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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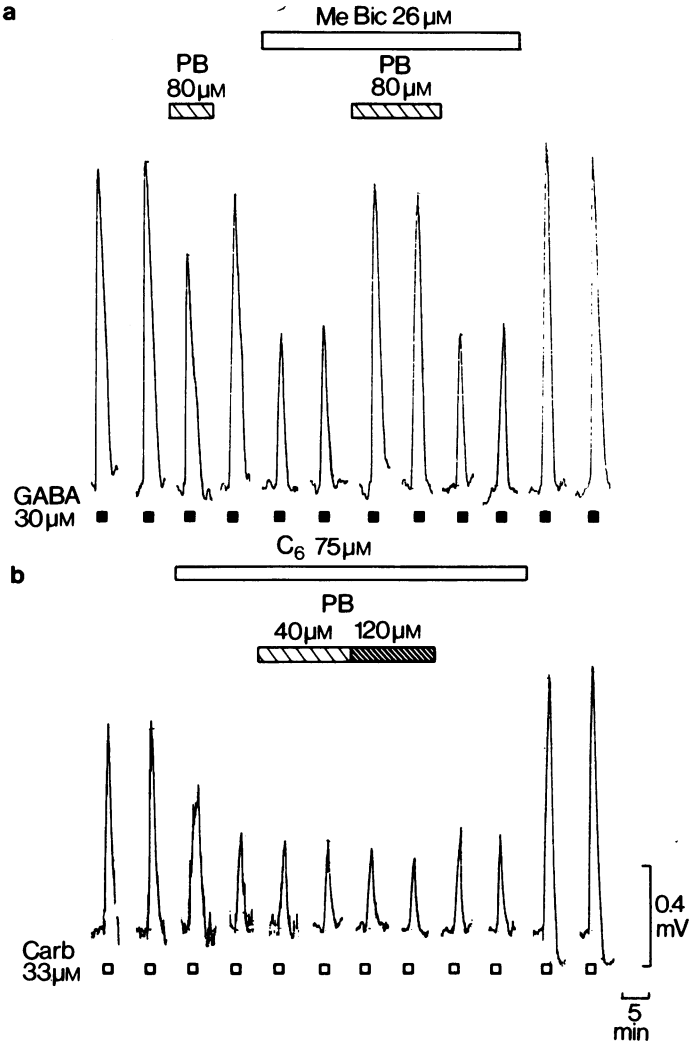


**Figure 1** Depolarizing responses to GABA (30 μM, **a**) and carbachol (33 μM, **b**) in two isolated superior cervical ganglia of the rat. (a) Reversal by sodium pentobarbitone (PB. 80 μM) of the depression in responses to GABA produced by bicuculline methochloride (MeBic. 26 μM). (b) Lack of effect of sodium pentobarbitone (40 and 120 μM) on the antagonism of responses to carbachol produced by hexamethonium ($C_6$ 75 μM). Gaps indicate periods >20 minutes.

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