Technical Report Documentation Page

1. Report No.	2. Government Accession No.	3. Recipient's Catalog No.
FAA-AM-75-14		

4. Title and Subtitle	5. Report Date
THE EFFECTS OF DEXTROAMPHETAMINE ON PHYSIOLOGICAL RESPONSES AND COMPLEX PERFORMANCE DURING SLEEP LOSS	November 1975
	6. Performing Organization Code
	8. Performing Organization Report No.

7. Author(s) E. A. Higgins, W. D. Chiles, J. M. McKenzie, P. F. Iampietro, J. A. Vaughan, G. E. Funkhouser, M. J. Burr, A. E. Jennings, and G. West

9. Performing Organization Name and Address

FAA Civil Aeromedical Institute
P. O. Box 25082
Oklahoma City, Oklahoma 73125

10. Work Unit No. (TRAIS)	11. Contract or Grant No.	13. Type of Report and Period Covered
		OAM Report

12. Sponsoring Agency Name and Address

Office of Aviation Medicine
Federal Aviation Administration
800 Independence Avenue, S.W.
Washington, D.C. 20591

14. Sponsoring Agency Code

15. Supplementary Notes

Work was performed under Task AM-A-74-PHY-65.

16. Abstract

On two separate occasions, performance of 10 male subjects was measured on the Civil Aeromedical Institute Multiple Task Performance Battery at 4-hour intervals for a period of 24 hours without sleep. Each subject received a capsule at 4-hour intervals beginning at 2000. On one occasion, the first three doses contained 5 mg each of dextroamphetamine sulfate followed by placebos for the remaining three capsules. On the other occasion, all capsules were placebos. Results of the experiment demonstrated that the dextroamphetamine sulfate sustained a high level of proficiency and alertness and delayed the effects of fatigue for 8 to 12 hours after the ingestion of the third and final drug capsule. Heart rate, rectal temperature, and urinary excretion rates of catecholamines were elevated with this drug. These increases could support the enhancement of proficiency and alertness demonstrated with amphetamines. Neither the subjects' feelings of fatigue nor the accuracy of their estimates of performance capabilities differed significantly in these two test conditions.

17. Key Words	18. Distribution Statement
Dextroamphetamine, Sleep loss, Complex performance, Urinary stress indicators, Body temperature, Heart rate	Document is available to the public through the National Technical Information Service, Springfield, Virginia 22151

19. Security Classif. (of this report)	20. Security Classif. (of this page)	21. No. of Pages	22. Price
Unclassified	Unclassified		$3.00 PC .95 MF

ACKNOWLEDGMENT

The authors express their appreciation to the personnel of the Stress Analysis Research Unit for the biochemical analyses of the urinary catecholamines and 17-ketogenic steroids. They also thank Mr. Peter Nelson of the Biostatistical Section for the statistical analyses of the physiological and biochemical data and the Medical Illustration staff for preparing the graphs.

THE EFFECTS OF DEXTROAMPHETAMINE ON PHYSIOLOGICAL RESPONSES AND COMPLEX PERFORMANCE DURING SLEEP LOSS

I. Introduction.

Dextroamphetamine sulfate is among those drugs (Schedule II) requiring strict controls because of their abuse and addiction potential. Currently, the main use of this and related drugs is as an aid to weight reduction, and then only under certain closely controlled conditions. It is also used in combination with scopolamine as an anti-motion-sickness drug.[6] A combination of scopolamine and dextroamphetamine is in use by the National Aeronautics and Space Administration for the astronauts. Six capsules were used by the crew of Apollo 11.[1]

The literature on amphetamines has been reviewed extensively by Weiss and Laties,[15] who concluded that amphetamines have their most beneficial effect in counteracting or preventing performance deterioration that results from fatigue and/or sleep loss. They concluded that amphetamines not only were more effective than caffeine, but also produced fewer and less severe side effects.

Although amphetamines promote a sense of alertness and well-being, little has been reported on the physiological aftereffects resulting from their withdrawal. They also may promote a false sense of performance capability, a condition that could have detrimental effects on skilled performance.

The purpose of this experiment is twofold: First, to identify and clarify possible differences between the subject's appraisal of his performance and objective test scores (test scores will also be related to his physiological responses while under the influence of dextroamphetamine sulfate), and second, to evaluate the subject's performance for several hours after withdrawal of the drug as well as during the use of it.

The results of this study are not to be interpreted as advocating the use of dextroamphetamine sulfate to ameliorate the effects of fatigue or sleep loss. It is representative of a drug type (stimulant), others of which might be as effective without the same degree of abuse and addiction potential.

