ENHANCEMENT OF HUMAN PERFORMANCE BY CAFFEINE AND THE AMPHETAMINES[1]

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I. INTRODUCTION

Although many drugs have been used in attempts to enhance performance, only caffeine and the amphetamines[2] have been studied extensively enough to permit a fairly thorough evaluation of their effects. Caffeine is more widely used, being found in coffee, tea, and cola drinks. Amphetamines, at least in this country, are legitimately available only on prescription but enjoy a wide illicit sale.

The main concern of this review is with the effects of these drugs on human performance. We shall also be concerned, however, with the question of whether, in the process of enhancing performance, effects are introduced that are considerably more dangerous and objectionable than low or impaired efficiency.

[1] The present paper is based, in part, on a review written by the authors for Stanford Research Institute Project No. SU-3024, Life Sciences Division, entitled "Drug Enhancement of Performance," and prepared under contract Nonr-2993 (00) for the Physiological Psychology Branch, Psychological Sciences Division, Office of Naval Research. The preparation of the present version was supported by grants MY-3229 and B-865 from the National Institutes of Health, U. S. Public Health Service.

[2] We shall discuss the following compounds under this rubric: Amphetamine Sulfate, U.S.P. [Benzedrine, *dl*-1-phenyl-2-amino-propane sulfate]; Dextroamphetamine Sulfate, U.S.P. [Dexedrine, *d*-1-phenyl-2-amino-propane sulfate]; Methamphetamine Hydrochloride, U.S.P. [Desoxyn, Pervitin, Syndrox, *d*-1-phenyl-2-methyl-amino-propane hydrochloride]. Unless otherwise noted, drugs were administered orally.

Many people believe that the ultimate cost of using drugs in this context far outweighs a temporary gain. This is an important problem which is indissolubly linked to enhancement of performance.

This review will consider the following types of performance: physical endurance and capacity, motor coordination and control, monitoring, learning, performance on verbal and arithmetic tasks, and subjective effects and judgment. Unless it seemed instructive to include them, inadequately controlled studies have been ignored. Discussions of other aspects of the actions of amphetamines as well as effects on performance may be found in reviews by Ivy and Krasno (58), Ivy and Goetzl (57), and Leake (70). A review by Landis (66) contains other information on coffee.

In our concluding remarks we shall discuss two main issues: 1) can caffeine and the amphetamines actually produce superior performance or do they merely restore to a normal level performance degraded by fatigue, boredom, or other influences?, and 2) are the performance-enhancing effects of these drugs counterbalanced by untoward effects to such an extent that their practical use is not feasible or desirable?

II. PHYSICAL ENDURANCE AND CAPACITY[3]

One reason for trying to find agents which enhance performance is that there are physical limitations on how long or how efficiently an individual can continue to perform a task requiring a high rate of energy output. The decline in the capacity to continue such a task or to perform other tasks is what most often is meant by fatigue.

A. Laboratory studies

Although many studies of caffeine were conducted in German laboratories toward the end of the nineteenth century, Rivers and Webber (93) are acknowledged to be the first investigators interested in enhancement of performance to have recognized the necessity for suitable controls, particularly the inclusion of placebo sessions. These authors studied their own performance on a Mosso ergograph (pulling a weight with a finger), under the influence of either caffeine citrate or the inactive agent. The subject was not told which of the two he had been given. A dose of 500 mg of caffeine citrate produced consistent increases in work output.

Foltz *et al.* (30) first worked their four subjects to exhaustion on a bicycle ergometer. Then, after a 10-minute rest, the subjects worked to exhaustion again. Caffeine sodium benzoate (500 mg) given i.v. during the rest period significantly increased work output during the second work period when compared to control injections. In a similar study, Foltz *et al.* (31) compared amphetamine (10 to 15 mg), methamphetamine (5 mg), caffeine sodium benzoate (500 mg), and placebo. The drugs were administered i.v. between 30 seconds and 30 minutes before the first work period. Amphetamine had no detectable

[3] The effects on physical fitness and athletic performance of various pharmacological and nutritive agents have been subjects of three other reviews (12, 49, 75).

effect on work output, methamphetamine produced a substantial effect, and caffeine fell somewhere in between. The large effect of methamphetamine and the small effect of amphetamine, in comparable dosages, is a curious one, for on other tasks, the effects of these two agents are quite similar. However, only two subjects were given amphetamine compared to four with the other drugs, so that the apparent difference could be the fault of sampling error.

These investigators also examined the effects of these agents on the performance of 23 untrained subjects (32). For this experiment, the subject, loaded with a knapsack equal to one-third his body weight, stepped up and down a 16-inch step every 3 seconds. He continued until he could no longer maintain this rate. After a rest, he again worked to exhaustion. On each experimental day a subject worked 3 periods. One hour before the first work period, the subjects took oral doses of amphetamine (10 mg), caffeine sodium benzoate (500 mg), or placebo. No significant differences among treatments emerged. However, the subjects improved so steeply with practice that a true drug effect may have been difficult to discern.

Alles and Feigen found that an oral dose of 10 mg of amphetamine kept performance on a Mosso ergograph from declining (2). Only a higher dose (20 mg) seemed to produce any increase in work capacity above the initial level. Caffeine, in doses up to 400 mg, produced a much less marked effect. Doses of 10 to 15 mg of amphetamine and 10 mg of methamphetamine produced increases in performance on both bicycle and hand ergometers in a well-controlled study by Cuthbertson and Knox (21). Knoefel (63) carried out a study with a bicycle ergometer in which he compared amphetamine, methamphetamine, and the dextro-isomers of both. He reported an increase in work output with 10 mg of methamphetamine and more activity from the dextro-isomer than from the racemic form. Lehmann *et al.* (71) made repeated studies on three subjects who rode a bicycle ergometer to exhaustion. They found the time to exhaustion was prolonged by 5, 10, or 15 mg of methamphetamine compared to placebo trials. Eighteen subjects in a study by Bujas and Petz (13) tried to maintain an 8.5-kg load as a test of static work. A dose of 15 mg of amphetamine 90 minutes before testing produced a statistically significant increase in static endurance compared to the placebo (206 *versus* 186 seconds).

These studies suggest that both caffeine and the amphetamines prolong the amount of time during which an individual can perform physically exhausting work. They also contain occasional hints that these drugs may raise the level of performance above the base line level. Such a small total number of subjects was involved, however, that these results cannot be classed as definitive.

B. Military field studies

Reports during World War II that the Germans were using methamphetamine to prolong endurance in their soldiers prompted the Allied Nations to study the effectiveness of this type of drug in the field. The most extensive series of experiments was conducted under the supervision of Seashore and Ivy (97). In all but two of the studies the subjects were soldiers, and attempts were made to mimic

actual military conditions as closely as possible. Four drug treatments were compared: caffeine sodium benzoate (450 mg); amphetamine sulfate (10 mg); methamphetamine hydrochloride (5 mg); and lactose placebo. The drugs were administered orally in identical capsules.

In the first study, the subjects participated in an all-day, 18- to 20-mile hike followed by guard duty from 6:00 P.M. to 3:00 or 4:30 A.M. Then testing started and lasted 1.5 hours. A first capsule of the drug was given at 6:00 P.M. and a second capsule of the same drug at midnight. The other studies involved training marches with full pack, driving a truck 18 to 20 hours per day, operating a tank for 5 hours per day, performing in hot-moist and hot-dry environments, and marching or operating a tank in the desert. The drugs generally were superior to the placebo in their effects on both subjective symptoms (*e.g.*, sleepiness) and motor tests (*e.g.*, motor coordination), but the effects on the former were more pronounced.

Somerville (103) also fatigued his subjects before testing. In one of his studies, two groups of 50 subjects each marched for 17 hours. One hour before the end of the march, one group received tablets containing 15 mg of amphetamine. The other group received an inert substance. At the end of the march, the subjects were evaluated on an obstacle course and in rifle marksmanship. No differences in the performance of these tasks appeared. In a second study, the subjects underwent a military exercise lasting 56 hours that included both day and night marches. During the last 22 hours, one group took a total of 30 mg of amphetamine, one a total of 35 mg of amphetamine, and the third received only lactose. While differences in the accuracy of rifle firing and times for covering the obstacle course were small, the latter were significantly shorter under the influence of the drug. A third experiment used officers taking part in a War Staff course. These were divided into three groups. One group received 20 mg of amphetamine on two occasions during the experiment; one received lactose; and one received nothing. The subjects had to complete, over a period of 72 hours, a program consisting of 9 exercises in staff duties. During the first 42 hours they did not sleep. The drug did not prevent sleep or improve performance.

Cuthbertson and Knox (21) performed two studies in the field. One involved the effects of 15 mg of methamphetamine on the performance of an 18-mile route march after 24 hours without sleep. No difference was found between the drug-treated and control groups on total time to cover the course. However, a few more of the men given control medication fell out of the march than the men given methamphetamine (7/28 *versus* 3/27). Two companies of infantry served in the second experiment, which lasted 2 days. On the first day, they marched 23 miles, then received 10 or 15 mg of amphetamine or a control capsule before going to sleep. On the second day, they marched 20 miles and "skirmished" with the "enemy" after which the drugs were given. They then "attacked." The amphetamine group slept less well, but was less fatigued in the morning. Seventy percent of the men given drug and 23% of the men given placebo thought the pills helpful. No "hangover" difference was apparent. A mimeographed report by Winfield (111) discusses the administration of amphetamine to RAF bomber

crews on prolonged missions. Winfield's survey demonstrated fewer complaints of fatigue after amphetamine than after placebos.

C. Athletic performance

The most thorough study of the effects of drugs on athletic performance was performed by Smith and Beecher (100).[4] Although 6 experiments were performed, the one in which they were able to impose the most rigid controls and experimental design was the first. The subjects were 15 college swimmers. Each swam his preferred event twice on each of 12 consecutive experimental days. The second swim began 15 minutes after the end of the first. On 4 of the 12 days, each subject received a dose of amphetamine sulfate equal to 14 mg/70 kg body weight; on 4 other days he received a control medication; and on the other 4 days he received a dose of secobarbital equal to 100 mg/70 kg. The interval between the medication and the swim was 2 or 3 hours for amphetamine and 55 minutes for secobarbital. These intervals apparently were based on preliminary studies. The same dose levels were used in the other experiments. The 12 experimental days were grouped into 6 competitive days (3 men per group) and 6 individual days. The events included the 100-yard butterfly, the 100-yard freestyle, the 200-yard freestyle, the 200-yard breaststroke, and the 200-yard backstroke. On the first swim, 14 out of the 15 subjects swam faster with amphetamine than with the placebo. The difference was statistically significant for both the absolute magnitude of the difference and the percentage improvement, which came to a mean of 1.16%. While such a change is small, one must remember, as the authors pointed out, that athletes may practice and train for months to produce such an improvement. (One percent of a 4-minute mile is 2.4 seconds—the difference between fame and oblivion.) On the second swim, only the 100-yard events were improved by amphetamine. When the subjects swam in competition, the drug tended to produce a smaller effect. Secobarbital impaired performance.

