amine metabolism in brain (Carlsson & Lindqvist, 1963; Neff & Costa, 1966; Burkard, Gey & Pletscher, 1967). During recent years, different pharmacological and isotopic methods have been elaborated for the study of *in vivo* synthesis and turnover of monoamines.

A study of the influence of some psychotropic drugs on catecholamine synthesis and turnover in the brain *in vivo* is presented. Catecholamine synthesis was studied by measuring the conversion of ^{14}C-tyrosine to ^{14}C-dopamine and ^{14}C-noradrenaline in rat and mouse brain (Sedvall, Weise & Kopin, 1968). Turnover of the amines was estimated from the decline in radioactivity following the pre-labelling of the brain amine stores by ^{14}C-tyrosine administration (Udenfriend & Zaltzman-Nirenberg, 1963). The influence of promethazine, chlorpromazine, haloperidol and desipramine was studied.

Chlorpromazine and haloperidol increased both accumulation and disappearance of ^{14}C-dopamine following administration of ^{14}C-tyrosine. Haloperidol and promethazine slightly increased the disappearance of ^{14}C-noradrenaline, whereas desipramine significantly decreased accumulation of ^{14}C-noradrenaline. The results are taken as evidence that desipramine selectively acts on noradrenaline neurones in the brain, whereas chlorpromazine and haloperidol primarily affect dopamine neurones where synthesis and turnover of the transmitter is increased.

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Excitation of cortical neurones by noradrenaline

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A recent study showed that the predominant effect of noradrenaline, applied iontophoretically to cortical cells, was one of excitation (Roberts & Straughan, 1968). The present experiments confirm these findings and deal with the pharmacology of this effect.

Eight hundred neurones from eighty-four adult cats have been studied; about half of the preparations were *encéphale isolé* (in which all possibly painful sites were treated regularly with local anaesthetics) and the remainder were anaesthetized with either a N_2O-halothane mixture, or a barbiturate.

In animals anaesthetized with N_2O-halothane, noradrenaline excited 61% of the neurones tested, depressed 14%, had a mixed effect on 7%, and had no effect on 18%. In the *encéphale isolé* preparations, noradrenaline excited 35%, depressed 18%, gave mixed responses on 12% and did not affect 35%. In the animals under barbiturate anaesthesia, only 8% of neurones were excited by noradrenaline, whereas 62% were depressed and 30% showed no response. This supports the suggestion of Roberts & Straughan (1968) that the use of barbiturate anaesthesia might be responsible for previous failures to obtain excitations with noradrenaline (Krnjević & Phillis, 1963).

Fifty-two cells have been tested so far with both noradrenaline and isoprenaline. The profiles of activity were similar for the two amines and in no case did a cell respond in opposite directions to the two; isoprenaline had about one third the excitant potency of noradrenaline. The effects of isoprenaline, however, persisted for twice as long as noradrenaline; following a contact time of 75 sec the excitant effects of isoprenaline (100 nA) lasted a further 10 min compared with about 5 min for noradrenaline.

Previously, we showed that dibenamine applied locally from another barrel of the multibarrelled micropipette would, on some occasions, selectively abolish noradrenaline excitations. A further antagonist at α-receptors for adrenaline has now been used. In all the nine cells tested, phentolamine (22 nA) produced a complete block of noradrenaline excitations within 6 min and this effect was reversible. At the height of the block, the response of the cell to other excitatory agonists (for example, acetylcholine or L-glutamate) was unaffected.

Two β-receptor antagonists, propranolol and 2-isopropylamino-1-(*p*-nitrophenyl) ethanol HCl (INPEA) have also been tested against noradrenaline excitations. Propranolol was more difficult to use than INPEA, for it was depressant ("local anaesthetic") in fifteen out of eighteen cells tested, and, because of this, it was often impossible to demonstrate a specific block of a noradrenaline response. INPEA (25 nA) produced a complete and specific block of noradrenaline excitations in seven out of nine cells tested within 2 min.

The block of noradrenaline excitations by α or β receptor blocking agents was similar in each of the three types of preparation used.

These results indicate that neuronal excitation by noradrenaline involves either a population of mixed α and β receptors or a different type of receptor.

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The effects of phenoxybenzamine on metabolism of ^{3}H-noradrenaline released from the isolated nictitating membrane

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When the noradrenaline (NA) stores of isolated nictitating membrane of the cat were labelled with ^{3}H-NA, stimulation of the nerves resulted in an increased outflow of ^{3}H-NA and metabolites, mainly ^{3}H-normetanephrine (NMN) and ^{3}H-4-hydroxy-3-methoxy-mandelic acid (Langer, 1968).

When the nerves were stimulated at 25 shocks/sec only about 35% of the total increase in radioactive products was due to ^{3}H-NA. The remaining 65% were accounted for by ^{3}H-NA metabolites.

When the frequency of stimulation was reduced to 4 shocks/sec, the ^{3}H-NA metabolites amounted to as much as 80% and ^{3}H-NA to only 20% of the total increase in outflow of labelled compounds.