II. Method.

Ten male paid volunteers (ages 20 to 28 years) served as subjects. Preceding the actual experiment, they spent 2 days in indoctrination and training on the Civil Aeromedical Institute Multiple Task Performance Battery (MTPB).[2] The battery included tasks that involved monitoring, group problem solving, mental arithmetic, pattern discrimination, and two-dimensional compensatory tracking. The subjects were tested in 2-hour sessions every 4 hours for a total of seven sessions. The task schedules for the first and second hours of each session were identical. The basic 1-hour task schedule required performance of the combinations of tasks shown in Table 1. Two different kinds of analyses were carried out. The first analysis was an appropriate expansion of a Lindquist Type VII analysis of variance design applied to each of the individual performance task measures. The second analysis, also an expanded Lindquist Type VII design, was applied to composite scores derived as follows: The measures taken during a given 15-

TABLE 1. One-Hour Task Schedule

	Time in Minutes			
	0-15	15-30	30-45	45-60
Warning Lights	X	X	X	X
Meters	X	X	X	X
Arithmetic		X		X
Pattern Identification			X	
Problem Solving	X	X	X	
Tracking				X

Note: X indicates task active

minute interval were combined so that each contributed equal variance to the resultant composite score. (See Chiles, Jennings, and West[3] for a more detailed description of the method of computation of the composite scores.) These composite scores were analyzed separately for each interval, and, in addition, the mean of the 15-minute composite scores for each hour of testing was analyzed. At the end of each test session, the subject was asked to estimate his level of performance during the preceding session, expressed as a percent of what he thought his "best" performance would be. At that same time, the subject was to indicate a subjective estimate of his state of fatigue by completing the 10-item Subjective Fatigue Checklist.[11]

Physiological responses consisted of heart rate (HR), which was obtained by using dry silver electrodes with a CM_5 lead[12] and measured continuously with an Electrocardiocorder (Avionics, Model 400), and rectal temperature (T_{re}), which was measured by an indwelling thermistor probe read from a portable bridge.

Urine samples were collected periodically, preserved with 1.2 N sulfuric acid, and frozen for later analyses. Biochemical analyses of the 17-ketogenic steroids (17-KGS) were made by a method described by Few,[4] and values were measured with a colorimeter in a Technicon Autoanalyzer system. Values for urinary epinephrine (E) and norepinephrine (NE) were made by using an automated differential fluorometric technique reported by Fiorica and Moses.[5] Urine dextroamphetamine was determined by a modified colorimetric method of Keller and Ellenbogen[7] and read from a Zeiss Spectrophotometer at a wavelength of 508 mμ. All concentrations were multiplied by the urine volume measured for each to obtain the total output.

After the training period, the 10 subjects were arbitrarily divided into two groups of five subjects each. Each group was tested twice, at 1-week intervals, in a double-blind design. For one test the subjects ingested only sugar (lactose) placebos at 4-hour intervals for a total of six capsules beginning at 2000. In the other test dextroamphetamine sulfate capsules were administered in three 5-mg doses at 2000, 2400, and 0400 and placebos in identical capsules were administered at 0800, 1200, and 1600. One group was tested first with the placebo and the other group was tested first with the dextroamphetamine.

Days 1 and 2	0830 - 1630	Training on the Complex Performance Task
Day 3	1630	Report to chamber area. Hook up chest leads and rectal probe, but no recording
	1700	Void and discard urine
	1800 - 2000	Complex performance, fatigue checklist, estimation of performance, urine sample No. 1, give capsule No. 1, start recording HR and T_{re}. (hourly)
	2000 - 2200	Free time
	2200 - 2400	Complex performance
	2400	Fatigue checklist, estimation of performance, urine sample No. 2, capsule No. 2
Day 4	0001 - 0200	Free time
	0200 - 0400	Complex performance
	0400	Fatigue checklist and estimation of performance, urine sample No. 3, capsule No. 3
	0400 - 0600	Free time
	0600 - 0800	Complex performance
	0800	Fatigue checklist and estimation of performance, urine sample No. 4, capsule No. 4
	0800 - 1000	Breakfast
	1000 - 1200	Complex performance
	1200	Fatigue checklist and estimation of performance, urine sample No. 5, capsule No. 5
	1200 - 1400	Lunch
	1400 - 1600	Complex performance
	1600	Fatigue checklist and estimation of performance, urine sample No. 6, capsule No. 6
	1600 - 1800	Supper
	1800 - 2000	Complex performance
	2000	Fatigue checklist and estimation of performance, urine sample No. 7, unhook release subjects

FIGURE 1. Schedule of events.