Nine track men served as subjects in experiment 2. Three ran 600 yards; 3 ran 1,000 yards, and 3 ran 1 mile. They ran in competitive groups of 3. Eight of the 9 subjects ran faster with amphetamine than with the placebo. The results of experiments 3 and 4, with track events and a marathon run, respectively, were in the same direction. Combining these three studies gave a statistically significant difference in favor of the drug.

Thirteen collegiate weight-throwers and shot-putters took part in experiment 5. Nine threw the 35-lb. weight; four put the 16-lb. shot. Both maximum and mean distances thrown were increased with amphetamine. Maximum distance scores improved 4.36%, while mean distance scores improved 4.39%.

In experiment 6, 16 swimmers each swam 6 times, 3 with amphetamine, 3 with a placebo. This time, the subjects were promised a steak dinner if they equalled or excelled their median competition time for the last 3 meets of the season. Despite the increase in speed evoked by this device, 11 of the 16 subjects

[4] A critique of these studies by Pierson (90a) has been adequately rebutted by Cochran, Smith, and Beecher (19a).

swam faster with amphetamine than with placebo, and the difference was statistically significant when the times for the 100-yard and the 200-yard events were combined.

Karpovich (60) studied running on a treadmill, swimming, and various track events. Neither 10 mg of amphetamine given 1 hour before testing nor 20 mg given 30 minutes before testing led to any improvement in performance. However, Karpovich might have detected improvement if, like Smith and Beecher, he had allowed at least 2 hours to elapse before testing in order to measure the peak effects of the drug [*cf.* Eysenck *et al.* (27) and Franks and Trouton (33)]. Haldi and Wynn (39) also failed to detect any effects on athletic performance. They studied 12 subjects, none of whom was an expert swimmer. Ninety minutes before a swim of 100 yards, the subjects ingested either placebo, 100 mg of metrazol, 5 mg of amphetamine, or 250 mg of caffeine. No drug effects could be found. However, not only was the dose rather small compared to that used by Smith and Beecher, but the use of subjects who were not trained swimmers probably introduced considerably more variability.

There is little doubt, then, that amphetamine can produce a significant enhancement of athletic performance, even in events in which, like putting the shot, one cannot see where endurance or fatigue would play a major role. These conclusions are not negated either by the Karpovich experiment or by the Haldi and Wynn experiment because of the difference in time since administration in the first case and the use of a lower dose and untrained swimmers in the second.

III. MOTOR COORDINATION AND CONTROL

This section deals with studies encompassing a wide range of tasks. They have been brought together because these tasks call mainly for relatively fine motor adjustments instead of gross muscular effort and endurance. Unfortunately, much of the evidence presented in this section is variable and contradictory, and few consistencies emerge. This situation is partly attributable to the neglect in many experiments of the crucial role played by slight variations in method. Small differences among the methods used to assess what is assumed to be a common underlying process, for example, reaction time, can lead to substantial differences in sensitivity to drug effects. In the reaction time study by Carpenter discussed below (16), for instance, the detection of an effect of caffeine depended on the brightness of the visual stimulus. Moreover, it also depended on dose level. The interaction of performance parameters and dose level is rarely assessed. Most of the investigations reported in this section employed one arbitrarily selected set of performance parameters, one dose level of the drug, and a single time of testing after drug. Without information about the interactions of these variables, the conclusions that we present must be regarded, for the most part, as provisional.

These conclusions may be listed as follows: 1) Caffeine has little or no effect on reaction time, whereas amphetamine seems to lower it, especially in fatigued subjects. 2) Caffeine impairs hand steadiness, whereas amphetamine seems to improve it. 3) Caffeine has equivocal effects on coordination, and amphetamine improves such performance, especially the more complex ones. 4) Both caffeine

and amphetamine can, to some extent, counteract decrement of motor performance produced by alcohol.

The individual studies are discussed below.

A. Reaction time

The effects of caffeine on reaction time are in dispute. Cheney (18, 19) found discriminative reaction time to a series of lights reduced by 4% after coffee (1 cup) and 8% after caffeine (180 mg, 2 hours before the test). The number of incorrect responses also was reduced. Unfortunately, the description of the experiment implies that every subject received the treatments in the same order—a procedure which makes it difficult to interpret these findings. Horst and Jenkins (55) reported a decrease in simple reaction time after the ingestion of 3 or 4 mg of caffeine/kg, as did Gilliland and Nelson (34) after either coffee alone or coffee plus added caffeine. Unfortunately, the use of coffee does not permit a precise statement of the amount of caffeine ingested. Moreover, the data with caffeine are then confounded with a mode of administration that contributes unique effects of its own unless the appropriate controls are included.

Lengthened reaction time after caffeine was reported by Hollingworth (52), Schilling (96), and Hawk (47). The last author had his subjects drink from 2 to 6 cups of coffee per day and found, when coffee drinking was terminated at the end of several weeks, that reaction time rose. This might have been the result of withdrawal, but the report is of only abstract length and not enough details are available to make a more definite statement. Schilling used an auditory reaction time task and administered 300 mg of alkaloidal caffeine 15 minutes before a 35-minute period during which reaction time was sampled every 5 or 10 minutes. While the author claimed an increase in reaction time after caffeine relative to placebo, our statistical analysis of his raw data gives a $t = 1.3$, which is not significant. Also, as shown by Hollingworth (52) and others, 50 minutes is probably too short a latency for peak drug effects to appear when caffeine is taken orally.

The most thorough study on caffeine was done a half century ago by Hollingworth (52). The care with which he devised appropriate controls has rarely been exceeded in contemporary research. Hollingworth found a dose-related effect on reaction time; smaller amounts of alkaloidal caffeine (60 to 240 mg) produced longer reaction times than placebo. Actually, Hollingworth says, the initial effect of the drug is a "briskness" which leads to false reactions, and the retardation in reaction time possibly follows because the subject becomes wary. Higher doses (300 to 360 mg) decreased reaction time within 2 hours. Hollingworth thought that the retardation seen with smaller doses was overcome by the extreme stimulation associated with these higher doses.

No differences between control medications and caffeine appeared in the reaction time studies of Thornton *et al.* (106), Adler *et al.* (1), and Seashore and Ivy (97). Lehmann and Csank (72) could demonstrate no shortening of simple reaction time after 600 to 900 mg of caffeine citrate. Thus, one is led to the

conclusion that caffeine, in ordinary doses, has little effect (or at least an inconsistent effect) on either simple or complex reaction time.

There also appears to be little effect of caffeine on the increase in reaction time produced by certain doses of alcohol. In a well-designed study, Carpenter (16) administered alcohol in doses of 0, 0.4, and 0.8 ml/kg to 9 subjects. Fifteen minutes were allowed for drinking. Capsules containing placebo, 1.47 mg caffeine/kg, or 2.94 mg caffeine/kg were ingested at the beginning of the drinking period. The first reaction time test (11 trials) began 30 minutes after ingestion of capsules. Subsequent tests followed every 10 minutes until 80 minutes post-ingestion. The reaction time apparatus presented a visual stimulus of either low or high intensity, and the subject responded by pressing a button. Alcohol increased reaction time in proportion to dose level. Caffeine had no over-all effect on reaction time. It did, however, increase the difference produced by variation in stimulus intensity. The data also suggest that caffeine lowered reaction time at the higher doses of alcohol when the high-intensity stimulus was used. The interactions shown in these results emphasize how much information is lost when experimenters arbitrarily select single values of performance parameters and drug dosages.

The effects of amphetamine are somewhat more consistent. Adler *et al.* (1) found a decrease in discriminative reaction time after 10 mg of *d*-amphetamine, even at a simulated altitude of 18,000 feet. Thornton *et al.* (106) found a small, not significant decrease in reaction time after amphetamine, but their experiment involved only 3 subjects. Lehmann and Csank (72) produced a marked shortening of simple reaction time after rather high doses (12.5 to 15 mg) of *d*-amphetamine. Goldstein *et al.* (35) observed no effect. They administered 10 mg of *d*-amphetamine 60 minutes before tests of both simple and discriminative reaction time. However, their results are confounded with a large practice-effect. The negative results of Rasch *et al.* (91) after 20 mg of amphetamine could also be due to confounding with a practice-effect, but their description of the experiment is too unclear for one to be sure. The above studies used non-fatigued subjects. From them we would conclude that amphetamine tends to reduce reaction time. This effect was also seen in fatigued subjects. Kornetsky *et al.* (65) found that 15 mg of *d*-amphetamine administered 90 minutes before testing eliminated the increase in discriminative reaction time engendered by 68 hours without sleep. Seashore and Ivy (97), also using fatigued subjects, found a significant decrease in discriminative reaction time following the administration of 10 mg of amphetamine or 5 mg of methamphetamine. The subjects had been awake for 24 hours at the time of testing. Tyler (109) reported that the deterioration in reaction time which occurred after 60 hours of sleep-loss was counteracted by amphetamine. The only study that showed no effect on the reaction time of fatigued subjects was the one by Cuthbertson and Knox (21). Thus, most of these studies indicate that reaction time lengthened by fatigue can be restored with amphetamine. Again, it must be underscored that differences in method probably contribute a great deal to the inconsistencies in the data.

B. Steadiness

Caffeine seems to impair the ability to maintain the arm in one position without tremor, while amphetamines seem to improve such ability slightly. Hollingworth (52) required the subjects to hold a metal stylus in a hole without touching the sides. He observed a pronounced unsteadiness that reached its peak about 3 to 4 hours after the administration of 360 mg of caffeine. Other investigators have confirmed these results. Thus, Hull (56) found increased tremor after 300 mg of caffeine citrate. Steadiness was also impaired after 300 mg of caffeine sodium benzoate (106), or after a cup of coffee (34). Adler *et al.* (1) found increased hand tremor after 420 mg of caffeine sodium benzoate. Switzer (104, 105) reported a 41 % increase in hand tremor 4 hours after 300 mg of caffeine citrate, and Lehmann and Csank (72) noted a significant decrease in steadiness after 600 to 900 mg of caffeine citrate. Only Seashore and Ivy (97) reported no effect on steadiness, but their subjects were fatigued, and this may account for the difference.

