The duration of anaesthesia produced by an intraventricular injection of 500 μg pentobarbitone sodium to rats withdrawn for 48 hr following various periods of barbitone administration has also been determined. The changes in sensitivity of the central nervous system indicated by this method were similar to those described above, tolerance being indicated by a markedly reduced sleeping time.

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Behaviour and EEG are affected on the day after hypnotic doses of nitrazepam and amylobarbitone sodium

C. R. B. JOYCE, ANN MALPAS*, J. ROWAN and D. F. SCOTT, *Department of Pharmacology and Therapeutics, London Hospital Medical College, and Department of Clinical Electroencephalography, London Hospital, London E.*1

Five and 10 mg nitrazepam have more pronounced effects on certain behavioural tasks than 100 and 200 mg of amylobarbitone sodium during the 3 hr immediately after daytime administration (Malpas & Joyce, 1969), as well as upon changes in the resting EEG (Volavka, Joyce, Maloney, Brawn, Summerfield, Topham & Scott, 1969). Over a longer period of time similar doses of pentobarbitone or quinalbarbitone cause statistically significant impairment on other psychomotor tasks (Goodnow, Beecher, Brazier, Mosteller & Tagiuri, 1951; Kornetsky, Vates & Kessler, 1959), but Ditt (1964) was unable to demonstrate any impairment in performance 10 to 16 hr after treatment with 5 or 10 mg of nitrazepam. We have now compared some behavioural and EEG effects of amylobarbitone and nitrazepam in the day following their administration as hypnotics in a double-blind cross-over trial.

Ten healthy male medical students took nitrazepam 5 or 10 mg, amylobarbitone sodium 100 or 200 mg, or placebo orally just before going to bed and were tested 13 and 17 hr later. Speed of motor performance and time to reach decisions at various information loads were estimated by means of a card sorting task (Crossman, 1953). All ratings of performance and EEG were completed before judges were informed of the treatments given. At 13 hr after treatment both doses of nitrazepam caused significant slowing of motor performance compared with placebo, but only the higher dose of nitrazepam significantly slowed information processing. Neither dose of amylobarbitone had significant effects on motor performance as compared with placebo, but the larger dose significantly lengthened decision time at all information loads and the lower dose did so at high information loads only. At 17 hr after treatment the effects were still apparent and in the same direction as before, but did not reach the 5% level of significance in any case. At 17 hr subjects were more likely to show the electrical changes associated with drowsiness and sleep after treatment with nitrazepam than with the barbiturate: changes with the latter were in turn more marked than those with placebo.

The subjects were apparently unaware that their performance was less efficient than usual. They considered themselves to be more alert at 13 hr after any drug treatment than at the same time after placebo and they did not report more subjective " hangover " effects after drug than after placebo.

The results imply that the effects noted in the first few hours after taking the drugs (Malpas & Joyce, 1969; Volavka, Joyce, Maloney, Brawn, Summerfield, Topham & Scott, 1969) are still detectable by objective but less easily by subjective measures, at least up to 17 hr later.

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Opioid and muscarinic anti-nociception

J. D. IRESON (introduced by G. B. LESLIE), *Department of Chemistry and Biology, Barking Regional College of Technology, Barking*

It is known that certain parasympathomimetic agents which penetrate to the brain abolish responses to noxious stimuli in laboratory animals. Leslie (1969) has shown this with oxotremorine, and Hendershot and Forsaith (1959) with eserine. The present experiments were performed to investigate the mechanism by which these agents produce their anti-nociceptive effect.

Two tests for anti-nociception were used, the electroshock test of Burn, Finney & Goodwin (1950), and the phenylbenzoquinone writhing test of Parkes & Pickens (1965). In both tests albino mice, weight range 18–22 g, were used.

Two classes of agents were investigated. One included morphine sulphate, nalorphine hydrobromide and the narcotic antagonist naloxone hydrochloride; the other included oxotremorine hydrochloride, eserine sulphate and atropine sulphate. In all experiments with the parasympathomimetic agents, the mice were pretreated with the quaternary muscarinic blocking agent atropine methylbromide (0·5 mg/kg). All test agents were administered subcutaneously.

Morphine was active in both tests, in the electroshock test at 5–20 mg/kg, and in the phenylbenzoquinone test at 0·1–0·4 mg/kg. Nalorphine was active in the phenylbenzoquinone test at 0·05–0·15 mg/kg., but showed only very slight activity in the electroshock test (100 mg/kg). Morphine and nalorphine were antagonized by naloxone in both the electroshock test (2·5 mg/kg) and the phenylbenzoquinone test (0·025 mg/kg). Morphine was potentiated by nalorphine (0·05 mg/kg) in the phenylbenzoquinone test, but antagonized by nalorphine (50 mg/kg) in the electroshock test.

A similar picture was seen with oxotremorine, eserine and atropine sulphate. Oxotremorine was active in both tests, at 0·01–0·02 mg/kg in the phenylbenzoquinone