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ACTIONS OF A MIXTURE OF AMPHETAMINE AND A BARBITURATE IN MAN

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The effects in man of a mixture of amphetamine and a barbiturate (15 mg of amphetamine sulphate and 300 mg of cyclobarbitone) and of each of the constituents separately were assessed on the performance of simple mental and motor tasks, on the pulse rate and on subjective reports. The mixture produced a pattern of effects which was different from that produced by either drug separately. It impaired the efficiency of the performance of tasks much less than did the barbiturate drug alone; it produced almost as big a rise in the pulse rate as did amphetamine alone; and it produced reports of feeling "elated" from many more subjects than did either drug separately, though there was no corresponding increase in reports of other feelings and sensations.

Amphetamine/barbiturate drug mixtures have been used in psychiatry for many years, especially in the treatment of agitated, anxious or depressed neurotic patients, and it seems that they continue to be fairly widely used even though many new drugs for treating psychiatric patients have been introduced. A number of such mixtures are available. Most contain dexamphetamine and amylobarbitone, usually in ratios of about 1:6.5 or 1:13 by weight, for example, Drinamyl (Smith, Kline & French) and Dexytal (Lilly) respectively. Why such mixtures might be especially effective does not seem to have been studied extensively. Barbiturate drugs and amphetamine have opposite effects on most responses both in man and in animals, and it has been suggested that, when the two types of drug are given in combination, their clinical effects can be "mutually corrective" in the sense that the advantages combine while the undesirable side-actions antagonize each other (Myerson, 1939).

Clinical reports (Myerson, 1939; Davidoff & Goodstone, 1942; Gottlieb & Coburn, 1944; Gottlieb, 1949; Grahn, 1950; Harris, 1953) suggest that amphetamine/barbiturate drug mixtures are probably used with three main kinds of object: (1) Where an amphetamine effect, that is, stimulation, is primarily desired, and the barbiturate drug is added to mitigate over-excitement, tachycardia or sleeplessness. (2) Where a barbiturate effect, that is, sedation, is primarily desired, and amphetamine is added to mitigate fatigue, drowsiness or inefficiency. The control of epilepsy is a further example of such a use. (3) Where what seems to be regarded as a special "mixture" effect is desired, that is, a more "balanced" and cheerful mood (Goodman & Gilman, 1955; Drill, 1958) and fewer side-effects than result from either

drug on its own. Effects on mood are particularly stressed in manufacturers' literature, and such effects are presumably also sought by the juvenile delinquents and others who are sometimes reported to take such drug mixtures.

Experiments with normal human volunteers suggest that amphetamine/barbiturate drug mixtures are apt to make subjects report feeling elated and sociable and that effects on the efficiency of performances are variable and probably largely depend on the nature of the task (Lanzetta, Wendt, Langham & Haefner, 1956 ; Laties, 1961). In neither the studies of Lanzetta *et al.* (1956) nor those of Laties (1961) were direct comparisons made with either drug separately, and it is therefore difficult to be sure how far the effects were due to the individual drugs or to a mixture of them. The findings of Nowlis & Nowlis (1956) suggest that with mixtures their subjects felt somewhat more expansive, elated and uninhibited than with amphetamine alone. In rats small doses of amphetamine and amylobarbitone, which on their own have little effect, when given in combination can markedly increase exploratory activity in a simple maze (Steinberg, Rushton & Tinson, 1961).

The purpose of the present investigation was to study the effects of amphetamine and of cyclobarbitone in single doses and of a mixture of these two drugs in the same doses on the performance of simple mental and motor tasks, on the pulse rate and on subjective reports in normal human subjects.

METHODS

The subjects were preclinical medical students in their fourth term, and the experiments were carried out in the course of practical classes in which the students learned simple ways of assessing in man effects of drugs acting on the central nervous system. Before the experiment it was explained that each subject would receive a tablet containing either amphetamine, or a barbiturate drug, or a mixture of the two, or lactose as a control ; the main effects of amphetamine and barbiturate drugs were described in general terms. Regarding the mixture, the subjects were told that " combinations of depressant and stimulant drugs are fairly widely used in medicine, but that such combinations had not been studied in previous practical classes."

Students worked in pairs, and each member of a pair acted in turn as subject and as observer for his partner. The experiments were carried out in cubicles, with one or two pairs of students and a demonstrator per cubicle. The general arrangements were similar to those described in previous papers (Wilson, Crockett, Exton-Smith & Steinberg, 1950 ; Paton & Steinberg, 1956).