Figure 1 shows the schedule of events that each of the two groups completed, once with the placebo and once with the drug. Subjects reported at 1630, at which time ECG electrodes were attached and the rectal probe was inserted. Subjects voided and discarded the first urine at 1700. Measurements were initiated directly after the first complex performance session at 2000. These were continued at 4-hour intervals for the ensuing 24-hour test period with the exception of HR and T_{re} observations, which were read each hour. Subjects did not sleep throughout the test period.

III. Results.

A. *Fatigue Checklist.* The Subjective Fatigue Checklist provided a scale of 0 to 20, with 0 representing extreme fatigue and 20 representing the condition of being totally refreshed. When only the placebo was used, the mean score was 8.9; when the dextroamphetamine was used, the mean score was 9.8. The numerical difference between the two conditions was not statistically significant.

B. *Subjective Performance Estimates.* The summary data for the performance estimates are shown in Table 2. These data present a compari-

TABLE 2. Comparisons of True Composite MTPB Scores With Estimated MTPB Scores

Session Clockhours	PLACEBO True Scores % S.E.M.	PLACEBO Estimated Scores % S.E.M.	PLACEBO Δ %	PLACEBO t	DRUG True Scores % S.E.M.	DRUG Estimated Scores % S.E.M.	DRUG Δ %	DRUG t
2000	72.5 ± 1.52	83.3 ± 3.38	10.8	3.10*	72.2 ± 1.41	81.8 ± 2.22	9.6	3.75**
2400	71.8 ± 1.68	81.4 ± 2.97	9.6	2.72*	72.4 ± 1.63	81.6 ± 2.54	9.2	2.85*
0400	67.8 ± 2.91	71.6 ± 3.22	3.8	1.18	72.9 ± 1.84	80.8 ± 1.85	7.9	3.51**
0800	65.1 ± 3.53	62.5 ± 5.44	-2.6	0.67	70.6 ± 2.15	75.3 ± 2.72	4.7	1.45
1200	66.1 ± 2.44	63.5 ± 3.50	-2.6	0.68	70.6 ± 2.35	75.3 ± 1.66	4.7	1.58
1600	67.1 ± 3.35	70.5 ± 4.44	3.4	0.64	69.8 ± 2.66	70.0 ± 4.22	0.2	0.03
2000	68.5 ± 2.09	74.8 ± 3.45	6.3	1.56	70.4 ± 2.32	73.3 ± 4.29	2.9	0.66
$\bar{X}$	68.4 ± 2.50	72.5 ± 3.77	4.1		71.3 ± 2.05	76.9 ± 2.78	5.6	

n = 10
* $p \leq .05$
** $p \leq .01$

son of the subjects' estimates of their relative performance levels and their calculated performance; calculated performance is expressed as the obtained composite score divided by the theoretical maximum score, this quotient then being multiplied by 100. When the drug was used, the subjects' estimates of performance were significantly higher than the calculated performance scores during the first three sessions. When only the placebo was used, the subjects' estimates were significantly higher during the first two sessions but decreased as the period without sleep increased, whereas when the drug was used, their estimates remained consistently higher than the calculated performances. However, when differences between estimated and calculated scores over the total testing period are considered, there was no statistically significant difference between the two conditions.

C. *Complex Performance.* Performance on the MTPB and the mean urinary excretion rate of dextroamphetamine are shown in Figure 2. The subjects' MTPB performance is expressed as overall composite score, with each point on the curve representing the average for each of the 2-hour sessions. An abbreviated summary of the results of the analysis of these and other data is shown in Table 3. In the analysis of the data shown in Figure 2, the main effects of drug condition and sessions were significant. In addition, the interaction of drugs with hours (first vs. second hour of a session) was significant. Figure 2 presents the data relevant to the first of these interactions; namely, the drug by sessions interaction. Although the overall effect of sessions was significant, it is clear that this is an average effect, and the important performance characteristic is the decline associated with the placebo condition. Individual "t" tests showed the difference between the drug and placebo conditions to be significant ($p \leq .05$) at 0400, 0800, and 1200.

The analyses of the other composite performance measures show essentially the same effect

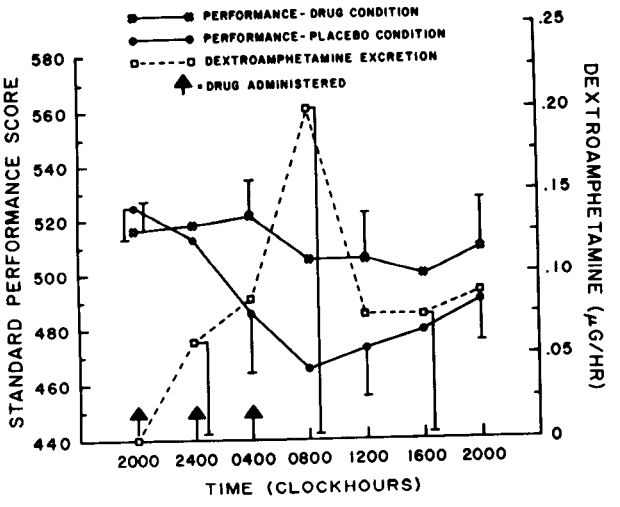

FIGURE 2. Standard composite MTPB scores through seven sessions ($\bar{X} \pm$ S.E.M., n=10). Mean urinary excretion of dextroamphetamine (broken line) is read on the right ordinate.

