SUSCEPTIBILITY TO METHYLPENTYNOL: EYELID CONDITIONING AND P.G.R. RESPONSE

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EYSENCK (1957a) has recently cogitated the relation between personality and drug response. He quotes McDougall (1929) as stating "I have observed in a number of cases that the marked extraverted personality is very susceptible to the influence of alcohol. The introvert, on the other hand, is much more resistant to alcohol". This is a remark capable of confirmation, for Eysenck (1953) has described at least two personality dimensions, each a continuum and each orthogonal to the other. These two dimensions were termed "Neuroticism-Normality" and "Extraversion-Introversion". A number of tests have been elaborated by Eysenck (1955, 1956, 1957b) for measuring such personality quantities.

Some of these tests were utilized by Bartholomew and Marley (1958) when scrutinizing a variety of somatic and personality variables that might affect response to methylpentynol ("Oblivon"). They noted that whereas a pronounced correlation existed between high neuroticism scores (as measured on the Maudsley Personality Inventory) and susceptibility to the drug, the only association between extraversion and susceptibility was a just statistically significant relation over the whole of that continuum as determined from the same questionnaire. Methylpentynol is a branched 6-carbon alcohol, and as the activity of an alcohol increases with the size of its molecule (Gaddum, 1956), one might have supposed that the results would have emphasized rather than contradicted McDougall's findings.

The relation between personality dimensions and conditioning ability has been explored by Eysenck (1955) and Franks (1954). Conditionability was discovered to be linked with introversion-extraversion (extraverts condition badly) but was unrelated to neuroticism.

It was decided to investigate the possibility that there might or might not be some association between conditioning (as measured by the eyelid response) and reaction to methylpentynol. In addition, and apart from the possibility

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of substantiating the thesis that susceptibility to the drug is not primarily related to the extraversion-introversion continuum, the opportunity would also present to assess the effect of methylpentynol on conditioning. If it acts as do other central nervous depressants (ethyl alcohol or amylobarbitone sodium) the effect of the drug should be to render the establishment and performance of conditioned responses more difficult. Previously it had been discovered that amylobarbitone sodium depresses, whereas dextroamphetamine sulphate facilitates the formation of conditioned reflexes (Franks and Laverty, 1955; Franks and Trouton, 1958).

METHODS

The conditioning procedure and apparatus have been described elsewhere (Franks, 1954, 1956) a special sound-proof conditioning laboratory having been constructed for the purpose (Franks, 1955).

The unconditioned stimulus was an air puff, and the conditioned stimulus a tone delivered through a pair of padded earphones. Two responses were recorded: the eyeblink and the psychogalvanic reflex (P.G.R.). A sequence of partial reinforcement was employed so that interspersed among 30 reinforced trials, consisting of an air puff paired with a tone, were 18 test trials (Acquisition trials) during which the tone alone was given. This was followed by 10 successive test trials (Extinction trials) in which, as before, the tone alone was presented. The procedure lasted approximately 25 minutes.

All stimuli were given and controlled electronically, the eyelid movements being measured by a photoelectric cell near the eye of the patient (Franks and Withers, 1955). This novel method of recording eyelid movements is particularly valuable when applied to mentally disturbed, sedated or otherwise abnormal subjects, since, unlike almost all other existing techniques, it is absolved from the cumbersome necessity of having electrodes or artificial eyelashes attached to the testee. On account of the lack of direct contact, many subjects remain unaware of the recording of their eyelid movements. A further refinement is that the small photoelectric cell is mounted on a pair of plain glass spectacles which move in sequence with the testee, who is consequently not constrained to keep his head rigidly still. The stimuli and responses were registered on a continuously recording inkwriting milliammeter.

The P.G.R. is a response which purports to assess sympathetic activity by measuring alterations in skin resistance when the subject perspires. It is an unsatisfactory index since the changes recorded depend upon a large number of variables, e.g. room temperature, humidity, atmospheric pressure, as well as the method of application of the electrodes. It was decided, therefore, to record the P.G.R. changes merely as events rather than attempt a quantitative evaluation of their magnitude. The technique employed was the Fere exsomatic method, a current of 14 microamps being passed through the subject (Franks, 1954). The electrodes, which should be dry, are placed on the thenar eminences of both hands.

Twenty-five subjects (9 males, 16 females) aged 19–54 years, in hospital for the treatment of neurotic or psychosomatic disorders, were prescribed 0·5 g. q.d.s. of methylpentynol for 5 days, a base-line of individual reaction being obtained by the immediate prior administration for the same period of an identical number of inert capsules. (The subjects had been weaned from all drugs at least 2–3 days before commencing the inert capsules.) During the 5 day regime of the latter, the Maudsley Personality Inventory was administered and

the initial control conditioning performed. It was imperative that these be done at a time when the individual was not in receipt of drugs, for as previously indicated, conditionability is modified by drugs affecting the central nervous system, and the ingestion of cerebral depressants (amylobarbitone sodium) is associated with an increase of extraversion as measured on the Guildford R scale (Franks and Laverty, 1955). The Maudsley Personality Inventory (adapted partly from the Guildford questionnaires) has been described elsewhere (Eysenck, 1957b; Franks, 1957) and is regarded as being a good measure of introversion-extraversion (a high score indicating extraversion) and of neuroticism. The subjects were finally conditioned on the fourth day of methylpentynol, the test-retest interval ranging from 6–10 days.