The methods used to assess the effects of the drugs are described below. Detailed information about similar tests, including their re-test reliability, has been given elsewhere (Steinberg, 1954).

Arithmetic. The subject added sums of four 2-digit numbers as quickly as possible. The score was the number of sums added correctly in 2 min.

Tapping. Using the index finger of his preferred hand, the subject tapped a key as quickly as possible. The key was connected to a resettable counter. The score was the number of taps in 60 sec. The subject could not see the counter while tapping, but he was told his score after each trial.

Dotting. A modified McDougall/Schuster disc-dotting machine was used. It consisted of a disc on which was marked a spiral of irregularly placed brass dots. The disc rotated behind a window. Starting at the centre of the spiral, the subject hit as many dots as possible with a metal stylus which was connected to an electric counter. The task required accurate hand–eye co-ordination. The score was the number of hits during one complete

exposure of the spiral which took 2 min. As in the tapping test, the subject could not see the counter while working, but he was told his score after each trial.

Pulse rate. The pulse rate was taken for 30 sec.

Subjective effects. Record sheets were provided for each subject on which he was asked to describe in his own words his "feelings and sensations" and the times at which they occurred throughout the experiment. When the experiment was over the subjects were invited to state what they thought their tablet had contained. The methods used to analyse these various records are described later.

The tests of performance were always carried out in the order in which they have been listed, and the pulse rate was always taken immediately before the first performance test. A complete set of observations occupied about 6 min. Before the testing began the students were given a standard amount of practice on all the tests. Tablets were taken on a relatively empty stomach at about 1.30 p.m., and immediately afterwards the pulse was taken and the performance tests were carried out. Twenty min after taking his tablet each subject ate a light lunch. Forty min after taking the tablet, and every 20 min thereafter, the subject had his pulse taken and he repeated the performance tests; the last set of tests began 100 min after the tablet had been taken. At the end of the afternoon, after the results had been tabulated and the subjects had said what they thought their tablet had contained, they were told what it had actually contained.

Each of the following had been compounded in the form of single yellow tablets with a bitter flavour and was administered with a draught of water: amphetamine sulphate 15 mg, cyclobarbitone 300 mg, these two combined in a mixture, and lactose as control. The doses of amphetamine and cyclobarbitone had in previous experiments been found to produce reliable but not excessive effects on some at least of the reactions under investigation (Wilson *et al.*, 1950). The proportion of barbiturate was greater than that in most of the proprietary mixtures used in psychiatry, the more so because amphetamine sulphate is generally regarded as less potent than dexamphetamine which is commonly used in these mixtures. Cyclobarbitone was used in preference to amylobarbitone because its shorter duration of action was more suitable for class experiments; the recommended hypnotic doses, by weight, of these two drugs are often similar (Osol & Farrar, 1955).

RESULTS

The subjects were divided into four groups according to the content of their tablet. Results were computed separately for each of these groups and differences between the groups were evaluated statistically.

Tests of performance

For each test the average score made at each trial by each of the four groups was computed. The initial score was taken as "basal," that is, the score made at the trial immediately after the tablet had been swallowed when there was no reason to suppose that the drugs had as yet had any effect. The initial scores of the four groups of subjects did not differ significantly; the mean initial scores and the results of one-way analyses of variance are shown in Table 1. Scores made at subsequent trials were expressed as mean changes from these initial scores and will be referred to as "difference scores." At each trial the difference scores made by each group were compared with those made by each other group by means of "t" tests, and the results of these comparisons which yielded significant differences are summarized in Table 2. The number of subjects in the four groups were: amphetamine 12, cyclobarbitone 13, mixture 14, controls 15, except where otherwise stated.

TABLE 1

INITIAL SCORES IN THREE PERFORMANCE TESTS AND INITIAL PULSE RATES

These values were obtained from four groups of subjects before the drugs took effect. The initial scores of the four groups were compared for each test separately by means of one-way analyses of variance; the four groups were found to be well matched

	Arithmetic Sums correct		Tapping No. of taps		Dotting No. of hits		Pulse Beats/min	
Group	Mean	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.
Amphetamine	11·58	3·68	360·92	48·78	204·67	36·58	71·16	14·83
Cyclobarbitone	11·69	3·59	352·69	43·68	189·17	29·97	73·38	6·86
Mixture	12·14	2·66	347·79	37·24	173·77	35·95	75·42	11·33
Control	13·67	4·20	359·93	42·38	190·83	34·69	75·06	8·17
F	1·018		0·285		1·379		0·432	
df	3, 50		3, 50		3, 45		3, 50	
P>	0·05		0·05		0·05		0·05	

