If the mechanism of uptake by platelets is indeed a model for uptake by neurons (Trenchard & Turner, 1975), then our results are indicative of a reduced 5-HT uptake at the neuronal level in E rats. Using the method proposed by Carlsson, Corrodi, Fuxe & Hökfelt (1969), we tried to further evaluate uptake of 5-HT in the brain. According to these authors the rate of 5-HT depletion caused by H75/12 compound (4-methyl-α-ethyl-*m*-tyramine) gives an indication of the rate of uptake at the level of the neuronal cell membrane.

The experiment was performed on 12 E rats and 12 NE rats. We observed that, when E rats are treated with H75/12 (25 mg kg^{-1}) for 1 h, the brain 5-HT level is decreased 21%. Under the same conditions the brain 5-HT level of NE rats is decreased 43%. The difference between these two percentages is significant ($0.02 < P < 0.05$).

This result is in agreement with the hypothesis that 5-HT uptake at the neuronal level is reduced in E rats. But investigations of uptake by synaptosomal preparations are necessary to provide further support for this hypothesis.

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Effects of *p*-chlorophenylalanine and α-methyltryptophan on rat social behaviour

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Previously we have studied the effect on rat motor activity of an inhibitor of 5-hydroxytryptamine (5-HT) synthesis, *p*-chlorophenylalanine (PCPA), and its reversal by the 5-HT precursor tryptophan (Marsden & Curzon, 1976). In the present communication the effects of PCPA on social behaviour are compared with those of α-methyltryptophan (AMTP), a drug which induces tryptophan pyrrolase and thus decreases brain 5-HT synthesis by depleting the precursor tryptophan (Sourkes, Missala & Oravec, 1970).

Male Sprague-Dawley rats (110–130 g) were housed 3 to a cage under a 12 h light/dark cycle for ten days. Six cages of rats were then injected with PCPA (200 mg/kg i.p.) and six with (±)-AMTP (150 mg/kg i.p.). Controls were injected with the vehicle medium (0.5% Tween in 0.9% saline). Various components of social behaviour in the home cage were observed for 5 min under red light during the first 90 min of the dark period. Observations were made 24 and 72 h after injection. Locomotor activity was measured simultaneously using an Animex activity meter. The amount of food eaten/24 h was also measured. Either 24 or 72 h after drug treatment the rats were killed and brain 5-HT and 5-hydroxyindoleacetic acid (5-HIAA) determined (Curzon & Green, 1970).

Both drugs reduced food intake during the first 24 h after injection but it was normal by 72 hours. PCPA markedly reduced 5-HT synthesis at 24 and 72 h with a significant decrease of 5-HT (24 h, −42%; 72 h, −53%) and 5-HIAA (24 h, −51%; 72 h, −67%). This was associated at 24 h (but not at 72 h) with increased locomotor activity ($P < 0.05$) and increased interactions between rats involving sniffing and biting ($P < 0.01$), fighting ($P < 0.01$) and mounting ($P < 0.01$). Self-grooming was decreased ($P < 0.05$). AMTP also decreased 5-HT turnover as brain 5-HIAA was reduced (24 h, −41%; 72 h, −43%) but 5-HT concentrations appeared to increase presumably due to the formation of α-methyl-5-HT (Roberge, Missala & Sourkes, 1972). In contrast to PCPA, AMTP had no significant effect on any of the above components of social behaviour or net locomotor activity. Self-grooming was increased at 24 h ($P < 0.01$) and at 72 h ($P < 0.05$) and burrowing was increased at 24 h ($P < 0.01$). α-Methyl-5-HT is formed by the action of tryptophan hydroxylase (Gal & Christiansen, 1975). To investigate whether α-methyl-5-HT was involved in the behavioural effects of AMTP tryptophan hydroxylase was inhibited by injecting PCPA (100 mg/kg) on three consecutive days to 24 rats and

AMTP (150 mg/kg) was then given to 12 of these rats 24 h after the last dose of PCPA. Twenty-four hours later there were no significant differences in social behaviour between PCPA and PCPA + AMTP treated rats.

The results suggest that when rats are given AMTP the formation of α-methyl-5-HT opposes the behavioural effects of decreased 5-HT synthesis.

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Reversal of the action of γ-aminobutyric acid (GABA) antagonists by barbiturates

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Certain hypnotic barbiturates have been reported to activate receptors for the central inhibitory neurotransmitter γ-aminobutyric acid (GABA) in the isolated frog spinal cord (Nicoll, 1975a, b). Also they prolong post-synaptic inhibition in the feline hippocampus which may be mediated by GABA (Nicholl, Eccles, Oshima & Rubia, 1975).

Sympathetic ganglion cells possess GABA-receptors which are analogous to those in the mammalian brain; activation of these receptors produces an easily measured depolarization (Bowery & Brown, 1974). This provided a model for testing the effect of barbiturates on GABA receptors.

Ganglion cell depolarization in the isolated desheathed superior cervical ganglion of the rat was recorded using extracellular $Ag^+/AgCl$ electrodes. The ganglia were superfused at 1 ml/min with Krebs solution at 25°C containing hyoscine (2.6 μM) (Brown & Marsh, 1975). GABA (1–300 μM) or carbachol (15–100 μM) were applied alternately for 1 min periods at 10–15 min intervals. Both produced a dose-dependent depolarization.

A depolarizing response to sodium pentobarbitone occurred only at high concentrations (>80 μM) and this was of low amplitude. A more striking effect, which could be observed at lower concentrations, was the reversal of the action of GABA-antagonists as shown in Figure 1a. When responses to GABA were reduced by bicuculline methochloride the simultaneous addition of sodium pentobarbitone restored responses to GABA. Pentobarbitone applied alone depressed responses to GABA and carbachol.

Pentobarbitone reversed the effects of other GABA antagonists, picrotoxin, tetramethylene-disulphotetramine (Bowery, Brown & Collins, 1975) and isopropyl bicyclo phosphate (Bowery, Collins & Hill, 1976). In contrast it did not reverse the antagonistic effect of hexamethonium against carbachol (Figure 1b). This selectivity for GABA was also apparent with strychnine: this depressed responses to GABA and carbachol equally (Bowery & Brown, 1974) but only the antagonism to GABA was reversed by pentobarbitone.

Thiopentone and amylobarbitone were as active as pentobarbitone whereas hexobarbitone and butobarbitone were less potent. Barbitone and phenobarbitone were inactive at concentrations up to 400 μM.

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