tic agonist, (Brown, unpublished observations, 1979), which, on the basis of the present interpretation, would be predicted to markedly inhibit catalepsy. Preliminary results suggest that this is the case.

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The effect of metoclopramide and haloperidol on tardive dyskinesia

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Tardive dyskinesia is a movement disorder which occurs in patients on long-term neuroleptic therapy, and has been attributed to the development of supersensitivity of dopamine receptors in the central nervous system (Marsden, 1975). Metoclopramide (MCP) has recently been reported to produce tardive dyskinesia (Lavy, Melamed & Penchas, 1978; Kataria, Traub & Marsden, 1978) but despite other evidence that MCP blocks dopamine receptors (Day & Blower 1975; Ahtee, 1975; Goldberg, Volkman & Kohli, 1978) it does not appear to have antipsychotic activity (Borenstein & Bles, 1965).

We have compared the effects of single intravenous doses of MCP (10, 20 and 40 mg), haloperidol (HL) (5 and 10 mg) and placebo (saline) in 8 patients (age 55 to 85 years, 6 female) with tardive dyskinesia secondary to long term neuroleptic treatment. The study was double blind and the order of drug administration randomised, with an interval of at least 7 days between each treatment. The patients' severity of dyskinetic movement (N.I.M.H. Psychopharmacology Research Branch 1975) and parkinsonism (Calne, Reid, Vakil, *et al.*, 1971) was rated immediately before, and at 1, 3 and 6 h after drug administration. In addition video recordings were made at the same time for later rating for dyskinesia by 4 observers. The total dyskinesia score for each patient at each time point was summed, and the results analysed by the Wilcoxon signed rank test (Siegel, 1956). The scored drug effects on dyskinesia were found to be similar both at the time of the study and from video playback. Patients improved significantly during the day whilst on placebo, and after all active treatments. The effects of HL 10 mg and MCP 40 mg on dyskinesia were significantly greater than placebo at 3 h ($P < 0.05$ and < 0.02 respectively) and of HL 5 and 10 mg and MCP 40 mg at 6 h ($P < 0.01$). No significant changes in parkinsonian features were noted.

These findings suggest that the dose of MCP used for studies of its antipsychotic activity (Borenstein & Bles, 1965) may have been too low. The effect of dopamine receptor antagonists on tardive dyskinesia may provide a useful method for investigating these drugs in man.

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Effect of some stimulants on sleep in man

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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 F_1–F_7 pair of electrodes were replaced by C_4–A_1. 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).

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