Brit. J. Pharmacol. (1957), 12, 479.

# THE EFFECT OF METHYLPENTYNOL IN MAN

BY

S. E. DICKER AND HANNAH STEINBERG
*From the Department of Pharmacology, University College London*

(RECEIVED JUNE 20, 1957)

Administration of methylpentynol to human subjects depressed their autonomic reactions to a difficult motor task and impaired their performance. Hexobarbitone affected neither autonomic reactions nor performance, though it impaired hand steadiness. The results suggest that the modes of action of methylpentynol and of hexobarbitone are different.

Methylpentynol has been shown to have a sedative action in animals (Margolin, Perlman, Villani and McGavack, 1951), and appears to reduce fear in rats (Dicker, Steinberg, and Watson, 1957). In human subjects the drug has been used to allay anxiety (Trotter, 1953 ; Bourne, 1954), without adversely affecting performance of motor tasks (Trotter, 1954). Furthermore, methylpentynol blocks transmission in autonomic ganglia (Quilliam, 1957).

As is well known, performance of difficult tasks can affect autonomic functions, indicated for example by pulse rate, blood flow, as well as respiration rate. Our purpose was to investigate whether methylpentynol would, first, alter such autonomic reactions to difficult tasks, secondly, affect performance in these tasks, and, thirdly, be distinguishable from a barbiturate in these respects.

## METHODS

The subjects were 20 male first-year medical students (average age 20) who were unfamiliar with the psychological and physiological techniques used. Each subject was seen once only and was given by mouth a drug or a control 25 min. before experiment. Drugs were dissolved in the same solvent ; the control consisted of the solvent alone. Eight subjects were seen between 12 and 1 p.m., the rest between 4 and 5 p.m., that is at least 3 hr. after a meal. Drugs and control were allocated at random and the subjects were not told which they received.

The subjects sat in an adjustable chair, and apparatus for recording pulse rate, blood flow and respiration was attached. Continuous recordings of these were taken ; skin temperature was measured at 60 sec. intervals. To measure respiration, an inflated rubber bag tied round the thorax of the subject was connected to a tambour and so to a pen recorder. Blood flow was measured by venous occlusion plethysmography (Lewis and Grant, 1925 ; Barcroft and Swan, 1953) from the left arm and skin temperature with a thermocouple (Paton and Steinberg, 1956) on the forehead.

The method for recording pulse rate was as follows: a small lever connected to a tambour (diameter 3 cm.) was fixed on the wrist over the radial artery. The oscillations of the lever were transmitted to a smaller tambour (diameter 8 mm.) supporting a mirror which reflected a light beam to a photo-transistor. Illumination of the photo-transistor produces a small electrical pulse which, amplified and converted into a pulse of a pre-set width (Fig. 1), is recorded by means of a pen on an Ediswan oscillograph. The electrical pulse activates a relay which short-circuits the input of the power amplifier, causing the pen to return to the base line. At the end of the pulse the relay opens, allowing the pen recorder to move again at a speed determined by the value of the time constant of C and R (Fig. 1). This movement continues until the arrival of the next pulse which terminates the discharge of C and brings the pen to base line. The amount of discharge is therefore proportional to the interval between successive pulses, that is to the pulse rate. This means, as can be seen from Fig. 4, that the faster the pulse beats, the smaller the amplitude of the tracing and conversely.

While these recordings were being made, the subjects were asked to carry out two psychological tests: a test of complex motor co-ordination and a hand steadiness test. The tests were given to different subjects in alternate orders. The whole experiment lasted about one hour.

The apparatus to test motor co-ordination was a modification of the Craik Triple Tester: it consists of a rotating horizontal drum round which is marked a spiral path of irregularly placed dots. The subject steers a wheel which guides a pointer on the drum. He is asked to drive the pointer over as many dots as possible, each "hit" being scored on an electric counter. The apparatus was used to assess the subject's performance and his "level of aspiration" (Eysenck and Himmelweit, 1946). Performance was the number of hits/trial of 45 sec. After each trial the subject was told his score and was asked to predict his performance in the next trial; the difference between score in the previous trial and prediction of the next performance was taken as the "level of aspiration." The subject made six trials separated by 1 min. intervals (see Steinberg, 1954).

