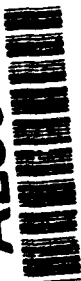


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Effects of Dextroamphetamine on Helicopter Pilot Performance: A UH-60 Simulator Study

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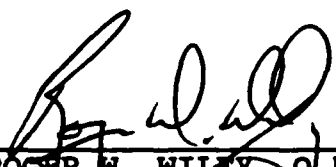
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19. ABSTRACT (Continue on reverse if necessary and identify by block number) To determine the efficacy and safety of using Dexedrine to sustain aviator performance during periods of sleep deprivation, a placebo-controlled study was conducted. Six U.S. Army helicopter pilots completed five, 1-hour flights in a specially-instrumented UH-60 simulator while their performance was evaluated via a computerized scoring system. Immediately following each flight, data were collected on electroencephalographic (EEG) activity, cognitive/psychomotor performance, and subjective mood ratings. The testing sessions began with flights at 0100, 0500, 0900, 1300, and 1700. One hour prior to each of the first three sessions on the drug-administration days, the aviators were given 10 mg of Dexedrine or placebo. Statistical analyses of the flight maneuvers revealed that Dexedrine improved aviator control on every maneuver with the exception of the hovering turns and the formation flight. Performance on the stationary hovers, the low level navigation, the climbs and descents, straight-and-level segments, standard-rate turns, and the left-descending turn all manifested at least one Dexedrine-related enhancement. The (continued)					
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times of day at which Dexedrine facilitated flight performance most noticeably were 0500, 0900, and 1700; there were only three instances in which statistically significant differences between Dexedrine and placebo occurred during the 0100 or 1300 flights. Analyses of the EEG and mood data showed that alertness was sustained significantly by Dexedrine. The cognitive testing did not reveal similar effects; however, this may have been due to low test sensitivity and short task duration. Psychomotor performance on a desktop flight simulation task indicated that Dexedrine tended to prevent a midday reduction in performance which was seen under placebo. Vital signs data showed there were significant Dexedrine-related increases in temperature, pulse, and blood pressure; however, none of these were clinically significant. Polysomnographic data indicated that recovery sleep was slightly less restful following the Dexedrine versus the placebo day probably because of the drug's long half-life. No adverse behavioral effects were observed in any of the subjects. In conclusion, the results of this study suggest that Dexedrine is safe and effective in sustaining helicopter pilot performance during short periods of sleep loss.

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Introduction

Aviation and other personnel are often faced with the requirement for sustained or continuous operations, particularly during times of military conflict. Technological advances, such as night vision devices, have created opportunities to operate effectively around the clock. However, while it is technically feasible, from an equipment standpoint, to work and fight throughout the day and night, the human element in the operational chain prohibits continuous, sustained work schedules because of the requirement for sleep and rest.

Increasingly, the Army is emphasizing the importance of ensuring that personnel receive adequate amounts of rest to maintain acceptable levels of operational performance. However, due to current battlefield doctrine (necessitating sustained or continuous operations), it is unrealistic to anticipate that proper crew rest policies will be maintained at all times. Thus, it is necessary to examine methods for maximizing our fighting strength under less than optimal circumstances such as those in which soldiers are fatigued and/or sleep deprived.

After a unit makes every attempt to enforce sleep discipline policies and invoke other nonpharmacological strategies, the only alternative for maintaining adequate levels of alertness and performance when aviators are sleep deprived is the administration of stimulant compounds. However, an examination of the literature shows that, while stimulant compounds (particularly dextroamphetamine) have been used operationally by the military since World War II, data from scientifically-controlled studies are scarce. Also, it is clear from the published studies that the predominant focus has been on the efficacy of single doses of stimulants to recover performance which already has deteriorated, rather than on the efficacy of stimulants to prevent the effects of sleep deprivation from ever occurring (Babkoff et al., 1992). Thus, research is needed to determine the utility of using stimulants to maintain aviator performance in situations where, for operational reasons, proper sleep cannot be obtained.

Of the stimulants available, amphetamines are the most promising in terms of affecting performance without inducing unwanted side effects, and research indicates that d-amphetamine is more potent than l-amphetamine for this purpose. Therefore, this investigation examined the efficacy of d-amphetamine (Dexedrine) as a prophylactic measure administered to aviators to sustain performance during periods of sleep loss.

Dextroamphetamine (Dexedrine)

Dexedrine (Smith, Kline, and French) is dextroamphetamine sulfate, supplied in 5, 10, and 15 mg Spansule sustained-release capsules, 5 mg tablets, and an elixir supplying 5 mg amphetamine per 5 ml (Physicians' Desk Reference, 1993). Amphetamines (and dextroamphetamine) belong to the general category of compounds referred to as sympathomimetic amines.

Although the various sympathomimetic amines differ in their effects based on differing amounts and types of central and peripheral stimulation (Benowitz, 1990), they have broad actions which can be classified as: 1) peripheral excitatory (stimulates certain smooth muscles like those in blood vessels of the skin, mucous membranes, and glands like salivary and sweat glands); 2) peripheral inhibitory on other smooth muscles (like those in the gut, blood vessels supplying skeletal muscles, and the bronchial tree); 3) cardiac excitatory (increased heart rate); 4) metabolic actions (increased glycogen conversion in liver and muscle); 5) endocrine actions (modulation of insulin and pituitary hormones); and 6) central nervous system (CNS) effects (increased wakefulness and motor activity with reduced appetite) (Weiner, 1980). Amphetamines have many, but not all of these effects.

The actions of amphetamines are similar to those of epinephrine. Amphetamine is referred to as a "mixed-acting" sympathomimetic amine because it exerts its effects in two ways: 1) by directly stimulating postsynaptic neurons and 2) by enhancing the release of norepinephrine and dopamine (Carlson, 1977).

Typical effects

Amphetamine has both CNS and peripheral effects (Weiner, 1980). Oral amphetamine elevates blood pressure (systolic and diastolic), but does not increase heart rate or cerebral blood flow. The bronchial muscle is slightly relaxed, but respiration rate and volume are unaffected. The urinary bladder sphincter is constricted. Gastrointestinal effects are not predictable. The CNS is stimulated, particularly with d-amphetamine, and the depressant effects of other drugs are lessened. Psychological effects of doses ranging from 10-30 mg are increased wakefulness, alertness, initiative, and concentration, with elevated mood, sometimes euphoria, improved task performance, and decreased fatigue. Amphetamines have been used to prolong performance of vigilance tasks, and in situations where performance has degraded due to sleep loss, amphetamines have produced improvements in tasks requiring sustained attention. Amphetamines alter sleep EEG by cutting in half the typical amount of REM sleep. They

alter the waking EEG by increasing desynchronous activity and producing a shift toward higher frequencies. Amphetamine suppresses the appetite probably via the lateral hypothalamus. Occasionally, amphetamine will produce a slight elevation in body temperature.

Dosage

The usual chronic oral dose of dextroamphetamine is 5 mg, 2-3 times daily; however, studies employing the drug to prolong wakefulness and performance typically employ larger doses in the range of 10-20 mg (Weiss and Laties, 1967). Prior to administering normal therapeutic doses to humans, a test dose of 2.5 mg is recommended since toxic manifestations have been seen (as an idiosyncrasy) after even a 2 mg dose, although reactions are rare with doses under 15 mg.

Pharmacokinetics

A single dose of two 5 mg tablets has been shown to produce an average peak blood level of 29.2 ng/ml at approximately 2 hours. The average half life is 10.25 hours (Physicians' Desk Reference, 1993).

Adverse reactions

The most common cardiovascular adverse effects are palpitations, tachycardia, and elevated blood pressure. The most common adverse CNS reactions are overstimulation, restlessness, dizziness, insomnia, euphoria, dyskinesia, tremor, and headache. The most common adverse gastrointestinal reactions are dryness of mouth, diarrhea, or constipation (Physicians' Desk Reference, 1993).

Tolerance and toxicity

Although the amphetamines can be toxic at doses only slightly higher than the recommended dose, tolerance develops quickly with repeated use. Ingestion of an acute dose of 1 mg/kg is considered life-threatening (Benowitz, 1990). In the event of acute intoxication, chlorpromazine and an alpha-receptor blocking agent should reduce both the CNS and the pressor effects of amphetamine (Weiner, 1980); however, Benowitz (1990) reports that there is no specific antidote. He recommends: 1) maintaining airways and assisting ventilation; 2) treating any symptoms of agitation, seizures, coma, and hyperthermia; 3) monitoring vital signs and ECG for at least 6 hours; 4) treating hypertension,

tachyarrhythmias, and arterial vasospasm; and 5) performing gastric lavage and administering charcoal and a cathartic.

Background

The fact that humans need sleep to maintain acceptable levels of performance is well documented. It is assumed that sleep serves the basic function of enforcing a rest period for the restitution of both the body and brain following periods of wakefulness (Horne, 1978). However, the exact mechanisms responsible for the restorative value of sleep have not been established.

There is little debate that sleep is a requirement, and that humans who are required to work long periods without proper sleep experience a number of problems. Krueger (1989) reviewed numerous studies on the effects of sustained work and sleep loss, and he summarized several of the more salient effects of sleep deprivation as follows: 1) increased mental "lapses" which have an impact on the speed and accuracy of responses; 2) reduced ability to acquire and recall information in complex tasks; 3) changes in brain activity associated with decreased alertness; and 4) an overall slowing of cognitive ability which reduces performance in conjunction with disturbed mood and decreased motivation. Furthermore, it was pointed out that humans cannot overcome the effects of sleep loss through any training mechanism, such as by gaining experience with performing under sleep-deprived conditions. However, pharmacological compounds (i.e., amphetamines) have been used to temporarily alleviate the fatigue and drowsiness associated with sleep deprivation.

Overcoming the effects of sleep loss is but one application of the amphetamines and other stimulants. Amphetamines have been used for a wide array of purposes which includes appetite suppression, treatment of narcolepsy, treatment of hyperactivity in children, and enhancement of athletic and other types of performance. Although their use for the first three indications has been well-accepted, the use of amphetamines to enhance physical performance or to sustain or restore mental performance under conditions of sleep deprivation has not been universally condoned. However, amphetamines and other stimulants have been used for these purposes in a number of settings.

Effects on physical performance

In athletic competition, stimulants have been used at least since the latter part of the nineteenth century when cyclists took caffeine to improve endurance (Wagner, 1991). By the early 1950s, amphetamines were being used by athletes; and over the

next several years, the problem of amphetamine abuse was severe enough to prompt special investigations by the medical community. It is estimated that about three percent of athletes continue to use amphetamines for their ergogenic effects. This is understandable given the positive effects of these drugs as described by Wagner (1991). Amphetamines (14 mg/70 kg) have been shown to improve performance in swimming, running, and weight throwing 2-3 hours postdose. Additionally, doses of 15 mg/70 kg have produced improvements in strength, speed, aerobic capacity, muscular power, and endurance.