TABLE 3. Abbreviated Summary of Analyses of Performance Measures

	Days	Drugs	Periods	Sessions	Drugs x Sessions
Individual Measures					
Red Lights	NS	S	S	S	NS
Green Lights	S	S	S	S	S
Meters	NS	NS	S	S	S
Arithmetic Time	NS	NS	S	NS	NS
Arithmetic Percent	NS	NS	S	S	NS
Pattern Identification Time	NS	NS	NS	NS	NS
Pattern Identification Percent	NS	S	S	NS	NS
Problem Solving Time	S	NS	S	S	NS
Problem Solving Percent	NS	NS	S	NS	NS

	Days	Drugs	Sessions	Hours	Drugs x Sessions	Drugs x Hours
Tracking Vector						
Absolute Error	NS	S	S	NS	NS	NS
Tracking RMS						
Vector Error	NS	NS	S	NS	NS	NS
Composite Measures						
1st 15 min.	S	S	S	NS	S	NS
2nd 15 min.	NS	S	S	NS	S	NS
3rd 15 min.	NS	S	S	NS	S	NS
4th 15 min.	S	S	S	NS	S	S
Overall	NS	S	S	NS	S	S

Note: S indicates significant at .05 level of confidence or better; NS indicates not significant.

and do not warrant separate comment. However, the analyses of the individual measures do suggest a different emphasis. Specifically, it is noted that the significant drug effects were found on only two of the individual measures other than the monitoring task measures. These two measures were "percent correct" on the pattern identification task and "vector absolute error" on the tracking task.

D. *Physiological and Biochemical Data.* The physiological and biochemical data were analyzed by the randomized block factorial method. The paired "t" test was employed to evaluate data during given time intervals. The hourly measurements of HR are shown in Figure 3. Mean rates for the dextroamphetamine condition were significantly higher than the rates for those receiving the placebo only ($p \leq .001$). Although both curves showed evidence of a circadian rhythm, there were no significant differences over time for either condition.

Rectal temperature as a function of time and drug condition is shown in Figure 4. The drug condition produced internal body temperatures that were significantly higher than those produced by the placebo condition. ($p \leq .001$). The curves for both conditions clearly indicate a 24-hour rhythm, as T_{re} decreased in the early morning hours even though the subjects were awake and active. The curves began to merge at about 1600 and were at normal levels by the end of the test period. The interaction between drug condition (drug/placebo) and time was significant ($p \leq .01$).

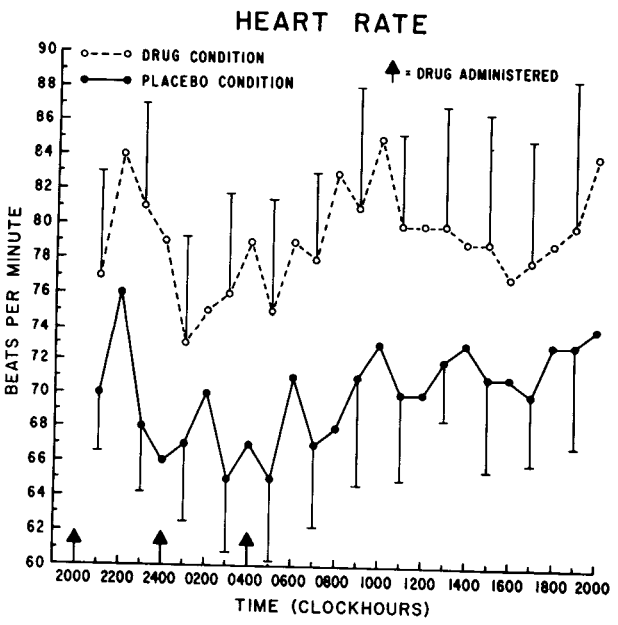

FIGURE 3. Hourly heart rate as a function of time ($\bar{X} \pm$ S.E.M., n=10).