In the hand steadiness test, the subject was asked to hold for two periods of 30 sec. a stylus (1.57 mm. diameter) in a hole of 3.175 mm. diameter without touching its side. The apparatus, a modification of the Whipple steadiness test (1914), is built in such a way that any contact of the stylus against the side of the hole is recorded on an electric counter at a rate of 20/sec. Hence the longer the contact the higher the score.

*Drugs.*—Methylpentynol was used in the form of "Oblivon" elixir (British Schering). The dose administered was 500 mg. in 8 ml. (Trotter, 1954). Hexobarbitone sodium (*B.P.*) was dissolved in the same solvent as methylpentynol, dose 150 mg. in 8 ml. This dose was chosen as the maximum which did not produce drowsiness. The solvent used for both hexobarbitone and control was flavoured to resemble "Oblivon" elixir and was supplied by the makers.

*Statistics.*—Changes in pulse rate and blood flow were expressed in percentages. Means are given with their standard errors. Chi-square and "Student's" *t* tests have been used. The Mann-Whitney U test (Mann and Whitney, 1947) was applied to results of psychological tests where the distributions were skewed.

## RESULTS

### *Autonomic Reactions*

*Preliminary Resting Period.*—At the beginning of the experiment, the subjects were asked to relax. All appeared restful and quiet, though the mean pulse rate of controls was higher than that of subjects with methylpentynol or hexobarbitone. During the period of 3 to 5 min. before the first psychological test, the mean pulse rate of controls was $76 \pm 1.2$/min. (7), that of subjects with methylpentynol $70 \pm 1.2$/min. (7), and with hexobarbitone $67 \pm 2.5$/min. (6). The differences between the control group and the groups with either drug were statistically significant, $t=3.141$, $P<0.01>0.001$ and $t=2.639$, $P<0.05>0.02$, respectively. Mean skin temperature was similar in the three groups: control $32.7 \pm 0.33°$, methylpentynol $31.1 \pm 0.39°$, and hexobarbitone $32.9 \pm 0.35°$. The tracings showed no difference in the rate of respiration.

*Experimental Period.*—While the tests were being explained both pulse rate and blood flow increased in control subjects. This is shown for the Triple Tester (Figs. 2 and 3).

During the actual performance of tests, pulse rate and blood flow increased markedly in controls and in subjects with hexobarbitone; the increases were especially striking during performances with the Triple Tester. By contrast, in subjects with methylpentynol pulse rate and blood flow remained practically unchanged (Figs. 2 and 3). During tests the respiration of controls became faster and shallower; in subjects with methylpentynol the respiration became markedly deeper, though its rate did not change noticeably (Fig. 4). Hexobarbitone did not seem to affect respiration. Skin temperature did not change appreciably in any group.