When enhancements of physical strength and endurance are desired, amphetamine is typically beneficial (Wagner, 1989). However, these drugs also exert physiological and mental or psychomotor effects.

Effects on physiology and simple task performance

Morselli et al., (1976) reported several basic amphetamine effects from their study of two different 20 mg preparations (salt-based and resinate). Blood work indicated that average peak plasma levels with these compounds occurred 4 hours post administration for both preparations while the peak blood-cells levels occurred at 4 hours for the resinate and 6 hours for the salt-based form. Increases in blood pressure (34 mmHg systolic, 25 mmHg diastolic after the salt; and 15 mmHg systolic and 7 mmHg diastolic after the resinate) were observed, but subsided completely within 4 hours. There was a slight decrease in heart rate during the first 45 minutes (in 4 of 6 subjects) with a subsequent slight (10-15 bpm) increase lasting 60-90 minutes. In addition, there were EEG amplitude reductions in the alpha range and increased fast activity 45-60 minutes postdrug. Some side effects (nausea, cramps, dry mouth, headache, etc.) were seen with both preparations although those with the salt base were more pronounced.

Skill on a letter matching test, a number comparison test, a memory test, and a test in which subjects placed metal pins into holes, was improved under both forms of amphetamine. No conclusive relationship was seen between blood levels and performance, but there was an apparent relationship between the rate at which amphetamine entered the blood stream and the occurrence of side effects.

Earlier investigations reviewed by Cole (1967) found similar results with regard to the pressor effects and task performance. It was reported that amphetamine increased both blood pressure and metabolic activity, as well as improving performance on intellectual tasks. Additionally, evidence showed that amphetamine enhanced motor task performance in both humans and

animals, and it was postulated that the drug-induced facilitation was a function of increased vigilance with which subjects attended to task-relevant cues.

Effects on vigilance

The vigilance enhancing effects of amphetamine during extended work periods are well documented. Payne (1953) and Payne and Hauty (1954) studied the ability of 5 mg Dexedrine and 20 mg of a caffeine derivative, as well as instructional manipulations, to prolong performance in a task where subjects monitored four dials and minimized pointer deviations throughout a 4-hour session. The results clearly indicated that both Dexedrine and caffeine prevented the performance decrements which occurred across time under the placebo and control conditions. Also, Dexedrine maintained performance for longer than the caffeine (4 versus 2 hours). A followup study (Haute and Payne, 1955) was designed to examine the impact of enhanced task cues, different instructional manipulations, and the effects of d-amphetamine (5 mg), time-released d-amphetamine, a caffeine derivative, and two compounds containing diphenhydramine (50 mg) combined with other drugs. Results showed that providing additional cues and intermediate work breaks improved overall task performance, and both preparations of d-amphetamine (and to some extent the caffeine) significantly curtailed declines in vigilance during the 7 hours. The amphetamines were clearly the most effective performance sustainers.

A later investigation of various doses of d-amphetamine (Payne, Hauty, and Moore, 1957) confirmed the performance sustaining effects noted earlier, and it was found that, with normal (presumably nonsleep-deprived) subjects, a 5-7.5 mg dose was optimal. However, a 10 mg dose also was effective, a finding which agrees with other investigators.

Effects on performance sustainment after sleep deprivation

Recently, Newhouse et al., (1992) expanded our knowledge of the utility of amphetamine for maintaining the performance of sleep-deprived subjects. Alertness, performance, and physiological changes were assessed in an experiment where 3 groups of subjects were sleep-deprived for 48 hours and then administered oral d-amphetamine (5, 10, or 20 mg), intravenous nicotine (0.39, 0.53, 0.79, or 1.05 mg), or the monoamine oxidase inhibitor l-deprenyl (20 or 30 mg) prior to an additional 12 hours of deprivation. Results indicated the nicotine administration produced only minor changes in performance and physiology without affecting alertness. L-deprenyl (30 mg) was better than nicotine in terms of accuracy improvement on logical

reasoning, but once again, alertness was unaffected. In contrast, the 20 mg dose of d-amphetamine produced marked improvements in addition/subtraction (lasting for over 10 hours) and gradual improvements in logical-reasoning (significant between 5.5 and 7.5 hours postdose). Also, there was an increase in alertness for 7 hours, blood pressure for 5 hours, heart rate (only after 8-10 hours), and temperature. The 10 mg dose exerted fewer performance effects which were shorter in duration, and no physiological effects. The 5 mg dose did not affect any of the measures. Interestingly, the observed performance enhancements with 20 mg continued even after the subjects' subjective feelings of increased vigor had subsided. Also, it should be noted that amphetamine improved performance without impairing judgement--findings consistent with those of Shappell, Neri, and DeJohn (1992) who determined that 10 mg/70 kg d-methamphetamine reduced the tendency of personnel in sustained operations to engage in faster, but more risky and impulsive responding, as they became fatigued.

This positive appraisal of amphetamine confirms an earlier study by Newhouse et al., (1989) in which sleep-deprived subjects were administered 5, 10, or 20 mg d-amphetamine and tested on alertness, cognitive performance, and subjective mood states. Subjects were given the drug following 48 hours of sleep deprivation, after which they were tested for an additional 12 hours. The results indicated 20 mg was effective in increasing sleep latency (up to 7 hours postdose) and self-ratings of alertness, mood, and vigor, while decreasing self-ratings of discomfort, and fatigue. In addition, 20 mg increased performance on addition/subtraction within 90 minutes postdose and maintained performance for over 10 hours. The same dose produced a more gradual increase in logical reasoning which was significant at 5.5 through 7.5 hours postdose. Choice reaction time was likewise improved by 20 mg in terms of speed (an effect which persisted for 10 hours postdose), but accuracy was not significantly improved. The decrements observed in the speed of completing a spatial rotation task were reversed only partially by amphetamine. The 10 mg dose typically exerted far fewer and smaller effects which were of shorter duration, and the 5 mg dose basically was ineffective.

These results are consistent with those of Hartmann, Orzack, and Branconnier (1977) who studied the effects of l-amphetamine (10 mg) and d-amphetamine (10 mg) on the mood, EEG, and performance of subjects exposed to a much shorter period of sleep deprivation (1 night). The authors found that subjective reports of decreased vigor and increased fatigue associated with sleep deprivation were not alleviated by either drug--a finding which is not too surprising in light of the earlier limited effects of 10 mg reported by Newhouse et al., (1989). However, cumulative omission errors in the vigilance task were reduced by

d-amphetamine, and d-amphetamine also was effective in maintaining EEG alpha activity at predeprivation levels in comparison to either placebo or l-amphetamine. The fact that d-amphetamine was the most potent of the two preparations supports the contention by others (Smith and Davis, 1977) that d-amphetamine is approximately twice as effective as l-amphetamine.

Effects on mood and motivation

Typically, the effects of amphetamines on mood and motivation are positive and can be summarized as increased euphoria, exhilaration, energy, talkativeness, mental capacity, and desire for work, while the negative effects are increased restlessness and anxiety (Weiss and Laties, 1967). Smith and Davis (1977) confirm these effects, but suggest there might also be a tendency toward increased end-of-day depression with amphetamine, although this was not confirmed statistically. Cole (1967) reviewed studies which reported that amphetamine given to college students produced a pleasurable sensation associated with optimism, friendliness, decisiveness, and light-headedness. The students were less drowsy, bored, dissatisfied, and depressed than a control group. Also, it was pointed out that students asked to estimate the number of correct problems they had solved under the influence of amphetamine overestimated more under amphetamine than placebo--an effect which substantiates the idea that amphetamines tend to improve overall attitude. Finally, it has been observed that amphetamines tend to create a nonspecific drive factor which increases the need to achieve while under the influence of the drug.

Effects on military performance

The above findings are of particular relevance to the military where it is often necessary for personnel to remain "on task" for extended duty periods without prolonged breaks. Babkoff and Krueger (1992) point out that stimulants have been used by the military since World War II to reduce fatigue and increase performance of soldiers assigned to special duties such as long-range reconnaissance and extended transport flights. Although stimulant use has not been well-studied in a field setting, occasional reports tend to substantiate their operational utility. Tyler (1947) found that volunteers from the Army, Marines, and civilian work camps were better at marksmanship, steadiness, and reaction time, and were more able to stay alert after 48 hours of sleep deprivation under the influence of 10 mg benzedrine sulfate given every 8-12 hours. More recently, Senechal (1988) reported that EF-111A Raven jet crews who were administered 5 mg Dexedrine during an Air Force strike on Libya in April of 1986 experienced positive effects in

terms of overcoming the fatigue of the mission itself and the sleep deprivation which occurred during earlier preparation for the mission. There were no in-flight or landing problems, and all of these electronic-jamming aircraft returned safely to base.

Cornum (1993) reported that dextroamphetamine also was used with 35 F-15C pilots who were flying combat air patrol missions during Operation Desert Shield/Storm. These pilots were not only flying long missions (6-11 hours), but they were sleep deprived and suffering from circadian desynchronization as well. To counteract potentially lethal performance decrements, the pilots were issued 5-6 dextroamphetamine tablets (5 mg) at the beginning of flights and were told to self-administer one tablet every 2-4 hours as needed to maintain alertness until landing. The aviators reported clear benefit from the drug, and the unit commander ultimately concluded that dextroamphetamine administration contributed significantly to the safety of operations. There were no reported adverse effects, even in personnel who took 10 mg at a time, and no aviators reported a need to continue the drug once proper work/sleep schedules were reinstated.

Studies summarized by Weiss and Laties (1967) provide further evidence of the facilitative effects of amphetamine in a military performance context. In one study by Seashore and Ivy (1953), two doses of either amphetamine (10 mg) or methamphetamine (5 mg) were shown to improve subjective reports of alertness and motor tests after subjects performed an 18-20 mile march and a night of guard duty. In another investigation by Somerville (1946), it was shown that 30 or 35 mg amphetamine (given in divided doses) enhanced rifle firing speed and accuracy during the final 22 hours of a 56-hour training exercise. However, it appeared from an earlier study that enhancements in marksmanship and obstacle course performance did not occur under amphetamine (15 mg) after the road march alone. Thus, the effects of amphetamine may be more pronounced in the presence of higher levels of fatigue such as those associated with sleep loss, rather than the fatigue associated only with increased physical activity.

Summary

In summary, the majority of amphetamine-related mood, attitude, and performance effects are favorable, especially when compared to the well-known negative effects of fatigue and sleep deprivation. Although some authors have failed to thoroughly confirm the advantages of amphetamines, particularly in nonsleep-deprived individuals, the majority of studies show favorable

results. Also, while other stimulants such as caffeine (Lieberman, 1992) and pemoline (Babkoff et al., 1992) show promise for maintaining alertness under conditions of prolonged work and fatigue, the amphetamines appear to be more beneficial in terms of consistency, duration of action, and minimal side effects. In fact, it has been concluded that "to date, the most promising stimulants to counteract performance decrements attributed to aircrew sustained operations are the amphetamines" (p. 269; Shappell, Neri, and DeJohn, 1992).

