DRUGS AND PERSONALITY

VII. THE EFFECTS OF STIMULANT AND DEPRESSANT DRUGS UPON PUPILLARY REACTIONS*

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1. INTRODUCTION

THERE has been relatively little work in psychology and psychiatry in which use has been made of the pupillary reaction to light and darkness; most of the work that has been done has been connected with the relatively slow reactions found in schizophrenia. This neglect is difficult to understand in view of the fact that this reaction and the autonomic innervation determining it are relatively well understood and do not present the same experimental and theoretical difficulties as the psychogalvanic reflex which is very much more widely used (Martin, 1960). In the present study, which forms part of a larger series, an attempt was made to investigate the influence of drugs on the reactivity of the pupil to changes in light stimulation.

2. THE EXPERIMENT

Details of drugs, experimental design and subjects have been given in a previous paper (Eysenck and Easterbrook, 1960). Eight subjects in all were tested under four drug conditions (d-amphetamine sulphate, sodium amylobarbitone, meprobamate, and a placebo), under an experimental design which ensured that each drug would be given once after each other drug and in each serial position. The experimental design, a balanced incomplete block, was completed twice, once for the subjects seen in the morning and once for those seen in the afternoon. The test under discussion here was only one of several applied to the same group of subjects under the same conditions. This test was the sixth to be carried out, immediately following the body sway test discussed in the previous paper.

The subject was seated in a flood-lit position with his head clamped in front of a cinecamera which was focused on the pupil of his left eye. A six-volt, twelve-ampere bulb was arranged to shine down a tube into his right eye, which was shielded from outside stimulation. After two minutes adaptation to the flood-lights, S was warned to fix his vision on a spot on the camera face, and records were made of left pupil size during (*a*) a period of five seconds when the right eye was unstimulated, followed by a period of twenty-five seconds with the stimulus "on" (contraction series), (*b*) a period of five seconds with the

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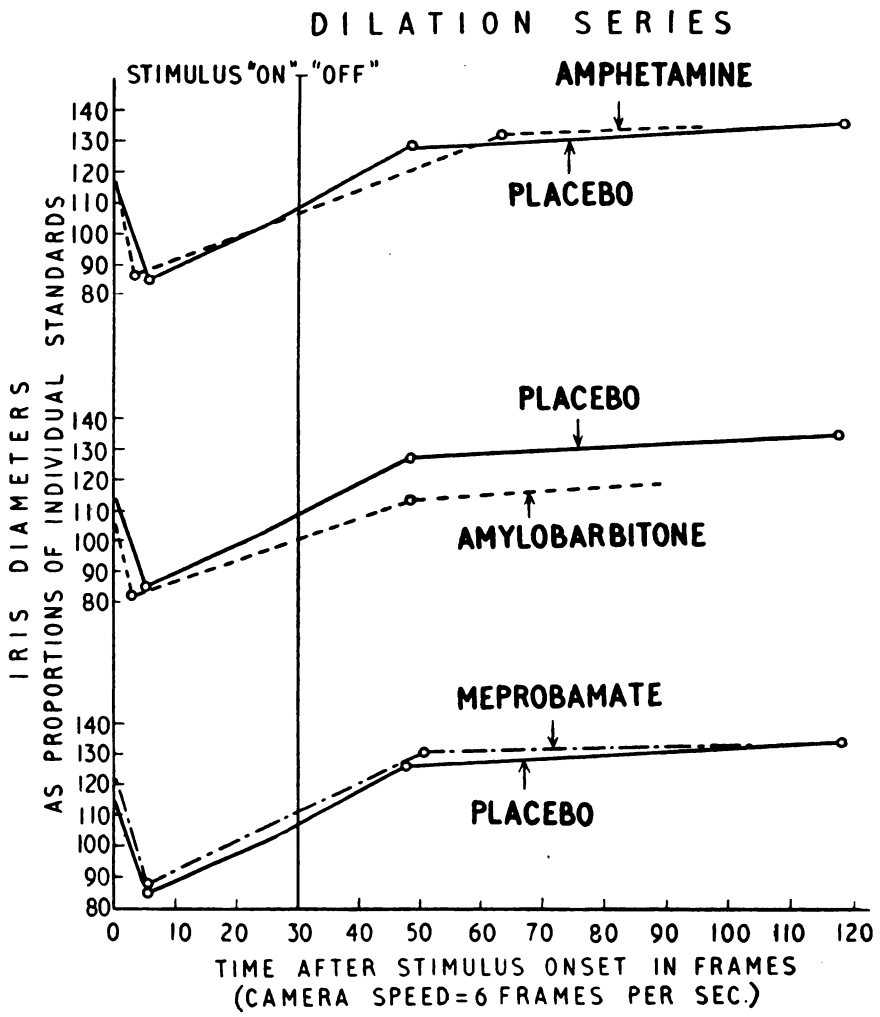