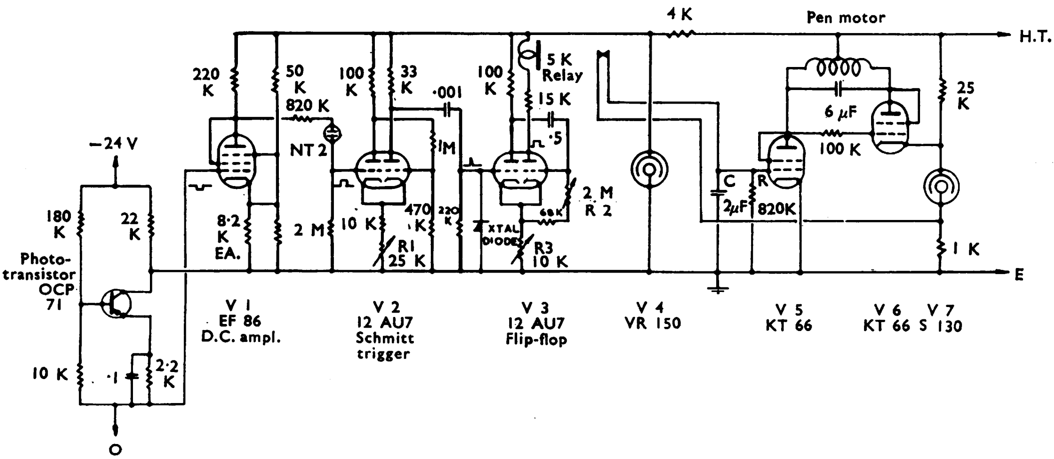


FIG. 1.—Diagram of the electronic circuit for the pulse rate recording device. When excited by a beam of light, the photo-transistor develops a negative voltage, which, amplified by $V_1$, is fed to a Schmidt trigger, $V_2$, built with a pre-set control, $R_1$. The output from the Schmidt trigger operates a "flip-flop," $V_3$, which produces a pulse; the width of the latter is pre-set by $R_2$. The purpose of $V_3$ is to ensure that the relay remains closed for sufficient time to allow the pen to return to base line. The voltage produced in the C/R network is amplified and fed to the pen recorder by means of a pair of power valves, $V_5$ and $V_6$.

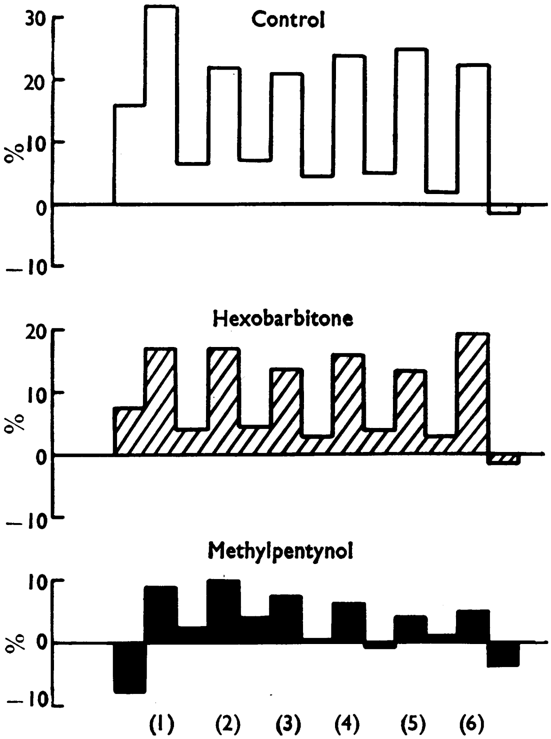


FIG. 2.—Changes in pulse rate (ordinate) during performance of Triple Tester, in control subjects and in those who had received hexobarbitone (150 mg.) or methylpentynol (500 mg.). The changes are expressed as % of resting levels. The numerals in parentheses show the order of the series of trials.

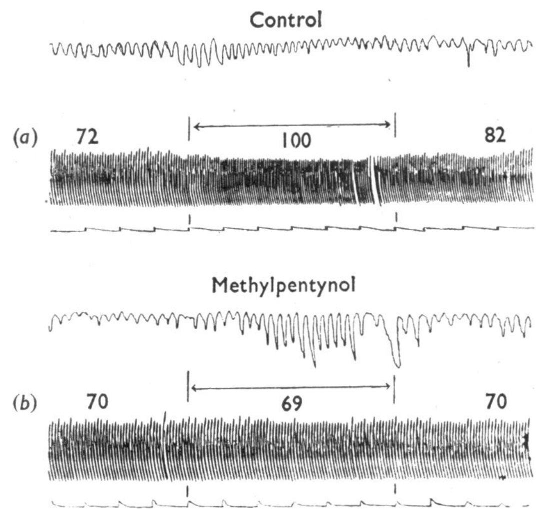


FIG. 4.—Respiration and pulse rate of (*a*) control subject and (*b*) a subject who had received methylpentynol before, during, and after a difficult test was performed. The test was carried out during the period between the vertical lines on each record. Upper trace, respiration; middle trace, pulse rate; lowest trace, time, 10 sec. The numerals give the pulse rate/min.