Thus, in situations where aviators are unable to receive proper restorative sleep/rest, amphetamines may be the key to preventing dangerous flight performance decrements. However, there have been no controlled studies on the efficacy of using amphetamines to sustain aviator flight performance in either the fixed-wing or rotary-wing environment.

Objectives

The present investigation was performed to determine the effects of dextroamphetamine (Dexedrine) in safely sustaining alertness and performance despite sleep loss in an aviation context. The study employed a variety of assessments to determine the effects of repeated 10-mg doses of Dexedrine on flight performance, mood, cognition, and CNS function of helicopter pilots performing around-the-clock flight operations.

Methods

Subjects

Six UH-60 qualified aviators (between the ages of 25 and 32, with a mean age of 27.8 years) were admitted to the protocol after signing appropriate consent forms and passing a medical evaluation. Subjects were not permitted to consume caffeinated beverages or any type of medication (other than acetaminophen or ibuprofen) for the duration of the protocol. Subjects were asked to significantly reduce or completely eliminate caffeine consumption beginning several days prior to the study (although none of the subjects reported normally using substantial amounts of caffeine). All of the subjects were non-smokers.

Apparatus

Physiological data

Oral temperatures were collected with an IVAC thermometer* (Model number 811). Pulse and blood pressure data were collected either with a Critikon vital signs monitor* (Model number 1846SX) or a conventional sphygmomanometer. An initial EKG was taken with a Marquette microcomputer augmented cardiograph system*.

UH-60 flight simulator

All simulator flights were conducted on site at the U.S. Army Aeromedical Research Laboratory (USAARL) at Fort Rucker, Alabama, using the UH-60 research flight simulator. This motion-base system includes an operational crew station, computer-generated visual display (which was set for standard daytime flight), environmental conditioning system, and a multichannel data acquisition system.

Flight data were acquired on a VAX 11/780 interfaced to a Perkin-Elmer* digital computer which controlled the UH-60 flight simulator. This system monitored a variety of aspects of simulator control, including heading, airspeed, and altitude control, global positioning system (GPS) readouts, switch positions, and operator console inputs. The acquired data were converted to root mean square (RMS) errors using specialized software routines developed at USAARL (Jones and Higdon, 1991).

EEG evaluations

The electroencephalographic (EEG) evaluations conducted during each subject's waking periods were performed with a Cadwell Spectrum 32*, neurometric analyzer. This device permitted the collection of 21 channels of EEG data which were stored on optical disk for subsequent analysis. The low filter was set at 0.53 Hz, the high filter was set at 70 Hz, and the 60 Hz notch filter was used. Subjects were outfitted with 25 Grass E5SH silver cup electrodes which were affixed to the scalp with collodion for the duration of the study. All active EEG channels were referenced to linked mastoids (A1 and A2).

*See manufacturers' list.

Desktop flight simulation task

A desktop flight simulation program (Microsoft Flight Simulator 4.0*), combined with a custom-designed, timed flight course (Microsoft Aircraft and Scenery Designer*), was used as an additional surrogate for flight performance. This novel task was run on an IBM 486 computer with VGA graphics. Flight control was via a realistic flight yoke (virtual pilot, CH Products*), with system interface using either mouse or keyboard, according to individual subject preference.

Mood questionnaire

The subjective evaluations of changes in mood were made with the Profile of Mood States (POMS) (McNair, Lorr, and Droppleman, 1981). The POMS is a 65-item paper and pencil test which measures affect or mood on 6 scales: 1) tension-anxiety, 2) depression-dejection, 3) anger-hostility, 4) vigor-activity, 5) fatigue-inertia, and 6) confusion-bewilderment. The answers were scored by hand using scoring templates.

Cognitive tests

Changes in basic cognitive abilities were examined with the Synthetic Work Environment, Version 2.0 (Elsmore, 1991). This task, which consisted of a Sternberg memory task, an arithmetic task, a visual monitoring task, and an auditory monitoring task, was administered via a Zenith 248 computer interfaced with a mouse and a 13-inch color monitor.

Polysomnography

Evaluations of whether subjects were experiencing sleep disturbances as a function of drug were made during subjects' sleep periods using a Nihon Kohden electroencephalograph* (model No. EEG-4321P). The EEG data were collected using a subset of the same electrodes attached for the recording of the waking EEG (C3, C4, O1, O2, A1, and A2). Four additional electrodes (SensorMedics*), affixed with adhesive collars immediately prior to each sleep period, were used to collect electrooculographic (EOG) and electromyographic (EMG) data. The time constant for the EEG channels was set at 0.3, and the high filter was set at 35 Hz. For EOG (recorded from the outer canthus of each eye), the time constant was 5.0 and the high filter was set at 10 Hz. For EMG (recorded with submental electrodes), a time constant of 0.003 and a high filter setting of 120 Hz were used. The 60 Hz notch filter was not employed.

Procedure

Each subject completed several simulator flights, electrophysiological evaluations, surrogate flight tasks, cognitive tests, and questionnaires under Dexedrine and placebo. The dose administration schedule was fully counterbalanced, and neither the subjects nor the experimenters were informed about the order of drug/placebo administration. Testing was scheduled for most of the time the subject was awake.

Flight performance

The flight performance evaluations required subjects to perform the maneuvers listed in Table 1. There were three parts to each flight. The first part consisted of tactical navigation in which the subject was required to use visual cues, GPS information, and time information to correctly navigate a prescribed course. The second part consisted of nontactical, upper-airwork in which the subject was required to perform precision maneuvers based upon instrument information. The third part consisted of nap-of-the-earth (NOE) flight in which the subject was required to follow a lead ship during flight at altitudes close to the earth over a prescribed course. The same sequence of maneuvers was used for every subject during each of the flights. These maneuvers were of the type typically flown in a UH-60 aircraft, and they are fully described in the Aircrew Training Manual (Department of the Army, 1988).

The low-level navigation portion of the profile began with four hovers. There was a straight 10-foot hover, a 10-foot hovering turn (360°), a stationary 40-foot hover, and a 40-foot hovering turn. These maneuvers were followed by the subject flying to five different check points using the global position system (GPS).

This part of the flight profile was segmented into eight maneuvers for scoring purposes (two stationary hovers, two hovering turns, and four navigation legs). During the straight hovers, subjects were required to maintain precise control over both altitude and heading, whereas during the hovering turns, subjects focused primarily on altitude control. During the low-level navigation, subjects were required to maintain proper control of altitude, slip, and roll while minimizing the deviation between their actual heading and the bearing to the next checkpoint.

Table 1.

Simulator flight maneuvers.

Maneuver	Description
Low hover	Maintain heading 150°, altitude 10 ft
Low hover turn	Heading from 150° to 330° while holding altitude of 10 ft above ground level
High hover	Maintain heading 330°, altitude 40 ft
High hover turn	Heading from 330° to 150°, while holding altitude of 40 ft above ground level
Navigate to checkpoint 1	Maintain GPS heading within 10 deg Maintain 700 feet MSL within 100 feet Arrive at checkpoint in 3 minutes
Navigate to checkpoint 2	Maintain GPS heading within 10 deg Maintain 600 feet MSL within 100 feet Arrive at checkpoint in 2 minutes
Navigate to checkpoint 3	Maintain GPS heading within 10 deg Maintain 600 feet MSL within 100 feet Arrive at checkpoint in 5 minutes
Navigate to checkpoint 4	Maintain GPS heading within 10 deg Maintain 600 feet MSL within 100 feet Arrive at checkpoint in 2 minutes
Navigate to checkpoint 5	Maintain GPS heading within 10 deg Maintain 700 feet MSL within 100 feet Arrive at checkpoint in 4 minutes
Transition	Establish heading 360°, airspeed 120 k, altitude 2000 ft MSL
Straight & level	Maintain the above parameters 1 min
Left standard rate turn	Perform 360° left standard rate turn maintaining airspeed and altitude
Straight & level	Maintain heading 360°, airspeed 120 k, and altitude 2000 ft MSL for 1 min
Climb	Climb from 2000 to 2500 feet while maintaining heading and airspeed (1 min)

Table 1 (Continued).

Simulator flight maneuvers.

Maneuver	Description
Right standard rate turn	Perform 180° right standard rate turn maintaining airspeed and altitude
Straight & level	Maintain heading 180°, airspeed 120 k, and altitude 2500 feet MSL for 1 min
Right standard rate turn	Perform 180° right standard rate turn maintaining airspeed and altitude
Climb	From 2500 to 3500 feet while maintaining heading and airspeed
TURN AFCS OFF	-----
Descend	Descend from 3500 to 3000 feet while maintaining heading and airspeed
Left descending standard rate turn	Perform 180° left standard rate turn while descending from 3000 to 2500 feet maintaining airspeed
Descend	Descend from 2500 to 2000 feet while maintaining heading and airspeed
Left standard rate turn	Perform 180° left standard rate turn maintaining altitude and airspeed
Straight & level	Maintain heading 360°, airspeed 120 k, altitude 2000 ft for 2 min
Right standard rate turn	Perform 360° right standard rate turn while maintaining altitude and airspeed
Descend	Descend from 2000 to 1000 feet MSL maintaining heading and airspeed

Table 1 (Continued).

Simulator flight maneuvers

Maneuver	Description
TURN AFCS ON - MOVE TO COORDINATES	
Execute terrain flight approach to LZ	Maintain airspeed until approach angle intercept; touch down in Y with zero ground speed
Perform formation flight takeoff (staggered left)	Maintain 3 rotor disk separation at 30° angle of leadship. Depart ground simultaneously with lead ship
Perform formation flight (staggered left)	Maintain 3 rotor disk separation at 30° angle; maintain altitude and airspeed
Perform formation flight (trail)	Maintain 3 rotor disk separation behind leadship; maintain altitude and airspeed
Perform formation flight approach (trail)	Maintain 3 rotor disk separation behind leadship; touch down with lead

The upper-airwork part of the profile consisted of several standardized maneuvers which the subjects were required to fly in a specific order during each of their training and test flights. The first group of maneuvers was flown with the automatic flight control system (AFCS) trim engaged (the normal mode when flying the UH-60), and the second group was flown with the AFCS trim turned off. The AFCS trim system enhances the static stability and handling qualities of the aircraft/simulator.

There were a total of 15 maneuvers in the upper-airwork profile. These consisted of 4 straight-and-levels (1 with AFCS off), 2 left standard-rate turns (1 with AFCS off), 3 right standard-rate turns (1 with AFCS off), 2 standard-rate climbs, 3 standard-rate descents (all with AFCS off), and 1 left descending turn (with AFCS off).