Although they found no effect in fatigued subjects on the hole-and-stylus steadiness test with 10 mg of amphetamine or 5 mg of methamphetamine, Seashore and Ivy (97) detected a significant improvement from these agents on arm-hand tremor and sway. They measured tremor and sway by having the subject hold a small ball attached to horizontal and vertical threads which operated ratchet mechanisms to give counts of movements in 4 directions. Postural sway, with the subject standing erect, also decreased after amphetamine and methamphetamine. Another study on fatigued subjects reported an improvement in steadiness and body sway after amphetamine (109). In non-fatigued subjects, *d*-amphetamine had no effect on body sway (28). A dose of 10 mg was followed 4.5 hours later by a dose of 5 mg. Thirty minutes later body sway was measured.

Both Thornton *et al.* (106) and Adler *et al.* (1) found with the stylus-hole method that amphetamine improved steadiness. Thornton *et al.* gave 20 mg of amphetamine, while Adler *et al.* obtained their results with 10 mg of amphetamine or 10 mg of *d*-amphetamine, both at ground level and at a simulated altitude of 18,000 feet. Methamphetamine (5 mg) had little effect under the latter conditions. Balloch *et al.* (5) found no effect from either 10 or 20 mg of *d*-amphetamine, nor did Goldstein *et al.* (35) after 10 mg of *d*-amphetamine.

Hauty (40) attempted to separate two components of hand steadiness in order to see whether they were differentially susceptible to drugs; these were high frequency, low amplitude tremor, and low frequency, high amplitude compensatory movements—what could be called "drift." The apparatus consisted of a stylus and a series of holes varying in size. The drug treatments consisted of 5 mg of *d*-amphetamine, 10 mg of *d*-amphetamine, 100 mg of secobarbital, 200 mg of secobarbital, placebo, and a no-drug control group. The results showed a significant difference between drugs when the smaller apertures were used; there was essentially no difference among drugs with the larger apertures. At the small ones, both doses of secobarbital tended to reduce tremor while both doses of

d-amphetamine tended to increase it. Only the increase relative to the no-drug group was statistically significant, however; the placebo group, interestingly enough, also demonstrated increased tremor. This is a useful and informative study because it explored both performance and pharmacological parameters to give us a notion of how they interact. It suggests, too, that the discrepancies among the various studies dealing with amphetamine may be due in part to the apparatus used to measure steadiness.

Newman and Newman (82) studied the effect of *d*-amphetamine and caffeine on disturbances of equilibrium and steadiness induced by alcohol. Sixty-six subjects ingested doses of ethyl alcohol equivalent to approximately 0.18 g/kg body weight in a concentration of 20%. This dose was repeated at intervals of 20 minutes through the experiment. When drugs were given, they were taken by mouth 45 minutes before the experiment. The doses were 15 mg of *d*-amphetamine and 300 mg of caffeine. The criteria used were balancing on one foot with eyes closed; hand steadiness; electroencephalogram (EEG); critical flicker frequency. Results were given in terms of the blood alcohol concentration at which "failure" occurred. The drugs had no effect on this concentration. Unfortunately, the authors seem to have given each subject the same order of treatments: alcohol first, alcohol plus *d*-amphetamine second, and alcohol plus caffeine third. This makes it difficult to interpret the data.

C. Coordination

The study of the complex muscular adjustments involved in performing skilled motor tasks is important in assessing the effects of a drug not only for intrinsic empirical value, but because the effects on such tasks may tell a great deal about how a drug acts. In this section, we shall discuss coordination tasks that range in complexity all the way from tapping a finger or a stylus to tracking a moving target.

Hollingworth (52), Horst *et al.* (53, 54), Thornton *et al.* (106), and Lehmann and Csank (72) observed an increased rate of tapping after caffeine. Neither Adler *et al.* (1) nor Flory and Gilbert (29) could find any effect of caffeine on tapping rate, while Gilliland and Nelson (34) claimed a slight increase. The effect of caffeine on this particular response is, therefore, equivocal, probably because the effect depends upon the specific technique employed to measure tapping rate, *e.g.*, whether the subject uses a stylus or his finger, whether he strikes alternate targets or a single one, *etc.* The same may be said about the effects of amphetamine. Thus, Adler *et al.* (1) produced no significant change in tapping rate with amphetamine, *d*-amphetamine, or methamphetamine nor did Balloch *et al.* (5) with *d*-amphetamine. No rise in the rate of working a thumb-operated manual counter followed a dose of 10 mg *d*-amphetamine in a study by Goldstein *et al.* (35). On the other hand, Simonson and Enzer (99) reported a rise with amphetamine but did not indicate the dose used. Lehmann and Csank (72) also noted an increased rate with *d*-amphetamine.

Hollingworth (52) also used a more complex test of coordination in which the subject had to insert a stylus successively into each of three holes. Here 60 or

120 mg of caffeine produced a slight decrease in the time required to complete the task; 180 or 240 mg seemed to produce an increase, and 360 mg seemed to produce a slight initial increase followed by a decrease. A similar task was employed in the study by Goldstein *et al.* (35). A dose of 10 mg of *d*-amphetamine did not change the rate at which subjects simultaneously touched, with a pair of rods, two pairs of disks. An interesting attempt to observe natural repetitive, coordinated movement was made by Golla *et al.* (37). They reported that 20 mg of amphetamine increased the speed of walking across a room and writing one's signature. This experiment, unfortunately, did not incorporate the controls necessary for a clear interpretation of the data. For example, the observer was aware of the drug that had been given.

One type of coordination task requires subjects to follow a moving target or to compensate for movement of a target; this is the skill called tracking. Horst *et al.* (53, 54) required their subjects to strike a pendulum at such a time and with such a force that it fell within a designated area. Caffeine impaired this performance by a considerable amount in doses of 3 to 4 mg/kg when the drug was given every day. Performance remained impaired for a few days after the caffeine regimen had ceased. A decrease in pursuit rotor performance (following a moving target on a turntable with a stylus) that occurred at simulated altitudes of 18,000 feet could be counteracted by amphetamines (1). *d*-Amphetamine, in fact, even with low oxygen pressure, improved performance beyond ground level control scores. Eysenck *et al.* (27) also employed the pursuit rotor. A dose of 10 mg of *d*-amphetamine administered 250 minutes beforehand produced a considerable increase in time-on-target score relative to placebo. An equivalent dose given 75 minutes beforehand produced a significantly smaller enhancement. This latency difference confirms Smith and Beecher's data (100).

One of the tests given fatigued subjects in the Seashore and Ivy (97) experiment required them to keep in level flight a model airplane that continually drifted off-course. All drugs used (caffeine sodium benzoate, 450 mg; amphetamine sulfate, 10 mg; methamphetamine, 5 mg) improved performance relative to the control agent, with the amphetamines proving somewhat more effective than caffeine. Newman (81) used the same task in two experiments. In the first, he compared a placebo and 10 mg of amphetamine given 1 hour before the start of a 1-hour run. No difference due to drug was found. Unfortunately, every subject underwent the same order of treatment: first placebo, then amphetamine. In the second study, the subjects were first deprived of sleep for 36 hours. After a 1-hour control run, they were all given 10 mg of amphetamine and, after a 1-hour test, worked again for 1 hour. Performance after drug was considerably better than pre-drug performance. But, in the absence of suitable controls—the author's failure to consider the effects of order of events—his conclusion that amphetamine produces effects on this task only in fatigued subjects must be regarded as questionable.

Using a simulated automobile driving device, Graf (38) gave his subjects a series of tests every 2 hours, starting at 6:00 P.M. and continuing until noon of the following day. Within each series, several road speeds were tested. The drug

preparations (6 mg of methamphetamine or 200 mg of caffeine) were administered at 1:00 A.M. Data were given for only one subject, and show a maximal effect 3 hours after administration, with methamphetamine producing both a greater and more prolonged action than the caffeine.

A combination of 10 mg of amphetamine and 100 mg of secobarbital sodium has been assessed by Laties (69) in a group performance situation (4 men per group) employing both sleep-deprived and non-sleep-deprived college men. The sleep deprivation period lasted approximately 36 hours. This combination of drugs significantly enhanced performance on both of the tasks employed. These required the subjects to work together in order to succeed. In one, the subjects tried to roll a ball up an inclined spiral plane that was mounted on a movable platform gripped by all four subjects. In the other, the subjects held a frame to which was attached an irregularly bent wire that they attempted to move through a small stationary ring. Performance on an individual task, a one-man version of the group ring-and-wire task, was also improved by the combination of drugs, making it less likely that factors peculiar to the group situation were responsible for its effectiveness.

The data available on coordination allow one to draw the provisional conclusion that the amphetamines can improve this kind of performance, with positive results more likely to appear when the task is complex rather than simple.

There are also reports in the literature of attempts with amphetamine or caffeine to combat the motor deterioration produced by sufficiently high doses of alcohol. Rutenfranz and Jansen (94) studied the effects of ethyl alcohol in doses of 0.5 g/kg and 1.0 g/kg in 2 subjects working on a task which simulated automobile driving. The performance decrement produced by the lower dose of alcohol was only partly counteracted by 200 mg of caffeine, but completely counteracted by 9 mg of methamphetamine. Such a dose of methamphetamine, however, could only partly counteract the decrement produced by the high dose of alcohol, an amount equal to about 6 ounces of 100-proof whiskey.

IV. MONITORING

As more and more human functions are appropriated by mechanical and electronic devices, more and more human activity shifts from detailed physical manipulation of the environment to making merely simple responses to the data conveyed by the device. The class of behavior that subsumes this sort of activity is called monitoring—a term coined by the British.

The number of experiments that have studied drugs in this context is relatively small. But a fairly definitive answer can be given, thanks to a brilliant series of studies carried out at the USAF School of Aviation Medicine at Randolph Field. These studies were aimed at the problems of performance decrement in prolonged monitoring tasks that also included a skill factor. The inclusion of a skill factor makes the task less pure as a monitoring task, but the experimental design and the variables studied make it more reasonable to call these experiments on monitoring rather than experiments on skill. Payne and Hauty (85) and Hauty and Payne (43) already have reviewed some aspects of this work. The task these

investigators chose as their tool was devised by Loucks in World War II for aviation cadet selection (Melton, 76). Called the USAF SAM Multidimensional Pursuit Test, it is based on an airplane-type cockpit in which a subject monitors a display of 4 dials. The dial pointers drift randomly from the null position. The subject's task is to restore the pointers to the null position and maintain them there concurrently by appropriate movements of a joy stick, rudder pedals, and throttle lever. The subjects in these studies were young airmen in basic training. The experimental procedure involved a training period of 50 minutes during which most subjects attained a stable level of proficiency (so that the skill factor did not enter into later performance), a 10-minute rest period for the introduction of drugs and other experimental treatments, and a final work period of several hours. During this final period most subjects showed a progressive decline in the amount of time that the 4 pointers were kept concurrently at the null position. [Sample performance curves are given in Payne and Hauty (85).]