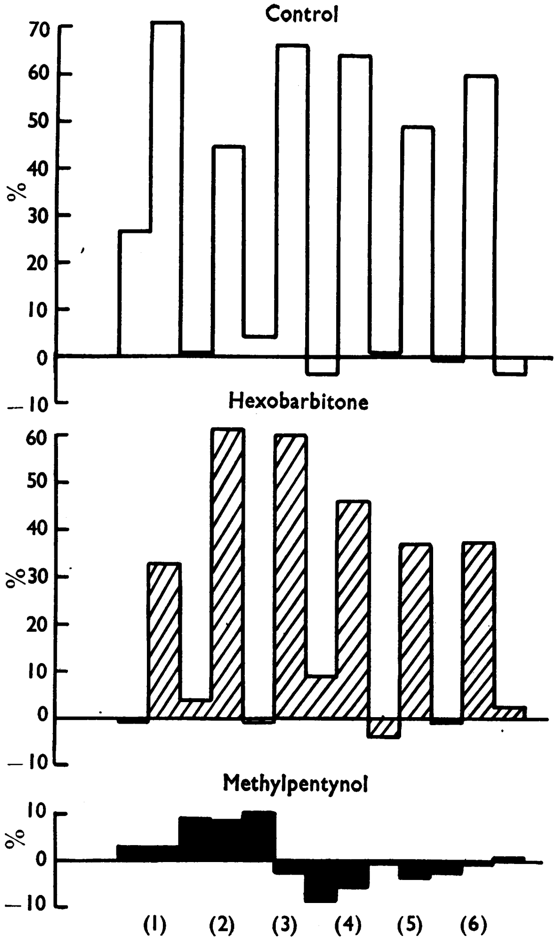


FIG. 3.—Changes in blood flow (ordinate) during performance on Triple Tester in control subjects and in those who had received hexobarbitone (150 mg.) or methylpentynol (500 mg.). Changes are expressed as % of resting level. The numerals in parentheses show the order of the series of trials.

### *Test Performances*

*Triple Tester.*—Performance improved with each trial in all three groups. The actual scores were, however, significantly lower in subjects with methylpentynol than in controls, $P=0.036$ (Fig. 5). Subjects with methylpentynol also had a lower "level of aspiration" than controls ($P=0.019$). Hexobarbitone did not affect performance or "level of aspiration" (Fig. 6).

*Steadiness Test.*—The performance of subjects with methylpentynol was similar to that of controls. The mean scores during 60 sec. were $195 \pm 53.3$ (6) and $193 \pm 74.7$ (5) respectively. Subjects with hexobarbitone, however, were nearly twice as unsteady. Their mean score was $377 \pm 33.6$ (6), ($t=2.390$, $P<0.05>0.02$).

