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.

REFERENCES

CROSSMAN, E. R. F. W. (1953). Entropy and choice time: the effect of frequency unbalance on choice responses. *Quart. J. exp. Psychol.*, **5**, 41–51.

DITT, J. (1964). Psychopharmakologische Untersuchungen mit "Mogadon". Congr. Germ. forens. soc. Med., Zurich, 17 October.

GOODNOW, R. E., BEECHER, H. K., BRAZIER, M. A. B., MOSTELLER, F. & TAGIURI, R. (1951). Physiological performance following a hypnotic dose of barbiturate. *J. Pharmac. exp. Ther.*, **102**, 55–61.

KORNETSKY, C., VATES, T. S. & KESSLER, E. K. (1959). A comparison of hypnotic and residual psychological effects of single doses of chlorpromazine and secobarbital in man. *J. Pharmac. exp. Ther.*, **127**, 51–54.

MALPAS, A. & JOYCE, C. R. B. (1969). Effects of nitrazepam, amylobarbitone and placebo on some perceptual, motor and cognitive tasks in normal subjects. *Psychopharmacologia (Berl.)*, **14**, 167–177.

VOLAVKA, J. V., JOYCE, C. R. B., MALONEY, M. J., BRAWN, W., SUMMERFIELD, J., TOPHAM, C. & SCOTT, D. F. (1969). Effect of nitrazepam, amylobarbitone sodium and placebo on the electroencephalogram of normal subjects. *Psychopharmacologia (Berl.)*, **14**, 178–183.

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

test, and at 0·03–0·12 mg/kg in the electroshock test. Eserine was active only in the phenylbenzoquinone test, at 0·03–0·06 mg/kg, being ineffective in the electroshock test at 0·3 mg/kg. Both agents were antagonized by atropine sulphate, 0·5 mg/kg, in both tests. As with morphine and nalorphine, eserine (0·03 mg/kg) potentiated oxotremorine in the phenylbenzoquinone test, but at 0·1 mg/kg antagonized it in the electroshock test.

By the use of crossed agonist and antagonist experiments we investigated the possibility that these two classes of agents were producing their anti-nociception by an action on the same system. The following results were obtained. Eserine (0·045 mg/kg) potentiated both morphine and nalorphine in both tests; morphine and nalorphine were not antagonized by atropine sulphate (0·5 mg/kg) in either test; neither oxotremorine nor eserine were affected by naloxone (2·5 mg/kg).

From these results it appears probable that there are at least two separate, centrally-sited, systems which can be involved in anti-nociception.

REFERENCES

BURN, J. H., FINNEY, D. J. & GOODWIN, L. G. (1950). *Biological Standardisation.* Oxford Univ. Press.

HENDERSHOT, L. C. & FORSAITH, J. (1959). Antagonism of the frequency of phenylquinone-induced writhing in the mouse by weak analgesics and non-analgesics. *J. Pharmac. exp. Ther.*, **125**, 237–240.

LESLIE, G. B. (1969). The effect of anti-parkinsonian drugs on oxotremorine-induced analgesia in mice. *J. Pharm. Pharmac.*, **21**, 248–250.

PARKES, M. W. & PICKENS, J. T. (1965). Conditions influencing the inhibition, by analgesic drugs. of the response to intraperitoneal injections of phenylbenzoquinone in mice. *Br. J. Pharmac. Chemother.*, **25**, 81–87.

A quantitative method for the assessment of physical dependence on narcotic analgesics in mice

I. MARSHALL* and MARTA WEINSTOCK, *Department of Pharmacology, St. Mary's Hospital Medical School, London, W.2*

In the past most quantitative assessments of the physical dependence properties of narcotic analgesic drugs were made in humans, monkeys and, more recently, in rats. It was generally agreed that mice were unsuitable for this type of study because their responses were too variable to permit objective measurement.

Following chronic treatment with morphine three times daily for one week, mice, when injected with nalorphine, exhibited signs of withdrawal which were characterized by persistent jumping. Other signs of withdrawal such as diarrhoea, micturition and piloerection were also present.

This characteristic jumping was also seen when chronic morphine administration was discontinued. Under these conditions the response was rather more variable and less intense than that elicited by nalorphine. This reduced intensity of withdrawal is consistent with the findings of numerous workers in other species.

The purpose of the investigation was to determine whether the number of jumps elicited by nalorphine in groups of mice could be used as a method of measuring the intensity of the withdrawal syndrome. The relationship between the number of jumps occurring in a given time and the dose of drug, the interval between injections and the dose increment was studied using morphine, methadone and pethidine.