In their first study [Payne and Hauty (84)] the investigators administered 5 treatments before a final work period of 4 hours. These were: no drug, lactose placebo, 5 mg of *d*-amphetamine, 20 mg of a caffeine derivative, and 0.65 mg of scopolamine plus 50 mg of diphenhydramine. *d*-Amphetamine completely arrested the usual decline in performance level with time; in fact, it raised performance above the level reached at the end of the 50-minute practice period. The caffeine compound also reduced performance decrement significantly, but not as strikingly as the *d*-amphetamine. The scopolamine-diphenhydramine combination significantly impaired performance.

A second experiment (41) was designed to investigate the single and joint effects of drugs, cues to pointer position, and statements about the length of the work period. The drug treatments comprised no drug; placebo; 5 mg of *d*-amphetamine; a slow-release dose (spread over 4 hours) of 6.3 mg of *d*-amphetamine sulfate; caffeine derivative (dose not specified); a combination of 5 mg of *d*-amphetamine, 50 mg of diphenhydramine, and 0.65 mg scopolamine; and 50 mg of diphenhydramine plus 0.65 mg of scopolamine. One-third of the subjects were given an auditory signal when all the pointers were at null; one-third were given a visual signal; and one-third had to rely on the usual method—visual scanning of the instrument panel. Half the subjects were told that they would perform for 4 hours, then be given a break. The other half were told that they would perform for 7 hours. All subjects worked for 7 hours, with a 15-minute rest at the end of 4 hours. The shorter goal proximity (4 hours *versus* 7 hours) resulted in better performance, even after the break at the end of 4 hours. An added auditory signal was more effective than an added visual signal, and both were better than the usual procedure.

The results with drugs were independent of the effects of additional cues. *d*-Amphetamine counteracted the usual decline in performance for the full 7 hours. It did not matter whether the drug was given as a single 5-mg capsule or in a sustained-release form. The caffeine derivative was also more effective than the placebo, but failed to match the amphetamine effect. Both of the mixtures containing scopolamine and diphenhydramine led to significantly worse per-

formances than did the placebo, but the mixture that contained the *d*-amphetamine excelled the one lacking it. An interesting difference between the effects of the stimulant drugs and the effects of the added cues appeared in this experiment. While both raised the level of performance, they did so in different ways. The supplementary signals merely raised performance without affecting the rate at which it fell off with time. The effective drugs, however, particularly *d*-amphetamine, exerted their effect mainly by arresting the decline in proficiency as the session progressed.

The same sort of dissociation between the effects of psychological and pharmacological treatments appeared in the third study of the series (86). Here the authors assessed the effects of two psychological variables. One was the amount of information conveyed about the position of the dial pointers—what the authors called "directive feedback." Three levels were imposed: no supplementary cue, a single peripheral visual signal (a light) whenever any one of the instrument settings drifted from null; and, one supplementary signal per instrument (4 lights). The other psychological variable was called motivation. Three levels were specified. In one, the control level, no supplementary cues about the effectiveness of performance were supplied. In the second, the score on the previous block of trials was posted on a pegboard. In the third, the subject could follow his progress through the entire session *via* the pegboard. The following medications were administered: a mixture of 0.65 mg of scopolamine plus 50 mg of diphenhydramine; 5 mg of *d*-amphetamine; placebo. A no-drug group was also included.

The more precise the supplementary cues and the more thorough the information about the subject's performance, the greater was his score. The drug treatments also produced the expected results: *d*-amphetamine arrested the decline in performance with time, while the scopolamine-diphenhydramine mixture accelerated it. As in the previous experiment, the *d*-amphetamine and the psychological variables exerted their benefits in different ways, the latter raising performance level but not changing its rate of decline, the drug counteracting the fall in performance. It is important to note how these results conflict with the hypothesis (see discussion) that amphetamine exerts its benefits simply by making the individual more highly motivated toward the task.

Payne *et al.* (87) then investigated the effect of *d*-amphetamine at various dose levels as a function of the time of administration during the work period. They studied dose levels of 1.25, 2.5, 5.0, 7.5, and 12.5 mg of *d*-amphetamine. These were given at the start, 1 hour after the start, or 2 hours after the start of a 4-hour work period. Two values were computed: the effect on loss of proficiency and the effect on gain of proficiency. Loss was taken to be the difference between the score on the last 30 minutes of the pre-experimental period (the practice period) and the score during the second hour after the drug. A plot of loss *versus* dose gave a quadratic function which showed that the larger the dose, the lower the loss, the asymptote of the function being reached at about 10 mg, and with no loss in performance detectable with doses of 7.5 mg and above. The interaction of dose and delay was not significant. A specified dose had the

same effect no matter when during the session it was given. Gain was taken to be the difference between the score during the last 30 minutes prior to the drug, and the score during the second hour after the drug. Here, too, the function was quadratic. Beyond about 5 mg, no significant additional benefit was realized; there is even a hint in the data of a decrement in gain beyond 10 mg.

The success of *d*-amphetamine in counteracting performance decrement led Payne and Moore (88) to examine other stimulant and depressant drugs with the same technique. We shall discuss only the stimulants, which were: *d*-amphetamine, 5 mg; mephentermine, 25 mg; and pipradrol, 2 mg. The work period lasted 4 hours. *d*-Amphetamine produced the best performance followed closely by mephentermine. Pipradrol at this dose level maintained performance at the pre-drug level throughout the session but did not generate the considerable increase in proficiency attained with *d*-amphetamine and mephentermine.

Up to this point, the work periods had not exceeded 7 hours. What effects would amphetamine produce on performance prolonged considerably beyond this length? Does it engender a "let down" when it wears off? Can it restore performance degraded by extremely prolonged work? An attempt to answer these questions was made by running 24 subjects for 30 continuous hours each (44). The subjects were divided into 3 drug treatment groups, the first medication being given after 1 hour of practice: 1) placebo at 9:00 A.M., day 1, and at 9:00 A.M., day 2; 2) placebo at 9:00 A.M., day 1, and 5 mg of *d*-amphetamine at 9:00 A.M., day 2; 3) 5 mg of *d*-amphetamine at 9:00 A.M., day 1, and 5 mg of *d*-amphetamine at 9:00 A.M., day 2. All three groups performed at a fairly steady level from 9:00 A.M. to midnight on day 1. No decline in proficiency was observed during this time. What was responsible for this lack of decrement is not known. At any rate, the first dose of amphetamine produced no effect on performance. From midnight to 6:00 A.M., performance fell steeply. During this time many subjects had hallucinations. (One saw a little man in a sombrero, holding an umbrella overhead, in the rpm dial. Another believed himself "at the end of a long dark alley walled by tall buildings leaning at crazy angles.") The occurrence of hallucinations was not related to whether amphetamine had been administered the morning before. At 6:00 A.M., performance picked up again, but fluctuated erratically, and, in the group given a placebo at 9:00 A.M. this second morning, never reached the proficiency levels of the day before. In the groups given *d*-amphetamine at 9:00 A.M. of day 2, performance returned to the high initial level of the preceding day after about an hour. No evidence of "let down" in the groups receiving amphetamine was detectable.

Two other experiments by the Randolph Field group (45, 46) were devoted to the study of oxygen deficiency. The first experiment (45) was designed to answer 3 questions. 1) Do normal oxygen levels restore work proficiency lowered by prolonged work and oxygen impoverishment? 2) Are the effects of amphetamine and normal air restoration additive in restoring proficiency? 3) How well will amphetamine sustain performance during interpolated periods of low oxygen? The subjects, after the usual training period, worked for 2 hours on the Multidimensional Pursuit Test while breathing a nitrogen-oxygen mixture containing

12% oxygen. They then worked for 1 hour while breathing 21% (normal) oxygen, and, finally, 1 hour again on 12% oxygen. The drug treatments—lactose placebo or 5 mg of *d*-amphetamine—were given before the start of the 4-hour work period. Amphetamine completely mitigated the marked decrement produced by oxygen impoverishment, except for the first hour after administration when the drug was in the process of being absorbed. Restoration of normal air only slightly arrested the decline in performance of the placebo group and had almost no effect on the amphetamine group. When put back on 12% oxygen, both groups declined at about the same rate.

In the second experiment (46) these investigators studied three different concentrations of oxygen: 60, 21, and 12%. Again, a lactose placebo or 5 mg of *d*-amphetamine was given before the start of a 4-hour work period. *d*-Amphetamine improved performance about equally at all concentrations of oxygen. Performance was better with 60% oxygen than with 21% oxygen, while performance with 12% oxygen was worse than with 21% oxygen. Only the latter difference, however, was statistically significant.

The conclusions that emerge from this series of studies are these: Amphetamine can sustain a high level of proficiency, can restore performance that has deteriorated, can counteract the effects of oxygen deficiency, and contributes something above and beyond what can be achieved with good human engineering design and high motivation. Moreover, it does this without engendering objectionable side-effects.

These conclusions are buttressed by other studies of monitoring. One of the earliest workers to study this type of behavior was Mackworth (73), whose well-known monograph contains an experiment in which his Clock Test was used to assess the action of amphetamine on vigilance. The apparatus consisted of a black pointer which rotated in steps. The pointer moved to a new position once every second, one hundred steps completing one revolution. No scale markings or reference points appeared on the white background. At irregular intervals—12 times in a 30-minute period—the pointer moved two steps instead of one. The subject's task was to press a key whenever a double-step occurred. After the first 30 minutes on this task the incidence of missed signals tended to rise from about 15% to about 25%, where it remained for the rest of the usual 2-hour test period. A dose of 10 mg of amphetamine 1 hour before the session completely counteracted the rise in missed signals. Moreover, the subjects responded more quickly when under drug to the signals they did detect. According to Holland's analysis of the vigilance situation (51), the probable effect of amphetamine in Mackworth's situation was a rise in the frequency of observing responses—looking more frequently at the clock. In tasks such as this, and in those used in the Randolph Field studies, the crucial element in proficiency is steady scanning of the "target." When scanning rate goes down [as it certainly did between midnight and 6:00 A.M. in the 30-hour study of Hauty and Payne (44), since the subjects began to snatch short periods of sleep] then performance falls too.

Two studies on a monitoring type of task by Kornetsky *et al.* (65) and Townsend and Mirsky (107) illustrate how, with some tasks, amphetamine may produce differential effects depending on whether this behavior is normal or impaired.

The task was built around an endless-belt filmstrip that presents letters to the subject at the rate of 1 per second. In one version of the task, the subject is required to press a response key whenever the letter *x* appears. In another version, he presses the key only when the *x* follows an *a*. Townsend and Mirsky (107) could detect no effects of 5 or 15 mg of *d*-amphetamine on either version when the drug was given 135 minutes beforehand. But Kornetsky *et al.* (65), who used subjects deprived of sleep for 68 hours at the time of testing, found significantly fewer missed signals with 15 mg of *d*-amphetamine on both versions. He administered the drug 90 minutes before testing.

