cerebral dopamine, there was still an increase in the concentration of dopamine in the brain after an injection of γ-hydroxybutyric acid. We have carried out experiments on both rats and mice to determine the effect of γ-hydroxybutyric acid on the cerebral concentrations of dopamine, and its metabolites, homovanillic acid and dihydroxyphenylacetic acid. There was a dose dependent increase in the concentration of all three substances 2 h after the injection of γ-hydroxybutyric acid. No increase in the concentration of dopamine was observed when γ-hydroxybutyric acid was administered to reserpine treated animals (Table 1). This result suggests that the action of γ-hydroxybutyric acid on the concentration of cerebral dopamine requires an unimpaired storage mechanism for dopamine.

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Central stimulant action of fenfluramine in the rat

B. J. EVERITT*† and N. B. HACKET (introduced by M. J. RAND)

Riker Laboratories (Aust.) Pty. Ltd., P.O. Box 122, *Hornsby, N.S.W.* 2077, *Australia*

Fenfluramine is structurally related to amphetamine and exhibits its anorectic action. After administration to rats at anorectic doses it is almost devoid of central stimulant activity (Le Douarec, Schmitt & Laubie, 1966; Alphin, Funderburk & Ward, 1964). However, high doses produce many amphetamine-like behavioural effects (Yelnosky & Lawlor, 1970).

The effects of fenfluramine and amphetamine have been compared on confinement motor activity in rats (Tedeschi, Fowler, Cromley, Pauls, Eby & Fellows, 1964). The apparatus restricts locomotor activity by confinement of single rats in an activity chamber which is small enough to permit vertical but not horizontal movements. The vertical movements are recorded with two photoelectric cells as interruptions of either one or both light beams.

Spontaneous confinement motor activity was greater with female than male rats. In addition, female rats exhibited a greater increase in activity than male rats after orally administered DL-fenfluramine (5 mg/kg) or D-amphetamine (1 mg/kg). However, male rats were used for a further comparison of fenfluramine and amphetamine in order to avoid effects arising from changes in drug metabolizing enzyme activity which might accompany hormonal changes in the oestrus cycle.

Three dose levels of DL-amphetamine and DL-fenfluramine, injected intraperitoneally, were used for calculation of the doses of each which produced a 200% increase in the average activity count over 25 min as compared to control rats tested at the same time. The following values were obtained: DL-amphetamine sulphate, 0·6 (95% confidence limits 0·4–0·9) mg/kg; DL-fenfluramine hydrochloride, 6·1

† Present address: Department of Pharmacology, University of Melbourne, Parkville, Victoria, Australia.

(95% confidence limits 3·7–9·9) mg/kg. These doses are anorectic in the rat and show that fenfluramine, like amphetamine, produces changes in the behaviour of rats which are indicative of central nervous system stimulation.

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Residual effects of a new benzodiazepine: flurazepam

A. J. BOND and M. H. LADER*

Department of Psychiatry, Institute of Psychiatry, University of London

Persistent behavioural and physiological effects after hypnotic doses of barbiturates and nitrazepam have been described by Malpas, Rowan, Joyce & Scott (1970). In a study using normal subjects with two doses of nitrazepam (5 and 10 mg) and amylobarbitone sodium (100 and 200 mg), electroencephalographic changes were apparent 18 h after ingestion. These changes were found on visual examination of paper records of the electroencephalogram (e.e.g.) taken while the subjects relaxed in a quiet, darkened room.

In a previous study we found e.e.g. changes and behavioural impairment 12 h after nitrazepam and butobarbitone sodium (Lader & Walters, 1971). We have extended this work to study the residual effects of a new benzodiazepine, flurazepam, in doses of 15 and 30 mg compared with those of butobarbitone sodium 150 mg and a placebo. Eight normal subjects received all four treatments at weekly intervals as part of a balanced design, using double-blind procedures. The drug was taken at 22.00 or 23.00 h and the psychological and physiological tests were carried out 12, 15 and 18 h later. The physiological tests consisted of e.e.g. recordings during an auditory reaction time task and the electroencephalographic averaged evoked response (A.E.R.) to the auditory stimuli (clicks) was also quantified. All experiments were carried out on-line, in real-time using a PDP-12A computer. The e.e.g. was analysed on-line by passing it through four broad wave band filters: 2·4–4·0 Hz, 4·0–7·5 Hz, 7·5–13·5 Hz and 13·5–26·0 Hz. The computer sampled each wave band at intervals between the auditory stimuli and calculated the mean rectified voltage in each wave band. The A.E.R. was computed using thirty-two epochs and the variance was calculated to check for artifacts. The main peaks had mean latencies of: P_1, 75 ms; N_1, 123 ms; P_2, 197 ms; N_2, 285 ms. Peak-to-peak amplitudes were computed in microvolts.

All wave bands showed significant changes which persisted through the day up to 18 h after the drug; for example, the 4·0–7·5 Hz wave band was significantly decreased by both drugs. A particularly sensitive measure was the mean voltage of the wave bands calculated as a percentage of the total voltage. Two components of the A.E.R.: P_1-N_1 and N_1-P_2 were significantly diminished. However, reaction time was not affected.