For each of these upper-airwork maneuvers, the subjects were required to maintain a constant air speed of 120 knots, but the specific targets for other parameters such as heading, altitude, roll, slip, etc., changed depending upon which maneuver was being flown. However, subjects always attempted to maintain

appropriate ideal flight parameters during each maneuver. The specific maneuvers, the measures examined, and the ideal parameters for each are presented in Tables 2 and 3.

The last part of the flight profile consisted of the subject following a lead ship through a standardized low-level course. There were four segments in this part of the profile, but only the middle two were graded. Specifically, subjects were evaluated on how well they followed the lead ship first in a 30-degree staggered-left configuration and then directly behind (trail formation). During both of these segments, the subjects were required to match the altitude of the lead ship while maintaining three rotor-disks of separation and a constant trail angle (30 degrees or directly behind the lead ship).

Root mean square (RMS) errors were calculated for each measure within each of the maneuvers (hovers, navigation, upper-airwork, and formation flight) in order to express how well subjects maintained specific headings, altitudes, air speeds, and other parameters. The formula for calculating RMS error is essentially the same as the formula for calculating a standard deviation with the exception that RMS errors reflect the amount of deviation from an ideal value rather than deviations from a mean. The RMS errors were transformed to their log natural values prior to analysis to minimize the influence of extreme scores.

The entire profile lasted approximately 1 hour, and during each profile, performance was measured using the simulator's computerized performance monitoring system which was described earlier. During each flight, a UH-60 pilot was present to instruct the subject and ensure the proper sequencing and timing of all flight maneuvers.

EEG evaluations

Each EEG session lasted approximately 40 minutes and began with a check to ensure electrode impedances were 5,000 Ohms or less. Any impedance problems were corrected by rotating a blunted needle gently inside of the problem electrode until an adequate signal was obtained. The subjects then were instructed to sit quietly with eyes closed for 1.5 minutes followed by 1.5 minutes of eyes opened while data were recorded. After the resting EEG, subjects were given a series of evoked potential tasks not reported here.

Table 2.

Upper airwork maneuvers (conducted with the AFCS on)
with parameters scored for each maneuver.

Maneuver	Duration (sec)	Parameters	Ideal values
Straight & level	60	Heading	360 degrees
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Roll	0 degrees
Left standard rate turn	120	Turn rate	3 deg/sec
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
Straight & level	60	Roll	20 degrees
		Heading	360 degrees
		Altitude	2000 feet MSL
		Airspeed	120 knots
Climb	60	Roll	0 degrees
		Heading	360 degrees
		Airspeed	120 knots
		Slip	0 ball pos
Right standard rate turn	60	Roll	0 degrees
		Rate of climb	500 feet/min
		Heading	360 degrees
		Airspeed	120 knots
Straight & level	60	Slip	0 ball pos
		Roll	20 degrees
		Altitude	2500 feet MSL
		Airspeed	120 knots
Right standard rate turn	60	Roll	0 degrees
		Heading	180 degrees
		Altitude	2500 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees
		Altitude	2500 feet MSL
		Airspeed	120 knots

Table 2 (Continued).

Upper airwork maneuvers (conducted with the AFCS on)
with parameters scored for each maneuver.

Maneuver	Duration (sec)	Parameters	Ideal values
Climb	60	Heading	360 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of climb	500 feet/min

Table 3.

Upper airwork maneuvers (conducted with the AFCS off)
with parameters scored for each maneuver.

Maneuver	Duration (sec)	Parameters	Ideal values
Descent	60	Heading	360 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of descnt	500 feet/min
Left descending turn	60	Turn rate	3 deg/sec
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees
		Rate of descnt	500 feet/min
Descent	60	Heading	180 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of descnt	500 feet/min
Left standard rate turn	60	Turn rate	3 deg/sec
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees

Table 3 (Continued).

Upper airwork maneuvers (conducted with the AFCS off)
with parameters scored for each maneuver.

Maneuver	Duration (sec)	Parameters	Ideal values
Straight & level	120	Heading	360 degrees
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Roll	0 degrees
Right standard rate turn	120	Turn rate	3 deg/sec
		Altitude	2000 feet MSL
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	20 degrees
Descent	120	Heading	360 degrees
		Airspeed	120 knots
		Slip	0 ball pos
		Roll	0 degrees
		Rate of descnt	500 feet/min

The EEGs for eyes-open and eyes-closed later were scanned visually for three relatively artifact-free 2.5-second epochs on which absolute power values were calculated for each of four bands. The results then were averaged together to produce one set of power values for each electrode site under eyes-closed and eyes-open. The activity bands were defined as follows: delta (1.0-3.5 Hz), theta (3.5-7.5 Hz), alpha (7.5-13.0 Hz), and beta (13.0-20.0 Hz).

Desktop flight simulation task

Following the EEG, subjects completed a 30-minute session on the desktop flight simulation task. This task required subjects to fly a timed course consisting of 21 "gates" positioned at various altitudes and headings. The first 15 gates were flown under nonturbulent conditions while gates 16-21 were made more difficult by the addition of 20-knot winds emanating from various directions. This task produced a summary score at the conclusion of each "flight." The score was calculated automatically from the elapsed time it took to fly the course, the number of gates missed, and the precision with which the subjects flew through each of the gates.

Questionnaire

The Profile of Mood States (POMS) was given immediately after each flight simulation test. Subjects were presented with a series of 65 words which described mood states, and for each "mood state" the subject indicated on a standardized answer sheet how well it described the way he was presently feeling. This test took approximately 5 minutes to administer, and yielded scores on the factors of tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment.

Cognitive performance evaluations

Following the POMS, subjects completed a 10-minute session on the Synthetic Work Environment. This test required subjects to simultaneously monitor and respond to four tasks which were presented on four quadrants of the computer screen. In the upper left quadrant, there was a Sternberg memory task which briefly presented the subject with a 6-letter memory set and subsequently required him to indicate whether or not a series of individually presented single letters (probes) had been present in the initial list. In the upper right quadrant, there was a 3-column arithmetic task which required the subject to perform additions on two numbers (each less than 1,000). In the lower left quadrant, there was a visual monitoring task in which the subject monitored a pointer moving from center to either end of a scale. The subject was required to reset the pointer to its center position prior to its reaching the end. In the lower right quadrant, there was an auditory monitoring task which required the subject to indicate when a high tone had been presented among several low tones. All responses were made via a mouse to avoid any distraction from attempting to locate response keys on the keyboard. This test yielded a variety of speed and accuracy scores for each task.

Polysomnography

The sleep recordings were made while the aviator was sleeping in a darkened, private bedroom. Each night on which sleep was allowed, the EOG and submental electrodes were placed, the subject was escorted into his bedroom at the proper time, the electrodes were plugged into the preamplifier, and the signal quality was checked. After the system was verified, the lights were turned out and the subject was permitted to sleep while electrophysiological data were recorded. A chart speed of 10 mm per s was used.

There were 3 nights during which polysomnographic data were collected. The first was a baseline night that occurred on Monday (following a Sunday adaptation night). The second was the recovery night on Wednesday, and the third was the recovery night on Friday. Data from each of these nights were recorded on a standard paper trace for analysis according to the rules set forth by Rechtschaffen and Kales (1968).

The number of minutes from lights out to the appearance of stage 2 sleep, the percentage of time subjects spent in stages 1-4 and REM sleep, the percentage of movement time, and the percentage of time subjects were awake during the night were calculated.

Test schedule

The test schedule is depicted in Table 4. Check-in time at the Laboratory was approximately 1800 on Sunday, at which point the study was explained, the informed consent agreement was signed, and the medical evaluation was conducted (if these steps had not been completed during the previous week). The medical evaluation consisted of a medical records review, completion of a medical questionnaire, and a physical examination which included a 12-lead EKG. Subjects with evidence of past psychiatric or cardiac disorder, allergic reactions to aspirin or yellow dye #5, or a history of sleep disturbances or any current significant illness would have been rejected, but none of these problems were identified in any of the volunteers.

After completion of the physical examination, the aviator's head was measured and electrodes were attached according to the International 10-20 guide. The aviator then was free to relax until bedtime (2300).

On Monday morning, the aviator was given a 2.5-mg dextroamphetamine test dose. Afterward, there were three simulator training flights followed by three EEG, performance, and mood testing sessions. At 2100, the aviator participated in physical exercise, and at 2300 hours, he retired for the day.

On Tuesday, there were three baseline simulator flights and three EEG, performance, and mood baseline tests. Every activity which occurred on Monday was repeated on Tuesday with the exception that the aviator was not allowed to go to sleep at 2300 in the evening. Instead, he was given his first drug/placebo dose at 2400 and subsequent doses were given at 0400 and 0800 on Wednesday.

Table 4.
Testing schedule.

TIME	SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
00-01				DEX/PBO		DEX/PBO	
01-02				simulator		simulator	
02-03		s l e e p	s l e e p	eeg	s l e e p	eeg	s l e e p
03-04				mini-sim poms synwork DEX/PBO		mini-sim poms synwork DEX/PBO	
04-05							
05-06				simulator		simulator	
06-07				eeg		eeg	
07-08		wake up	wake up	mini-sim poms synwork DEX/PBO	wake up	mini-sim poms synwork DEX/PBO	wake up breakfast
08-09		testdose breakfast simulator	breakfast simulator	breakfast simulator	breakfast simulator	breakfast simulator	RELEASE
09-10							
10-11		eeg	eeg	eeg	eeg	eeg	
11-12		mini-sim	mini-sim poms synwork lunch	mini-sim poms synwork lunch	mini-sim poms synwork lunch	mini-sim poms synwork lunch	
12-13		poms synwork lunch simulator					
13-14			simulator	simulator	simulator	simulator	
14-15		eeg	eeg	eeg	eeg	eeg	
15-16		mini-sim	mini-sim poms synwork	mini-sim poms synwork	mini-sim poms synwork	mini-sim poms synwork	
16-17		poms synwork					
17-18		simulator	simulator	simulator	simulator	simulator	
18-19	arrive med exam	eeg	eeg	eeg	eeg	eeg	
19-20	eeg hookup	mini-sim poms	mini-sim poms synwork	mini-sim poms synwork	mini-sim poms synwork	mini-sim poms synwork	
20-21		synwork dinner pt	dinner pt	dinner pt	dinner pt	dinner pt	
21-22							
22-23	freetime	shower poms bed time	shower	shower poms bed time	shower	shower poms bed time	
23-24	bed time		poms		poms		

Note: DEX= Dexedrine (10 mg); PBO= Placebo

On Wednesday, simulator testing began 1 hour after each drug/placebo administration (for the first three sessions) followed by two additional nondrug sessions as well. Other tests followed each simulator flight--just as on previous days. Thus, there was a total of five equally-spaced test sessions completed on this day (at 0100, 0500, 0900, 1300, and 1700). Afterwards, the aviator ate dinner, exercised, and retired for the day.

