200% of control. The potentiating action of viloxazine on depressant responses can be summarized as follows: noradrenaline, unlesioned sides, 2 cells (average potentiation 169%); lesioned sides, 4 cells (209%); 5-HT, unlesioned sides, 2 cells (203%); lesioned sides, 7 cells (182%).

Viloxazine is not a tricyclic antidepressant but has been shown to act similarly to tricyclics in potentiating cortical cell responses to monoamines in unlesioned animals (Jones & Roberts, 1977b). There is evidence to suggest that viloxazine is an inhibitor of NA uptake into brain tissue. (Lippmann & Pugsley, 1976). It would therefore seem likely that potentiation of responses is due to uptake blockade. However, the potentiating effects of viloxazine appear to be unimpaired following lesions which should have caused degeneration of presynaptic terminals. The potentiation therefore may be dissociated from the blockade of reuptake. Bevan, Bradshaw & Szabadi (1975a,b) have reported other evidence for a similar conclusion with regard to tricyclics.

Viloxazine is much less effective in blocking the reuptake of 5-HT. Nevertheless it strongly potentiates responses to 5-HT in both lesioned and unlesioned hemispheres. This further suggests a dissociation between the potentiation of monoamine responses and the blockade of reuptake.

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Effects of mazindol on the *in vitro* uptake of monoamines by the rat brain

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Previous studies have revealed that the anorectic drug mazindol is an extremely potent inhibitor (being 4–5 times more potent than desipramine) of rat brain noradrenaline (NA) uptake *in vivo* as assessed by the effect of drug pretreatment on the ability of intracerebroventricularly injected 6-hydroxydopamine to lower brain NA levels (Sugrue, Shaw & Charlton, 1977). Using the same method mazindol, unlike tricyclic antidepressants, also blocked dopamine (DA) uptake. Pretreatment with mazindol had essentially no effect on the ability of *p*-chloroamphetamine to lower the concentration of 5-hydroxytryptamine (5-HT) in the rat brain. The interpretation of this finding is that mazindol is devoid of effect on 5-HT uptake *in vivo* (Sugrue *et al.*, 1977). The relative lack of effect of mazindol observed on 5-HT uptake *in vivo* contrasts with *in vitro* findings. For example, mazindol has been observed to block 5-HT uptake by rat striatal synaptosomes (Koe, 1976, Kruk & Zarrindast, 1976). The objective of this study was to investigate the effects of mazindol on the uptake of NA, DA and 5-HT by synaptosome rich homogenates obtained from selected regions of rat brain. Two experimental approaches were used. In the first, drugs were directly added to the incubation medium at the start of the preincubation period (*in vitro* experiments). In the second, rats were injected i.p. with the drug under study 1 h prior to death and synaptosomal [^{3}H]-monoamine uptake subsequently determined (*ex vivo* experiments).

Male Wistar rats weighing 180–220 g were used. The uptake of [^{3}H]-DA into synaptosome rich homogenates of corpus striatum and the uptake of [^{3}H]-NA and [^{3}H]-5-HT into synaptosome rich

homogenates of hypothalamus were measured according to Horn & Snyder (1972).

Mazindol rivalled desipramine and (+)-amphetamine in blocking the *in vitro* uptake of [^{3}H]-NA and [^{3}H]-DA by hypothalamic and striatal synaptosomes respectively. Of the compounds studied for inhibition of [^{3}H]-5-HT uptake mazindol, desipramine and fenfluramine were of comparable potency and all three compounds were less potent than either chlorimipramine or imipramine.

Following 1 h pretreatment mazindol was approximately 2.5 times more potent than desipramine in blocking hypothalamic synaptosomal [^{3}H]-NA uptake. Mazindol, by contrast with tricyclic antidepressants, also inhibited striatal [^{3}H]-DA uptake. At 1 h after injection of desipramine, fenfluramine and chlorimipramine (each 20 mg/kg i.p.), [^{3}H]-5-HT uptake by hypothalamic synaptosomes was blocked 14.6 ± 2.5 ($P<0.05$), 36.9 ± 2.1 ($P<0.001$) and 50.9 ± 1.0% ($P<0.001$) respectively. By contrast, [^{3}H]-5-HT uptake was not significantly inhibited (4.6 ± 2.3%) following 1 h pretreatment with mazindol (30 mg/kg, i.p.).

Results from *ex vivo* experiments agree with data from *in vivo* studies. For example, mazindol is not only more potent than desipramine in blocking NA uptake but is also essentially devoid of effect on 5-HT uptake. In contrast to the *ex vivo* and *in vivo* findings mazindol blocks 5-HT uptake *in vitro* and has a potency comparable to that of desipramine and fenfluramine, drugs which significantly inhibit the *ex vivo* uptake of the monoamine. Why mazindol is active in blocking 5-HT uptake *in vitro* but not *ex vivo* and *in vivo* is not readily apparent. Furthermore, these findings suggest that it may be invalid to extrapolate an *in vitro* inhibition of monoamine uptake to the *in vivo* situation.

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Effect of acute α-methyldopa administration on catecholamine levels in anterior hypothalamic-preoptic and medullary nuclei in rat brain

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α-Methyldopa (α-MDOPA) is now considered to produce a major component of its hypotensive effect via the central actions of its metabolite, α-methylnoradrenaline (Henning, 1975). Injection of α-methylnoradrenaline into specific areas within the anterior hypothalamic-preoptic (AH/PO) region and into the nucleus (n.) tractus solitarius in the medulla oblongata produces a fall in blood pressure in anaesthetized rats (Struyker-Boudier, Smeets, Brouwer & Van Rossum, 1975; De Jong & Nijkamp, 1976). These authors have suggested that these areas may be directly involved in producing the hypotensive effect of α-MDOPA. However, no studies have yet looked at levels of the metabolites of α-MDOPA in these areas after α-MDOPA injection. We have therefore, examined the effects of acute administration of α-MDOPA on catecholamine levels in several AH/PO nuclei and in the n. tractus solitarius and n. tractus spinalis nervi trigemini in the medulla oblongata.

Nuclei were dissected from fresh 400 μm thick coronal sections of brain tissue from adult Sprague-Dawley rats. Nuclei from three animals were pooled and catecholamine levels were estimated by modifying the radiochemical-enzymatic assay procedure of Van Der Gugten, Palkovits, Wijnen & Versteeg (1976). After acute administration of α-MDOPA (200 mg/kg s.c.) levels of both noradrenaline and dopamine declined in all nuclei. Noradrenaline levels were lower 12 h after α-MDOPA than 4 h and ranged from 16 ± 6.7% (mean ± s.e. mean, $n = 5$) of control in the n. interstitialis striae terminalis (100 ± 6.7%, $P < 0.001$) to 23 ± 5.1% of control in the n. preopticus medialis (100 ± 12.7%, $P < 0.001$). At 12 h no noradrenaline was detected in the medullary nuclei. Endogenous dopamine levels were undetectable in the medullary nuclei. At 4 h after α-MDOPA dopamine could not be detected in the n. anterior (hypothalami), n. lateralis (hypothalami) and n. preopticus medialis while dopamine levels had been reduced to 19 ± 8.9% of control in the n. interstitialis striae terminalis (100 ± 29.3%, $P < 0.05$) and 13 ± 6.9% in the n. preopticus lateralis (100 ± 32.1%, $P < 0.05$). Dopamine levels were still depressed at 12 hours. α-Methyldopamine