V. LEARNING

Drugs can contribute to efficiency not only by maintaining or improving ongoing performance but by speeding the rate at which new behavior is acquired. The question of whether drugs that enhance performance can also hasten learning is an interesting one. It is somewhat surprising to find no more than a handful of studies devoted to it.

Switzer (104) observed the effects of caffeine on "inhibition of delay." The conditioned stimulus (CS) was a 21-second light. The unconditioned stimulus (US) was an electric shock applied for 1.2 seconds at the end of the 16th second of the CS. The galvanic skin response (GSR) served as the measure of conditioning. The subjects in the study received 300 mg of caffeine citrate or a lactose placebo 4 hours before a session. A session was run on each of 5 experimental days. Administration of caffeine resulted in a significantly shorter response latency to the CS than did the placebo (9.84 *versus* 11.72 seconds); that is, the rise in GSR amplitude during the CS occurred earlier after caffeine. The drug also produced a significantly greater amplitude of response.

To investigate extinction, Switzer (105) used a CS (light) that lasted 0.95 second. The US, electric shock, overlapped the CS by 0.15 second and continued for 1.05 seconds following the termination of the CS. Capsules of either caffeine citrate (300 mg) or lactose placebo were ingested 4 hours before a session. On each of the 4 days when an extinction session was run, the subject underwent a series of unreinforced CS's followed by 1 or 2 CS-US pairings. Even during extinction caffeine increased the amplitude of the GSR.

Hull's (56) subjects learned nonsense syllable lists, each of which was 16 syllables long, by the anticipation method (giving the next item in the series). After taking 300 mg of caffeine citrate or a lactose placebo, the subjects relearned two lists from the previous day, then, starting 3.5 hours after ingestion of the drug, learned two new series to a criterion of 2 perfect repetitions. Caffeine significantly increased the number of anticipatory intrusions. These were defined as giving, instead of the correct word, a word that came later in the series. The length of anticipatory displacements (the number of syllables skipped) also increased significantly. Despite this, caffeine affected neither the number of trials needed to attain the criterion, nor retention.

The experiments by Switzer (104, 105) and by Hull (56) suggest that caffeine does not affect either the development or extinction of a response, but simply provokes a tendency to respond early or more strongly. Hollingworth's (52)

observation is in accord with this view. He attributed the lengthened reaction time found after moderate doses of caffeine to the subjects' attempts to inhibit quick, false reactions. The data available do not allow one to make any further statements about caffeine and learning.

The data on amphetamine are also sparse. Franks and Trouton (33) investigated the effects of *d*-amphetamine on eyeblink conditioning. A puff of air served as the US and a tone as the CS. Eyelid movements were recorded photoelectrically. The drug treatments consisted of sodium amobarbital (270 mg), *d*-amphetamine (10 mg), or placebo 45 minutes before the start of the session, or 10 mg of *d*-amphetamine 2 hours before the start. The subjects given *d*-amphetamine 2 hours before the experiment became conditioned more quickly than the placebo group, while the amobarbital group became conditioned less quickly. The group given *d*-amphetamine 45 minutes before conditioning did not differ from the placebo group. [This latency of effect confirms the statement by Smith and Beecher (100) that 2 to 3 hours are required to attain the peak effects of such a dose level.] It would have been useful to have observed whether the groups differed after the effects of the drugs had worn off, because then one could have said whether the effects on conditioning were permanent or whether they were transitory and reflected merely, perhaps, a greater responsiveness to the conditioned or unconditioned stimuli.

d-Amphetamine (5 or 15 mg) given 90 minutes before testing did not affect the ability of rested subjects to learn which of 10 stimulus-lights were connected to which of 10 response-buttons (64). The subject had to press the appropriate button when a light flashed. In subjects deprived of sleep for 68 hours before testing, 10 mg of *d*-amphetamine at 44 hours and 15 mg at 68 hours significantly improved both time and error scores (65). The data reported by Eysenck *et al.* (27) of pursuit rotor performance indicated that the subjects given 10 mg of *d*-amphetamine 250 minutes before the session rose in proficiency at a greater rate than those given a placebo or 10 mg of *d*-amphetamine 75 minutes before the session. If the relevant variable were not a drug, most psychologists would not hesitate to call this an increase in rate of learning. Under the circumstances, however, one is justified in calling for more fundamental evidence before accepting such a conclusion. Simply promoting a greater rate of improvement in proficiency is insufficient proof, in view of the numerous effects of amphetamine on motor performance. A more convincing experiment would be one in which the increased rate of gain in proficiency was carried over to a subsequent occasion.

Amphetamine, then, seems to hasten conditioning, to restore in part the degraded rate at which a new discrimination is learned by sleepy subjects, and to increase the rate at which subjects acquire proficiency in a motor skill. But there are no data to answer the more important question of whether these effects are permanent or transient.

VI. SIMPLE AND COMPLEX VERBAL AND ARITHMETIC TASKS

A variety of tasks explicitly designed to assess verbal and arithmetic behavior has been studied by investigators interested in drug effects. These range from

crossing out numbers or letters to standard intelligence tests. Neither the results of the simple nor the results of the complex tasks offer much hope of an affirmative answer to the question: "Can drugs help to raise the level of 'intellectual' performance in normal subjects?"

Barmack (9) found that 120 mg of caffeine increased the number of addition problems attempted, the same effect he had found previously with 10 mg of amphetamine (6). Gilliland and Nelson (34) also reported that the ingestion of one or two cups of coffee 100 minutes previously increased the rate of adding. The subjects in the experiment by Kleemeier and Kleemeier (62) showed significant increases in rate of addition and multiplication after 10 mg of amphetamine. McNamara and Miller (74) used written multiplication problems to measure the effects of 20 mg of amphetamine given 2 hours previously. Neither the number of problems attempted in a 12-minute period nor the number of errors was altered by the drug, but the presence of a substantial practice effect makes this result ambiguous. A dose of 10 mg of *d*-amphetamine produced no effect on rate of addition in the study by Goldstein *et al.* (35). In the test used by Hollingworth (52), the subjects had to add *17* to a number on a card and give the answer orally. The time required to perform 50 calculations consistently decreased after caffeine over a wide range of dose levels (60 to 360 mg). Graf's (38) subjects worked arithmetic problems for 3 continuous hours. At 60 and 120 minutes after the beginning of the session, solutions of the drug were administered by mouth. On methamphetamine days the dose was 3 mg per administration. On caffeine days the dose was 100 mg per administration. (It is not clear whether a placebo was given on control days.) After a 90-minute pause for lunch, there were three more 30-minute work periods separated by 30-minute rest periods. The rate of addition fell off less on caffeine days than on control days, but methamphetamine led to a substantial rise in rate above the control level. Thus, there is some evidence that caffeine and amphetamine can improve performance on arithmetic tasks, especially if the experimental sessions are long.

Compensation for the effects of alcohol has also been tested with arithmetic problems. Graf (38) administered 30 g of alcohol to 2 male subjects and 20 g to 2 female subjects; the subjects worked for 1 hour, took alcohol plus drug, then worked for 2 more hours. Then followed a 30-minute rest, 30 minutes of work, 90 minutes for lunch, and 90 minutes of work. Methamphetamine (9 mg to males, 6 mg to females) not only counteracted the decrease in performance induced by alcohol but raised performance above control (no alcohol) levels. Caffeine (150 mg to males, 100 to females) prevented a fall in performance after alcohol but produced no enhancement.

A number of tasks requiring the subject to remain attentive has been investigated. Hollingworth (52) observed a slight increase in speed of typing and a considerable decrease in typing errors after a dose of 180 or 360 mg of caffeine. Hollingworth also observed an increased rate of naming colors on a card after caffeine in doses of 72 to 216 mg. Berdie (11) found no effect on a similar color-naming task of 15 mg of amphetamine given 2 hours before the test. Barmack and Seitz (10) found no effect of 10 mg of amphetamine on the number of letters

their subjects could reproduce after seeing a group of 8 flashed on a screen. Several investigators have examined the efficiency of crossing-out certain letters or digits randomly distributed among other letters or digits, and reported slight but variable stimulation by caffeine in one instance (52), and significantly faster performance after 600 to 900 mg of caffeine citrate in another (72). Lehmann and Csank (72), Adler *et al.* (1), and Tyler (109) also reported improved performance after amphetamine.

Dill *et al.* (25) gave subcutaneous injections of 20 mg of amphetamine to subjects working at a simulated altitude of 10,000 to 24,000 feet. This treatment affected neither arithmetic performance nor a simple coding task, but the decrease in oxygen concentration had no effect by itself, indicating that the task was insensitive.

Thus, on simple tasks such as arithmetic problems and cancellation, both caffeine and amphetamine can at times improve performance. Determination of whether this represents a true facilitation or merely an antidote to boredom requires that more demanding tasks be used.

A digit-symbol substitution test derived from the Wechsler Adult Intelligence scale was incorporated into experiments by Townsend and Mirsky (107) and Kornetsky *et al.* (65). The Townsend and Mirsky experiment demonstrated no effect of 5 or 15 mg of *d*-amphetamine. Kornetsky *et al.*, who used sleep-deprived subjects, found that the loss in performance produced by 68 hours without sleep disappeared after the administration of 15 mg of *d*-amphetamine. In a more complex task—solving war staff problems—Somerville (103) found that the administration of amphetamine, even to subjects without sleep for 42 hours, did not facilitate performance.

Andrews (3) could find no effect of amphetamine (10 mg) on the solution of syllogisms. Hecht and Sargent (48) could find no effect on rate of solving anagrams. In both experiments, however, the interval between drug administration and testing (30 minutes and 60 minutes, respectively) may not have been long enough to detect effects produced at the time of peak drug action. Two-move chess problems were used as the criterion by Holck (50); the problems and solutions were taken from a book. A dose of 200 mg of caffeine, subcutaneously, produced no demonstrable effect on performance of this task.

During the 1930's, several investigators (*e.g.*, 77, 78, 95) claimed that amphetamine could raise intelligence test scores. These studies suffer badly from the lack of adequate controls, *i.e.*, random allocation of subjects to treatments, placebo groups, double-blind designs, *etc.* The early promising results have not been duplicated by later work. Thus, Barmack (8) found no effect of 10 mg of amphetamine on the Otis Test scores of college students. Cutler *et al.* (22) gave mentally defective children 5 mg of amphetamine per day for 3 months and 7.5 mg per day for the next 3 months. This double-blind study could demonstrate no effect of the medication on intelligence test scores. Another group gave mentally defective subjects 5 mg of amphetamine per day for the first week, 10 mg per day for the second, and 15 mg per day for the third and fourth weeks of their well-controlled study (79). The authors concluded, "It is apparent that

treatment with amphetamine does not increase intelligence, learning capacity, speed and accuracy of voluntary attention, fluency, or memory in mental defectives."