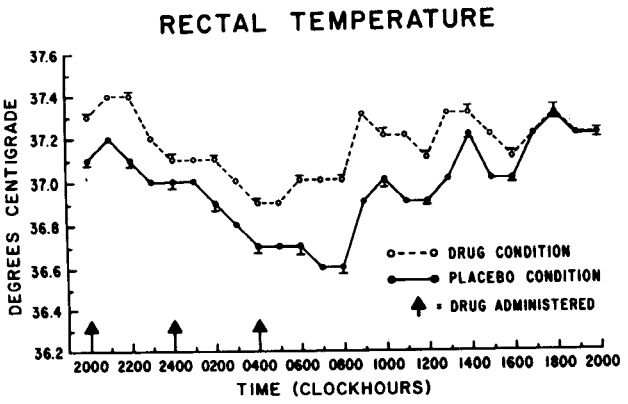

FIGURE 4. Hourly rectal temperature as a function of time ($\bar{X} \pm$ S.E.M., n=10).

Excretion of 17-KGS and dextroamphetamine is shown in Figure 5. Although the peak for the steroid fraction under the drug condition appears earlier and at a level about 0.1 mg/hr lower than the peak for the placebo condition, the only significant difference for this measure is for time ($p \leq .001$). This generally reflects the expected diurnal rhythm effect.

The curves for urinary excretion of E and the excretion of dextroamphetamine during the drug condition are shown in Figure 6. Epinephrine excretion rates for the drug condition are elevated over those for the placebo condition ($p \leq .001$). The degree of elevation increases over time ($p \leq .05$) for the drug condition but drops to the level of the placebo condition by the end of the 24-hour period. The drug condition by time interaction was also significant ($p \leq .001$).

Figure 7 shows the curves of NE excretion rates for the two conditions and the urinary excretion rate for dextroamphetamine. The curves show the NE excretion levels to be, on the average, higher under the drug condition than under the placebo condition. Although the difference is significant ($p \leq .05$), the excretion pattern is variable. The time course of NE excretion in the drug condition is biphasic, with one peak at 2400 and a second, slightly higher peak at 1200. None of the interaction effects among drugs, groups, and time was statistically significant.

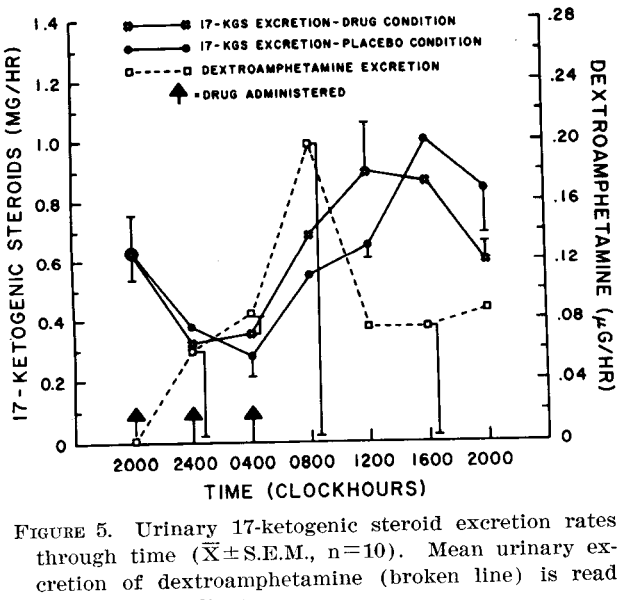

FIGURE 5. Urinary 17-ketogenic steroid excretion rates through time ($\bar{X} \pm$ S.E.M., n=10). Mean urinary excretion of dextroamphetamine (broken line) is read on the right ordinate.

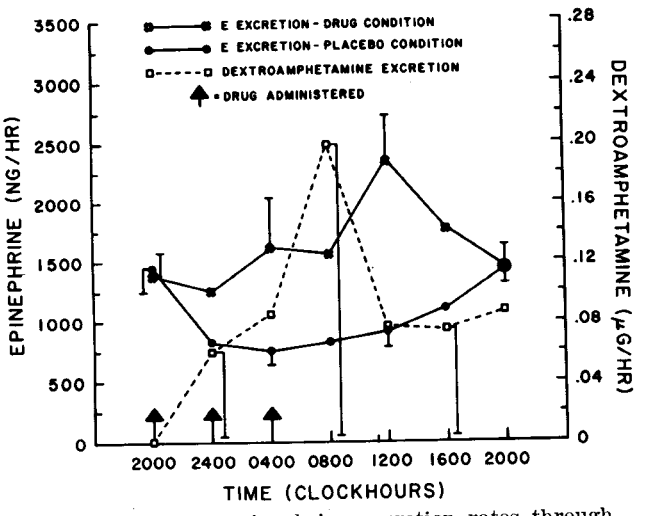

FIGURE 6. Urinary epinephrine excretion rates through time ($\bar{X} \pm$ S.E.M., n=10). Mean urinary excretion of dextroamphetamine (broken line) is read on the right ordinate.

