J. Physiol. (1961), **158**, *pp.* 411–425
With 11 *text-figures*
Printed in Great Britain

THE EFFECT OF SOME CATECHOLAMINES UPON A MONOSYNAPTIC REFLEX PATHWAY IN THE SPINAL CORD

BY H. McLENNAN

From the Department of Physiology, University of British Columbia, Vancouver, Canada

(*Received* 6 *March* 1961)

In 1937 Schweitzer & Wright described an inhibitory effect, following intravenous injections of adrenaline, upon the knee-jerk reflex in cats anaesthetized with chloralose. They found that the depression was not related to the blood-pressure changes produced, and that there was often an increase in the strength of the reflex muscle contraction preceding the depression. Later experiments by Bernhard & Skoglund (1953) and by Sigg, Ochs & Gerard (1955) indicated that either enhancement or inhibition of the reflex could be observed after systemic administrations of adrenaline, the effect depending in part upon the extent to which higher levels of the central nervous system were left intact to influence the spinal neurones, and also upon the depth of anaesthesia. Sigg *et al.* showed that inhibition was the only observed reaction to intravenous adrenaline in the deeply anaesthetized spinal animal. The effects obtained were interpreted by Schweitzer & Wright as indicating a direct action of adrenaline upon the spinal neurones, and this view has been accepted by later authors. On the other hand, in their studies of the effects of certain drugs on single motor neurones of the spinal cord Curtis, Eccles & Eccles (1957) failed to find any actions of adrenaline other than those which could be interpreted as due to vascular changes.

Interest in a possible direct effect of the catecholamines upon cord neurones has been raised again as an extension of attempts to identify an active ingredient in extracts of central nervous system (defined as containing Factor I) (Florey, 1954), which cause a reversible inhibition of the knee-jerk reflex following topical application to the exposed cord (Florey & McLennan, 1955) and seem to contain a substance active at inhibitory synapses (McLennan, 1960*b*). Factor I is able also to cause inhibition of impulse generation in the slowly-adapting neurone of the stretch receptor organs of crayfish (Florey, 1954), and in a recent study of a number of known compounds on this preparation McGeer, McGeer & McLennan (1961) showed that the catecholamines were active. Average threshold concentrations required to prevent impulse generation were: for L-

adrenaline, 18 μM/l., for DL-noradrenaline, 1·9 μM/l. and for 3-hydroxytyramine 0·1 μM/l. There was some indication that D-noradrenaline was considerably more active than the L-isomer. Since 3-hydroxytyramine is a normal constituent of the brain (see e.g. Carlsson, 1959) and would therefore be expected to occur in the Factor I extracts, and since it is by far the most active compound so far known to affect the crayfish neurone, these experiments were carried out to investigate its effects upon the knee-jerk reflex as possibly explaining the actions thereon of Factor I. The relationship of the results obtained to inhibition of the reflex by stimulation of the bulbar reticular formation (Magoun & Rhines, 1946) has also been explored.

METHODS

All experiments have been performed on cats weighing 2·8–3·2 kg, anaesthetized with chloralose (65 mg/kg) and urethane (250 mg/kg). Movements of the leg in response to stimulation of the patellar tendon by means of an automatic hammer (Schweitzer & Wright, 1937) were recorded on a kymograph, together with the carotid blood pressure in some experiments. Taps were delivered to the tendon at rates of 6/min or 12/min.

Substances were administered intravenously into the radial vein, or topically to the spinal cord. For the latter, the vertebral column overlying segments L 7–S 2 was opened from the dorsal side, the dura covering the cord removed, and the cord itself raised up on small glass rods to ensure that the applied solutions reached all parts of the surface. All solutions to be applied to the cord were warmed to 35° C, and between tests the cord was covered by a pool of warm sodium chloride solution, 0·9 g/100 ml.

The catecholamines used were all hydrochlorides, obtained commercially. Since there appears to be a contaminant in the 3-hydroxytyramine as supplied (McGeer *et al.* 1961) it was recrystallized from alcohol-ether before use. Solutions were made freshly in 0·9% sodium chloride solution.

Factor I extracts were prepared by the method of Florey & McLennan (1955). In some experiments a more purified material obtained by passage of the crude extract through a cellulose column, and recombination of the two active fractions resulting (McLennan, 1960*a*), was used, with identical results on the reflex activity.

Stimuli to the ipsilateral bulbar reticular formation were delivered with a bipolar concentric needle electrode placed in position after fixing the cat's head in a stereotaxic instrument. Points stimulated were in the area described by Magoun & Rhines (1946). In the majority of experiments the electrode tip lay within the limits of 12–14 mm posterior, 1–2 mm lateral and 7·5–9 mm below the Horsley–Clarke zero co-ordinates. Stimulation at a frequency of 50/sec, 0·1 msec duration and 3–5 V was sufficient to cause a marked inhibition of the reflex. At the end of each experiment the brain was removed and fixed in formalin and the position of the electrode determined after cutting sections of the tissue and staining with cresyl violet.

RESULTS

Intravenous administration

Schweitzer & Wright (1937) reported that the intravenous administration of 100–400 μg of adrenaline led in some cases to complete abolition of the knee-jerk reflex after a latency of less than 4 min, and the recovery from the depression was slow and sometimes incomplete. They noted also

that the inhibition was frequently preceded by a period of enhanced reflex contraction. Sigg *et al.* (1955) essentially confirmed these results, without, however, finding that complete abolition of the reflex was ever obtained; they further stated that noradrenaline gave similar but less pronounced effects.