Cattell (17) found no effect of 200 or 400 mg caffeine citrate, either on an intelligence scale or on a test of factual knowledge. However, his subjects began the tests only 20 minutes after taking the drug, which was probably insufficient time for peak effects to appear. Flory and Gilbert (29) evaluated the effects of 300 mg of caffeine citrate and 15 mg of amphetamine sulfate on rate of reading, reading comprehension, and on a vocabulary and analogies test. No effects of the drug were apparent.

The evidence at hand, therefore, indicates that neither amphetamine nor caffeine possesses properties which lead to improved intellectual performance except, perhaps, when normal performance has been degraded by fatigue or boredom.

VII. JUDGMENT AND MOOD

Is there a psychological price that must be paid for the use of drugs that enhance performance? Only two aspects of this question will be discussed here: 1) Do drugs that enhance performance impair judgment? 2) Do such drugs produce changes in mood that could be considered deleterious?

A. Effects on judgment

If one conceives of judgment as the appropriateness of behavior to the environment, then a drug could impair judgment in two ways. One would be directly related to certain subjective effects of the drug, *e.g.*, inflated estimates of one's ability to continue physically fatiguing work or to stay awake while driving an automobile. Such an impairment in judgment would be due to a lack of correlation between the subjective and performance-modifying effects of a drug. A second type of impairment would be more difficult to relate directly to known effects of the drug, for instance, reckless driving, poor tactics in a military operation, and so on. Neither of these facets of judgment has received much study. What little published work exists, moreover, treats only the amphetamines.

Davis (23) made two statements about judgment in his summary article on the British experience with stimulants during World War II. First, he stated that "the subject who has taken amphetamine usually judges the effects more favorably than the experimenter." Second, he claimed that amphetamine may induce a person to persist in inappropriate behavior. Winfield (111), however, in studying RAF bomber crews on combat missions, reported that no evidence of recklessness or lack of judgment was apparent after 10 or 15 mg of amphetamine. Somerville (103) was another investigator who could find no effect of amphetamine on judgment in a military situation. Officers working on an arduous 72-hour program of staff duty exercises were not permitted to sleep during the first 42 hours. Two opportunities for sleep were given during the last 30 hours, one for 4 hours, and one for 6 hours. The men worked in groups of 10 or 11, and their

performance was judged by general staff officers familiar with the tasks. Three treatments were chosen: no drug (N = 23), placebo (N = 25), and active drug (N = 25). Subjects in the active drug group received 20 mg of amphetamine in divided doses between the 32nd and 42nd hours. This dose was repeated between the 56th and 66th hours. Identically appearing inert capsules were given to those in the placebo group at the same times. The supervisory officers were asked to pay particular attention to any evidence of deficiencies in judgment. (They were kept unaware of which subjects received the active drug.) Little evidence was seen of the drug's producing any adverse effect upon judgment.

The ability of a subject to predict his future performance on the Air Force SAM Pursuit Confusion Task was not affected by 5 mg of *d*-amphetamine, according to Hauty and Payne (42). The subject estimated how long he would be able to keep a stylus in contact with a moving target on his next trial. Since he performed the task while viewing the apparatus in a mirror, interference effects from habitual perceptual-motor behavior produced a high degree of uncertainty about his performance. He thus had to depend heavily on immediate past performance in making his estimate for the next trial. Performance was measured 1 hour after the administration of the drug. Neither the algebraic nor the absolute differences between estimated and actually attained proficiency proved to be statistically significant, nor did the drug produce any changes in performance.

Smith and Beecher (102), whose work on amphetamine and athletic performance was discussed earlier, also gathered data on how accurately their subjects estimated their speed. A dose of 14 mg amphetamine/70 kg given 2 or 3 hours before the trial led subjects swimming alone and unfatigued to give lower estimates than those they gave under control conditions. This occurred in the face of an actual improvement in speed. Amphetamine did not produce this result, however, when the subjects were tired or when they competed with two other swimmers. The authors were unwilling to conclude that the drug impaired judgment. That it probably did affect time-estimation is indicated by the results of two other investigators. Goldstone *et al.* (36) presented each of their subjects with a series of audible signals of varying duration and then had them judge whether each signal was greater or less than 1 second in duration. The judgments were made 30 and 60 minutes after taking capsules containing either 15 mg of *d*-amphetamine, 200 mg of secobarbital, or a placebo. Compared to the placebo, *d*-amphetamine led subjects to overestimate the length of the signal, with the effect greater after 60 minutes than after 30 minutes. Using a totally different technique, Dews and Morse (24) showed a similar effect in a situation that required subjects to space successive key-presses a certain minimum length of time apart in order to win money. The subjects tended to press slightly earlier when they worked 30 minutes after an oral dose of 5 mg of *d*-amphetamine.

A mild time-distortion is therefore likely to occur with the amphetamines. It is also clear that much more work is needed before we can answer the question of whether the amphetamines have more general effects upon the judiciousness of decisions.

B. Effects on mood

The dominant subjective effect of the amphetamines, a general increase in feelings of alertness and well being, was reported in the early uncontrolled studies. Nathanson (80) was the first to study the effects of an amphetamine in a controlled fashion. He gave either 1) 10 mg of amphetamine before breakfast and 10 mg before lunch, or 2) 20 mg of amphetamine before lunch, or 3) placebos. Each subject (all were members of a hospital staff) was given a scaled questionnaire with instructions to open it and answer the questions in the evening. In reporting the results, Nathanson pooled his drug data, presumably because he found little difference between the two dosage schedules. A total of 55 subjects were in the drug groups, 25 in the placebo group. The differences were dramatic. Thirty-seven of the subjects that received the drug, but only one of those receiving the placebo, reported euphoria and feelings of exhilaration. Thirty of those on drug reported an increase in energy and in the desire and capacity for work; again, only one individual in the placebo group responded in this way. Comparable figures for an increase in talkativeness were 31 and 1; for feeling less fatigued from the day's work, 34 and 1; for feeling an increase in mental activity and efficiency, 23 and 0. On the negative side, 10 in the drug-group felt more fatigued from the day's work *versus* 2 in the placebo-group. And, while no one in the placebo-group reported any insomnia that night, 17 of those who had received the active drug reported either mild or moderate difficulty in going to sleep. Surprisingly little has been added to our knowledge of the effects of the amphetamines on verbal descriptions of mood since this early questionnaire study.

Bahnsen *et al.* (4) also studied the actions of amphetamine in an everyday context. They gave the drug to adult men and women, partially adjusting dose to weight by giving 20 mg to the men and only 10 mg to the women. There were 100 subjects in the experimental group and 95 in the group given placebos. The drug was taken in the morning of a normal working day and the subjects filled out extensive questionnaires before drug administration, at about 5:00 P.M. that afternoon, and the next morning. Apart from the usual lessening of fatigue, they reported "a considerable increase in the desire for work" and "the feeling that it is relatively easy to perform a task." Other items showing large differences between the drug and placebo groups were reports of general well being, good humor, exhilaration, talkativeness, restlessness, excitement, and anxiety. All these sensations were increased by the drug. A study by Jacobsen and Wollstein (59) in which they gave 15 mg of amphetamine to young men yielded similar findings.

One early and frequently cited attempt to study the effects of amphetamine on a wide variety of tasks as well as on mood was marred by an inadequate randomization procedure (14, 15, 108). In discussing one aspect of the results, Turner and Carl wrote: "It will be noted that the 'starting points' for the four groups differ from each other to a considerable degree and particularly that the 'P' (Placebo) group registered well above the others at first administration. It is quite likely that this condition is explicable in part through the fact that about one-third of the subjects in the 'P' group were under 21 years of age, who had

been so classified in order to avoid the necessity for securing the parental authority to administer Benzedrine; and, as indicated previously that there is a rather clear tendency for young subjects to register higher scores" (108, p. 166). Since the age-bias therefore was considerable, the results of the study are impossible to interpret.

As part of an intensive investigation of boredom and fatigue, Barmack (6) studied the effects of amphetamine on several mood variables. The subjects filled out rating scales after each of eight 15-minute work periods, during which they added pairs of 6-place numbers. The drug (or placebo) was given between 15 and 40 minutes before the first of the work periods. Each of 36 subjects served twice, once after 10 mg of amphetamine and once after the placebo, with both possible orders of administration used equally often. The results were clearcut: with only a placebo, subjects reported that they became bored, inattentive, fatigued, sleepy, relaxed, and irritated as time wore on. The drug, while it did not abolish these decrements completely, reduced them considerably. Approximately the same result occurred when a slightly higher dose of amphetamine, 15 mg, was used with another task, the Poffenberger pursuitmeter (7). In this second experiment the drug was given one-half hour before the beginning of eight 15-minute work periods. The effects of 60 mg of ephedrine hydrochloride were equivocal.

Barmack (9) also studied the effects of 120 mg of caffeine on several mood variables as part of his investigation of its effects on addition. The drug slowed the development of boredom, fatigue, inattentiveness, and sleepiness, but had little effect either on the number of additions attempted or upon subjective ratings made early in the work session. The caffeine was given either 1, 2, or 3 hours before the start of the session in order to discover whether the effect was merely a function of time of administration. It was not; the subjective ratings seemed to be affected only if the subject had been working for a while, irrespective of the time since drug administration. A somewhat similar result was shown for *d*-amphetamine by Pearson and Byars (90). They found that 5 mg of the drug affected only slightly the subjective ratings of fatigue made by men who simply sat around filling out checklists every one and one-half hours for 6 hours, starting at 9:30 A.M.

Ten mg of amphetamine reduced the fatigue of men working at a simulated altitude of 16,000 feet, but did not bring their ratings back to the level found under ground control conditions, according to Seitz and Barmack (98). The judgments of fatigue were made 2 hours after the subjects had taken either the drug or a placebo. Adler *et al.* (1) found that 10 mg of amphetamine, 10 mg of *d*-amphetamine, 5 mg of methamphetamine, 420 mg of caffeine sodium benzoate, and 5 mg of amphetamine plus 225 mg of caffeine sodium benzoate all reduced the number of subjective symptoms reported at simulated altitudes of 15,000 and 18,000 feet.

Amelioration of the feelings of fatigue developed by prolonged work is the most fully documented subjective effect of the amphetamines. During the second World War, investigators in many countries tried to find out how well

these drugs worked and how much had to be paid for their use in the way of adverse side-effects. Work done in the United States has been reported by Seashore and Ivy (97) and Tyler (109); in Canada, by Somerville (103); in Great Britain, by Cuthbertson and Knox (21), Davis (23), and Winfield (111).