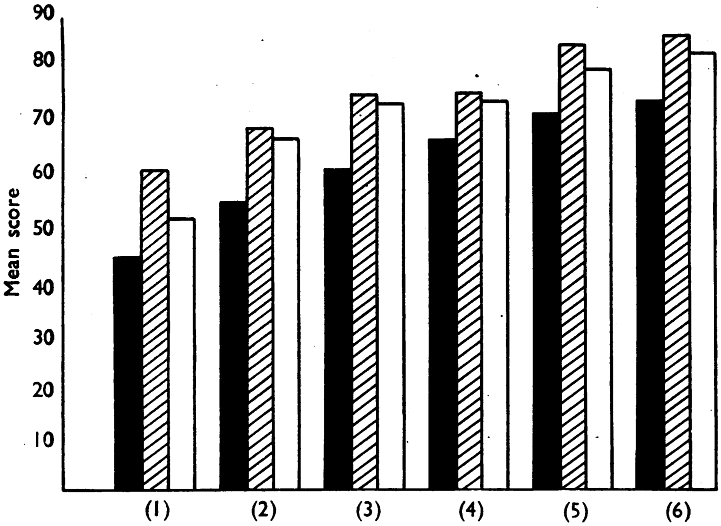


FIG. 5.—Performance on Triple Tester. Ordinates are the mean scores in 6 trials. Open columns, controls; cross-hatched columns, hexobarbitone (150 mg.); solid columns, methylpentynol (500 mg.). The numerals in parentheses show the order of the series of trials.

*Subjects' Sensations*

At the end of the experiment subjects were questioned about their sensations, and their answers were classified as (a) "tense," (b) "relaxed," (c) "drowsy" and (d) "normal." Table I shows that most subjects with methylpentynol felt "relaxed," while most controls felt "tense" ($P=0.04$).

TABLE I

DISTRIBUTION OF SUBJECTS' SENSATIONS

| | Methylpentynol | Control | Hexobarbitone |
|---|---|---|---|
| Tense .. | 1 | 5 | 0 |
| Relaxed .. | 5 | 1 | 3 |
| Drowsy .. | 1 | 2 | 3 |
| Normal .. | 1 | 1 | 3 |

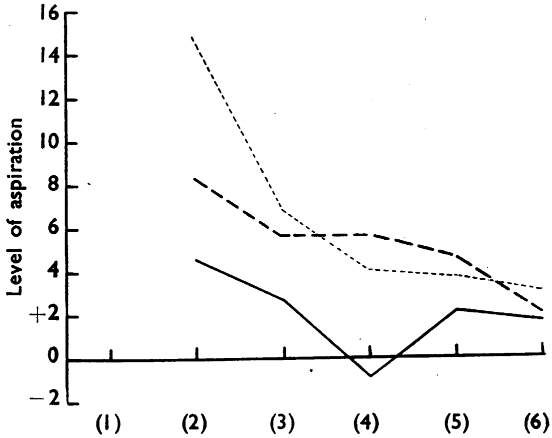


FIG. 6.—"Level of aspiration": difference between performance and prediction (ordinate). It will be noted that only 5 predictions could be made after the first trial. Full line, methylpentynol; dotted line, hexobarbitone; broken line, control. The numerals in parentheses show the order of the series of trials.

## DISCUSSION

On the assumption that increases in pulse rate and blood flow are reactions to the situation created by the performance or anticipation of difficult tests, it seems that methylpentynol is effective in that it decreases these autonomic responses. Subjects with methylpentynol, however, performed worse with the Triple Tester than controls and their "level of aspiration" was also lower; their prediction, however, was not more accurate. This suggests that, unlike controls, they were indifferent about their performance. This raises the question of whether people faced with a difficult task benefit from the damping down of their autonomic reactions by methylpentynol. According to experiments reviewed by Farber (1955) anxiety may sometimes help performance. It may be noted that both the performance and the "level of aspiration" of subjects with hexobarbitone were similar to those of the controls, though their autonomic reactions remained fully responsive. This does not seem to be entirely attributable to the relatively small dose of hexobarbitone administered, as, during the resting period, the pulse rate of subjects with hexobarbitone remained lower and during the hand steadiness test their performance was worse than that of controls.

It would appear from the present investigation that the effect of methylpentynol on human subjects faced with a difficult task is to make them perform worse and mind less.

We are grateful to British Schering Ltd. for generous supplies of "Oblivon" elixir, and to Miss Joan Nunn, Mr. P. E. Taylor, Mr. F. B. Ives and Mr. F. Ballhatchet for technical assistance. We want to express our thanks to Mr. G. L. Read, who designed and made the electronic apparatus for recording the pulse.

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