On Thursday, the aviator repeated the same schedule which was used on Tuesday. There were three test sessions during the day, and as was the case on Tuesday night, the aviator was not allowed to go to bed at 2300. Instead he was given the first dose in his second series of drug/placebo doses at 2400.

On Friday, the aviator repeated the Wednesday schedule, beginning his simulator flight at 0100 hours and completing the other sessions at 4-hour intervals until 2000. At 2300, he retired for the day.

On Saturday, the aviator was awakened at 0700 and prepared for departure from the Laboratory. He was examined by the flight surgeon (and given an up-slip) before being released to travel home.

Results

General

The primary objective of this research was to assess the efficacy of using Dexedrine to sustain helicopter pilot performance during periods of sleep deprivation. To accomplish this goal, the data from the two deprivation periods were analyzed to compare both the magnitude and time-course of Dexedrine's effects relative to placebo. Thus, the analyses each consisted of at least the two primary factors of drug (Dexedrine versus placebo) and session (0100, 0500, 0900, 1300, and 1700).

Flight performance

BMDP 4V (Dixon et al., 1990) was used to conduct a series of analyses of variance (ANOVAs) on the transformed RMS errors from each maneuver in the flight profile. The first two within-subjects factors for each maneuver were drug (placebo, Dexedrine) and session (0100, 0500, 0900, 1300, and 1700). Maneuvers which were flown more than once during each flight profile included a third factor designated iteration (there were two iterations of straight hovers, two iterations of hovering turns, four navigation legs, four straight-and-levels, three right-standard-rate turns and descents, and two left-standard-rate turns and

climbs). Significant main effects and interactions from these ANOVAs were followed by appropriate posthoc analyses consisting of simple effects and/or contrasts to pinpoint the location of noteworthy differences.

Straight hovers

The 3-way ANOVA (drug x session x iteration) on how well the subjects controlled heading and altitude during the 10-foot and 40-foot hovers indicated no 3-way interaction, but there was a 2-way interaction between drug and hover iteration on heading control ($F(1,5)=22.86$, $p=.0050$). Analysis of simple effects showed this occurred because there was better performance under Dexedrine than placebo during the 40-foot hover ($p<.05$) while there was no difference between the drug conditions in the 10-foot hover. In addition, there was a consistent main effect on the drug factor with regard to heading control. Overall, Dexedrine produced better control than placebo ($p<.05$).

Hovering turns

The analysis on altitude control during the 10-foot and 40-foot hovering turns revealed no interactions, but there was a significant effect ($F(1,5)=84.03$, $p=.0003$) attributable to iterations. Overall, altitude control was found to be better during the 10-foot hovering turn than during the 40-foot hovering turn.

Low-level navigation

The ANOVA on how well the subjects maintained correct headings, altitude control, slip control, and roll control while using the GPS to navigate the low-level course revealed several effects. There was a 2-way interaction between drug and session on altitude control ($F(4,20)=3.89$, $p=.0171$) because of better performance under Dexedrine than under placebo at 0500, 0900, and 1300 ($p<.05$). There were no differences between the drug conditions at the other sessions.

There were also main effects due to iteration and drug. The iteration main effect occurred on heading control ($F(3,15)=12.55$, $p=.0002$), altitude control ($F(3,15)=7.03$, $p=.0036$), slip control ($F(3,15)=19.71$, $p<.0001$), and roll control ($F(3,15)=46.53$, $p<.0001$). Contrasts comparing the individual iterations showed that both heading and roll control were worse in the third iteration than in the first, second, or the fourth iteration, and the second was better than the fourth as well ($p<.05$). However, roll control was worse during the first iteration than it was

during either the second or the fourth. Slip control was poorer during the third iteration than during any of the others, and altitude control was poorer during the fourth iteration than during the first, second, or third ($p < .05$). These effects are depicted in Figure 1.

In addition to the iteration effects, there were drug main effects on altitude control ($F(1,5)=7.70$, $p=.0391$) and slip control ($F(1,5)=17.39$, $p=.0087$). In both cases, performance was better under Dexedrine than placebo.

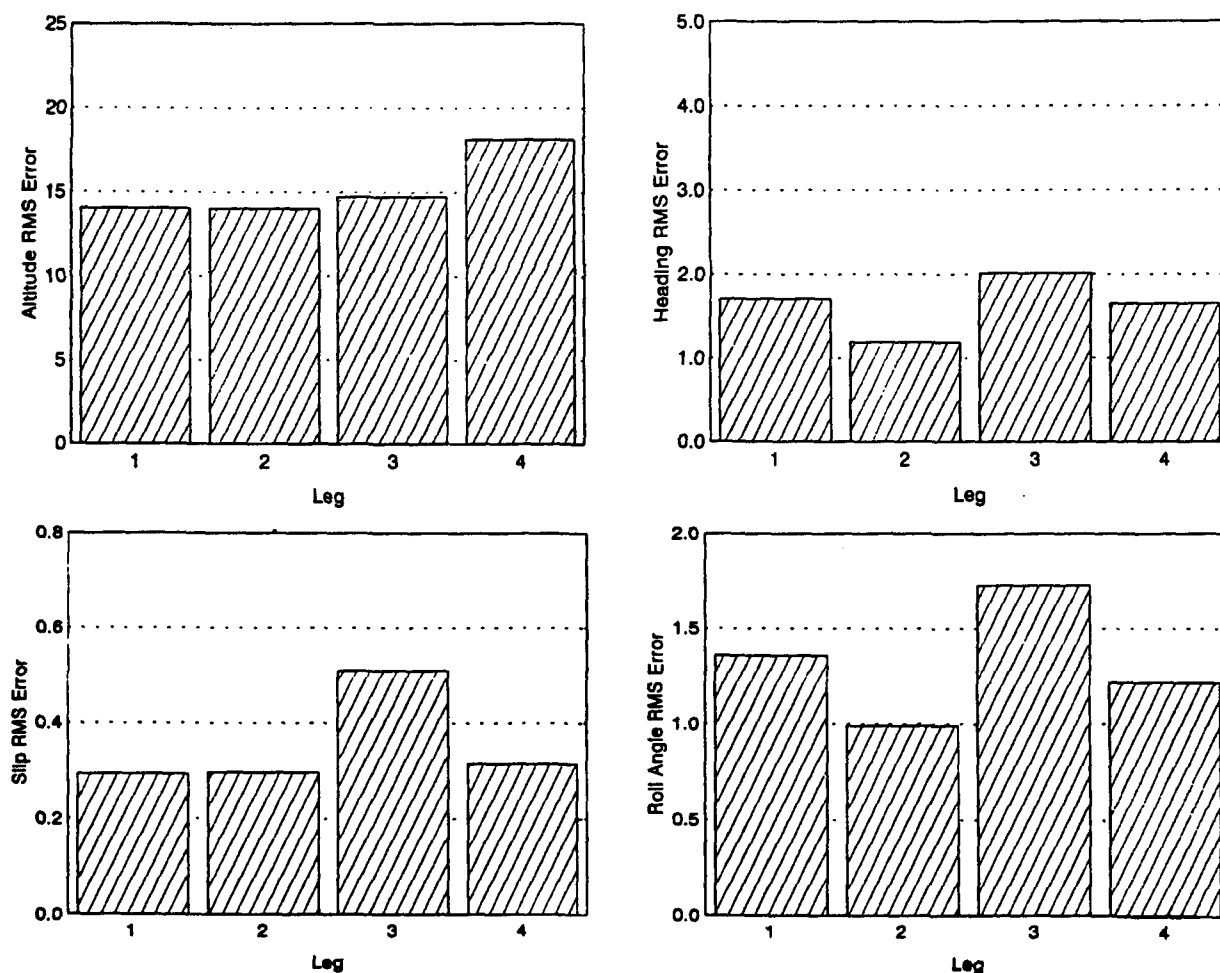


Figure 1. Heading, altitude, slip, and roll control as a function of iteration during the low-level navigation.

Straight and levels

The 3-way analysis of variance (drug x session x iteration) conducted on heading control, air speed control, altitude control, slip control, and roll control during the four straight-and-level (SL) maneuvers indicated there were several interactions and main effects. There was a 3-way interaction among drug, testing session, and iteration on altitude control ($F(12,60)=4.13$, $p=.0001$). Analysis of simple effects showed this was due to better performance under Dexedrine than placebo during SL 2 at 0500, SL 3 at 0100 and 0900 hours, and SL 4 (with no AFCS) at 0500, 0900, and 1300 ($p<.05$). There were no statistically significant differences between Dexedrine and placebo across any of the sessions during SL 1, and there were no differences between the two drug conditions during any of the SLs at the last session of the day (see Figure 2).

There was a 2-way interaction between the testing session and the SL iterations on altitude control ($F(12,60)=4.90$, $p<.0001$) which was attributable to differences among the sessions during the 3rd SL ($p<.05$) which were not present during SLs 1, 2, or 4. Specifically, it was found that altitude control (regardless of drug) in the third SL was better at 0100 than at 0500, 1300, or 1700, but worse than altitude control at 0900 (see Figure 2).

There was a 2-way interaction between drug condition and SL iteration on altitude control ($F(3,15)=7.09$, $p=.0034$) which was due to better performance under Dexedrine during all four iterations. The reason for the interaction apparently was that there was a much smaller improvement from placebo to Dexedrine during the first SL than during the others (see Figure 3).

Next, there were interactions between drug condition and session on both heading control ($F(4,20)=4.92$, $p=.0063$) and roll control ($F(4,20)=5.07$, $p=.0055$), which for both measures was due to better performance under Dexedrine than placebo at the 0900 session. Dexedrine also improved roll control at the 1700 session ($p<.05$) where there was a tendency toward a similar effect on heading. There were no differences between the two drug conditions on either measure (heading or roll) at the 0100, 0500, or 1300 sessions.

There were also several significant main effects. The first involved the iteration factor on heading control ($F(3,15)=21.19$, $p<.0001$), altitude control ($F(3,15)=4.61$, $p=.0177$), air speed control ($F(3,15)=9.78$, $p=.0008$), and roll control ($F(3,15)=83.77$, $p<.0001$). In the case of both heading and roll, there was better overall performance during the first SL than during all of the others, and the second and third iterations were better than the fourth. The second and third iterations did not, however, differ

from one another on heading control, but on roll control, the second was worse than the third. For airspeed control, performance during the first three iterations was better than performance on the last ($p < .05$), and altitude control tended to be affected similarly. All of these effects are depicted in Figure 4. The fact that the last iteration was always flown less accurately than the others was expected since the AFCS trim had been turned off for SL 4.