The clinical response to methylpentynol was graded into three, the unexpected and considerable incidence of toxic phenomena determining a classification—depending on the presence or absence of abnormal signs in the central nervous system—of nil, minimal, and maximal toxic categories (Marley and Bartholomew, 1958).

The prototypes of these clinical gradings will be briefly portrayed. A maximal toxic reaction (Clinical Grading 3) was deemed to be present if it included a majority of the following picture: dilated pupils reacting sluggishly to all stimuli, sustained nystagmus on conjugate lateral gaze, diplopia, ptosis, loss of tone in the lower facial musculature, dysarthria, and a fine tremor of the protruded tongue. A cerebellar type of ataxia might be found in the limbs or an admixture of this with posterior column type of ataxy and a positive Romberg's sign. Alterations in the mental state included mood disturbance and impairment of attention, concentration and abstract thought. A minimal toxic reaction (Clinical Grading 2) was epitomized by little more than nystagmus on conjugate lateral gaze, and slight unsteadiness of gait or drowsiness. Mood changes were also evident. The designation of nil toxicity (Clinical Grading 1) is self-explanatory.

Results

Conditioning and Personality

Only the eyeblink response will be considered since there was too much adaptation of the P.G.R. to the unconditioned stimulus for the latter to be regarded as a consistent measure of conditioning. A correlation of $-0{\cdot}21$ ($p>0{\cdot}05$) was noted between acquisition of the conditioned eyeblink response of the 25 subjects and their rating on the extraversion-introversion scale of the questionnaire. A correlation of $-0{\cdot}20$ ($p>0{\cdot}05$) was found between resistance to extinction and the rating on the extraversion-introversion scale. The correlations between conditioning and neuroticism were $-0{\cdot}048$ ($p>0{\cdot}05$) for the acquisition trial and $-0{\cdot}059$ ($p>0{\cdot}05$) for the extinction trial. (The raw extraversion and neuroticism scores had been corrected so that the two personality dimensions of extraversion-introversion and neuroticism-normality would be independent of one another.) These results, while not statistically significant, are consistent with the argument that conditionability is related to the introversion-extraversion dimension and not to neuroticism.

Susceptibility to Methylpentynol, Conditioning and Personality

The clinical gradings, personality ratings, and the results for the conditioning of the 25 subjects are depicted in Table I.

TABLE I

Relation Between Clinical Gradings of Susceptibility to Methylpentynol and Mean Extraversion Rating (E), Mean Neuroticism Rating (N), and Mean Number of Conditioned Eyeblink Responses

Clinical Grading	Number of Patients	E	N	Mean Number of Trials for Conditioning Eyeblink Response	
				Acquisition	Extinction
1	6	9·9	9·5	7·2	2·8
2	9	13·0	15·2	8·3	3·8
3	10	8·6	17·6	4·7	2·2

It is obvious that in this series susceptibility to methylpentynol is unrelated to the extraversion-introversion continuum but appears to be linked with high scores for neuroticism. The relation to conditioning is more obscure, and it might seem from ranking the mean scores for the number of trials required before the establishment of the conditioned eyeblink response that susceptibility to the drug is not associated with conditionability. On the other hand, if the drug dose-response curve is assumed to be steep, which is probable (the curve would be more likely to follow a geometric than an arithmetic progression) the mean acquisition scores of 8·3 and 7·2 for the eyeblink response could be regarded as coming from individuals at the lower end of the dose-response curve, whereas the mean acquisition score of 4·7 would be from subjects at the upper end of the dose-response curve, and the discrepancy in ranking for the minimally susceptible group would be unimportant. A case could therefore be advanced for an association between ease of conditioning and maximum susceptibility to methylpentynol, although no similar trend is apparent between the rate of extinction of the conditioned eyeblink response and susceptibility. It would be more realistic to assume, however, that no real relation has been demonstrated between eyeblink conditioning and liability to intoxication with the drug.

Depressant Effects of Methylpentynol on Conditioning and P.G.R.

The mean number of conditioned eyeblink responses for each subject prior to and during the regime on methylpentynol are shown in Table II.