TABLE 2

STATISTICAL COMPARISON OF CHANGES IN PERFORMANCE AND IN PULSE RATE UNDER THE INFLUENCE OF DIFFERENT DRUGS, BY MEANS OF "t" TESTS

Changes were measured 40, 60, 80 and 100 min after taking drugs, as shown in Figs. 1 to 4. The table shows all values of "t" which were significant at the 0.05 level of probability or less; those with an asterisk just failed to reach that level of significance

		Min after taking drug			
Task and comparison	*df*	40	60	80	100
Arithmetic					
Amphetamine v. cyclobarbitone	23	2·16	2·74	2·70	NS
Mixture v. amphetamine	24	NS	2·60	2·74	NS
Tapping					
Cyclobarbitone v. control	26	3·56	3·40	2·56	2·76
Mixture v. cyclobarbitone	25	2·64	2·40	2·03*	2·93
Mixture v. amphetamine	24	NS	2·39	NS	NS
Dotting					
Cyclobarbitone v. control	22	3·31	3·23	2·75	2·19
Mixture v. control	23	2·69	2·01*	2·35	1·90*
Cyclobarbitone v. amphetamine	22	4·32	2·49	NS	NS
Pulse					
Amphetamine v. control	25	2·11	2·97	2·76	3·04
Mixture v. control	27	2·15	NS	2·42	3·13

Arithmetic. Fig. 1 shows that the performance of the controls remained virtually stable in successive trials and that the drugs produced relatively little change. The difference scores of the amphetamine group were, however, consistently higher than those of the controls, and the difference scores of the cyclobarbitone group were consistently lower than those of the controls; the difference scores of these two groups were in general significantly different from each other (Table 2). The scores of the mixture group lay between those of the cyclobarbitone and the control groups but did not differ significantly from either of them, though they were significantly lower than those of the amphetamine group 60 and 80 min after taking the tablets. Errors made in the arithmetic test were analysed in a similar way to the "sums correct" scores and the results showed similar trends, but the absolute values were too small to justify conclusions.

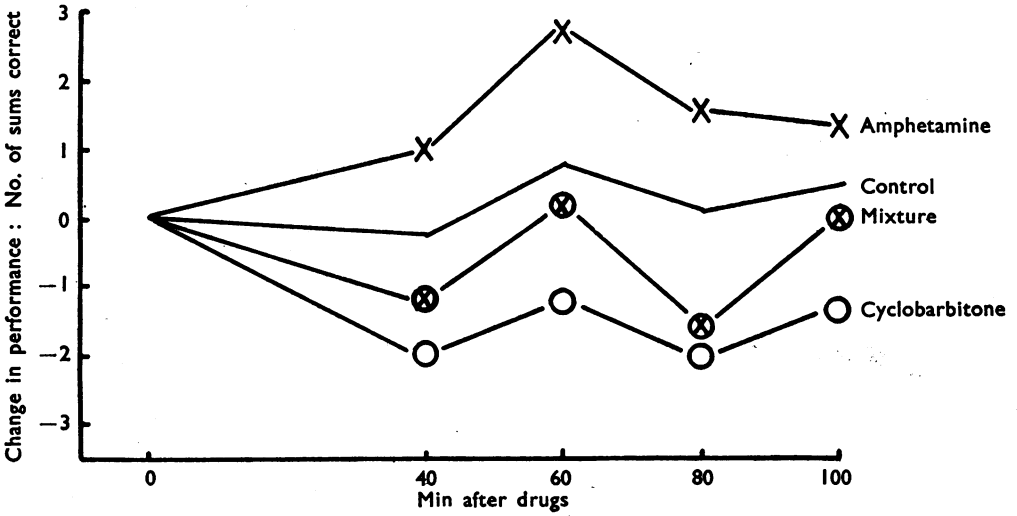

Fig. 1. Arithmetic test. The mean scores of four groups of subjects are expressed as differences from initial scores at 0 min after the drug. The groups received respectively amphetamine sulphate 15 mg, cyclobarbitone 300 mg, these two combined in a mixture and lactose as control. Each group repeated the test at 40, 60, 80 and 100 min after taking the drug, and positive scores mean that performance improved compared with initial scores.

