EFFECT OF DIAZEPAM ON OCULOMOTOR BALANCE

Blurred vision and diplopia are recognized adverse effects of benzodiazepine tranquillizers (Meyler, 1966), but the mechanisms by which they are produced have been little explored. We have, therefore, examined the ocular effects of diazepam in six healthy volunteers, aged 18-22 years, with good vision and ocular motility.

Diazepam (10 mg), or an identical placebo tablet, was administered orally at 13.00 h under double-blind conditions, the order of treatments being randomized. The subjects had not eaten since breakfast. The following measurements of ocular function were made before administration of the drug and at 1.5 and 3 h after: (a) visual acuity using standard Snellen charts; (b) oculomotor balance at distance using a Maddox rod, and at near with Mills test; (c) near point of convergence using a near point rule; (d) amplitude of accommodation using a subjective method with a near point rule, and an objective method with a retinoscope (Wagstaff, 1966); (e) visual fields using a Friedman-Bedwell analyser with a neutral density filter set initially at 2.20 log units; and (f) saccadic eye movements using a technique involving reflection of infra-red light from the cornea. Horizontal saccades of 7° were produced by asking the subject to look from one target to another in time to a metronome set at 80/minute. Only four subjects gave technically satisfactory records of saccadic movements.

Results are shown in Table 1. Oculomotor balance was changed little or not at all by placebo treatment, but after diazepam five of the six subjects showed a change of up to three prism

Table 1 Ocular effects of diazepam. The values given are the means for six subjects, with the exception of saccadic movements, which were calculated from the results of four subjects. Changes from the control value at 1.5 h and 3 h after administration of diazepam or placebo are given in the upper half of the table, and actual values in the lower half.

Measurement	*Diazepam*			*Placebo*		
	Control value	*Change at 1.5 h*	*Change at 3 h*	*Control value*	*Change at 1.5 h*	*Change at 3 h*
Oculomotor balance (prism dioptres)						
(a) at distance		+1.0 ESO*	+1.4 ESO*		+0.1 EXO	+0.3 EXO
(b) at near		+2.0 EXO*	+1.3 EXO*		0.0	0.0
Near point of convergence (cm)	5.8	+3.7*	+2.1*	5.6	+0.4	+0.4
Amplitude of accommodation (dioptres)						
(a) subjective	10.6	−1.2	−0.4	11.3	+0.1	0.0
(b) objective	6.7	−0.7	−0.2	6.7	+0.2	+0.2
	Control value	*Value at 1.5 h*	*Value at 3 h*	*Control value*	*Value at 1.5 h*	*Value at 3 h*
Visual fields (reduction in log units from 2.20 neutral density)						
(a) right eye	1.1	2.8	1.7	1.7	0.9	1.0
(b) left eye	1.3	3.0	1.5	2.3	1.3	1.3
Saccadic movements (Ratio: mean amplitude/mean peak velocity)						
(a) to right	1.65	2.02	1.68	1.95	1.70	1.45
(b) to left	1.61	2.34	1.91	1.75	1.79	1.98

* Significantly different from value after placebo treatment at $P < 0.01$ on analysis of variance.
ESO, Esophoria.
EXO, Exophoria.

dioptres towards esophoria at distance, while the remaining subject showed no change. On the other hand, oculomotor balance at near altered by up to five prism dioptres in the direction of exophoria after treatment with diazepam. These changes were significant at the 1% level on analysis of variance. Near point of convergence receded in all six subjects following diazepam treatment, compared with a minimal change after placebo. Again, the difference between the responses to the two treatments was significant. Although visual field testing showed a greater decrease in the threshold contrast sensitivity after diazepam administration than after placebo, the difference was not significant. Visual acuity remained unchanged throughout these experiments.

Recordings of saccadic eye movements showed a marked increase in the number of corrective saccades after diazepam treatment. The effect of the drug on the velocity of the movement was examined by calculating the ratio of the mean amplitude of ten saccadic movements to the mean peak velocity reached during these saccades. This allowed for changes in velocity which were amplitude related. An increase in this ratio indicated a reduction in velocity relative to amplitude. Although the ratio increased after diazepam administration, the change did not reach statistical significance, partly because this investigation was technically satisfactory only in four subjects.

The changes produced by diazepam in these experiments resemble those found by Westheimer & Rashbass (1961) with amylobarbitone sodium. A change in distance heterophoria in the direction of esophoria, and a change in near heterophoria in the direction of exophoria were seen. A reduction in the amplitude of the fusional range results. A recession of the near point of convergence occurred, but no change in the amplitude of accommodation was seen. Miller (1962) reported that chlordiazepoxide in doses of 20 mg daily for a week produced some degree of lateral exophoria for both near and far vision, but Austen, Gilmartin & Turner (1971) did not find a significant change in near heterophoria with single doses of chlordiazepoxide (10 mg) in normal subjects. Our results indicate that, as with amylobarbitone sodium, administration of single doses of diazepam (10 mg) reduces the fusional range, presumably by interfering with the mechanism which organizes eye vergence movements (Westheimer & Rashbass, 1961), and this accounts for the blurred vision and diplopia which have been reported to occur with this drug.

Rashbass (1959) and Norris (1968, 1971) showed that barbiturates and benzodiazepines suppressed slow tracking eye movements and increased corrective saccades. The peak velocity of the saccades, however, was reduced by benzodiazepines (Gentles & Thomas, 1971). Our findings in four subjects support these observations.

Rose Brand, J. Saunders & J. Stewart-Jones

Department of Ophthalmic Optics & Visual Science, The City University, Cranwood Street, London EC1V 9HH

A. Richens

Department of Clinical Pharmacology, St. Bartholomew's Hospital, London EC1A 7BE

Received February 25, 1974

References

AUSTEN, D.P., GILMARTIN, B.A. & TURNER, P. (1971). The effect of chlordiazepoxide on visual field, extraocular muscle balance, colour matching ability and hand-eye co-ordination in man. *Br. J. Physiol. Optics*, **26**, 161-165.

GENTLES, W. & THOMAS, E.L. (1971). Effect of benzodiazepines upon saccadic eye movements in man. *Clin. Pharmac. Ther.*, **12**, 563-574.

MEYLER, L. (1966). *Side Effects of Drugs*. Amsterdam: Excerpta Medica Foundation.

MILLER, J.G. (1962). Objective measurements of the effects of drugs on driver behaviour. *J. Am. med. Ass.*, **179**, 940-943.

NORRIS, H. (1968). The time course of barbiturate action in man investigated by measurement of smooth tracking eye movement. *Br. J. Pharmac.*, **33**, 117-128.

NORRIS, H. (1971). The action of sedatives on brain stem oculomotor systems in man. *Neuropharmacology*, **10**, 181-191.

RASHBASS, C. (1959). Barbiturate nystagmus and the mechanism of visual fixation. *Nature, Lond.*, **183**, 897-898.

WAGSTAFF, D.F. (1966). The objective measurement of the amplitude of accommodation. *The Optician*, **151**, 105-109.

WESTHEIMER, G. & RASHBASS, C. (1961). Barbiturates and eye vergence. *Nature, Lond.*, **191**, 833-834.