The findings of Sigg *et al.* have been confirmed in the present series of experiments. The intravenous administration of 100–400 μg of L-adrenaline

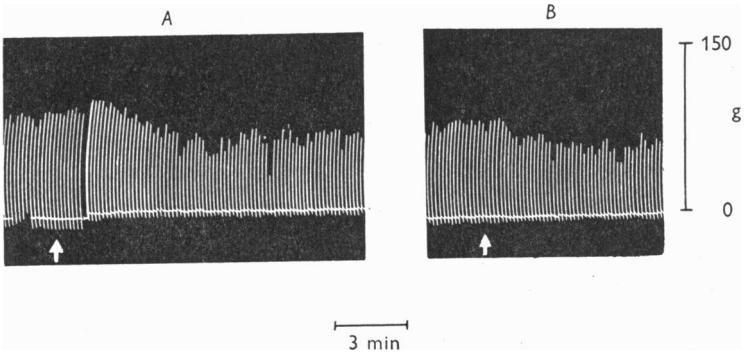

Fig. 1. The effects of the intravenous administration of (*A*) 150 μg L-adrenaline HCl and (*B*) 150 μg DL-noradrenaline HCl on the knee-jerk reflex.

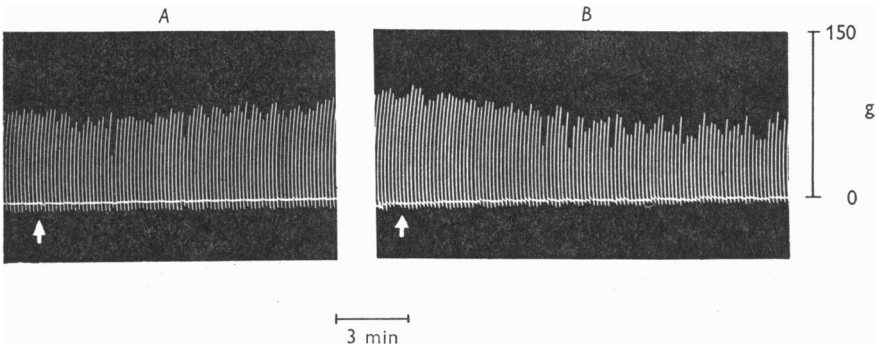

Fig. 2. The effect of the intravenous injection of 400 μg of 3-hydroxytyramine on the knee jerk, (*A*) before and (*B*) 10 min after the administration of β-phenylethylhydrazine hydrogen sulphate 10 mg/kg.

hydrochloride resulted normally in an enhancement of the reflex movement after a delay of 1–2 min, succeeded by depression of the reflex over the next 5–10 min with slow recovery thereafter (Fig. 1*A*). A similar but less marked effect was observed with equivalent amounts of DL-noradrenaline (Fig. 1*B*). Complete abolition of the reflex was never observed.

By contrast, 3-hydroxytyramine in equivalent dose was considerably less active than adrenaline in causing depression of the reflex and often had no