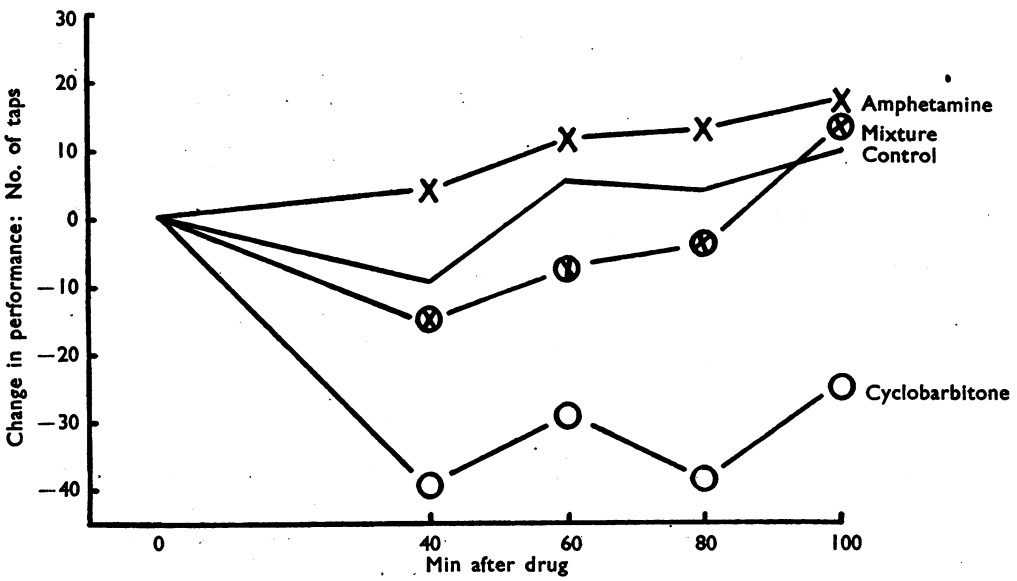

Fig. 2. Tapping. The mean scores of four groups of subjects as for Fig. 1.

Tapping. The effects of the drugs are shown in Fig. 2. The performance of the controls improved slightly in successive trials. The amphetamine group showed a similar trend; their improvement was throughout slightly greater than that of the controls, but at no time was the difference between the two groups statistically significant. Cyclobarbitone, on the other hand, markedly impaired performance,

and the net drop compared with the controls was of the order of 30 to 40 taps/min, which is about 10% of initial scores. The differences in mean change between the cyclobarbitone and control groups were significant at every trial. The scores of the mixture group, on the other hand, were indistinguishable from the scores of the controls; and like the control scores they were significantly different from the cyclobarbitone scores but not from the amphetamine scores. There were two inconsistencies: at 60 min the difference between mixture and amphetamine scores reached statistical significance, and at 80 min the difference between the mixture and cyclobarbitone did not. These inconsistencies were probably due to sample variances which were uncharacteristically small and large respectively.

Dotting. The performance of the controls (n=12) markedly improved in successive trials and, at the final trial, Fig. 3 shows that they made on average