IV. Discussion.

A. *Fatigue Checklist.* The period without sleep led the subjects to describe their general condition as being characterized by moderate fatigue under both the drug and the placebo conditions. The difference of less than one unit on the 20-point scale is small (less than 5 percent). It is of interest that the drug did not appear to result in a measurable difference on the fatigue parameter, especially since performance was maintained at a significantly higher level under the drug condition than under the placebo condition. Perhaps the subjective parameter being assessed by the scale was not directed at the proper domain; i.e., greater emphasis should have been placed on the detection of feelings, alertness, or sleepiness rather

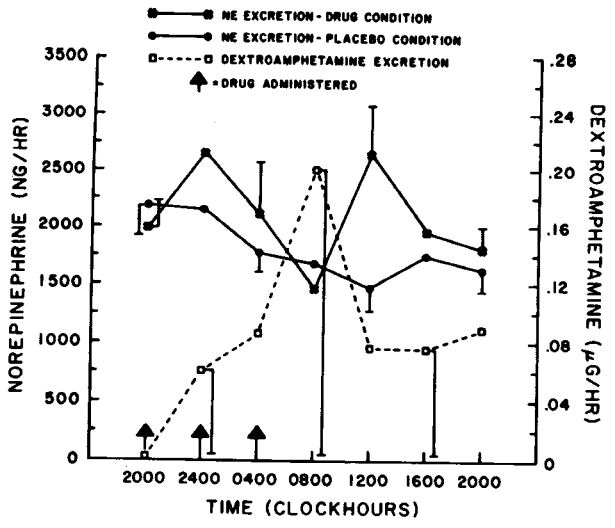

FIGURE 7. Urinary norepinephrine excretion rates through time ($\bar{X} \pm$ S.E.M., n=10). Mean urinary excretion of dextroamphetamine (broken line) is read on the right ordinate.

than fatigue *per se*. In any event, the checklist failed to reveal differences under conditions in which objective measures of performance revealed substantially significant differences.

B. *Subjective Performance Estimates.* The accuracy of the subjects' estimates of their performance is difficult to ascertain because the method for computing the "true" score necessarily contained some arbitrary elements. Whereas the true score was based on an equal-variance measure of overall performance, it is very unlikely that the subjects had precise feedback on the monitoring tasks; further, since the estimates were made at the end of a session, we would not expect the subjects to remember with any great accuracy the levels of performance maintained. It is likely that, with appropriate feedback and sufficient training, the subjects could learn to produce rather good estimates during the earlier periods of the session. Thus, the term "overestimate" should be interpreted in a relativistic manner. However, the estimates were generally accurate in that, under both conditions, as the level of performance decreased, the estimate also decreased. Overall, the very small difference in the accuracy of the estimates under the two conditions implies that the drug did not lead to overestimation of performance capabilities.

C. *Complex Performance.* If we think of the totality of the different task combinations of the MTPB as being a "job" (as the term "job" is used in everyday discourse), then the overall composite score may be thought of as an index of how well that job is performed. Thus, the general finding was that performance of the job was better under the dextroamphetamine condition than under the placebo condition. As shown in Figure 2, performance under the drug condition was better than under the placebo condition from 0400 until the end of the experiment, even though the last drug capsule was ingested at 0400. The continued, though not statistically significant, superiority of the drug condition at 1600 and 2000 may have resulted from the continued presence of the drug in the subjects' systems, or it may have been the result of the drug's having allowed a less fatiguing night without sleep. The data do not allow an assignment of weight to the contribution of these two possible factors.

If we consider the elements of the task complex, we see that there is a large variation in the susceptibility of the individual tasks to the possible deleterious effects of sleep loss and, by inference, the alleviation of those effects by dextroamphetamine. The most sensitive tasks appear to be the lights and meters tasks, both of which involve performance of monitoring. In addition, the tracking task and the pattern identification task were performed significantly better under the drug condition than under the placebo condition. Considering first the monitoring tasks, it should be noted that these tasks require systematic scanning of the performance panel to achieve good performance. Good monitoring performance generally depends on the ability of the subject to divert his attention from ongoing tasks requiring relatively sustained attention (such as mental arithmetic) and his ability to rapidly detect and respond to "abnormal states" of the monitoring tasks. The structure of the pattern identification task requires a good sense of timing. The standard pattern (a six-bar histogram graph) is present for 5 seconds and each of two comparison patterns is present for only 2 seconds. Thus, the subject must divert his attention from whatever other tasks are active to the pattern identification display at specific times if the briefly presented problem elements are to be seen and identified. Similarly, the subject must be able to shift his attention back and forth between the tracking task display and the other tasks in order to