As discussed previously (pp. 3–4), Seashore and Ivy (97) conducted a series of eight field trials in which various stimulants were tested on infantry soldiers, truck drivers, and tank drivers. The one experiment reported in detail concerned the effects of 10 mg of amphetamine, 5 mg of methamphetamine, and 450 mg of caffeine sodium benzoate. The drugs and a placebo were given orally. An all-day hike was followed by continuous guard duty from 6:00 P.M. to 3:00 or 4:30 A.M. The experimenters then administered the 1.5 hour-long test battery, results from which have been described earlier. The data of interest to us here come from a check list given to the subjects some time during this period. One dose of the drugs was given at 6:00 P.M. and another at midnight. Each of 16 subjects received a different agent on each of four weekly occasions. The order was balanced so that no drug was favored. All three stimulants increased the estimates of how long the subjects thought they could have continued on guard duty. Amphetamine produced the fewest negative subjective symptoms. These included excessive sleepiness, vertigo, difficulty in concentrating, slowness in reasoning, nervousness, inward tension, restlessness, indifference, exhaustion, and tremor. Caffeine produced the next lowest incidence of subjective symptoms. Methamphetamine in the dose employed differed only slightly from the placebo. A comparison of positive subjective symptoms also showed amphetamine to be first, caffeine second, methamphetamine third, and the placebo last. The positive symptoms were: no sleepiness, talkativeness, excitement, and exhilaration. The authors also said that they "were often able, by the more buoyant attitude and behavior exhibited, to distinguish subjects receiving Benzedrine from those receiving the other two stimulants." The rest of the experiments in the series generally confirmed the results of this one, although the effects were less pronounced.

Tyler (109) carried out a series of studies on the performance of large groups of men forced to remain awake for as long as 112 hours. In one 72-hour experiment, he gave 10 mg of amphetamine every 8 to 12 hours, starting at either the 36th or 48th hour of wakefulness. The drug decreased the difficulty subjects had in remaining awake. Drug-induced mood changes were nearly absent, perhaps because no very systematic attempts were made to observe them, although Tyler attributed the lack of mood changes to the high motivational level of his subjects. One interesting finding was that more amphetamine subjects than placebo subjects were willing to volunteer for a 35-mile forced march with full pack on their third night of sleep deprivation. This may be indicative of deficiency in judgment, because they already had made two night marches totalling 69 miles and, according to Tyler, a third was out of the question since their feet were sore and blistered.

A rather surprising lack of effectiveness of amphetamine was reported by Somerville (103). Experiments were carried out on Canadian soldiers engaged in

obstacle course running, night and day marches, and prolonged staff duty exercises. Doses of amphetamine varied from 15 mg 1 hour before the end of the fatiguing activity to 40 mg given in divided doses over a 72-hour period. The differences that did occur were in the direction of a slight alerting effect of the drug. The only statistically significant difference was the number of subjects in the staff duty exercise experiment who thought the drug helped keep them awake (21 of 25 in the amphetamine group, 7 of 25 in the placebo group). Flory and Gilbert (29) and Cranston *et al.* (20) also failed to find significant subjective effects after amphetamine, as did Goldstein *et al.* (35). The failure of Kenyon and Pronko (61) to find mood changes (as measured by adjective sorting) after 10 mg of *d*-amphetamine could have been due to the shortness of the period between drug administration and testing (45 minutes). Another possibility that could account for the lack of subjective effects in the above studies is the insensitivity or inappropriateness of the measuring device. Dureman and Scholander (26) compared two kinds of subjective rating scales for sensitivity to drug effects. One contained 28 expressions related to non-specific activation; the subject checked, for each item, "more than," "alike," or "less than." The other consisted of three graphic rating scales representing "clearness of mind," "wakefulness-alertness," and "power of concentration"; the subjects rated these in three graded levels. On the check list, 10 mg of amphetamine produced a substantial increase in score, the greatest effect occurring at 180 minutes after administration of the drug. Many more subjects reported no effect on the rating scale after exactly the same dose. Subjective effects are just as dependent upon techniques of measurement as are performance effects, although it is rare to find investigators who act on this principle.

In contrast to some of the above results, Davis (23), in his short summary of the British World War II studies, reported an abundance of subjective effects with amphetamine. He stated that in subjects kept awake all night a dose of 15 mg of amphetamine may cause them to feel "more alert than usual and ready for anything. They may become mildly elated and confident, without doubts and anxieties and the discomfort of the tension usually experienced before starting a test. On the other hand, tests which without amphetamine are regarded as boring may engage their interest and become absorbing. They may feel able to concentrate on them without the usual diversion of their attention by extraneous events. Attention may seem to be narrowed and focused upon the task in hand."

Davis also believed that 15 mg of amphetamine often leads to impulsive and inappropriate activity, irritability, and restlessness, when the task given to the subject constrains his activity or calls for separate responses that must be made to separate stimuli at about the same time. This author reported great variability in response to the drug and saw more mood change and overt behavior change than anyone else. Thus: "Individual differences are large and unpredictable, and the effects differ in the same individual from occasion to occasion. Sometimes individuals become excited, restless, and garrulous. Some become irritable and quarrelsome, others emotionally labile.... Irresponsible behaviour, euphoria and airy, dreamy or drunk feelings may also result from a 15 mg dose." Unfortunately, no quantitative data were given, nor were the methods of observa-

tion. Davis did not state whether these kinds of data were systematically gathered or whether his statements were the result of casual observations. One cannot judge the validity of his conclusions under these circumstances.

Cuthbertson and Knox (21) kept soldiers without sleep for 24 hours, then marched them 18 miles. A dose of 15 mg of methamphetamine was given just before the march. The 55 subjects were divided into three squads. All the members of one squad were given the drug, all the members of the second were given a placebo, and the third squad was made up of approximately equal numbers of drug and placebo subjects. By arranging matters in this way, rather than randomly assigning both treatments within each squad, the authors made possible an interesting reanalysis of their data that shows how the euphoriant effect of the drug was magnified by placing like-treated subjects together. In the all-drug group, 10 of 18 subjects reported having experienced euphoria during the march, whereas in the all-placebo group, only 1 of 17 reported euphoria; the difference was statistically significant (chi-square = 8.38, dF = 1, $P < .01$). But the incidences of euphoria in the group with approximately half the subjects on drug and half on placebo, were 1 out of 8 for the former and 0 out of 10 for the latter. Thus, it seems that the euphorigenic effect was much more pronounced when everyone in the group received the drug. This social facilitation effect has been studied, with other drugs, by Wendt and the Nowlises at the University of Rochester (83).

Lasagna *et al.* (68) examined how amphetamine and several other drugs affected the reports of mood of two widely disparate groups, normal volunteers (predominantly university students) and former narcotic addicts. (Data from a third group of old, chronically ill patients were not very satisfactory, since many of the patients were unable to cooperate fully.) The subjects filled out a standard questionnaire 30 minutes, 1 hour, and 2 hours after receiving the drug. Normal subjects received a subcutaneous injection of either saline placebo, 20 mg of amphetamine, 2 or 4 mg of heroin hydrochloride, or 8 or 15 mg of morphine phosphate. Sodium pentobarbital, in doses of 50 and 100 mg, was given intravenously. The former addicts were given either the saline placebo, 20 or 30 mg of amphetamine, 4 or 6 mg heroin hydrochloride, or 15 or 22.5 mg of morphine phosphate. All doses were per 70 kg of body weight. The subjects did not know which drugs they were getting.

Amphetamine surpassed all the other drugs in its ability to create a pleasant state in normal subjects. It achieved the highest score on a euphoria index compiled from the questionnaire items. This contrasted sharply with the dysphoria produced by the two opiates. It also was the most popular drug when subjects were asked to rate them all on a "most pleasant" to "most unpleasant" scale at the end of the experiment. Fifteen of the 20 subjects put amphetamine on the "pleasant" side of the midpoint; the rest called it "unpleasant." Only five of them called the placebo pleasant; one called it unpleasant, and the rest found it neutral. Amphetamine was much more popular than any of the other drugs, with pentobarbital second, and the opiates liked by few subjects and heartily disliked by most.

Amphetamine also greatly improved the mood of the former addicts according

to the results of the euphoria index rating. In fact, on this score, which reflected only the first 2 hours after drug administration, it produced as pleasant a reaction as did the opiates. (As might be expected, because of their special history, the former addicts contrasted greatly with the normal subjects in enjoying the opiates.) Amphetamine did not maintain its popularity on the ratings made at the end of the entire experiment, apparently because the former addicts were unhappy with the insomnia and other side-effects that sometimes resulted. Thirty subjects thought it pleasant; eight either called it neutral or had no reaction, and nine called it unpleasant. (The 20- and 30-mg dose data were combined because they did not differ significantly.) In contrast, one subject called the saline placebo pleasant, 25 called it neutral, and 4 called it unpleasant.

Another approach to the study of the effects of drugs on mood was taken by the group at the University of Rochester (83). They have used a variety of agents in an extensive exploration of changes in affect in subjects working together in four-man groups. The primary tool has been a list consisting of 100 to 200 adjectives on which the subject is asked to check those that apply to him. Amphetamine alone was used in some of the early work of this group. A dose of 10 mg of amphetamine typically increased the checking of such words as "businesslike, talkative, capable, enterprising, independent, nervous, jittery," and it decreased the checking of such words as "lazy, languid, nonchalant."

Smith and Beecher (101) also showed that amphetamine produces a positive mood report. A variety of doses—usually 14 mg/70 kg, sometimes 7 or 21 mg/70 kg—influenced the way their college runners, swimmers, and weight throwers checked a list of adjectives quite similar to the one used by the Rochester group. The authors summarize their findings in this way:

"The increased feeling of mental and physical activation was the most definite amphetamine effect . . . there was more checking of such words as active, vigorous, and energetic on amphetamine than on placebo days; less checking of sluggish, weak, drowsy, and tired; more checking of alert and clearheaded; less checking of mentally slow; more checking of efficient, ambitious, industrious, and effective; and more checking of excited, on edge, anticipative, tense, jittery, and restless on amphetamine than on placebo days. The second most definite amphetamine effect was increased elation. There was more checking of elated, exhilarated, happy, cheerful, and overjoyed and less checking of depressed and moody on amphetamine days than on placebo days. A third positive effect was increased boldness. The subjects checked bold, boastful, cocky, self-confident, playful, and domineering more, and insecure less, on amphetamine days than on placebo days. The fourth definite effect was greater friendliness, as indicated by more checking of friendly, talkative, good-natured, obliging, and trustful and less checking of grouchy, unsociable, and sarcastic" (p. 1509).