TABLE II

The Mean Numbers of, and Standard Deviations of, Acquisition and Extinction Trials of Conditioned Eyeblink Responses Both Before and With Methylpentynol

	Acquisition Trials		Extinction Trials	
	Before Methyl-pentynol	With Methyl-pentynol	Before Methyl-pentynol	With Methyl-pentynol
Mean	5·6	6·3	2·1	2·6
S.D.	4·1	5·0	1·8	2·2

In order to evaluate the statistical significance of these results, a control group of similar subjects tested and retested after an equal interval without methylpentynol would be required. This information is not available, but data do exist for a group of 20 normal subjects retested after a time lapse of 14–21 days. The mean number of acquisition and extinction conditioned eyeblink responses for this normal control group are presented in Table III.

TABLE III

The Mean Number of, and Standard Deviations of, Acquisition and Extinction Trials of Conditioned Eyeblink Responses in a Control Group under Test-Retest Conditions

	Acquisition Trials		Extinction Trials	
	Test	Retest	Test	Retest
Mean	8·0	14·4	3·7	5·6
S.D.	5·3	6·4	1·4	1·6

The group of normal subjects, as expected, increase in eyeblink conditioning significantly from test to retest ($p<0·01$). The group receiving methylpentynol do not evince an increased conditioning score from test to retest conditioning ($p>0·05$). Although the two groups are not strictly comparable, the results suggest that methylpentynol reduces conditionability.

Although the P.G.R. data cannot be used as a measure of conditioning since there was often no response to the unconditioned stimulus, they can still be considered as indicators of sympathetic autonomic activity. The mean number of P.G.R. responses to the 18 acquisition test trials for the normal group and for that receiving methylpentynol were compared.

TABLE IV

The Mean Number of, and Standard Deviations of, P.G.R. Responses in a Group With and Without Methylpentynol, and in a Control Group from Test to Retest

	Methylpentynol Series (25 subjects)	
	Number of P.G.R. Responses Before Methylpentynol	Number of P.G.R. Responses With Methylpentynol
Mean	3·3	0·6
S.D.	1·5	0·6
	Control Series (20 subjects)	
	Number of P.G.R. Responses on Initial Testing	Number of P.G.R. Responses on Retest
Mean	2·5	3·0
S.D.	1·5	1·8

The mean number of P.G.R. responses is significantly reduced after methylpentynol ($p<0·05$) although no significant alteration in the mean number of P.G.R. responses occurred in the control group from test to retest, suggesting that methylpentynol has a depressant effect on sympathetic conditioning as measured by the psychogalvanic response ($p>0·05$). Examination of the case records confirms this: thus whereas in the control group, 11 of the 20 subjects gave P.G.R.s initially and 14 gave P.G.R.s on retest, in the group receiving methylpentynol, 14 of the 25 subjects gave P.G.R.s initially but only 3 on retest.

DISCUSSION

It was hoped in the present investigation to provide evidence that susceptibility to the higher alcohol methylpentynol bore no relation either to extraversion or conditioning. While this has proved correct up to a point, the correlation between extraversion and conditionability was not statistically significant, so that the protocol of this paper would be more suitably confined

to stating that liability to intoxication with methylpentynol and ability to condition seem to be unrelated factors. There was however a definite association between high neuroticism scores on the Maudsley Personality Inventory and susceptibility to the drug.

The results are interesting in that they are at variance with an observation of Pavlov's (Pavlov, 1927). Pavlov noted a difference in the behaviour of his dogs. Certain of the animals developed conditioned salivary responses with ease, which, once established, were retained for a long while. Other dogs developed positive conditioned responses with difficulty, and, once formed, they were easily disrupted and extinguished. Pavlov also noted that animals which conditioned well were resistant to bromides, whereas dogs of the same body weight but which conditioned with difficulty required only an eighth of this amount of bromide and reacted badly to anything in excess.

Methylpentynol possessed a depressant effect on conditioning ability, a finding in conformity with that of Hilgard and Marquis (1940) who noted that central nervous depressants (sodium bromide) retard the formation, and accelerate the rate of extinction of conditioned responses. Methylpentynol may act by blocking the formation of the central changes associated with conditioning, and also by interfering with the peripheral performance of these conditioned responses. A peripheral neuro-muscular blocking activity by this drug has been demonstrated in animals (Quilliam, 1955; Nicholls and Quilliam, 1956).

Summary

Twenty-five subjects were prescribed 0·5 g. q.d.s. of methylpentynol for 5 days preceded by a similar period on inert capsules.

During the period on inert capsules, the patient completed the Maudsley Personality Inventory and the control conditioned eyeblink and psychogalvanic responses were obtained. The final conditioned eyeblink and psychogalvanic responses were determined on the fourth day of the course of methylpentynol.

No relation was found between susceptibility to the drug and conditioning ability. Methylpentynol possessed a depressant effect on eyeblink conditioning.

There was no relation between susceptibility to methylpentynol and extraversion scores obtained from the Maudsley Personality Inventory, although there seemed a definite association between high neuroticism scores determined from the same questionnaire and susceptibility to the drug.

Methylpentynol has a depressant effect on sympathetic conditioning as measured by the psychogalvanic response.

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