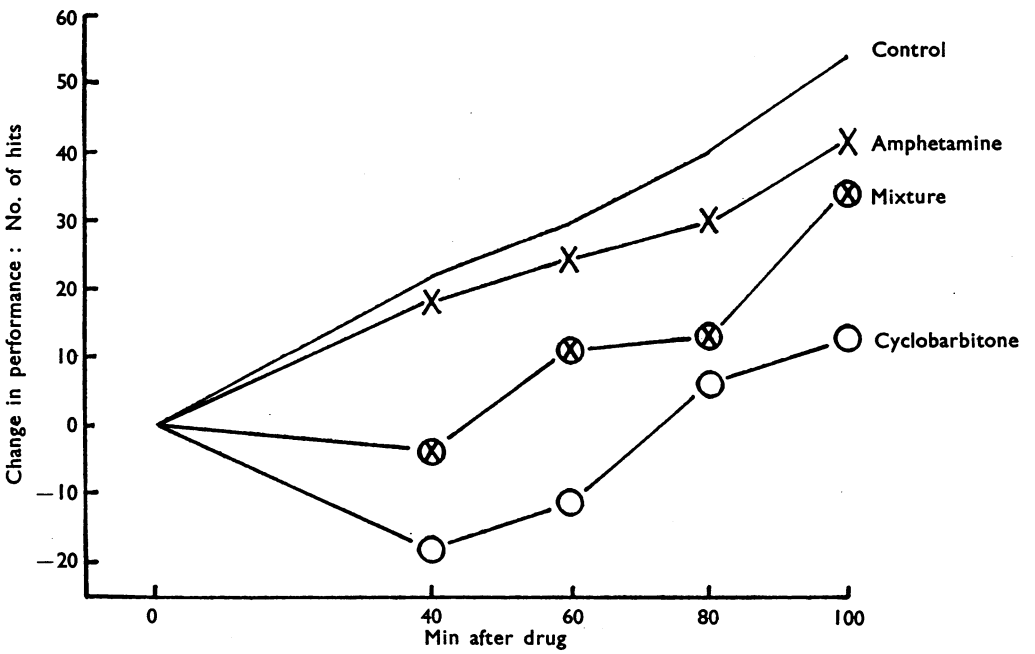

Fig. 3. Dotting. The mean scores of four groups of subjects as for Fig. 1.

53.59 more hits than at the first trial (t=5.45 ; *df* 11 ; $P<0.001$). The amphetamine group improved almost as much, and did not differ significantly from the control group at any time. The scores of the cyclobarbitone group (n=12), on the other hand, were throughout well below those of the control and amphetamine groups; the mean net drop in performance compared with the controls was of the order of 30 to 40 hits, which is about 20% of initial scores. The differences between the scores of these two groups were found to be statistically significant at every trial after the initial one. The scores of the mixture group (n=13) lay, once again, between those of the cyclobarbitone and the amphetamine groups, though because of the large variability they were significantly different from neither of them; the

mixture scores were, however, in general significantly lower than the control scores. Fig. 3 shows also that the slopes of the four curves from the 40 min trial onwards are relatively similar: the amount of improvement, from the 40 min trial to the final trial, did not differ significantly among the four groups of subjects ($F=0.121$; df 3, 45; $P>0.05$), that is, the drugs did not seem to affect the rate of learning this skill but only the level of performance.

Pulse

Pulse rates were expressed as the number of beats/min, and changes were computed and analysed in a similar way to the results of the performance tests, and are summarized in Table 2. The effects of the drugs are shown in Fig. 4. The pulse rate of the controls remained relatively stable throughout, and the rate

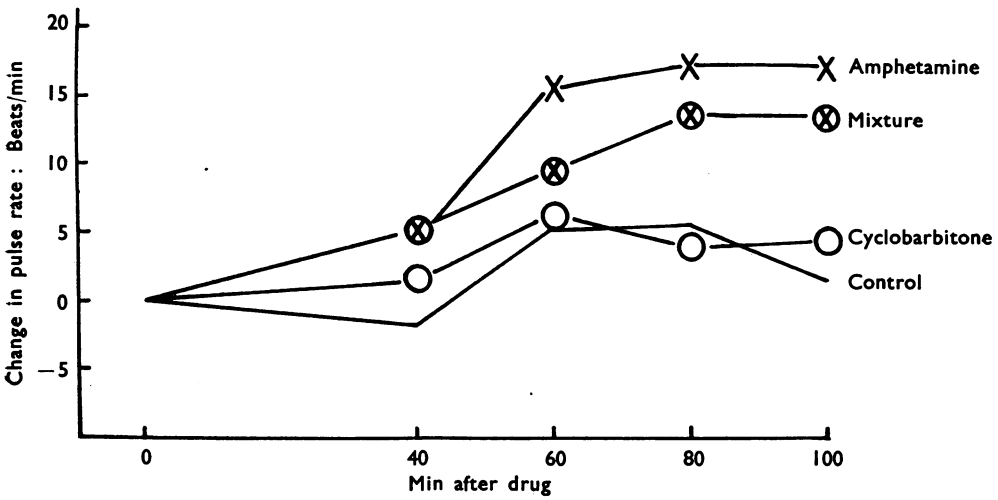

Fig. 4. Pulse rate. The mean pulse rates of four groups of subjects as for Fig. 1.

of the cyclobarbitone group was indistinguishable from that of the controls. In the amphetamine group, on the other hand, the pulse rate rose, and this rise was throughout significantly greater than the change in the controls. By 80 min after taking tablets, the mean rise in the amphetamine group was 17 beats/min, and this persisted to the end of the experiment. The rise in the pulse rate of the mixture group was slightly less than in the amphetamine group but was still in general significantly greater than that among the controls.

