Values were obtained as follows: ADTN, 140 nM; dopamine, 168 nM; benztropine, 180 nM; nomifensine, 200 nM and noradrenaline, 920 nM.

These results indicate that [^{3}H]-ADTN is accumulated primarily into dopaminergic terminals by active, high-affinity transport processes.

A.D. is in receipt of an M.R.C. studentship for training in research methods.

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Further observations of the effects of noradrenaline and dopamine on cortical neurones

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Single cortical neurones can respond both with excitation and depression to microelectrophoretically applied noradrenaline and dopamine (Bevan, Bradshaw & Szabadi, 1975). In a previous study (Bevan *et al.*, 1977) we found that these cells invariably respond in the same direction to the two catecholamines, being either excited by both drugs or depressed by both drugs. We also observed that excitatory responses to both catecholamines can be antagonized by phenoxybenzamine and haloperidol, phenoxybenzamine showing a more pronounced effect on responses to noradrenaline, and haloperidol a more pronounced effect on responses to dopamine. We report here some further studies comparing the two catecholamines.

Single neurones were studied in the prefrontal and parietal cortices of halothane anaesthetized rats. Drugs were applied by microelectrophoresis.

The effects of noradrenaline and dopamine were compared on 136 cells. Every cell responded in the same direction to the two catecholamines (103 excited, and 33 depressed by both drugs). On 68% of the cells excited and on 82% of the cells depressed, noradrenaline had a greater apparent potency than dopamine. The mean equipotent current ratio was 2.8 (excitatory responses) and 3.2 (depressant responses). We compared the transport numbers of noradrenaline and dopamine using four micropipettes: the mean transport number of noradrenaline was 0.330, and that of dopamine 0.376. Within each micropipette dopamine had a higher transport number than noradrenaline (t test: $P<0.001$, $P<0.02$, $P<0.02$, $0.1>P>0.05$). Thus the greater apparent potency of noradrenaline than dopamine in our experiments probably reflects a genuine biological potency difference rather than a difference between the mobilities of the two drug molecules.

In neither the prefrontal nor the parietal region was there any significant correlation between the relative potencies of noradrenaline and dopamine and the depth in the cortex at which a neurone was encountered ($r<0.1$, $P>0.2$ in both regions). Our results therefore fail to confirm the report of Bunney & Aghajanian (1976) that neurones in the upper layers of the prefrontal cortex are more sensitive to noradrenaline while cells in the lower layers are more sensitive to dopamine.

We also examined the effects of α- and β-flupenthixol on excitatory responses to the catecholamines, using acetylcholine as a control agonist. On every cell tested ($n=8$), α-flupenthixol (5–10 nA) antagonized responses to dopamine without affecting responses to acetylcholine. On 2 cells responses to both catecholamines were equally antagonized; on 6 cells responses to noradrenaline were affected less than were responses to dopamine. In contrast, β-flupenthixol (10–50 nA) had no specific effect on 9 of the 14 cells tested, although on 3 of the remaining 5 cells responses to dopamine were affected more than were responses to noradrenaline. These findings agree with previous observations of a greater effectiveness of α-flupenthixol than β-flupenthixol as a dopamine antagonist (see Iversen, 1975).

This work was supported by the North Western Regional Health Authority and the Mental Health Foundation.

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Effect of etorphine on brain stem neurones in the rat: a microiontophoretic study

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Morphine and levorphanol, applied microiontophoretically to brain stem neurones produce a stereospecific depression of spontaneous firing and a non-stereospecific excitation (Bradley & Bramwell, 1975, 1977). In this study the effects of the potent narcotic etorphine were compared with those of morphine and D-ala-leucine enkephalin, either on the same neurones or on different neurones.

Male albino rats were prepared under urethane anaesthesia as described previously, and single neurones were recorded from the brain stem reticular formation. Drug solutions used included 25 mM etorphine hydrochloride, pH 5.0; 5 mM 2D-ala,5D-leucine enkephalin (B.W. 180-C), pH 4.9: 25 mM morphine hydrochloride, pH 4.8; 25 mM naloxone hydrochloride, pH 4.6; 25 mM dextrophan tartrate, pH 4.0.

Etorphine, applied with a current of 25–50 nA for 1–4 min, reversibly depressed 76/94 spontaneously firing neurones and excited none. Depression developed slowly (latency 33 ± 3 s, mean $\pm$ s.e. mean, $n = 55$), increasing with time of application, until either a plateau response was achieved or the neurone stopped firing altogether. Spontaneous recovery took 14 ± 1 min ($n = 20$). In the main, however, recovery was induced with naloxone, which invariably reversed and on 20/25 occasions powerfully antagonized etorphine depressions. Naloxone-antagonizable depressions were never produced by dextrorphan (25 nA).

Comparisons of the effects of etorphine and morphine were made on 22 occasions. Of the 18 neurones depressed by atorphine, 5 were excited by morphine, 1 responded biphasically and only 2 neurones were depressed. In addition, morphine excited 3/4 neurones not responding to etorphine.

B.W. 180-C, applied with a current of 0–25 nA for 1/2 to 3 min reversibly depressed 37/44 and excited none. These depressions were antagonized by naloxone on 5/7 occasions. Though dextrorphan was without effect on these neurones, etorphine depressed 8/8 neurones also depressed by B.W. 180-C. In addition, morphine depressed 7 neurones, excited 2 and produced a single biphasic response among 16 neurones also depressed by B.W. 180-C.

Though not observed with etorphine, tachyphylaxis to B.W. 180-C depressions was seen on 5 occasions, making it difficult to conduct antagonism studies.

This tachyphylaxis to B.W. 180-C but not to etorphine depressions raises the possibility that these two classes of opiate might interact with different receptors. Furthermore, the complete lack of excitation with the potent narcotic agonist, etorphine, provides further proof that naloxone-reversible depression represents the pharmacologically significant action of opiates on brain stem neurones.

We are very grateful to Burroughs Wellcome for supplying B.W. 180-C, Endo Laboratories for supplying naloxone and Reckitt and Colman for supplying etorphine.

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