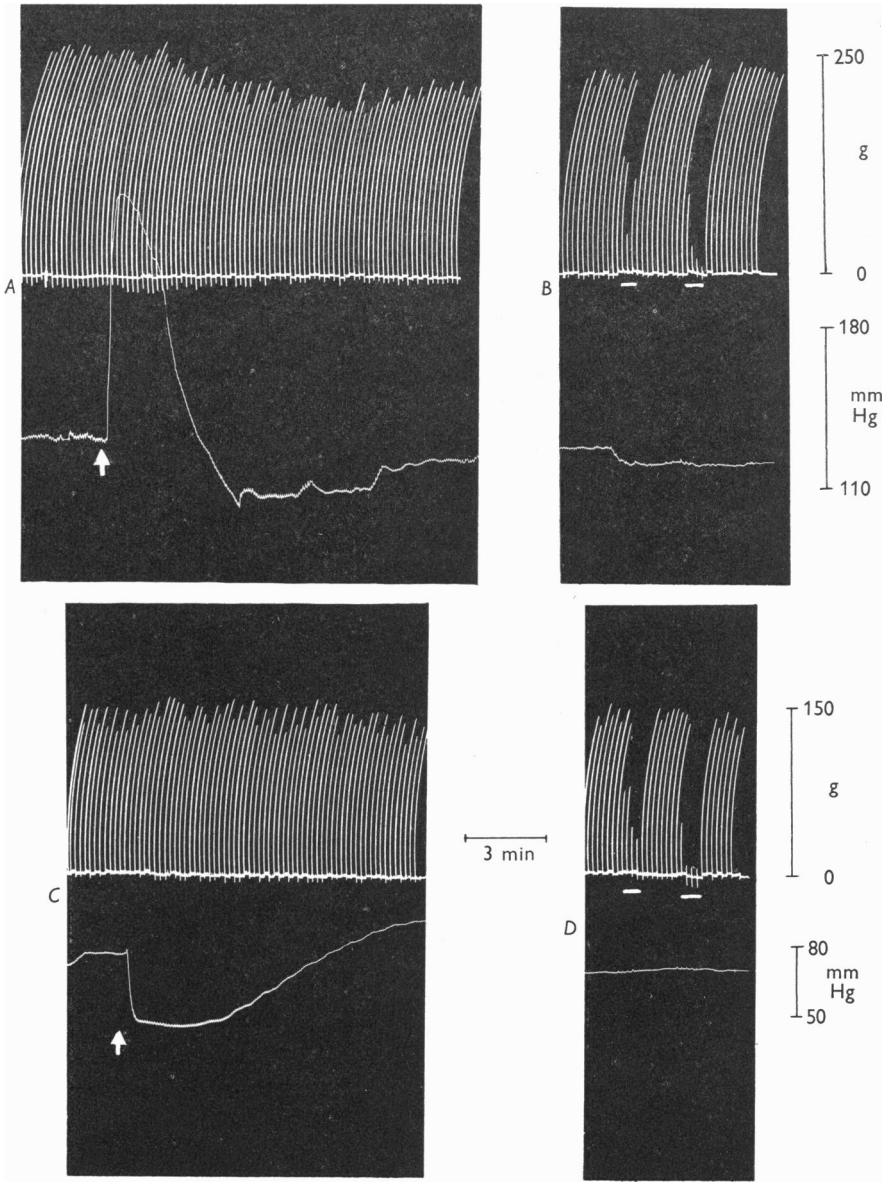

Fig. 3. The effect of Dibenzyline on the knee-jerk reflex and the carotid blood pressure in response to 300 μg adrenaline intravenously and on the inhibition produced by stimulation of the bulbar reticular formation. *A* and *B*, before; *C* and *D* 30 min after Dibenzyline, 15 mg/kg, I.V. Two strengths of reticular formation stimulation ($2\frac{1}{2}$ and 5 V) are shown in *B* and *D*.

detectable effect (Fig. 2*A*). That some activity in this respect was possessed by 3-hydroxytyramine was indicated, however, by the observation that after treatment of the animal with an inhibitor of monoamine

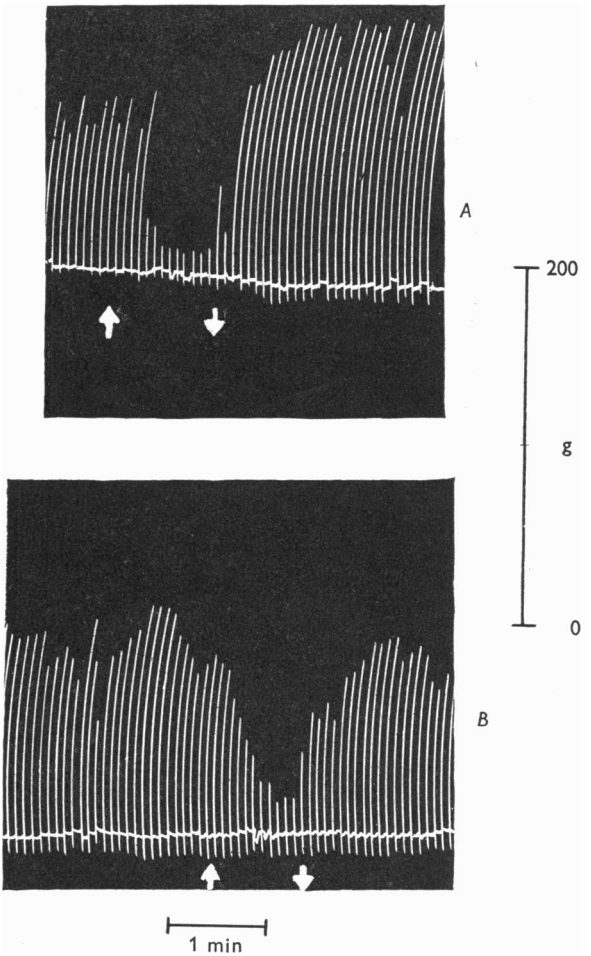

Fig. 4. The effect of topical application of Factor I solution to the exposed spinal cord on the knee-jerk reflex, (*A*) before and (*B*) 90 min after chlorpromazine, 15 mg/kg, I.V. The solution was applied to the cord at the first arrow in each case, and washed off with saline at the second. Note the post-inhibitory potentiation in (*A*).

oxidase (β-phenylethylhydrazine), an inhibition of the reflex appeared (Fig. 2*B*), and the pressor action of the 3-hydroxytyramine was prolonged. The depressant action of adrenaline on the reflex could similarly be potentiated by this agent.

The inhibition produced by adrenaline could be prevented by the administration of Dibenzyline (phenoxybenzamine), chlorpromazine or promazine. This is shown for Dibenzyline in Fig. 3. These drugs block excitatory adrenergic receptors ('alpha' in the terminology of Ahlquist (1948)). Dichloro*iso*proterenol (1-(3,4-dichlorophenyl)-2-*iso*-propylamino-ethanol hydrochloride), which specifically blocks the inhibitory 'beta' receptors (Powell & Slater, 1958) had no effect on the depression of the reflex produced by intravenous adrenaline.