FIG. 1A.

stimulus "on" followed by a period of twenty-five seconds with the stimulus "off" (dilation series), and (*c*) a series of twenty-five cycles in each of which one second of stimulation was followed by four seconds without. The film was subsequently projected at an enlargement of about twenty to one on to a ground glass screen and iris sizes were measured with calipers automatically feeding their settings into a recorder. The following readings were then taken: (*i*) initial diameter, (*ii*) minimum diameter after stimulus onset, (*iii*) maximum compensatory dilation within five seconds of stimulus onset, (*iv*) the first subsequent diameter not exceeded for fifty frames, (*v*) the final maximum diameter, i.e. the largest size reached during the whole of the experiment, as well as the time in frames between each incident.

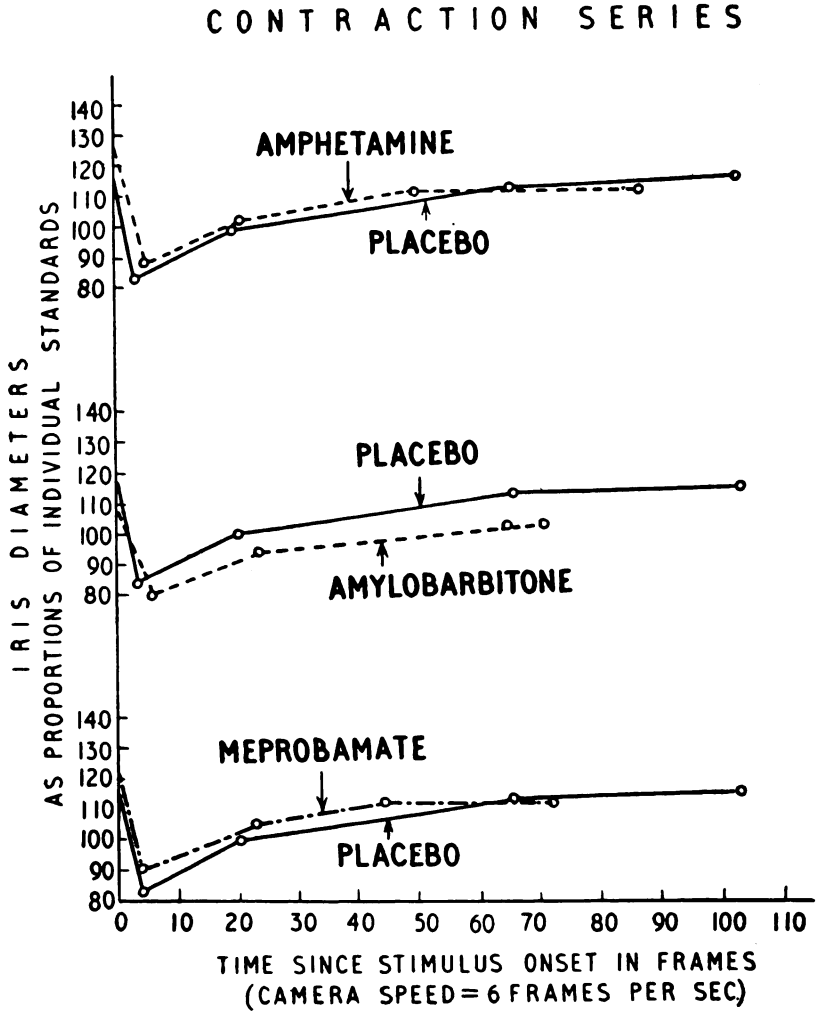

FIG. 1B.

3. RESULTS

(a) *Iris Size Response to Stimulation*

In both the "contraction" records and the "dilation" records the iris contracted rapidly to a minimum within 2–6 frames of onset of the stimulus, and then showed a compensatory dilation with cyclic variation to a maximum. During the first five seconds with stimulus "on" the data duplicated one another, so it was possible to estimate the test-retest reliability of the measures. Using a coefficient of consistency* on the readings of maximum compensatory dilation within five seconds of stimulus onset (which were to serve as standards —see below), the consistency of the scores was found to be sufficiently high ($r_c = \cdot 988$) to justify considerable reliance on these data as read.

* $r_c = 1 - Vsb/Vsw$, in which Vsb signifies the variance attributable to subjects between replications on the same subjects and Vsw signifies the variance attributable to subjects within replications.

The mean iris diameters at the point of maximum compensatory dilation within five seconds of stimulus onset for both the "contraction" and the "dilation" records under the different treatments are shown in Table I (see also Figs. 1a and 1b). In these data, the effect of drugs is significant when tested against the replication variance ($F=14\cdot0$ with 3/3 degrees of freedom (d.f.)). The meprobamate treatment produced the largest and the amytal the smallest iris diameters.