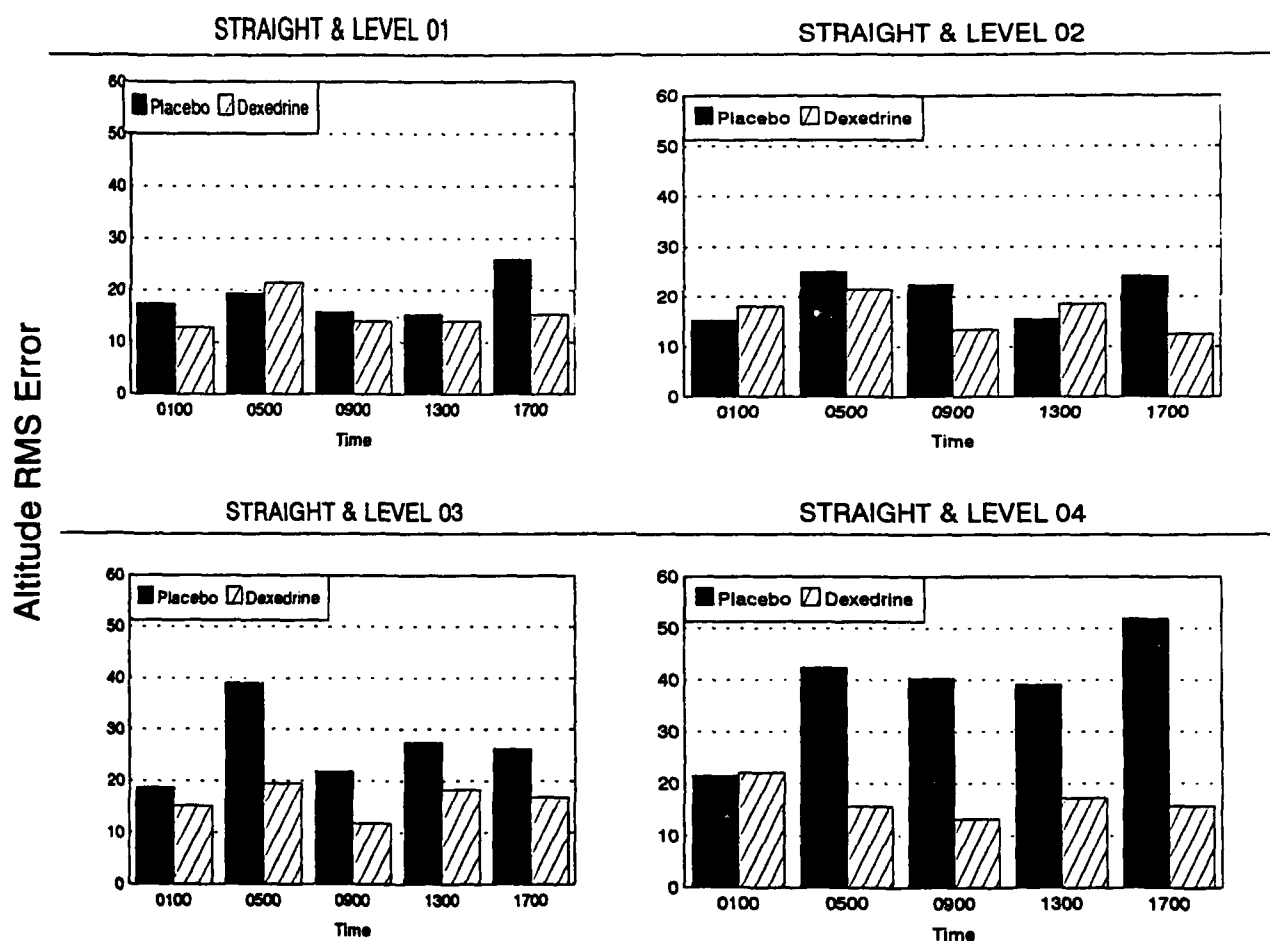


Figure 2. Altitude control as a function of drug, session, and iteration during the straight-and-level.

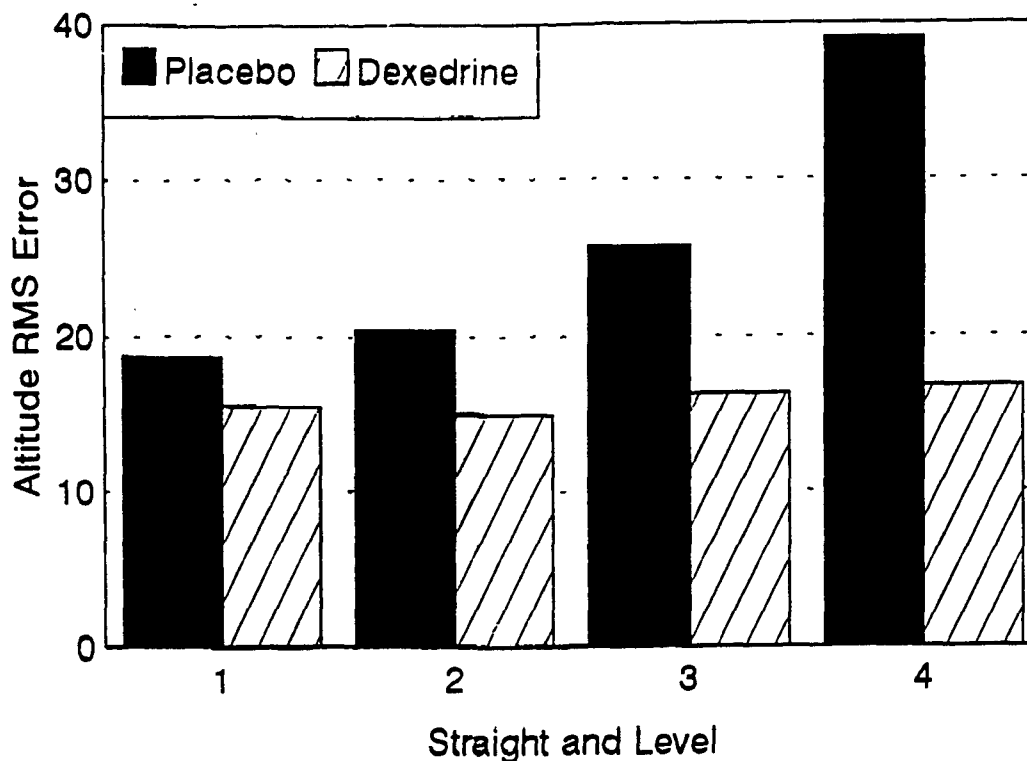


Figure 3. Altitude control as a function of drug and iteration during the straight-and levels.

Next, there were main effects on the session factor where altitude control ($F(4,20)=5.75$, $p=.0030$) declined from the 0100 session to the end of the day (with the exception that there was no loss of control accuracy at 1300). Air speed control ($F(4,20)=4.17$, $p=.0129$) was likewise poorer at the end of the day than at the beginning. Airspeed RMS errors were larger at 1700 than at 0100, 0500, and 1300 ($p<.05$), and airspeed control at 1700 tended to be worse than what was observed at 0900.

Finally, there were main effects attributable to overall differences between Dexedrine and placebo on control of heading ($F(1,5)=18.35$, $p=.0078$), altitude ($F(1,5)=39.82$, $p=.0015$), and air speed ($F(1,5)=23.34$, $p=.0048$). In every case, performance under Dexedrine was superior to performance under placebo.

Left standard-rate turns

The two left standard-rate turns (with AFCS and without AFCS) were analyzed in a 3-way analysis of variance for drug, session, and iteration effects. The specific parameters evaluated were turn rate accuracy, and altitude, air speed, slip, and roll control. The ANOVA indicated that, while there

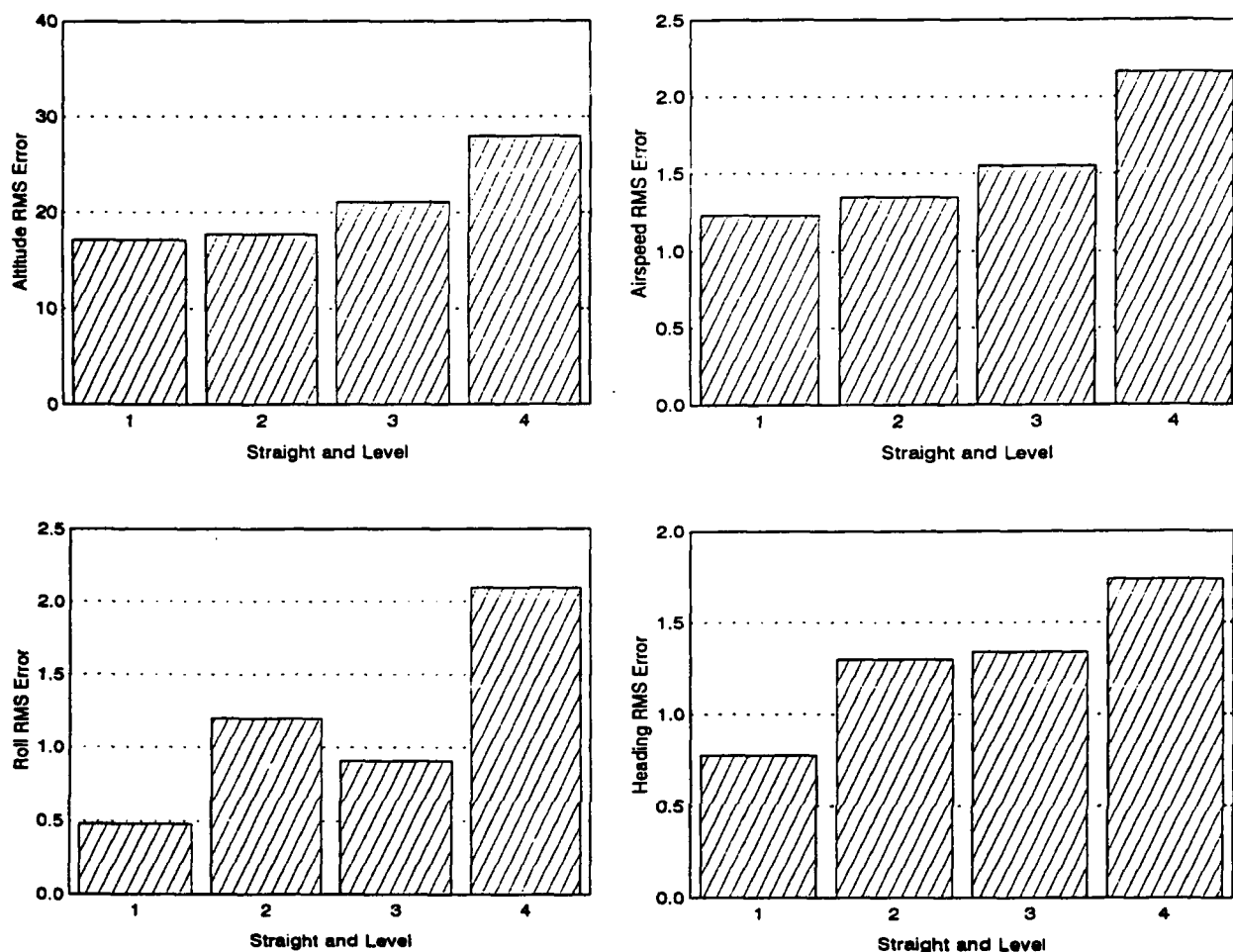


Figure 4. Heading, altitude, air speed, and roll control as a function of iteration during the straight-and-levels.