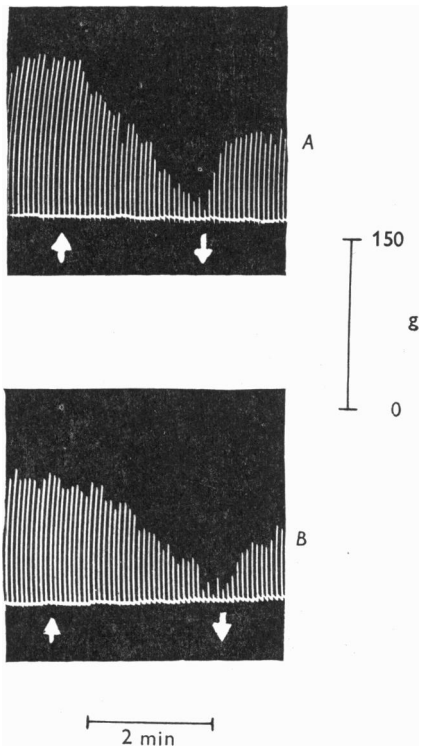

Fig. 5. The effect of topical application of 3-hydroxytyramine 50 g/l. to the cord, (*A*) before and (*B*) 30 min after Dibenzyline 20 mg/kg, I.V. The solution was applied at the first and washed off at the second arrow.

Topical administration

Florey & McLennan (1955) first reported the prompt and reversible inhibition of the knee-jerk reflex following topical application of concentrated solutions of Factor I to the exposed spinal cord. The effect is shown in Fig. 4*A*. A similar inhibition can be observed following the application of a drop of a solution of 3-hydroxytyramine to the cord (Fig. 5*A*). The concentrations of 3-hydroxytyramine which have been used in these

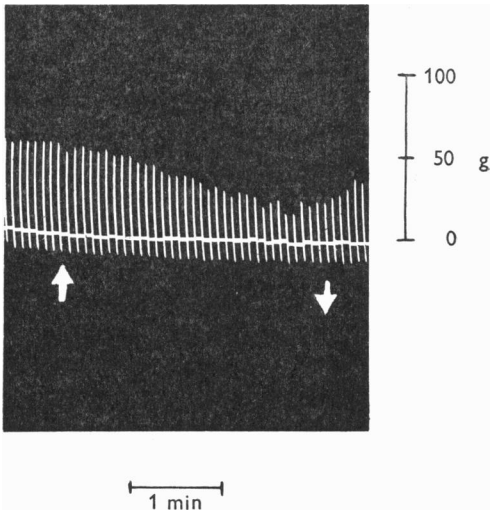

Fig. 6. The largest observed inhibition of the knee-jerk reflex obtained with DL-noradrenaline 100 g/l. applied to the cord.

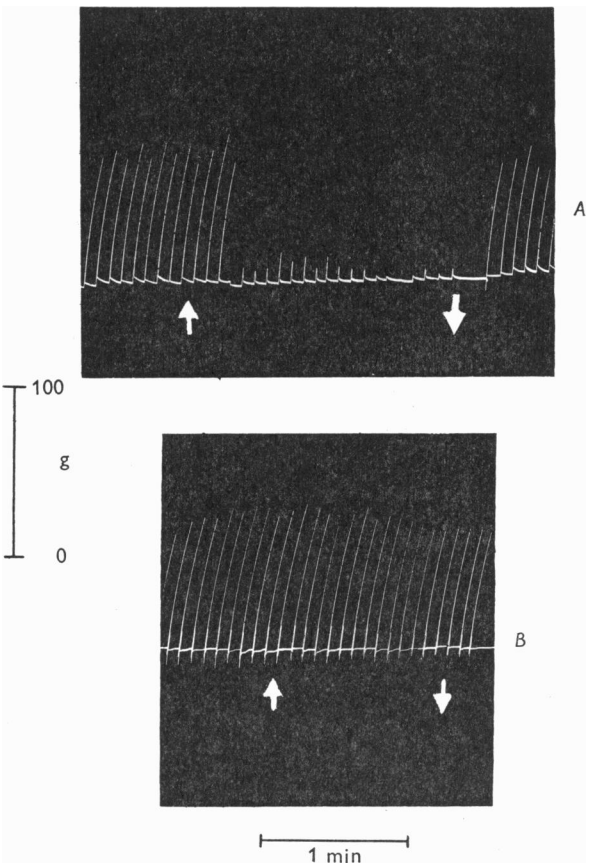

Fig. 7. Blocking of the inhibitory effect of 3-hydroxytyramine (50 g/l.) applied to the cord, by strychnine. (*A*) before and (*B*) after strychnine sulphate 0·1 mg/kg I.V.

experiments are high (25–50 g/l.), but inhibition can be obtained with less concentrated solutions provided that sufficient time of contact with the cord is allowed.

Adrenaline and noradrenaline are much less active than 3-hydroxytyramine when applied topically to the cord. Figure 6 shows the largest effect observed with 100 g/l. of DL-noradrenaline; 3-hydroxytyramine on the same preparation produced complete inhibition in about 30 sec with a solution of 25 g/l. Adrenaline was even less effective than noradrenaline.

The inhibitory effects of topically applied Factor I and 3-hydroxytyramine, unlike those of intravenous adrenaline, are not antagonized by the promazines or by Dibenzyline (Figs. 4 and 5). The effects of both are, however, prevented by strychnine in small doses (Fig. 7, and Florey & McLennan, 1955) and are similarly affected by the administration of dichloro*iso*proterenol, which blocks inhibitory 'beta' receptors, but has little effect on 'alpha' receptors (Powell & Slater, 1958) (Fig. 8). The effects obtained after topical and intravenous administration of the catecholamines are therefore different both in the relative strength of action of the three compounds tested and in the blocking of their effects by various pharmacological agents.

