JOUVET, M. (1967). Sleep and altered states of consciousness, p. 86. Editors: Kety, S. S., Evarts, E.V. & Williams, H. L. Baltimore: Williams and Wilkins.

JOUVET, M. (1969). Science, 163, 32-41.

KORNETSKY, C., MIRSKY, A. F., KESSLER, C. K. & DORFF, J. E. (1959). J. Pharmac. exp. Ther., 127, 46-50.

KÖNIG, J. F. R. & KLIPPEL, R. A. (1963). The Rat Brain. A stereotaxic atlas of the forebrain and lower parts of the brain stem. Baltimore: Williams and Wilkins.

LIDBRINK, P., CORRODI, H., FUXE, K. & OLSON, L. (1972a). Brain Res., 45, 507-524.

LIDBRINK, P., JONSSON, G. & FUXE, K. (1972b). Acta pharmac. tox., 31, Suppl., 1, 26.

LOIZOU, L. A. (1969). Brain Res., 15, 563-566.

LONGO, V. G. (1962). Electroencephalographic atlas for pharmacological research, Rabbit brain research, II. Amsterdam: Elsevier.

MICHEL, F., KLEIN, M., JOUVET, D. & VALATX, J. L. (1961). Comp. Rend. Soc. Biol., 155, 2289-2292 OLSON, L. & FUXE, K. (1971). Brain Res., 28, 165-171.

PEYRETHON-DUSAN, D. (1968). Imprimerie des Beaux Arts, Lyon, pp. 1-111.

Rossi, G. F., FAVALE, E., HARA, T., GIUSSANI, A. & SACCO, G. (1961). Arch. Ital. Biol., 99, 270–292.

ROUSSEL, B. (1967). Imprimerie des Beaux Arts, Lyon, pp. 1-144.

TAYLOR, K. M. & LAVERTY, R. (1969). Eur. J. Pharmac., 8, 296-301.

UNGERSTEDT, U. (1968). Ibid., 5, 107-110.

UNGERSTEDT, U. (1971a). Acta physiol. scand., Suppl. 367, 1-48.

UNGERSTEDT, U. (1971b). 6-Hydroxydopamine and catecholamine neurons. Editors: Malmsfors, T. & Thoenen, H., p. 101. North-Holland: Amsterdam.

## Lorazepam on visuo-motor co-ordination and visual function in man

In any study of centrally acting drugs in man involving a response to a visual stimulus, the possibility of a drug effect on the peripheral visual apparatus must be considered. This is especially true for benzodiazepine drugs. Miller (1962) reported that chlordiazepoxide in doses of 20 mg daily produced significant exophoria and reduced visual acuity. Hedges, Turner & Harry (1971) showed that there was a significant dose-related reduction in critical flicker frequency, disc-dotting and reaction times by the benzodiazepine drug, lorazepam, in doses of 0.5, 1.0 and 2.0 mg, the maximum effect being seen at 4 or 6 h.

We have examined the effect of lorazepam in normal volunteers to determine if a dose sufficient to produce significant impairment of hand-eye co-ordination (a recognized test in the evaluation of centrally acting drugs—Molson, Mackey & others, 1966; Large, Wayte & Turner, 1971), was associated with change in tests of visual function.

Six healthy volunteers (aged 19–21 years) with normal colour vision and visual acuities of 6/4.5 or better in both eyes, and in good health, who were receiving no other medication, were given lorazepam 1.0 and 2.0 mg and a placebo in tablet form in random order based on two latin-square designs, under double-blind conditions, each treatment being separated by at least one week. The investigations were made at the same time in the afternoon after a standard light lunch. Subjects avoided coffee, tea, alcohol and nicotine on the test days. Tests were made before and at  $1\frac{1}{2}$  and 3 h after the treatment. The subjects had been familiarized with the procedures before the investigation. In the hand-eye co-ordination test they had reached a plateau of performance to minimize further learning effects.

The tests were of (a) refraction (b) visual acuity (c) amplitude of accommodation (d) oculomotor balance (e) visual fields (f) hand-eye co-ordination, and were made





according to Austen, Gilmartin & Turner (1971). The only modification was that a nylon-tip pen was steered along a spiral of dots on a paper sheet in the co-ordination test.

Results were submitted to analysis of variance and showed a significant doserelated increase in tracking errors in the hand-eye co-ordination test (P < 0.001), the maximal effect being seen at  $1\frac{1}{2}$  h (Fig. 1). No significant changes were found in any of the other tests of visual performance.

This finding supports the results of Hedges & others (1971) except that the time course showed a maximum at  $1\frac{1}{2}$  h compared with the 4 or 6 h found by those authors. This may be due in part to differences in time of day and in conditions of fasting or food intake between the studies.

Thus, doses of a centrally acting drug, lorazepam, sufficient to produce significant impairment in a test of hand-eye co-ordination did not significantly alter peripheral visual function in the tests used.

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## REFERENCES

AUSTEN, D. P., GILMARTIN, B. A. & TURNER, P. (1971). Br. J. Physiol. Opt., 26, 161-165.
HEDGES, A., TURNER, P. & HARRY, T. V. A. (1971). J. Clin. Pharmac., 11, 423-427.
MILLER, J. G. (1962). J. Am. med. Ass., 179, 940.
MOLSON, G. R., MACKAY, J. A., SMART, J. V. & TURNER, P. (1966). Nature (Lond.), 209, 516.
LARGE, A. T. W., WAYTE, G. M. & TURNER, P. (1971). J. Pharm. Pharmac., 23, 134-135.