

- GOLDBERG, L.I., VOLKMAN, P.H. & KOHLI, J.D. (1978) A comparison of the vascular dopamine receptor with other dopamine receptors. *Ann. Rev. Pharmac. Toxicol.* **18**, 57-59.
- KATARIA, M., TRAUB, M. & MARSDEN, C.D. (1978). Extrapyramidal side effects of metoclopramide. *Lancet* (ii), 1254-1255.
- LAVY, S., MELAMED, E. & PENCHAS, S. (1978). Tardive dyskinesia associated with metoclopramide. *Br. med. J.* **1**, 77-78.
- MARSDEN, C.D. (1975). The neuropharmacology of abnormal involuntary movement disorders (the dyskinesias). *Modern Trends in Neurology* **6**, 141-166.
- N.I.M.H. PSYCHOPHARMACOLOGY RESEARCH BRANCH (1975). Development of a dyskinetic movement scale. *Early Clinical Drug Evaluation Unit Intercom.* **4**, 3-6.
- SIEGEL, S. (1956). *Nonparametric statistics for the behavioural sciences*. McGraw-Hill. N.Y.

Effect of some stimulants on sleep in man

A.N. NICHOLSON AND BARBARA M. STONE

Royal Air Force Institute of Aviation Medicine, Farnborough, Hampshire.

Sleep analysis has been used to investigate the effect of caffeine in man, (Brězinová, 1974; Karacan, Thornby, Anch, Booth, Williams & Sallis, 1977; Nicholson & Stone, 1977), and such studies may help to understand the activity of stimulants. We have extended our previous work to three other drugs, methylphenidate hydrochloride (10 and 20 mg), pemoline (20 & 40 mg) and fencamfamine hydrochloride (10 and 20 mg). Caffeine (300 mg) was included as an active control, and its effect on sleep was similar to that observed previously (Nicholson & Stone, 1977).

The subjects were six healthy male volunteers aged between 20 and 31 years adapted to the sleep laboratory. From a week before and during the study the subjects drank decaffeinated coffee (Boots Pure Drug Company). Both doses of each drug were studied in all subjects, and with each active compound the subject ingested matching placebos of the other three drugs. The tablets were taken at 'lights out', and experiments were separated by seven days. Details of recording techniques, statistical procedures and analyses are given elsewhere (Nicholson, Stone, Clarke & Ferres, 1976), except that the F₁-F₇ pair of electrodes were replaced by C₄-A₁. The study was double blind with a balanced random order.

Mean sleep onset latencies were not changed. Mean total sleep times (TST) were reduced with methylphenidate (20 mg) and pemoline (40 mg) ($P < 0.01$ and < 0.05 respectively), but not with fencamfamine. The effect with pemoline was due to grossly disturbed sleep in one subject. However, the effects of methylphenidate and fencamfamine were seen in all subjects. Duration of awake activity was increased with each dose ($P < 0.05$), and duration of drowsy sleep was

increased with methylphenidate (20 mg) ($P < 0.01$). The percentage of drowsy sleep was also increased with methylphenidate (20 mg) ($P < 0.001$) and fencamfamine (20 mg) ($P < 0.05$). The higher doses of methylphenidate and fencamfamine delayed the first REM period ($P < 0.001$ and < 0.05 respectively), and the duration of REM sleep was decreased with methylphenidate (10 & 20 mg) ($P < 0.05$ and 0.001 respectively), and with fencamfamine (20 mg) ($P < 0.05$). The percentage REM sleep was also decreased by methylphenidate (20 mg) ($P < 0.001$) and fencamfamine (20 mg) ($P < 0.05$).

Methylphenidate and fencamfamine possess stimulant activity in man as indicated by sleep studies. Fencamfamine, like caffeine and methylphenidate, increases awake activity and drowsy sleep, but it does not reduce TST. Both drugs increase the latency of the first REM period, and reduce duration of REM activity. It would appear that the alerting effect of these drugs may involve reduced sleeping times as well as increased wakefulness during the sleep period.

The drugs were kindly supplied by Ciba Laboratories (methylphenidate hydrochloride), Medo-Chemicals Ltd. (pemoline) and E. Merck Ltd. (fencamfamine hydrochloride).

References

- BRĚZINOVÁ, V. (1974). Effect of caffeine on sleep. EEG study in late middle age people. *Br. J. clin. Pharmac.*, **1**, 203-208.
- KARACAN, L., THORNBLY, J.L., ANCH, A.M., BOOTH, G.H., WILLIAMS, R.L. & SALLIS, P.J. (1977). Dose related sleep disturbances induced by coffee and caffeine. *Clin. Pharmac. Ther.*, **20**, 682-689.
- NICHOLSON, A.N. & STONE, B.M. (1977). Studies on the sleep of the young adult after caffeine. *Br. J. clin. Pharmac.*, **4**, 717P.
- NICHOLSON, A.N., STONE, B.M., CLARKE, C.H. & FERRES, H.M. (1976). Effect of N-desmethyldiazepam (nordiazepam) and a precursor, potassium clorazepate, on sleep in man. *Br. J. clin. Pharmac.*, **3**, 429-438.