maintain good performance. In contrast, the presentation of a problem on the arithmetic task is accompanied by a rather loud noise produced by the resetting of the keys of the response mechanism as well as the onset of the nine, rather bright Nixie tubes used to present the problem elements. On the group problem-solving task, although the feedback lights are no more visible than the monitoring lights, the group nature of the task tends to compel the typical subject to attend to this task with some care; namely, all of the subjects are—or, if they pay attention, can be—aware of how each individual subject is performing on this task. Thus, a certain amount of group pressure is exerted on individual subjects to perform well. In fact, occasionally a subject is found who, if he is poor on one or more of the other tasks, will simply let those tasks go in order not to be obviously poor on the group problem-solving task. Another factor to be considered in evaluating the individual tasks is the consistently observed tendency of subjects to attach different priorities to the different tasks. As noted above, the problem-solving task is given rather high priority, as is the arithmetic task; in this latter case the reason is, perhaps, that many people feel a need to demonstrate that they are reasonably proficient at carrying out simple addition and subtraction.

Performance of the task complex as a whole requires skill in the domain of time sharing. The subject, to perform well, must be able to shift his attention rapidly from one type of activity to another. In this sense, the monitoring tasks can be thought of as providing an index of the "channel capacity" that the subject has to spare after giving what he considers to be adequate attention to the major tasks; i.e., those tasks to which he gives priority. Pursuing this line of reasoning to its conclusion, then, we would say, at the descriptive level, that the dextroamphetamine mitigates the performance effects of the period of sleep loss by preventing the reduction of the subject's channel capacity.

These general findings are clearly in line with those of previous investigators as reviewed by Weiss and Laties.[15] Thus, the major contribution of the present study, with respect to performance measurements, lies in the methodological refinement permitted by the MTPB; namely, the MTPB brought out the differential effects of sleep loss as affected by dextroamphetamine in relation to the nature of the task demands.

D. *Physiological and Biochemical Effects.* Stolman and Stewart[13] report that the amphetamines reach a maximum excretion rate between 3 and 12 hours after ingestion and that an average of 29 percent of the dose is excreted in 24 hours, but there is a wide individual variation in excretion rate. The mean total excretion of dextroamphetamine for the subjects in this experiment was 15.6 percent, ranging from a low of 2.6 percent to a high of 43.3 percent in the 24-hour period for which measurements were made. The average rate of excretion of the drug remained at an elevated level throughout the study, and the post-drug levels did not go below that observed in the samples taken 4 hours after ingestion of the first capsule. When this finding is considered in conjunction with the data of Stolman and Stewart,[13] it would appear that (on the average) substantial amounts of the unmetabolized drug could remain in the subjects' systems at the end of the experiment.

The data indicate that dextroamphetamine is sympathomimetic, particularly evidenced by the cardiovascular and the temperature regulation systems. Wurtman,[16] in reviewing the results of a number of investigators, describes the role of the catecholamines in the mechanisms of the physiological effects of amphetamine on the central nervous system. Amphetamine liberates stored NE from nerve endings in the brain.[13] However, the amine thus released is not metabolized before it leaves the nerve ending, and thus it is able to exert continuing physiologic effects.[8] The uptake of H^3-norepinephrine is blocked by amphetamine.[8 9] Since uptake appears to be a major mechanism for catecholamine inactivation in adrenergic nerves, this blockade in the brain probably lengthens the period that NE molecules released at central synapses remain effective. Amphetamine may also interfere with the metabolism of catecholamines by monoamine oxidase.[10] The definitive increases in urinary E (Figure 6) and NE (Figure 7) levels with dextroamphetamine over those of the placebo-condition level lend support to this interpretation. The substantially higher value of T_{re} under the drug condition than under the placebo condition (Figure 4) probably occurs because the amphetamine decreases perspiration and increases vasoconstriction, both of which conserve

heat, and also because it increases muscle tone for greater heat production. Further, relatively large amounts of NE may be released from the hypothalamus, the site of central regulation of body temperature. The myocardium contains numerous sympathetic nerve endings and can take up significant quantities of catecholamines. The elevated HR (Figure 3) with dextroamphetamine may reflect the role of the catecholamines in augmenting cardiac output under stress.

Differences in the excretion patterns of E and NE may be traced to the anatomical sites at which each was secreted. Most of the E originates in the adrenal medulla, where it is secreted sporadically, the quantities related to the intensity of the stimulus, while most of the NE is stored in adrenergic vesicles located in the several organs containing sympathetic innervation. Thus, the rate of release and subsequent excretion of NE may differ from one organ to another, resulting in the irregular pattern through time.

Dextroamphetamine has little apparent effect on 17-KGS excretion (Figure 5), since the excretion rate with the placebo is not different from that with the drug and excretion patterns under both conditions are probably the result of diurnal variation.