Subjective effects

The subjects' reports of "feelings and sensations" were scrutinized, and the contents were classified into the following five categories: (1) "elation" (described by words like elated, euphoric, lighthearted, happy); (2) "haziness" (hazy, muzzy, dazed, head swimming, dizzy); (3) "drowsiness" (drowsy, tired, sleepy, fatigued, lethargic, mentally slow); (4) "jitteriness" (jittery, excited, agitated); and (5) physical symptoms suggesting autonomic effects (tachycardia, awareness of heart beat, flushing, feeling hot or cold, sweating). The number

of subjects was counted who had reported any of the symptoms contained in each category, at any time during the experiment. No account was taken of the number of times a subject reported the same symptom, nor of the number of symptoms reported within each category.

Fig. 5 shows the results expressed as the percentage of subjects in each of the four groups reporting symptoms within the five categories. "Jitteriness" and

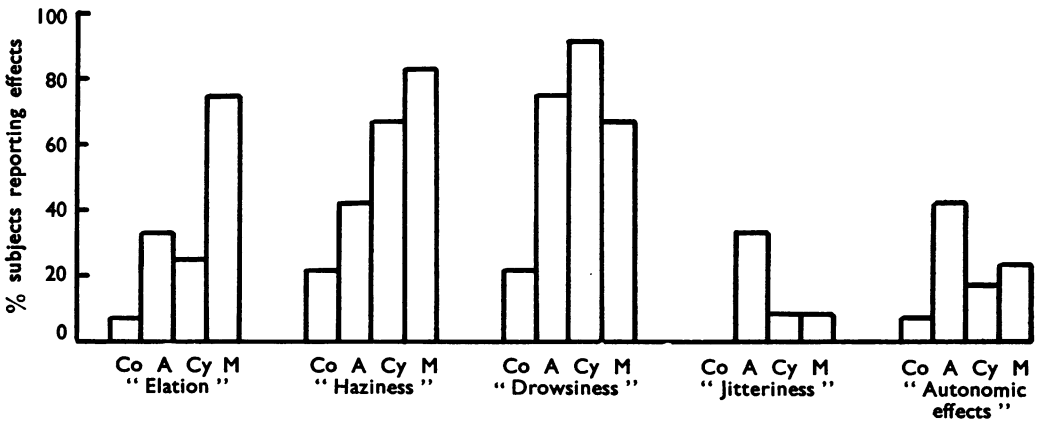

Fig. 5. Subjective effects. The incidence of "elation," "haziness," "drowsiness," "jitteriness" and "autonomic effects" was expressed as the percentage of subjects who reported such feelings and sensations in each of four groups. Co=control group; A=amphetamine group; Cy=cyclobarbitone group; M=mixture group.

"autonomic effects" were reported too rarely to allow analysis. The significance of the differences between the four groups of subjects in respect of "elation," "haziness" and "drowsiness" was calculated by means of χ^2 tests. χ^2 values with a chance probability greater than 0.05 were considered not significant. The number of subjects for whom records were available was amphetamine 12, cyclobarbitone 12, mixture 12 and controls 14. The analysis showed: (*a*) Subjects who had received *any* drug reported symptoms significantly more often than control subjects (for "elation" $\chi^2=4.70$; *df* 1; $P<0.05$; for "haziness" $\chi^2=5.68$; *df* 1; $P<0.025$; for "drowsiness" $\chi^2=11.30$; *df* 1; $P<0.001$). (*b*) The three drug groups did not differ significantly among each other in the frequency with which they reported symptoms of "haziness" or "drowsiness," but they did differ significantly in respect of "elation" ($\chi^2=6.97$; *df* 2; $P<0.05$); few subjects given amphetamine or cyclobarbitone separately reported "elation," but a very large proportion of mixture subjects—9 out of 12—did ($\chi^2=5.08$; *df* 1; $P<0.025$). (*c*) There was no significant association between the three symptom categories, and this suggests that whether a subject reported symptoms within any one category was relatively independent of whether he also reported symptoms in either of the other two categories.

Analysis of the subjects' statements as to which drug they thought they had been given produced the following results. Most subjects were able to discriminate accurately whether or not they had been given a drug at all—only 1 control subject thought he had been given a drug, and 4 subjects given drugs thought they were

controls—($\chi^2 = 30.01$; *df* 1 ; $P < 0.001$), and the accuracy of this discrimination was unaffected by the kind of drug they had been given ($\chi^2 = 2.27$; *df* 2 ; $P > 0.05$). However, only the subjects who had received cyclobarbitone were able to identify their particular drug correctly more often than would be expected by chance ($\chi^2 = 11.13$; *df* 1 ; $P < 0.005$); 10 out of 13 cyclobarbitone subjects were in fact correct.