Stimulation of the reticular formation

Magoun & Rhines (1946) reported that stimulation of the ventromedial part of the reticular formation in the lower brain stem caused inhibition of spinal reflexes, a finding which has been amply confirmed. Recently, Cranmer, Brann & Bach (1959) reported that this reticular inhibition could be prevented by Dibenzyline infused intravenously at a rate of 0·025 mg/min, and restored by adrenaline infused or injected directly into the substance of the brain.

Evidence for a blocking action of a single large dose (20 mg/kg) of Dibenzyline (or of chlorpromazine) on the inhibitory effect of reticular formation stimulation could not be obtained in these experiments (Fig. 3). By contrast, the effect was antagonized by the administration of 7 mg/kg of dichloro*iso*proterenol (Fig. 9). The action of the adrenergic blocking agents on the inhibition due to reticular formation stimulation thus parallelled that obtained in the experiments in which 3-hydroxytyramine was applied to the cord, in that blocking agents for 'alpha' receptors were ineffective while that active at 'beta' receptors prevented the inhibitory effects. Strychnine in low doses was also able to antagonize partially the effect of reticular formation stimulation (Fig. 10): higher doses of strychnine could not be satisfactorily tested, since in such experiments the animals invariably jerked convulsively when the reticular formation was stimulated.

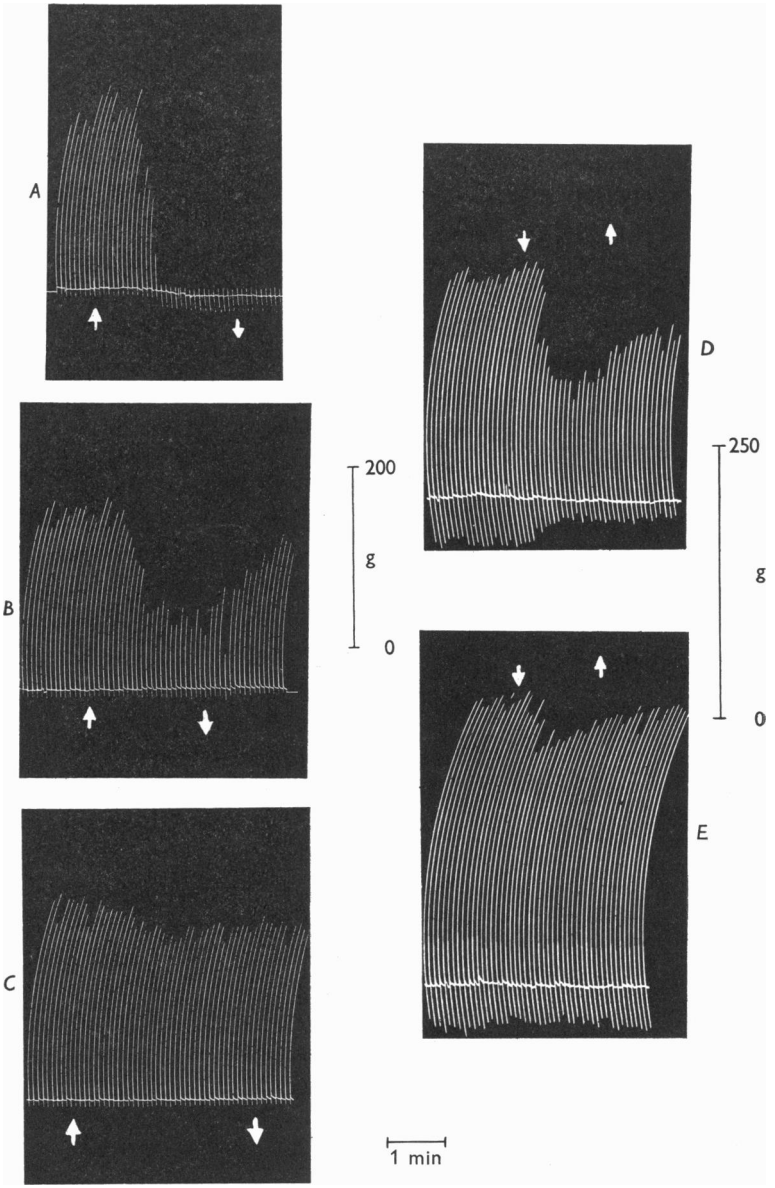

Fig. 8. The blocking action of dichloro*iso*proterenol on the inhibition of the knee-jerk reflex produced by topical application of Factor I (*A*, *B* and *C*) and, from a different experiment, of 3-hydroxytyramine, 50 g/l. (*D* and *E*). *A* and *D* before, *B* 1½ hr, *C* 3 hr, *E* 1¾ hr after dichloro*iso*proterenol, 10 mg/kg, I.V.

