administered clonidine (300 μg/kg) on the other hand was significantly antagonized by phentolamine (5 μg/animal, ICV).

The β-adrenergic antagonist propranolol possesses no antinociceptive activity when peripherally administered (Cicero, Meyer & Smithloff, 1974). However, when given alone, propranolol (10 μg/animal, ICV) exhibited some antinociceptive effect but it did not potentiate the activity of concurrent subcutaneous doses of morphine (2.5 mg/kg), pentazocine (15 mg/kg) or clonidine (300 μg/kg, s.c.).

Cicero *et al.* (1974) have shown previously that peripherally-administered α-adrenergic antagonists enhance the antinociceptive effects of morphine in mice. The present study shows this is also true when these agents are restricted to the central nervous system by virtue of their ICV route of injection; also, that the antinociceptive activity of a partial agonist is also enhanced, whilst that of clonidine is attenuated. Whilst the enhancement of the action of narcotic agonists and partial agonists by α-adrenergic antagonists is entirely consistent with the previously demonstrated effects of ICV NA, the significance of the antinociceptive effect of ICV propranolol requires further study.

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The uptake of mescaline by rat brain synaptosomes

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It has previously been reported that single cortical neurones can respond with excitation or depression to microelectrophoretically applied mescaline (Bevan, Bradshaw, Roberts & Szabadi, 1974). It has also been reported that these neuronal responses can be potentiated by the tricyclic antidepressant desipramine (Bevan, Bradshaw & Szabadi, 1975). It is of interest to know whether this potentiation could be due to the blockade of the uptake of mescaline into presynaptic terminals. Iversen (1967) has reported that mescaline has a very low affinity for noradrenaline uptake mechanisms in the periphery, but there are no data concerning the uptake of mescaline into brain tissue.

I have therefore examined the uptake of (^{14}C)-mescaline (specific activity 5.2 mCi/mmole, New England Nuclear Corpn) and, for the purposes of comparison, (^{14}C)-(−)-noradrenaline (specific activity 5.0 mCi/mmole, Radiochemical Centre Ltd.) into synaptosomes prepared from rat cerebral cortex according to the method of Thornburg & Moore (1973). After incubation, the mescaline or noradrenaline content of each sample was assessed by liquid scintillation spectrometry, and the protein content determined using the method of Lowry, Rosebrough, Farr & Randall (1951). The uptake of mescaline or noradrenaline was thus expressed as pmoles/mg protein for each sample. All values are expressed as mean ± s.e.

In agreement with earlier reports, for example, Horn, Coyle & Snyder (1971), the accumulation of noradrenaline was found to be a temperature-dependent process (K_m = 0.628 ± 0.033 μM, V_m= 192.3 ± 7.4 pmoles/mg protein). Mescaline was also accumulated by an active uptake process (K_m= 1.24 ± 0.27 μM, V_m= 26.34 ± 8.02 pmoles/mg protein); however, for equivalent concentrations, the uptake of mescaline was much lower than that of noradrenaline. For example, at a concentration of 0.628 μM, the K_m of noradrenaline, the uptake of mescaline was 10% the uptake of noradrenaline.

The effect of desipramine on the uptake of noradrenaline and on the uptake of mescaline was then examined. Desipramine competitively inhibited the uptake of noradrenaline (K_i desipramine = 0.0499 ± 0.0052 μM). However, desipramine, within a concentration range 0.05-5 μM, did not affect the uptake of mescaline.

The effect of mescaline on the uptake of noradrenaline was also examined. Mescaline was found to inhibit the active accumulation of noradrenaline in a non-competititive manner (K_i mescaline = 10.548 ± 0.697 μM).

The data presented here suggest that the active accumulation of mescaline into synaptosomes from the cerebral cortex is not brought about via the noradrenaline uptake mechanism. Furthermore, since the uptake of mescaline was not affected by desipramine, uptake blockade cannot explain the potentiation of neuronal responses to mescaline by desipramine.

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Depleting effects of reserpine on intracellular catecholamines in rat coeliac-mesenteric ganglion

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Since the introduction of formol-induced fluorescence methodology for the histochemical demonstration of biogenic amines these have been studied in sympathetic ganglia not only in adrenergic post-ganglionic neurones but also in small intensely fluorescent (sif) cells (Eranko & Harkonen, 1963) present in these ganglia. Sif cells have been equated (Grillo, Jacobs & Comroe, 1974) with the small granular cells revealed by electron microscopy in sympathetic ganglia (Williams & Palay, 1969). Recently, Lever, Lu, Presley & Santer (1974) have demonstrated chromaffin-positive (CH+) small cells with a similar distribution to sif cells in a variety of sympathetic ganglia employing glutaraldehyde tissue fixation prior to dichromate treatment. Current speculation suggests that small cells in sympathetic ganglia may have an inhibitory effect on post-ganglionic transmission acting either interneuronally or in a local endocrine capacity.

The aim of the present investigation was to test the lability of sif and CH+ cells to reserpine in terms of their specific fluorophore emission and chromaffin positivity respectively in adult rat coeliac-mesenteric ganglia. Two reserpine dosage schedules were applied (a) 5 mg/kg i.p. 6 h before sacrifice and (b) 5 mg/kg i.p. at 36, 24 and 12 h before the animals were killed. Control animals were correspondingly injected with saline. After single injections of reserpine there was a statistically significant ($P < 0.001$) reduction in the % of chromaffin-positive and a statistically significant ($P < 0.001$) increase in the % of chromaffin-negative small cells compared with controls. Although after single injections of reserpine specific amine fluorophore was not detected in principal ganglionic neurones, no obvious reduction in fluorophore emission from sif cells was apparent. However, after prolonged reserpinization (3 x 5 mg/kg) not only was there a highly significant reduction in the % of chromaffin-positive small cells but fluorimetric measurements from sif cell cytoplasmic areas were significantly ($P < 0.001$) lower (by a factor of 2) than from comparable cells areas in control animals.

Our results are more definitive than those of Van Orden, Burke, Geyer & Lodoen (1970) who reported 'slight variable reduction in fluorescence intensity' from sif cells following two reserpine injections.

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