Ritter *et al.* (92) took another approach to the problem of uncovering possible deleterious effects of a drug. They reasoned that "the psychologic stress imposed upon individual organisms by the adjustments involved in getting along together toward some common goal may constitute a sufficient condition for the exposure of latent unwanted effects of *d*-amphetamine." The task they chose was the

USAF SAM Two-Hand Coordination Test (76), modified so that each subject had control of one handle but only one subject could see the turntable and the stylus that the team attempted to keep in contact with the moving disc. At the end of the task each subject was asked to make ratings of his attitudes toward the task itself, his own performance, and his partner's performance. A dose of 5 mg of *d*-amphetamine, given 1 hour before the start of the group session, significantly improved the subjects' attitudes toward the task. Attitudes toward one's own and his partner's performance were also more positive after *d*-amphetamine but the changes were smaller and not statistically significant. Thus, the drug did not cause adverse effects; on the contrary, what effects it did have were all positive.

A 5-mg dose of *d*-amphetamine produced a more favorable attitude toward the prolonged tracking task used by Payne and Hauty (84) than any other pharmacological treatment. The attitude score associated with a caffeine derivative was higher than that with the placebo, but far less than that with *d*-amphetamine. By analyzing the relation between attitude scores and performance, the authors showed further that the effects of the drugs on performance could not be ascribed to favorable attitudes (*cf.* 69).

Several investigators have combined a barbiturate with an amphetamine in the hope that the combination would prove an equally good stimulant but without the negative effects occasionally reported. Unfortunately, no direct extensive comparisons have been made with the amphetamine alone. There is some evidence that the combination produces somewhat more euphoric and outgoing behavior (83). Laties (69) studied the effects of 10 mg of amphetamine plus 100 mg of secobarbital on the mood of college students who worked in four-man groups when deprived of sleep for about 36 hours and when not deprived of sleep. The Nowlis Adjective Check List was used several times before and during the experiment. About 2.5 hours after oral drug administration, whether sleep-deprived or not, subjects reported more friendliness, more involvement with their tasks, more social initiative, and more elation than they did after placebos. This picture is strikingly similar to that reported by Smith and Beecher (101) for amphetamine alone: more friendliness, more activation, more boldness, and more elation.

Lanzetta *et al.* (67) used a slightly smaller dose of the same combination, 7.5 mg of amphetamine and 75 mg of secobarbital, in a study of three-man groups working on a task that the subjects believed was being used as an evaluation procedure for their military reserve unit. Under the influence of the drugs, subjects checked more adjectives on a check-list that connoted "a relaxed, positively affective, cooperative, phenomenal state," while they checked fewer adjectives that connoted "an anxious, obstructive state."

About the only reliable information on the subjective effects of caffeine apart from the work by Barmack (9) comes from Hollingworth's monograph (52). Hollingworth gauged these effects by inspecting the diaries his subjects were asked to keep. Although, because of the hard work involved in the tests, many subjective complaints were noted on control days, a greater incidence was noted

on days during which caffeine, in doses of 240 mg and more, had been given. The most prominent symptoms included nervousness, feverishness, headache, irritability, and disturbed sleep.

VIII. CONCLUDING REMARKS

The foregoing evidence indicates that a very wide range of behavior (with the notable exception of intellectual tasks) can be enhanced by caffeine and the amphetamines—all the way from putting the shot to monitoring a clock face. Moreover, the superiority of the amphetamines over caffeine is unquestionable.

Two questions are implicit in these conclusions. 1) How do these drugs enhance performance; can they actually produce superior performance or do they merely restore performance degraded by fatigue, boredom, and so on? 2) What is the "cost" of obtaining this enhancement; is it great enough to prohibit the practical use of these agents, particularly the amphetamines?

Davis (23), who studied amphetamine, and Barmack (6, 7, 9), who studied both amphetamine and caffeine, are among those who claim that these agents produce their effects not by an increase in capacity, but by making people more interested in the task, or as Barmack (6) states, because their effect is to allay the development of unfavorable attitudes toward the task. Davis' evidence is unconvincing, but Barmack supports his argument with data. One of his most cogent findings in this regard was the lack of effect of caffeine on subjects who had just started working *versus* its effects on subjects who had been working for 2 hours. Also, he found with amphetamine that the greatest differences between active drug and placebo (on adding 6-place numbers) occurred toward the end of the work-period and paralleled reports of boredom, irritation, and inattention by the control subjects.

To support this contention we also have the data of Kornetsky *et al.* (65), who found that *d*-amphetamine affected performance only in subjects suffering from prolonged sleep-loss. Furthermore, Hauty and Payne (44) showed that in highly motivated subjects, *d*-amphetamine did not produce the same superiority in performance relative to placebo that it produced in subjects who typically showed early decrement of performance. Finally, Mackworth's (73) results showed only a restoration by amphetamine to normal performance on a vigilance task, and no enhancement. Moreover, a number of experiments have failed to show any effects at all in non-fatigued subjects.

Opposing these data and their interpretation, however, are arrayed data at least equally convincing. Among the most cogent are those of Smith and Beecher (100) on athletic performance. Smith and Beecher (experiment 5) found that amphetamine significantly decreased the time to swim an event, even in college swimmers so highly motivated that they often exceeded, with placebo, the best times that they had made in intercollegiate competition. Smith and Beecher also found (experiment 1) that the effects of amphetamine were more apparent in rested than in fatigued subjects. Furthermore, shot-putting and weight-throwing displayed the greatest proportionate modifications by the drug. It is difficult to see how fatigue, lack of interest, or boredom could be significant factors in such an acute expenditure of effort.

Some of the findings of the Randolph Field investigators also support the notion that drugs can have effects above and beyond a mere restoration of previously impaired performance. Their data frequently showed a sizable increase in proficiency after the administration of *d*-amphetamine relative to the highest score achieved during the pre-drug period (41, 45, 84, 88). Even though this increased proficiency may not be statistically significant when the studies are evaluated individually, the consistency of this finding suggests that the effect is a real one. Another consistent finding of these investigators is a difference in the kind of improvement produced by psychological and pharmacological variables; only drugs were able to forestall the decline in proficiency with time. Other investigators who have found performance improved beyond the control level in non-fatigued subjects include Adler *et al.* (1), Lehmann and Csank (72), and Eysenck *et al.* (27). The results of Adler *et al.* are particularly noteworthy. In their experiment, *d*-amphetamine not only restored to normal some kinds of performance degraded by exposure to a simulated altitude of 18,000 feet, but brought other kinds to levels better than that seen at ground level. And the two studies by Hauty *et al.* (45, 46) conclusively demonstrated on a monitoring task that *d*-amphetamine could prevent proficiency decline even with the added challenge of inadequate oxygen. Payne *et al.* (87) also offered data that contradict Barmack's finding (6) that the difference between amphetamine and placebo is exaggerated toward the end of a long work period. They found an equivalent effect of a particular dose no matter when during the period it was given.

Actually, neither Barmack's data nor those of the other investigators who hold similar views can justify their position that drugs that enhance performance do so only by inducing favorable attitudes. It is quite likely that drugs such as the amphetamines produce at least two independent effects—performance changes and attitude changes. The fact that these parallel one another does not necessarily confirm a deterministic relationship; nor does it make it unnecessary to show that attitudinal variance can account for performance variance. Indeed, in the only investigations to take this crucial step, the subjective data argued against the hypothesis that the amphetamines improve performance merely by inducing favorable attitudes toward the task. Payne and Hauty (84) found that favorable dispositions toward tasks which arose from special instructions were not reflected in performance. They also demonstrated that very significant variation in drug response occurred independently of attitude variation. Pearson (89) obtained similar results; he could demonstrate no more than a very slight correlation between fatigue ratings and performance decrement. One can point to even more dramatic disparities; for instance, although alcohol may increase confidence in the ability to drive an automobile, we have every reason to doubt that this parallels an increased ability to perform the task.

The associated claim that only performance degraded by fatigue and similar states can be helped by drugs also suffers from a logical defect. Obviously, if one is working just below a task ceiling the effect of an agent is more difficult to detect than if performance is well below that ceiling. One should not confuse ease of detection with mechanism of action.

There are strong indications, therefore, that the amphetamines, and perhaps

caffeine as well, can do more than merely restore performance degraded by factors such as muscular fatigue, sleep deprivation, and boredom.

The evidence for answering the second question—is there a cost to the enhancement obtained?—is mostly negative. Both from the standpoint of physiological and psychological cost, amphetamines and caffeine are rather benign agents. Except for reports of insomnia, the subjective effects of the amphetamines in normal doses are usually favorable. Moreover, no one has ever presented convincing evidence that they impair judgment. Caffeine seems somewhat less benign. Hollingworth's (52) subjects, after doses of about 240 mg and above, reported such symptoms as nervousness, feverishness, irritability, headache, and disturbed sleep. Caffeine also produces a significant increase in tremor. At dose levels that clearly enhance performance, the amphetamines seem not only more effective than caffeine, but less costly in terms of side-effects.

These statements refer only to the acute effects of caffeine and the amphetamines. Are additional costs incurred when these drugs are taken chronically to enhance performance? Do they lead to addiction? There appears to be no experimental evidence from which to answer this question. The clinical reports show that occasional individuals, usually persons with neurotic or psychotic symptoms, habitually take extremely high doses. However, there is no evidence of physical dependence; abrupt cessation of the drug produces hardly any effect, apart, perhaps, from a transient somnolence (56a, 62a, 112). Caffeine also does not produce physical dependence. Withdrawal in habitual coffee drinkers seems mainly to lead to an increased incidence of headaches for a day or two (66). Some degree of tolerance develops to both; neither is addicting in the sense that narcotics are. In view of the wide use enjoyed by these drugs, the incidence even of habituation, so far as one can tell from the literature, is quite low. [The sociological aspects of the use of these drugs, particularly the amphetamines, are discussed by Leake (70)].

A final word is in order about our present state of knowledge. Strikingly few attempts have been made to determine the basic parameters of drug action and performance. Such work is essential if we are ever to develop broad principles. What little we have learned has had to be inferred from work rarely designed to yield unambiguous answers. The question of whether the effects of amphetamine are dependent upon the amount of degradation of performance existing at the time the drug is taken has been discussed above. Few other broad questions have stimulated even this amount of work. A few examples should suffice to make the point. (a) We suspect that amphetamine affects coordination and tracking tasks differentially depending upon the complexity of the task used (Sect. III). But task complexity has rarely been made the subject of explicit study. (b) Work with lower animals suggests that the effects of the amphetamines on response rate are in part dependent upon the rate at which the subject is responding when given the drug (23a); almost no systematic work on human performance has been done (24). (c) There is a hint that the mood changes due to any drug depend upon the environment of the subject; more specifically, there is some evidence that amphetamine leads to more profound changes when the subject

is surrounded by others also on the drug. Little has been done to determine the variables operating here (21, 83). (d) We have no information on whether tolerance develops to the effects of these drugs on performance as it does, say, to the anorexigenic effects of the amphetamines. It is clear that the notion of drug-behavior interaction, which is proving so important in behavioral pharmacology (98a), should be applied more frequently to work on the human level.

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