V. Summary and Conclusions.

Performance of a complex task was maintained at a significantly higher level during a period of 24 hours without sleep when subjects were given 15 mg of dextroamphetamine sulfate in three 5-mg doses at 4-hour intervals. However, subjective measures showed that neither feelings of fatigue nor the accuracy of self-estimates of performance efficiency were significantly affected by the administration of the drug as compared to a placebo control condition. Increases were found in the levels of HR, T_{re}, and urinary catecholamine excretion. Excretion of urinary dextroamphetamine reached a peak about 4 hours after administration of the third and final drug capsule, but excretion levels were still quite elevated at the end of the study. Presumably because of the continued presence of the drug, the various biochemical and physiological parameters showed effects for 8 to 16 hours after the last drug capsule was administered, and performance was also maintained at a higher level throughout the withdrawal period.

The results of this study should not be interpreted to suggest that the detrimental effects of sleep loss can be prevented by the administration of dextroamphetamine sulfate. Although the difference between the presleep loss and the sleep loss conditions was not statistically significant, performance under the drug condition during the morning and afternoon hours of the second day suggested some loss of efficiency. The only inference permitted by a strict interpretation of the results is that performance would be expected to be maintained at a higher level under dextroamphetamine than without it. It should also be noted that, since dextroamphetamine is generally regarded as one of the most effective stimulants, more common, legal stimulants (such as caffeine) would not be expected to insure satisfactory performance levels under conditions of sleep loss.

In the realm of methodology, the detailed analysis of the performance data suggests that monitoring tasks embedded in a task complex provide the most sensitive indicators of the impact of stresses such as sleep loss. The implication of this finding is that tasks that would typically be regarded as peripheral to the main duties of the operator, and are thus assigned a lower priority, are likely to suffer even though the major, high priority tasks appear to be unaffected by sleep loss.

REFERENCES

1. Berry, C. A.: Summary of Medical Experience in the Apollo 7 through 11 Manned Spaceflights, AEROSPACE MED., 41(5): 500–519, 1970.
2. Chiles, W. D., E. A. Alluisi, and O. S. Adams: Work Schedules and Performance During Confinement, HUM. FACTORS, 10:143–196, 1968.
3. Chiles, W. D., A. E. Jennings, and G. West: Multiple Task Performance as a Predictor of the Potential of Air Traffic Controller Trainees, FAA Office of Aviation Medicine Report No. AM–72–5, 1972.
4. Few, J. D.: A Method for the Analysis of Urinary 17-Hydroxycorticosteroids, J. ENDOCRINOL., 22:31–46, 1961.
5. Fiorica, V., and R. Moses: Automated Differential Fluorometric Analysis of Norepinephrine and Epinephrine in Blood Plasma and Urine, BIOCHEM. MED., 5:483–504, 1971.
6. Graybiel, A., C. D. Wood, J. Knepton, J. P. Hoche, and G. F. Perkins: Human Assay of Antimotion Sickness Drugs, AEROSPACE MED., 46:1107–1118, 1975.
7. Keller, R. E. and W. C. Ellenbogen: The Determination of D-Amphetamine in Body Fluids, J. PHARMACOL. EXP. THER., 106:77–82, 1952.
8. Glowinski, J., and J. Axelrod: Effects of Drugs on the Disposition of H^3-Norepinephrine in the Rat Brain, PHARMOCAL. REV., 18:775–785, 1966.
9. Glowinski, J., and J. Axelrod: Effects of Drugs on the Uptake, Release, and Metabolism of H^3-Norepinephrine in the Rat Brain, J. PHARMACOL. EXP. THER., 149:43–49, 1965.
10. Glowinski, J., J. Axelrod, and L. L. Iversen: Regional Studies of Catecholamines in the Rat Brain. IV: Effects of Drugs on the Disposition and Metabolism of H^3-Norepinephrine and H^3Dopamine, J. PHARMACOL. EXP. THER., 153:30–41, 1966.
11. Pearson, R. G., and G. E. Byars, Jr.: The Development and Validation of a Checklist for Measuring Subjective Fatigue. USAF School of Aerospace Medicine Report No. TR–56–115, 1956.
13. Vogt, M.: The Concentration of Sympathin in Different Parts of the Central Nervous System Under Normal Conditions and After the Administration of Drugs. J. PHYSIOL., 123:451–481, 1954.
14. Weiss, B. G., and V. G. Laties: Enhancement of Human Performance by Caffeine and the Amphetamines. PHARMACOL. REV., 14:1–36, 1962.
15. Wurtman, R. J.: *Catecholamines.* Little, Brown, and Co., Boston, 1966, pp. 79–83.