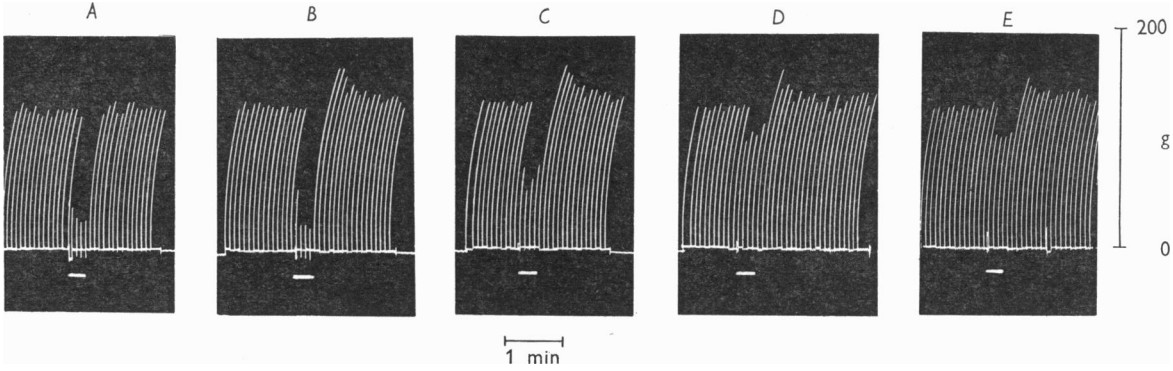

Fig. 9. Inhibition of knee-jerk reflex by stimulation (3½ V) of the reticular formation, (*A*) before, (*B*) 15 min, (*C*) 1 hr, (*D*) 1½ hr and *E* 3½ hr after dichloro*iso*proterenol, 7 mg/kg, I.V.

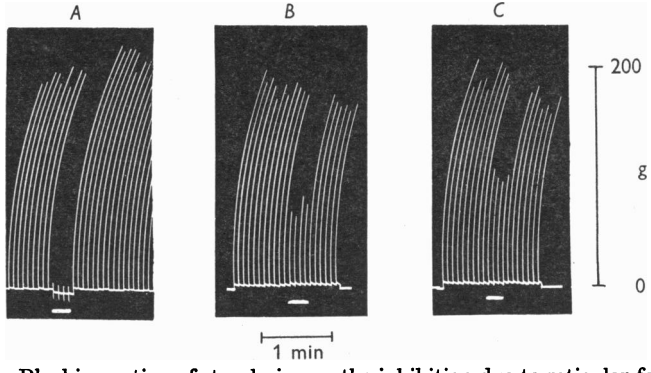

Fig. 10. Blocking action of strychnine on the inhibition due to reticular formation stimulation (5 V). (*A*) before, (*B*) after strychnine sulphate, I.V., 0·025 mg/kg and (*C*) after 0·05 mg/kg.

Treatment of an animal with reserpine depletes its brain of the catecholamines, including 3-hydroxytyramine (Carlsson, Rosengren, Bertler & Nilsson, 1957) and the level of the latter is rapidly restored after the administration of large doses of L-3, 4-dihydroxyphenylalanine (DOPA) (Carlsson, 1959). The experiments described above suggested the possibility that 3-hydroxytyramine was in some way implicated in the inhibition of the knee-jerk reflex brought about by reticular formation stimulation, and therefore that depletion of the endogenous stores of this substance might prevent the occurrence of the inhibition.

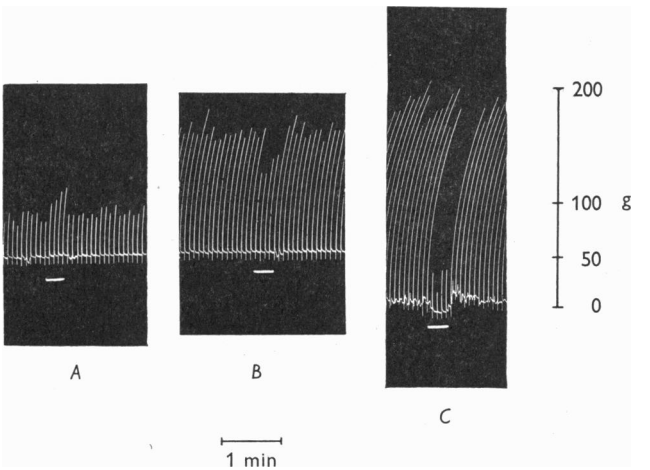

Fig. 11. Stimulation of the reticular formation in an animal treated for 3 days with reserpine. (*A*) control, (*B*) 2 hr after the administration of L-DOPA, 100 mg/kg, I.V. and (*C*) 3½ hr after DOPA. The strength of stimulation was 5 V in all cases. Note the small size of the reflex contractions in the reserpinized animal, and the enhancing effect of the stimulation; and the increased size of the contractions with reappearance of the normal inhibitory response after DOPA.

Cats were prepared by the intraperitoneal administration of reserpine 0·5 mg/kg for 3 days before the experiment, and a stimulating electrode was placed in the reticular formation at a point which in normal animals always gave a good inhibitory response (see Methods). In some cases the normal inhibitory response could not be obtained at all under these conditions (Fig. 11*A*), and instead stimulation usually gave rise to an enhancement of the reflex response. In other instances the usual inhibitory response was still produced by stimulation, but a much stronger stimulus than usual was required to elicit the effect. Following the intravenous administration of L-DOPA (100 mg/kg) the inhibitory response to the same stimulus gradually reappeared (Fig. 11, *B* and *C*). In those cases in which reserpine had caused the threshold for stimulation to be raised, it was reduced to the normal level following the administration of DOPA.

