interrupted by periods of exaggerated gnawing and sniffing. On the other hand, when the SP was injected either immediately dorsal to, or anterior to the zona reticulata the animals always responded with a postural bias or turning in the opposite direction. SP injections made posterior to the zona reticulata, or injections of saline given into any of these regions, failed to elicit any form of stereotyped behaviour.

Although there was considerable variation between animals in the striatal concentrations of dopamine (range 0·9–1·9 $\mu g\,g^{-1}$ wet wt) and HVA (range 0·32–1·02 $\mu g\,g^{-1}$ wet wt), bilateral differences in the striatal contents of these substances in saline-injected controls were less than 10%. In the low dose employed here SP had no effect on the steady-state level of dopamine in the striatum. However, Table 1 clearly indicates that SP-induced contralateral turning was accompanied by a pronounced increase in ipsilateral striatal HVA concentrations ($P < 0.001$), and that turning towards the injected side was characterized by a significant decrease in this metabolite ipsilaterally ($P < 0.001$). SP injections at sites which did not elicit turning caused no significant change in striatal HVA concentrations.

Since the neurons in the substantia nigra are known to be susceptible to excitation by electrophoretically-applied SP (Davies & Dray, 1976), it seems reasonable to speculate that the SP-induced contralateral turning observed here results from the unilateral stimulation of the ascending nigrostriatal dopaminergic pathways, especially as the HVA concentrations in the corresponding striata were raised accordingly.

The critical placement of the SP injection is also interesting, because it emphasises that the application of SP to other cells in the neighbourhood of the zona reticulata ultimately reduces impulse traffic in the ascending dopaminergic neurons on that side and leads to ipsilateral circling. The nature of the synaptic connections in the region of the substantia nigra is not fully understood, but it is possible that in this case SP may be acting indirectly upon the zona reticulata through the intervention of an inhibitory interneuron.

Although the mode of action of SP remains to be determined, this preliminary study serves to illustrate that SP possesses demonstrable physiological activity when injected in small doses into the substantia nigra, an area of the brain which possesses high concentrations of SP and which could conceivably utilize this peptide as an endogenous synaptic transmitter.

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A simplified decerebration technique in cats and its applicability to neuro-cardiovascular drug studies†

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Elimination of higher central nervous system (cns) structures by decerebration has been carried out by a variety of techniques. However, these methods are not entirely satisfactory as they either require specialized instrumentation (Kent, Drane & Manning, 1971) result in massive trauma and blood loss (Chai & Wang, 1962) or do not completely eliminate higher cns influence on hind brain activity (Borison, Clark & Rosenstein, 1963). The purpose of our work was to develop a technique that would avoid these problems.

We modified a stainless steel microspatula (spatula, micro, stainless steel, mirrowed finish, No. 57949-022, VWR Scientific) into an instrument that could be

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mounted on to a David Kopf stereotaxic apparatus and passed through a coronal plane of the brain. In detail, 4·8 mm of the spooned end of a 154 mm long spatula was cut and discarded, leaving the flattened end and most of the shaft. The flattened end was shortened by 11 mm and the edges rounded off, resulting in a device with a final length of 95 mm. Two holes (1/18 in) were bored through the shaft 3·90 and 8·75 mm from the tip of the flattened end. These holes served as a pivot and a locking point, respectively. The device is shown in Fig. 1.

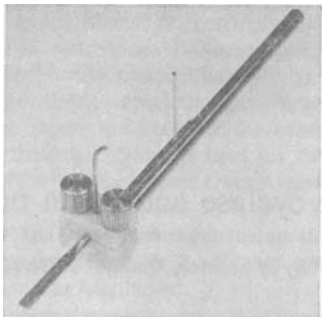

FIG. 1. Modified stainless steel microspatula used for decerebration.

For midcollicular decerebration, the modified microspatula was mounted on to a stereotaxic apparatus (Fig. 2) and lowered sequentially through two 1/4 in burr holes in the cranium. The burr holes were centred 5 mm from either side of the midline. In the locked vertical position, the device was lowered through the cerebral cortex and mesencephalon until it made contact with the baso-occipital bone. The stereotaxic co-ordinates used to place the modified microspatula were those of Snider & Niemer (1961) (ANT 1·5; RL +5 and −5). The pin was removed from the locking point and the decerebrating device was oscillated along the ventromedial contour of the baso occipital bone using minimal applied pressure (Fig. 2). If resistance was encountered to the oscillating motion, the instrument was raised to a higher level and gently moved side to side until bone was felt. The upper edge of the baso-occipital bone on the opposite side of the cranial opening could be easily felt and served as a landmark for limiting further lateral movement.

Inspection of the brain after decerebration indicates complete section of the intercollicular tegmentum and tectum. The ventral most portions of the corticospinal tracts usually remain intact. Most importantly, the arterial basilar arterial network is left intact and no evidence of significant bleeding in the area can be found.