were no 3-way interactions, there was a 2-way interaction between drug and left-standard-rate-turn (LSRT) iteration on turn rate accuracy ($F(1,5)=13.67$, $p=.0140$), air speed control ($F(1,5)=9.57$, $p=.0270$), and roll control ($F(1,5)=6.69$, $p=.0491$). Analysis of simple effects revealed that each of these effects was due to better performance under Dexedrine than under placebo ($p<.05$) at the second iteration (with AFCS off), while drug conditions did not differ during the first iteration (with AFCS on). There was a supportive main effect on the drug factor for roll control ($F(1,5)=17.38$, $p=.0087$) as well as a significant drug effect on altitude control ($F(1,5)=10.43$, $p=.0232$)--both of which were due to enhanced performance under Dexedrine. In addition, there were clear iteration main effects on turn rate accuracy ($F(1,5)=18.92$, $p=.0074$), altitude control ($F(1,5)=9.43$, $p=.0278$), air speed control ($F(1,5)=14.50$, $p=.0125$), slip control ($F(1,5)=22.08$,

$p=.0053$), and roll control ($F(1,5)=360.52$, $p<.0001$), all of which were because the first iteration (with AFCS on) was better than the second iteration (with AFCS off).

Climbs

The two straight climbs also were evaluated with a 3-way ANOVA (drug x session x iteration) in terms of how well subjects maintained precise control over heading, airspeed, slip, roll, and rate-of-climb. Both climbs were conducted with the AFCS engaged.

The ANOVA revealed that there were no significant 3-way or 2-way interactions; however, there were main effects on iteration, session, and drug. The iteration effects were observed on heading ($F(1,5)=9.46$, $p=.0276$), slip ($F(1,5)=37.55$, $p=.0017$), and roll control ($F(1,5)=55.67$, $p=.0007$), and in each case, they were due to poorer overall performance in the second versus the first climb during the upper airwork profile. The session effect involved rate of climb accuracy ($F(4,20)=3.07$, $p=.0399$) and was attributable to a performance decline from 0100 to 0900, which was followed first by an improvement from 0900 to 1300, and then by a decline from 1300 to 1700 ($p<.05$). These results are depicted in Figure 5. In addition to this overall session effect, a drug main effect was found on the accuracy of heading control ($F(1,5)=6.37$, $p=.0530$). Subsequent examination of the means showed that Dexedrine significantly improved performance in comparison to placebo.

Right standard-rate turns

The three right standard-rate turns (RSRTs) were evaluated in terms of how well subjects maintained an accurate turn rate, and how well they controlled altitude, air speed, slip, and roll during each drug condition, session, and iteration. The first and second RSRTs were flown with the AFCS trim engaged, and the third RSRT was flown with the AFCS trim off.

The 3-way ANOVA revealed there was only a single interaction on this maneuver, but there were several main effects. The interaction was a significant 2-way between drug and session on turn rate accuracy ($F(4,20)=2.99$, $p=.0439$) which tended to be due to enhanced performance under Dexedrine in comparison to placebo at both the 0100 and 0500 sessions. Performance did not change as a function of drug condition during the later parts of the testing days (see Figure 6). In addition, there were significant main effects on iteration, session, and drug. Iteration effects were found on the RMS errors for turn rate ($F(2,10)=27.39$, $p=.0001$), altitude ($F(2,10)=9.75$, $p=.0045$), air speed

($F(2,10)=7.76$, $p=.0092$), slip ($F(2,10)=8.20$, $p=.0078$), and roll ($F(2,10)=31.80$, $p<.0001$). In every case, with the exception of slip, errors were greater during the third RSRT (with AFCS off) than during the first or second RSRT ($p<.05$). The slip data were peculiar in that they suggested performance on the second RSRT was better than performance on both the first and the third RSRT ($p<.05$).

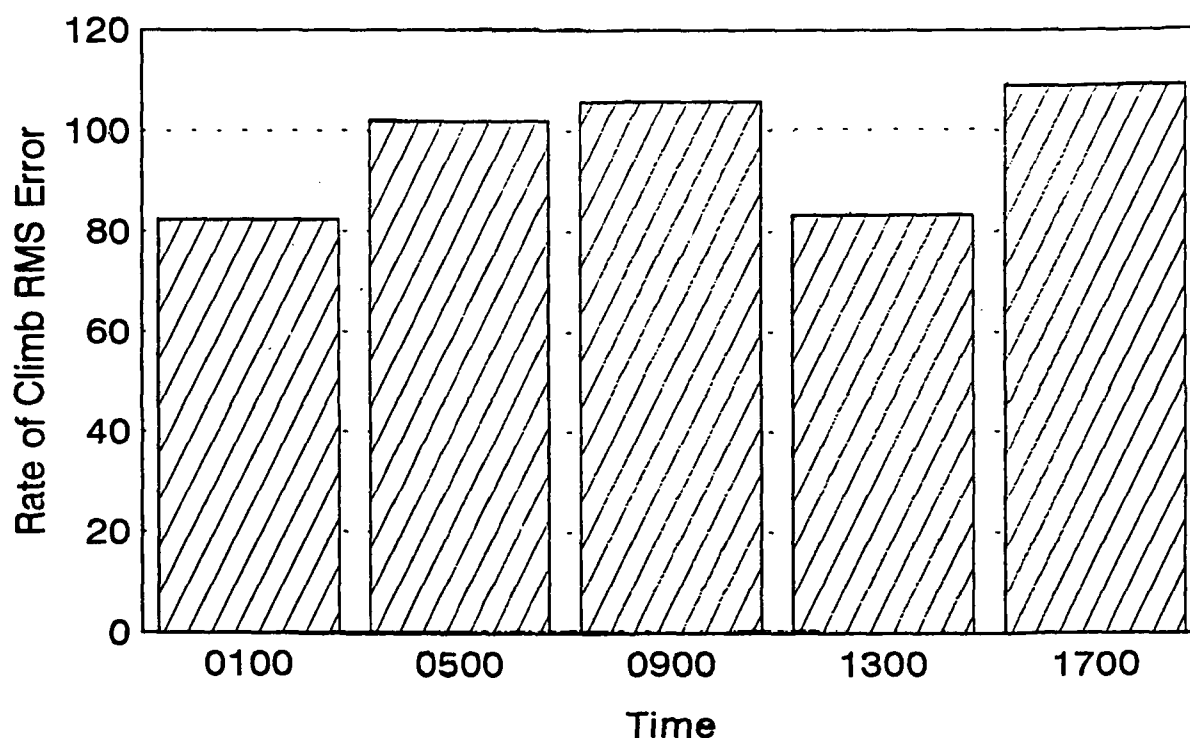


Figure 5. Rate-of-climb accuracy as a function of testing session during the climb.

The main effect for session involved only air speed control ($F(4,20)=2.96$, $p=.0451$) where there was a difference in performance at the 0500 session in comparison to both the 0100 session and the 1700 session (the 0500 session was worse than the other two). In addition, there was a drug main effect on air speed control ($F(1,5)=16.61$, $p=.0096$) as well as a similar effect on altitude control ($F(1,5)=16.26$, $p=.0100$). In both cases, there were significant enhancements attributable to Dexedrine.

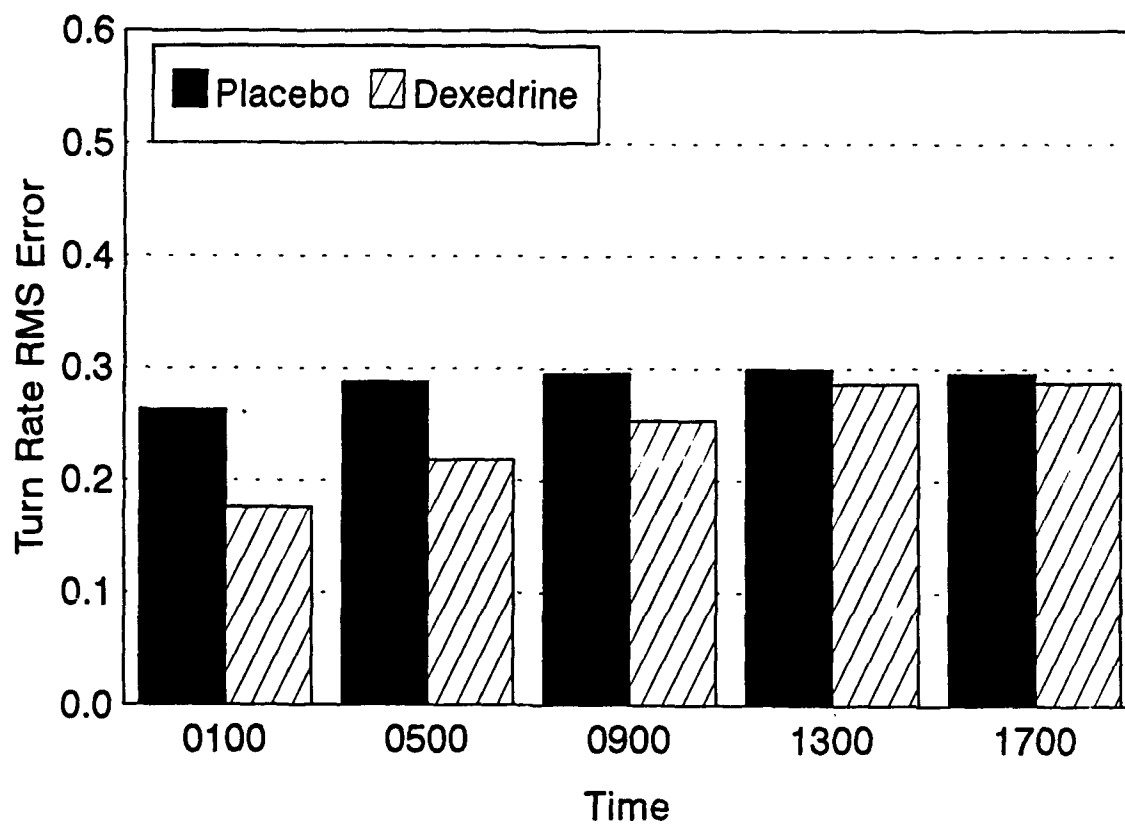


Figure 6. Turn rate accuracy as a function of drug and session during the right standard-rate turn.