It was noted that in some experiments (as in that of Fig. 11) the size of the reflex contraction obtainable in animals treated with reserpine was small, and that this was greatly improved after the L-DOPA treatment. This observation suggests that 3-hydroxytyramine may, in addition to its inhibitory effects, have an excitatory function at some other site in the central nervous system; or since DOPA and 3-hydroxytyramine are precursors of noradrenaline and adrenaline, that the restoration of the stores of these substances is in some manner responsible for the increased response.

The finding that reticular formation stimulation in the animal treated with reserpine, at a site which normally would have resulted in inhibition of the reflex, can instead result in an enhancement would seem to indicate that this mechanism is not dependent on stores of catecholamines in the brain. Magoun & Rhines (1946) showed that stimulation of some points in the reticular formation resulted in increased reflex responses: the present results might be interpreted as indicating a generalized action in this direction which is normally masked by inhibition, but which appears when the inhibition is prevented by reserpine.

TABLE 1. The inhibitory effects of catecholamines and of Factor I on the knee-jerk reflex; and the actions of adrenergic blocking agents

	Inhibitory actions of				Inhibitory actions	
	3-hydroxy-tyramine	Nor-adrenaline	Adrenaline	Factor I	Antagonized by	Not antagonized by
Intravenous administration	0 or +	+ or ++	++	0	Dibenzyline, chlorpromazine	Dichloro-*iso*proterenol
Topical application	+++	+	0	+++	Dichloro-*iso*proterenol, strychnine	Dibenzyline, chlorpromazine
Reticular-formation stimulation	—	—	—	—	Dichloro-*iso*proterenol, strychnine, reserpine pre-treatment	Dibenzyline, chlorpromazine

0, no action; + weak action; ++ moderate action; +++ strong action.

DISCUSSION

A summary of the results described above is set forth in Table 1. It is apparent from the table that the actions of topically applied 3-hydroxytyramine and Factor I are similar, and that their inhibitory effect on the knee-jerk reflex is prevented by the same drugs as those which antagonize the inhibitory effect of stimulation of the bulbar reticular formation. A reasonable conclusion would seem to be that a catecholamine active at the 'beta' type of adrenergic receptors is in some way connected with the physiological inhibitory process. This statement is borne out by the

following points: (1) the inhibitory effect of stimulation of the bulbar reticular formation was prevented by treatment of the animal with reserpine, which depletes its stores of catecholamines; and was restored by the administration of DOPA, which replenishes the stores; (2) the action was also prevented by treatment of the animal with dichloro*iso*proterenol which specifically blocks the 'beta' receptors. The blocking of the effects of reticular formation stimulation by Dibenzyline, which was reported by Cranmer *et al.* (1959), was not obtained with the somewhat different conditions used in this study.

The results further suggest that the catecholamine involved is likely to be 3-hydroxytyramine rather than adrenaline or noradrenaline. This conclusion is reached since topical application of 3-hydroxytyramine to the exposed spinal cord caused a complete and reversible inhibition of the reflex, whereas noradrenaline had only a much weaker action in this respect and adrenaline little or none. This effect of 3-hydroxytyramine was prevented by administration of dichloro*iso*proterenol.

It seems likely that the inhibitory effect of intravenously administered adrenaline upon the reflex, originally reported by Schweitzer & Wright (1937), cannot be another aspect of the same mechanism as that described above. With topical application the order of potency (3-hydroxytyramine $\gg$ noradrenaline $>$ adrenaline) was the reverse of that seen with intravenous injection; however this might possibly be due to differences in penetration through the blood–brain barrier or to differing rates of destruction. The actions after intravenous administration, moreover, were abolished by Dibenzyline and by chlorpromazine, while these drugs were without effect on both the 'topical' inhibition and that due to reticular formation stimulation. Schweitzer & Wright showed that the effect was not related directly to vascular changes; but the interpretation of these results and of those obtained by Bernhard & Skoglund (1953) following intra-arterial administration to the cord is difficult.

The inhibitory action of extracts of mammalian brain (Factor I extracts) upon the knee-jerk reflex was reported by Florey & McLennan (1955). These extracts have properties in this regard very like those of 3-hydroxytyramine solutions, and the possibility implied by the findings of McGeer *et al.* (1961) on the crayfish stretch receptor neurone, that the extracts might owe part of their activity to 3-hydroxytyramine, is strengthened. The action of the pharmacological agents used here, i.e. the blocking of Factor I action by dichloro*iso*proterenol and by strychnine but not by Dibenzyline or chlorpromazine, parallelled that found for 3-hydroxytyramine and for reticular formation stimulation, and bears out the suggestion that Factor I extracts may owe their activity on the cord to 3-hydroxytyramine. It is noteworthy that some areas of the brain showing

high Factor I activity as assayed with the crayfish neurone, e.g. the caudate nucleus (Florey & Florey, 1958), also have high contents of 3-hydroxytyramine (Carlsson, 1959).

From the present experiments the suggestion that 3-hydroxytyramine is released from the endings of the reticulospinal tract neurones at their inhibitory synapses upon the motor neurones may be postulated. It should be noted that the inhibitory effects both of reticular formation stimulation and of topically applied 3-hydroxytyramine can be prevented by strychnine, which is known to inactivate inhibitory synapses at spinal motor neurones (Curtis, 1959).