Transection of the brain of cats anaesthetized with chloralose and artificially respired by this technique

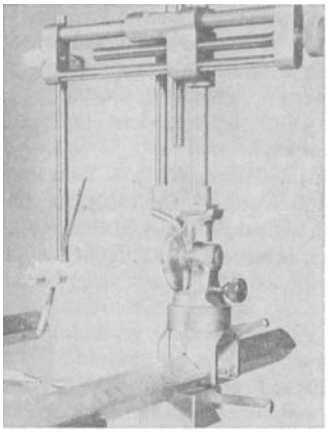

FIG. 2. Microspatula mounted on to a stereotaxic apparatus.

produces an immediate but transient (<1 min) increase in arterial pressure. Within 30 min the level of arterial pressure is identical to that seen before decerebration (Table 1). An increase in heart rate is also observed, but in contrast to arterial pressure, the increase in heart rate persists (Table 1) for the duration of the observation period (2 h). The effect of our decerebration technique on the arterial pressure response to baroreceptor deactivation was tested by performing a 30 s bilateral carotid occlusion before and after decerebration. The decerebration technique did not dampen the response (Table 1); indeed a greater pressor response to baroreceptor deactivation was observed (Table 1).

Table 1. *Cardiovascular status of animals before and after decerebration.*

	Mean arterial pressure mm Hg (n = 7)	Heart rate beats min^{-1} (n = 6)	Pressor response to bilateral carotid occlusion mm Hg (n = 6)
Control	121 ± 7	172 ± 13	41 ± 8
After decerebration	118 ± 13	208 ± 9*	66 ± 6*

* Significantly different from control ($P < 0.05$).

The cardiovascular status of the animals following decerebration (i.e. level of arterial pressure and heart rate as well as presence of a carotid occlusion response) indicated that the functional integrity of medullary cardiovascular centres remained intact. The greater

heart rate and carotid occlusion response after decerebration may indicate the presence of some degree of inhibitory tone to medullary cardiovascular centres by the higher centres. This preparation is well suited for investigating the site of action of drugs that affect the cardiovascular system through a central mechanism.

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Selective block of cardiovascular adenylate cyclase activation *in vivo*

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Stimulation of β-adrenoceptors by sympathomimetic drugs increases tissue cyclic 3′-5′-adenosine monophosphate (cyclic AMP) concentrations by activating an adenylate cyclase system which regulates cyclic AMP biosynthesis (Robison & Sutherland, 1970). The increase in cyclic AMP concentrations is presumed to mediate pharmacological responses to sympathomimetic drugs despite evidence of dissociation between inotropic responses and adenylate cyclase activation in cardiac tissue (Wastila, Su & others, 1972; Benfey, Kunos & Nickerson, 1974).

The present report describes an investigation of the ability of β-adrenoceptor blocking agents to block adenylate cyclase activation by isoprenaline in cardiac and vascular tissues *in vivo*. The blocking agents studied are known to have different selectivities in blocking cardiostimulant and vasodilator responses to isoprenaline *in vivo*.

Female white rats (Fisher Strain), 150–250 g, were anaesthetized by an intraperitoneal (i.p.) injection of pentobarbitone sodium (50 mg kg^{-1}) and anaesthesia maintained by additional doses as needed. The femoral vein was isolated and cannulated and the trachea cannulated to facilitate respiration. The animals were killed by removal of the heart (atria and ventricles) and aorta approximately 50 min after an intraperitoneal injection of physiological saline or theophylline (45 mg kg^{-1}) and 1 min after an intravenous injection of physiological saline or (±)-isoprenaline (10 μg kg^{-1}). Some animals received an injection of propanolol (0·5 mg kg^{-1}), practolol (4 mg kg^{-1}) or H 35/25 (4 mg kg^{-1}) 15 min before the isoprenaline injection.

The doses of isoprenaline and blocking agents used were selected in preliminary experiments using theophylline-pretreated rats anaesthetized with pentobarbitone. Heart rate and blood pressure were recorded in these experiments on a Hewlett Packard Model 7700 polygraph via a Statham PT06 transducer attached to a cannula inserted in a carotid artery. In these experiments, isoprenaline (10 μg kg^{-1}) significantly increased heart rate and decreased diastolic blood pressure; both of these effects were abolished by pretreatment with propranolol (0·5 mg kg^{-1}). Practolol (4 mg kg^{-1}) significantly reduced the effect of isoprenaline on heart rate but not on blood pressure. H 35/25 (4 mg kg^{-1}) significantly reduced the effect of isoprenaline on blood pressure but not on heart rate. In all of the animals in which heart rate and blood pressure were measured, blocking agents were administered in the same time sequence as in the animals from which heart and aorta samples were removed, i.e. 25 min after theophylline (45 mg kg^{-1}, i.p.) and 15 min before isoprenaline (10 μg kg^{-1}, i.v.).

The heart and aorta samples were homogenized with glass tissue homogenizers in cold trichloroacetic acid solution, centrifuged and the resulting supernatants washed with diethyl ether as described by Brown, Albano & others (1971). The cyclic AMP content of heart and aorta extracts was then determined by a protein-binding assay procedure based on the competition between unlabelled (tissue) and tritium-

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