TABLE I

Mean Iris Diameters in Millimetres
At Point of Maximum Dilation Within Five Seconds after Stimulus Onset

	Treatments			
	Placebo	Amphetamine	Amylobarbitone	Meprobamate
"Contraction" records ..	1·450	1·480	1·355	1·517
"Dilation" records ..	1·470	1·460	1·347	1·475

The mean for each subject was calculated from the eight available measures of iris diameter at the point of maximum compensatory dilation (within five seconds of stimulus onset). There are eight measures on each subject because there are 4 conditions×2 series. All other readings were then converted to ratio scores, using these means as 100, and subsequent tests were made with the data in this form. Table II shows the means for each treatment of these ratio scores at each point at which readings were made. The pattern of treatment effects confirms that noted in Table I.

TABLE II

Mean Iris Diameters

As Percentages of Individual Standards Taken at the Point of Maximum Compensatory Dilation Within the First Five Seconds After Stimulus Onset

	Treatments			
	Placebo	Amphetamine	Amylobarbitone	Meprobamate
Contraction Records:				
Pre-stimulation	116·9	125·5	107·5	123·0
Minimum with stimulus "on"	83·9	86·9	81·1	89·9
Maximum in 5 seconds after stimulation	99·7	102·4	93·9	105·5
First true maximum*	112·6	111·0	102·4	111·7
Grand maximum*	114·9	112·5	102·7	112·2
Dilation Records:				
Pre-stimulation	114·9	118·4	106·9	122·6
Minimum with stimulus "on"	84·9	86·5	81·9	87·5
Maximum in 5 seconds after stimulation	101·7	100·9	93·0	102·1
First true maximum†	127·5	132·5	114·4	131·4
Grand maximum	135·0	135·0	118·6	134·4
Means	109·20	111·16	100·24	112·03

* The "first true maximum" was defined as the first maximum diameter after stimulus onset that was not exceeded for 50 frames (8·33 seconds). The "grand maximum" was the largest iris diameter observed in the record.

† In the dilation records the stimulus had been turned off after five seconds.

Two points may be made about the calculations in Table II. First, in the absence of the light stimulus (i.e. in the "dilation records") the grand maxima

for the placebo, amphetamine and meprobamate treatments may be the same. Second, despite this, the averages of all treatments but amphetamine and meprobamate differ from one another at the ·01 level of significance, so that there is a general effect of treatments on iris diameter.

(b) *Iris Responsiveness*

The changes in iris diameter in Table II are responses to stimulation or to withdrawal of stimulation. The speeds at which such changes occur are indices of responsiveness in some sense to stimulation or to withdrawal of stimulation and are likely to have fundamental importance. The matrices of time lapse between the points at which readings were taken showed no significant relations to treatment; calculations were therefore made for each individual of the net amount of change between adjacent points per unit time difference (in frames). Table III displays these mean rates of change under each treatment, with two related calculations.

TABLE III

Net Change in Iris Size Between Reference Points

(Unit averages ·44 mm./seconds)

Reference Points From–To	Treatments			
	Placebo	Amphetamine	Amylobarbitone	Meprobamate
Stimulus onset–minimum	−7·88	−9·10	−6·09	−7·42
Minimum–C/maximum in 5 seconds*	1·03	0·96	0·69	0·87
Total change in 5 seconds	8·91	10·06	6·78	8·29
C/maximum in 5 seconds–1st true maximum with stimulus "on"	0·280	0·309	0·209	0·282
C/maximum in 5 seconds–1st true maximum with stimulus "off"	1·100	0·795	0·875	0·934
Difference off–on	0·820	0·486	0·666	0·652

* Compensatory maximum within the first 5 seconds after stimulus onset.

The data in Table III suggest that two dimensions underlie the differences between treatments in speed of change of iris diameter. The first is clearly *responsiveness to stimulation*, indicated by the contraction "rates" (amylobarbitone reduces responsiveness and amphetamine increases it). The concomitance of the mean rates of compensatory dilation (stimulus "on") with those during contraction suggest that the rates of compensatory dilation (stimulus "on") vary directly with the rates of contraction to the stimulus. In more general terms *negative adaptation* (or "habituation") to this stimulus seems to proceed more rapidly when *sensitivity* to the stimulus is greater. However the rates of dilation with the stimulus "off" that are shown in Table III are not apparently related to the rates of compensatory dilation. (All drugs retard this, as compared with placebo.)

None of the matrices whose means are displayed in Table III showed a significant effect of drugs when analysed individually, although the differences between amphetamine and amylobarbitone in total change in the first five seconds and in the rate of compensatory dilation (stimulus "on") are significant by t test. Nonetheless the effects seemed to present a pattern.