DISCUSSION

In the present experiments the mixture made more subjects feel " elated " than either drug separately, without producing a corresponding increase in reports of other feelings and sensations ; it impaired the performance of simple mental and motor tasks much less than did cyclobarbitone alone ; but it produced almost as big a rise in the pulse rate as did amphetamine alone. These effects may appear to be somewhat complex and inconsistent, but they can be largely deduced from the effects of the two drugs when given separately.

On the performance of simple skills, barbiturate drugs and amphetamine usually have opposite effects: barbiturates tend to impair efficiency and amphetamine tends to improve it, though improvements are apt to be harder to demonstrate than impairments and may only occur under special conditions (Steinberg, 1959 ; Plotnikoff, Birzis, Mitoma, Otis, Weiss & Laties, 1960). In the present experiments, cyclobarbitone had the most marked effect on performance ; it made efficiency, as measured by scores in three tests, consistently worse. The amphetamine group, on the other hand, performed consistently better than the controls in tapping and arithmetic, but the differences were small and not statistically significant. This failure of amphetamine to produce a significant improvement was probably due to the fact that the tasks were short and carried out under competitive conditions. The students were therefore probably working near the limits of their capacity, and there is evidence which suggests that amphetamine does not then lead to much further improvement (Hauty & Payne, 1958 ; Smith & Beecher, 1959). Amphetamine had in fact been found to improve tapping performance in previous experiments which were similar except that subjects were not told their scores until after the experiment was over ; these subjects had less incentive to work hard and to obtain high scores, and so there was room for improvement when the drug was given (Steinberg, 1961). In the present investigation the results of the dotting task are also compatible with this interpretation. Subjects consistently reported dotting to be the most interesting of the three tasks and seemed to be trying hard to improve their own scores and to beat each other's scores in successive trials ; amphetamine produced no improvement at all on performance in this test. Nevertheless, when amphetamine and cyclobarbitone were given together as a mixture the effect in all three performance tests was intermediate between the results obtained with either drug separately ; in other words, although amphetamine produced little or no improvement of performance on its own, it was able to mitigate the deleterious effects of cyclobarbitone. This " hidden " effect of amphetamine was shown most clearly with tapping ; cyclobarbitone alone produced a marked impairment ; amphetamine alone produced but little improvement ; but when amphetamine was given together with cyclobarbitone it restored the performance practically to the

normal value. This effect of amphetamine was similar to what has often been demonstrated with fatigued subjects: with many kinds of prolonged task amphetamine has been shown to act not by increasing the absolute level of efficiency but by counteracting the deleterious effects of fatigue and so maintaining the normal level of performance for longer than was possible without the drug (see, for example, Mackworth, 1950; Payne & Moore, 1955; Kornetsky, Mirsky, Kessler & Dorff, 1959).

The pulse rate was increased by amphetamine, but was unaffected by cyclobarbitone. When both drugs were given together the rise due to amphetamine was not appreciably reduced. Thus, although the use of the mixture demonstrated a "hidden" effect of amphetamine on the performance tests, no comparable effect of cyclobarbitone on the pulse rate was found; the barbiturate drug was ineffective in counteracting the amphetamine-induced tachycardia, in spite of the relatively high proportion of cyclobarbitone in the mixture.

Reports of "feelings and sensations" were found to be very similar with amphetamine and cyclobarbitone. The changes induced by these two kinds of drug were similar both in quality and incidence; even "drowsiness" was reported almost equally often with amphetamine and cyclobarbitone. Hence one might expect that the mixture would produce as many or even more effects than the separate drugs. The most striking effect actually occurred with "elation" which was reported by a far greater proportion of subjects who had received the mixture than among subjects given single drugs. This suggests that, by giving a combination of amphetamine and a barbiturate drug, effects on mood can indeed sometimes be accentuated as has been observed clinically. On the other hand, it will be remembered that the mixture did not produce significantly more reports of "haziness," "drowsiness," "jitteriness" or of "autonomic effects" than either drug alone. It might be interesting to explore effects on feelings and sensations further by using methods of assessment which are more detailed and take account of the times of onset and the duration of effects.

The results of the present experiments therefore suggest that an amphetamine/barbiturate drug mixture can produce a pattern of effects which is different from that produced by either constituent separately. It is possible that by varying the experimental conditions, especially by using the two kinds of drug in different doses and proportions, further variations in the pattern of effects could be obtained, and that findings of this kind might be useful to clinicians.

