoked from the PBN might reflect a species difference; however, this remains to be resolved.

In conclusion the present evidence suggests that the cardiovascular responses evoked from the lateral PBN are in part mediated by a bicuculline-sensitive mechanism within the NTS. It is suggested that this pathway might also be an important relay in the pathway whereby lobule IXb activation influences circulatory control in the decerebrate rabbit. These data support the notion that the PBN plays an integral role in central cardiovascular control mechanisms.

The technical assistance of Mr M. A. Goring and Miss A. J. Bradley is gratefully acknowledged. These studies were supported by programme grants from the British Heart Foundation and MRC.

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