tion of 1 μM to 5 mM. Analysis of the kinetic data obtained provided evidence that DABA entry is mediated by both high and low affinity carriers. Further evidence that DABA entry occurs by more than one transport process was obtained from the Inui constant ratio test (Inui & Christensen, 1966). When cortical slices were incubated in the presence of equimolar [^{3}H]-DABA and [^{14}C]-GABA the ratio of entry of the two radionuclides was found to depend upon the loading concentration. DABA entry was progressively favoured in comparison to GABA entry as the loading concentrations of both amino acids were raised.

The specificity of the uptake of (−)-DABA (1 μM and 1 mM) was examined. GABA and DABA were relatively potent inhibitors of DABA (1 μM) uptake, whereas an equal concentration of histidine did not produce significant inhibition. In contrast, DABA and histidine were markedly more potent as inhibitors of DABA (1 mM) uptake than was GABA.

It is concluded from these experiments that (−)-DABA is transported into cortical slices by a carrier which has high affinities for both DABA and GABA and by a second lower affinity carrier which prefers DABA as a substrate to GABA. On the basis of a comparison of the effects of inhibitors on [^{3}H]-DABA and [^{3}H]-GABA uptake it is estimated that approximately 26% of DABA uptake at 1 μM does not occur by the high affinity carrier whereas at 1 mM DABA this proportion rises to more than 60%.

A.J.K. is an MRC postdoctoral fellow.

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Uptake of 2-amino-6,7-dihydroxy-1,2,3,4- tetrahydronaphthalene (ADTN) into rat brain synaptosomes

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The 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (ADTN) molecule contains the dopamine skeleton held in a rigid cyclic conformation. It possesses potent dopamine-like activity and has been found to stimulate locomotor activity (Elkhawad & Woodruff, 1975); to be equipotent with dopamine in its ability to activate dopamine-sensitive adenylate cyclase (Miller, Horn & Iversen, 1974) and to inhibit the firing of cells in the rat nucleus accumbens (Woodruff, McCarthy & Walker, 1976). Recently, we have reported the binding of [^{3}H]-ADTN to receptors on rat brain synaptic membranes (Roberts, Woodruff & Poat, 1977) and in this study we have investigated the possible uptake of ADTN into dopaminergic neurons.

Crude synaptosomes (P_2) were prepared from rat striatum and incubated in Krebs-bicarbonate medium at 37°C containing [^{3}H]-ADTN (0.3 μM). Uptake was linear for at least 4 min and was energy-dependent, as evidenced by the inhibitory effects of lowered temperature and added metabolic inhibitors.

The uptake was mediated by two distinct systems ($K_m = 0.3$ μM; $V_{max} = 0.3$ nmol/mg protein/4 min and, $K_m = 3.1$ μM; $V_{max} = 1.0$ nmol/mg protein/4 min, respectively). Similar systems (K_m's 0.3 and 7.5 μM) were found in the cerebellum, a region devoid of dopaminergic terminals. However, the capacity of these systems were substantially less than in the striatum (V_{max} of 0.028 and 0.125 nmol/mg protein/4 min respectively).

Subcellular distribution studies of striatum demonstrated that of the accumulated [^{3}H]-ADTN, 62.3% was localized in the synaptosomal and, 28.6% in the mitochondrial fractions. TLC of alcoholic tissue extracts indicated that following a 20 min incubation, at least 50% of the radioactivity was attributable to unmetabolized [^{3}H]-ADTN.

To investigate the specificity of the ADTN uptake system, synaptosomes were incubated with [^{3}H]-ADTN (0.3 μM) in the presence of a range of concentrations of drugs known to interact with dopaminergic mechanisms and, IC_{50} values determined.

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.

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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).

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