Dr D. R. Curtis has kindly investigated the effects of 3-hydroxytyramine iontophoretically applied from a micro-electrode to single neurones of the spinal cord. The results which he has obtained were uniformly negative, and render the above suggestion of a transmitter action for 3-hydroxytyramine less attractive. The action of strychnine in blocking the effects of applied 3-hydroxytyramine, however, is difficult to explain in other terms in the light of present views on its mode of action.

SUMMARY

1. The inhibitory effects of adrenaline, noradrenaline and 3-hydroxytyramine on the knee-jerk reflex have been studied by intravenous administration or topical application to the exposed spinal cord, and compared with those produced by stimulation of the bulbar reticular formation.

2. Intravenous adrenaline caused a prolonged depression of the reflex, in confirmation of reports by other workers; noradrenaline was less potent in this respect and 3-hydroxytyramine almost inactive. The effects could be potentiated by administration of an inhibitor of monoamine oxidase, and that caused by adrenaline prevented by Dibenzyline or by chlorpromazine.

3. Topical application of 3-hydroxytyramine to the cord caused a complete and reversible inhibition of the reflex; noradrenaline was less active and adrenaline inactive. The effect of 3-hydroxytyramine was not blocked by Dibenzyline or chlorpromazine, but was prevented by dichloro-*iso*proterenol and by strychnine.

4. Stimulation of the bulbar reticular formation produced an inhibition of the reflex which was also unaffected by Dibenzyline or chlorpromazine but which was blocked by dichloro*iso*proterenol and by strychnine. Depletion of the catecholamines of the brain by pre-treatment of the animal with reserpine also prevented the effect of stimulation, and the inhibition could be restored by the administration of L-DOPA.

5. The inhibitory action of Factor I-containing extracts of mammalian brain on the reflex is similarly prevented by dichloro*iso*proterenol and strychnine, but is unaffected by Dibenzyline or chlorpromazine. It is suggested that Factor I extracts may owe their activity on the knee jerk to 3-hydroxytyramine.

6. The possibility is considered that the transmitter substance active at the inhibitory synapses of the reticulospinal tract upon motor neurones is 3-hydroxytyramine.

I am indebted to Dr George Ling and Dr P. L. McGeer for much helpful discussion and for generous supplies of the drugs used. Mr R. Walker rendered invaluable technical assistance. This work was supported by a grant from the National Research Council of Canada.

REFERENCES

AHLQUIST, R. P. (1948). A study of the adrenotropic receptors. *Amer. J. Physiol.* **153**, 586–600.

BERNHARD, C. G. & SKOGLUND, C. R. (1953). Potential changes in spinal cord following intra-arterial administration of adrenaline and noradrenaline as compared with acetylcholine effects. *Acta physiol. scand.* **29**, Suppl. 106, 435–454.

CARLSSON, A. (1959). The occurrence, distribution and physiological role of catecholamines in the nervous system. *Pharmacol. Rev.* **11**, 490–493.

CARLSSON, A., ROSENGREN, E., BERTLER, Å. & NILSSON, J. (1957). Effect of reserpine on the metabolism of catecholamines. In *Psychotropic Drugs*, ed. GARATTINI, S. & GHETTI, V. pp. 363–372. Amsterdam: Elsevier.

CRANMER, J. I., BRANN, A. W. & BACH, L. M. N. (1959). An adrenergic basis for bulbar inhibition. *Amer. J. Physiol.* **197**, 835–838.

CURTIS, D. R. (1959). Pharmacological investigations upon inhibition of spinal motoneurones. *J. Physiol.* **145**, 175–192.

CURTIS, D. R., ECCLES, J. C. & ECCLES, R. M. (1957). Pharmacological studies on spinal reflexes. *J. Physiol.* **136**, 420–434.

FLOREY, E. (1954). An excitatory and an inhibitory factor of mammalian central nervous system, and their action on a single sensory neuron. *Arch. int. Physiol.* **62**, 33–53.

FLOREY, E. & FLOREY, E. (1958). Studies on the distribution of Factor I in mammalian brain. *J. Physiol.* **144**, 220–228.

FLOREY, E. & MCLENNAN, H. (1955). Effects of an inhibitory factor (Factor I) from brain on central synaptic transmission. *J. Physiol.* **130**, 446–455.

MAGOUN, H. W. & RHINES, R. (1946). An inhibitory mechanism in the bulbar reticular formation. *J. Neurophysiol.* **9**, 165–171.

MCGEER, E. G., MCGEER, P. L. & MCLENNAN, H. (1961). The inhibitory action of 3-hydroxytyramine, gamma-aminobutyric acid (GABA) and some other compounds towards the crayfish stretch receptor neurone. *J. Neurochem.* (in the Press).

MCLENNAN, H. (1960*a*). The fractionation and purification of Factor I. *J. Physiol.* **151**, 31–39.

MCLENNAN, H. (1960*b*). Evidence for the presence of an inhibitory transmitter substance in Factor I extracts. *J. Physiol.* **153**, 55–56*P*.

POWELL, C. E. & SLATER, I. H. (1958). Blocking of inhibitory adrenergic receptors by a dichloro analog of isoproterenol. *J. Pharmacol.* **122**, 480–488.

SCHWEITZER, A. & WRIGHT, S. (1937). The action of adrenaline on the knee jerk. *J. Physiol.* **88**, 476–491.

SIGG, E., OCHS, S. & GERARD, R. W. (1955). Effects of the medullary hormones on the somatic nervous system in the cat. *Amer. J. Physiol.* **183**, 419–426.