A new 8×4 matrix was therefore composed using the means for each of the two groups of four subjects that composed a block, of the following

measures: rate of contraction, rate of compensatory adaptation within the first five seconds, rate of compensatory adaptation to the first true maximum (stimulus "on") and the total (without regard to sign) of the first two slopes ("total change in first five seconds"). Thus we are using averages of 4 indices of responsiveness to stimulation. Each of the treatment means on these measures was expressed as a percentage of the total across treatments, so that the four indices became comparable and could be averaged. The mean percentages obtained were: placebo, 26·8; amphetamine, 29·1; amytal, 20·1; and meprobamate, 24·0. This matrix shows a significant drug effect ($F=10·0$ with 3 and 18 d.f.) and t tests of the difference between adjacent means ($SE_d=1·72$) showed all differences except those between the placebo and either meprobamate or amphetamine to be significant (at $P=·05$).

A similar large matrix could not be composed to test the observation that the rates of dilation after cessation of stimulation (and the difference of these rates from those for compensatory dilation) may reflect a second dimension of difference between treatments. However, this possibility cannot be confidently rejected. The difference between the scores for placebo and amphetamine treatments in the "Difference Off–On" (whose means are shown in Table III) yields a t of 2·09, while a t of 2·12 would be significant at the ·05 level of confidence.

(c) *Effects of Repeated Stimulation*

The records which had been made of the changes in iris diameter during the period of two minutes when 25 one-second flashes of light were presented at regular intervals revealed no indication of differences between treatments beyond those of general iris size. The records themselves were imperfect, due to a great number of long blinks or winks. These cases of lid closure were apparently bilateral and affected the phenomenon under investigation by interrupting the stimulation. In several records the lid closure coincided with the stimulus onset quite neatly. The repetition of short flashes of light seemed to produce a higher incidence of lid closures than did the continuous stimulation, particularly under the three drugs.

4. Discussion

The results reported above leave no doubt that the drugs used strongly affected the response of the pupil to light stimulation and its recovery. Responsiveness to stimulation is quickly retarded by the depressant drugs, particularly amylobarbitone, as compared with placebo conditions; it is increased by amphetamine as compared with placebo conditions. It appears at the same time that negative adaptation (of the contraction response) is most rapid under conditions in which sensitivity to the stimulus is greatest, i.e. under stimulant drugs, and proceeds more slowly under conditions in which sensitivity to the stimulus is least, i.e. under depressant drugs and particularly under amylobarbitone.

The data suggested that in addition to this pharmacological effect in responsiveness to stimulation (or sensitivity) there was also present another factor related to rates of dilation with the stimulus off. This type of dilation appeared to be retarded by all the drugs but most of all by amphetamine. In view of the border-line significance of this finding we cannot be sure that there does in fact exist a second dimension of this type in the data, and a repetition of the experiment would be necessary before any certain conclusion could be

arrived at. However such an investigation might be eminently fruitful. A single line of behaviour—pupil dilation—is here manifestly sensitive to both continuation and cessation of stimulus energy, and it is the suggestion of these data that its two hypothetical mechanisms are differently affected by drugs.

Our main interest from the theoretical point of view had lain in the effects of repeated stimulation because it would be predicted from the drug postulate, which was outlined in the first paper of this series, that adaptation to repeated stimulation (inhibition) should proceed more rapidly and more strongly under depressant than under stimulant drugs. The large number of eye-blinks elicited by the testing procedure makes it impossible to use the data in any definitive fashion. The frequently observed fact that the lid closure coincided with stimulus onset may be evidence of some form of conditioning, the conditioned stimulus being the time interval between light flashes. If this is so and if, as has been argued elsewhere, introverts condition more easily than extraverts (Eysenck, 1957), this conditioned reaction would be likely to cut down the amount of light stimulation received by introverts as compared with extraverts, thus confounding the prediction. This may be overcome in future research by spacing the light stimuli at irregular intervals.

5. Summary and Conclusions

The effects of d-amphetamine sulphate, sodium amylobarbitone and meprobamate were compared with those of a placebo in respect of their power to influence subject's pupillary reactions to light stimulation. The main findings were: (*i*) that amylobarbitone retards responsiveness, while amphetamine increases it, and (*ii*) that drug conditions favouring rapid adaptation to the stimulus also appeared to produce greater sensitivity to the stimulus.

References

Eysenck, H. J., *Dynamics of Anxiety and Hysteria*, 1957. London: Routledge & Kegan Paul.

Eysenck, H. J., and Easterbrook, J. A., "Drugs and personality: VI. The effects of stimulant and depressant drugs upon body sway (static ataxia)", *J. Ment. Sci.*, 1960, **106**, 831.

Martin, I., "Somatic reactivity", *in* Eysenck, H. J. (Ed.), *Handbook of Abnormal Psychology*, 1960. London: Pitman.