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REFERENCES

DAVIDOFF, E. & GOODSTONE, G. L. (1942). The amphetamine-barbiturate therapy in psychiatric conditions. *Psychiat. Quart.*, **16**, 541–548.

DRILL, V. A. (1958). *Pharmacology in Medicine*, 2nd ed., p. 402. New York: McGraw Hill.

GOODMAN, L. S. & GILMAN, A. (1955). *The Pharmacologic Basis of Therapeutics*, p. 141. New York: MacMillan.

GOTTLIEB, J. S. (1949). The use of sodium amytal and benzedrine sulphate in the symptomatic treatment of depressions. *Dis. nerv. Syst.*, **10**, 50–52.

GOTTLIEB, J. S. & COBURN, F. E. (1944). Psychopharmacologic study of schizophrenia and depressions: intravenous administration of sodium amytal and amphetamine sulphate separately and in various combinations. *Arch. Neurol. Psychiat.*, **51**, 260–263.

GRAHN, H. V. (1950). The depressed patient; management with the aid of new medication. *Amer. Practitioner*, **1**, 795–797.

HARRIS, N. (1953). The modern treatment of depressive states. *Med. Press*, No. 5975, 460–463.

HAUTY, G. T. & PAYNE, R. B. (1958). Effects of analeptic and depressant drugs upon psychological behavior. *Amer. J. pub. Health*, **48**, 571–577.

KORNETSKY, C., MIRSKY, A. F., KESSLER, E. K. & DORFF, J. E. (1959). The effects of dextroamphetamine on behavioral deficits produced by sleep loss in humans. *J. Pharmacol. exp. Ther.*, **127**, 46–50.

LANZETTA, J. T., WENDT, G. R., LANGHAM, P. & HAEFNER, D. (1956). The effects of an "anxiety-reducing" medication on group behavior under threat. *J. abn. soc. Psychol.*, **52**, 103–108.

LATIES, V. G. (1961). Modification of affect, social behaviour and performance by sleep deprivation and drugs. *J. psychiat. Res.*, **1**, 12–25.

MACKWORTH, N. H. (1950). *Researches on the Measurement of Human Performance.* London: H.M.S.O.

MYERSON, A. (1939). The reciprocal pharmacologic effects of amphetamine (benzedrine) sulphate and the barbiturates. *New Engl. J. Med.*, **221**, 561–564.

NOWLIS, V. & NOWLIS, H. H. (1956). The description and analysis of mood. *Ann. N.Y. Acad. Sci.*, **65**, 345–355.

OSOL, A. & FARRAR, G. E. (1955). *United States Dispensatory*, 25th ed. U.S.A.: Lippincott.

PATON, W. D. M. & STEINBERG, H. (1956). A class experiment on ganglion block in human subjects. *Brit. med. J.*, ii, 622–626.

PAYNE, R. B. & MOORE, E. W. (1955). The effects of some analeptic and depressant drugs upon tracking behavior. *J. Pharmacol. exp. Ther.*, **115**, 480–484.

PLOTNIKOFF, N., BIRZIS, L., MITOMA, C., OTIS, L., WEISS, B. & LATIES, V. (1960). Drug enhancement of performance. *SRI Project No. SU-3024 for Psychol. Serv. Div. O.N.R.*, Washington, D.C.

SMITH, G. M. & BEECHER, H. K. (1959). Amphetamine sulphate and athletic performance. I. Objective effects. *J. Amer. med. Ass.*, **170**, 542–557.

STEINBERG, H. (1954). Selective effects of an anaesthetic drug on cognitive behaviour. *Quart. J. exp. Psychol.*, **6**, 170–180.

STEINBERG, H. (1959). Effects of drugs on performance and incentives. In LAURENCE, D. R. (ed.), *Quantitative Methods in Human Pharmacology and Therapeutics*, pp. 76–87. London: Pergamon.

STEINBERG, H. (1961). Methods and problems of measuring drug-induced changes in emotions and personality. *Rev. Psychol. Appliquée*, **11**, 361–372.

STEINBERG, H., RUSHTON, R. & TINSON, C. M. (1961). Modification of the effects of an amphetamine-barbiturate mixture by the past experience of rats. *Nature (Lond.)*, **192**, 533–535.

WILSON, A., CROCKETT, G. S., EXTON-SMITH, A. N. & STEINBERG, H. (1950). Clinical evaluation of effects of drugs on medical students as a teaching method. *Brit. med. J.*, ii, 484–488.