Descent

The three standard-rate descents were each examined in terms of how well subjects maintained designated heading, air speed, slip, roll, and rate-of-descent parameters. All three iterations were flown with the AFCS trim turned off. The RMS errors for each measure were analyzed with a 3-way ANOVA (drug x session x iteration).

There were several significant interactions and main effects. Analysis of the rate-of-descent measure revealed a 3-way interaction ($F(8,40)=28.00$, $p<.0001$) which was due to differential drug effects as a function of testing sessions under the first, second, and third descents. Specifically, the analysis of simple effects showed there was better performance under Dexedrine than placebo during the 1700 session across all three iterations ($p<.05$). However, each iteration was affected differently by the drug earlier in the testing day. The first descent revealed enhanced performance under Dexedrine at the 0900 session, while the second descent showed a similar effect at 0500. The third descent showed Dexedrine-related improvements at both of these sessions ($p<.05$). None of the iterations were affected by the presence or absence of Dexedrine at 1300 (see Figure 7).

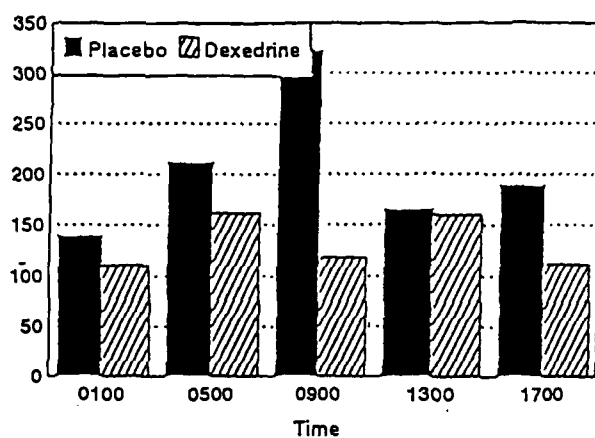
Besides the 3-way interaction, there was a 2-way interaction between testing session and iteration for rate of descent ($F(8,40)=23.35$, $p<.0001$). Analysis of simple effects indicated this was attributable to differences among the testing sessions during the first descent and the second descent which were not present during the third ($p<.05$). For the first, there was better performance at 0100 than at 0500, and for the second, there was better performance at 0100 than at 0900 or 1700 ($p<.05$). Also, during the second descent, there was better performance at 1700 than at either 0500 and 0900, while performance at 1700 was worse than performance at 1300 (see Figure 7).

In addition, there was an interaction between drug and iteration on the rate-of-descent measure ($F(2,10)=35.12$, $p<.0001$). Analysis of simple effects revealed this interaction was due to significantly better performance under Dexedrine than placebo during both the second and third iterations of the descent ($p<.05$), while the same type of drug effect was only marginally significant during the first.

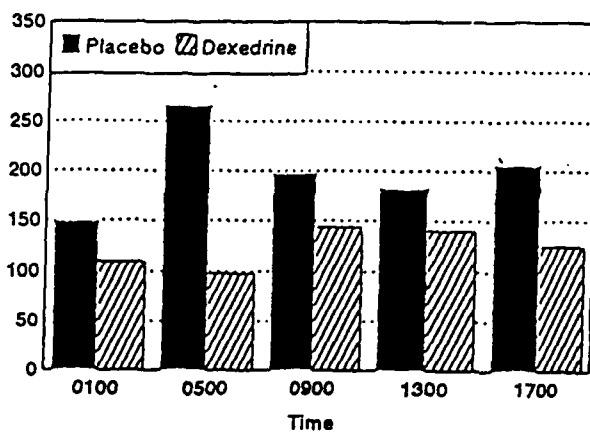
The rate-of-descent measure also was found to be affected by a combination of session and drug ($F(4,20)=12.50$, $p<.0001$) across all iterations taken together. In this case, there were marked differences between the two drug conditions at 0500, 0900, and 1700 where Dexedrine was, once again, responsible for improved

Rate Of Descent RMS Error

DESCENT 01



DESCENT 02



DESCENT 03

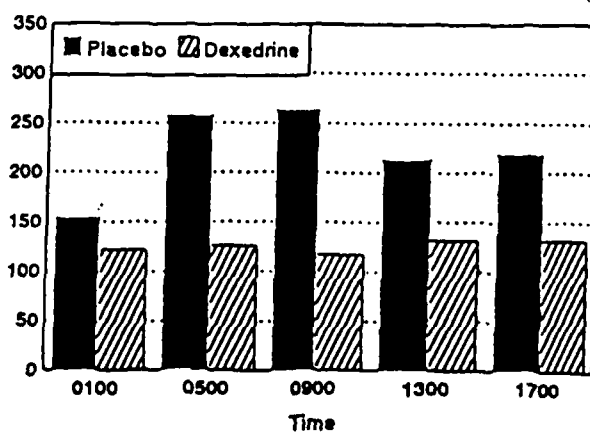


Figure 7. Rate-of-descent as a function of drug, session, and iteration during the straight descents.

performance ($p < .05$). There were no drug effects at 1300 and only a marginal effect at 0100.

There were main effects on all three factors in the ANOVA. With regard to the iteration factor, differences were found on the measures of slip ($F(2,10)=19.86$, $p=.0003$), roll ($F(2,10)=4.58$, $p=.0387$), and rate of descent ($F(2,10)=10.47$, $p=.0035$). Subsequent contrasts revealed that rate-of-descent was better during the second iteration than during either the first or the third ($p < .05$). Conversely, both of the other measures indicated better performance during the first iteration than during either of the other two, and slip control was better during the second descent than during the third as well (see Figure 8). With regard to the session factor, there was once again an effect on rate-of-descent. This was attributable first to the fact that performance at 0100 was better than performance during every other session except for the one at 1300, and second to the fact that performance at 0500, 0900, and 1300 was worse than performance at 1700 (see Figure 9). With regard to the drug factor, it was found that performance enhancements were evident under Dexedrine in comparison to placebo on both airspeed control ($F(1,5)=6.66$, $p=.0494$, and the maintenance of stable rate of descent ($F(1,5)=29.24$, $p=.0029$).

Left descending turn

There was only a single descending turn performed during the flight profile, and this maneuver was scored in terms of how well subjects were able to maintain a correct rate-of-turn, and the appropriate airspeed, slip control, roll, and descent rate. The left descending turn was the second maneuver to be conducted once the AFCS was turned off. Results were analyzed in a 2-way ANOVA for drug and session.

This analysis indicated a drug x session interaction on slip ($F(4,20)=3.86$, $p=.0175$), as well as a main effect on the session factor ($F(4,20)=4.28$, $p=.0115$). The interaction was due to substantially better performance under Dexedrine than placebo during the sessions at 0500, 0900, and 1700 ($p < .05$), while there were no differences at 0100 or 1300 (see Figure 10). The session main effect was because of a decline in performance from 0100 to 0900 which subsequently dissipated by the last session of the day (i.e., performance was worse at 0500, 0900, and 1300 than it was at 1700).

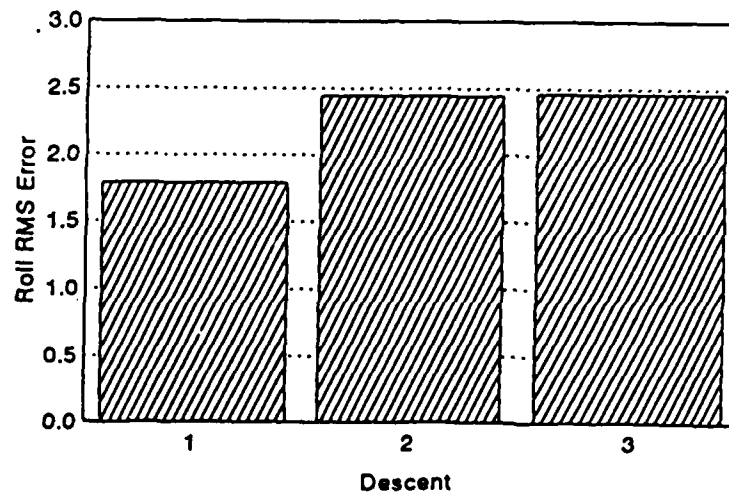
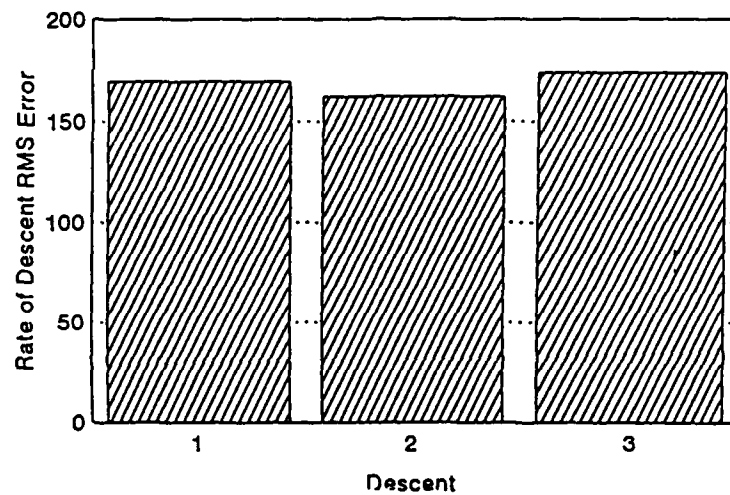
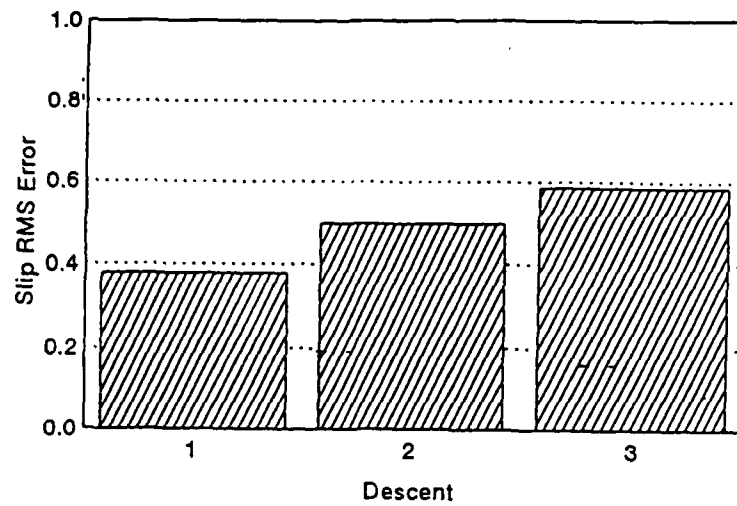


Figure 8. Slip, roll, and rate-of-descent as a function of iteration during the straight descents.

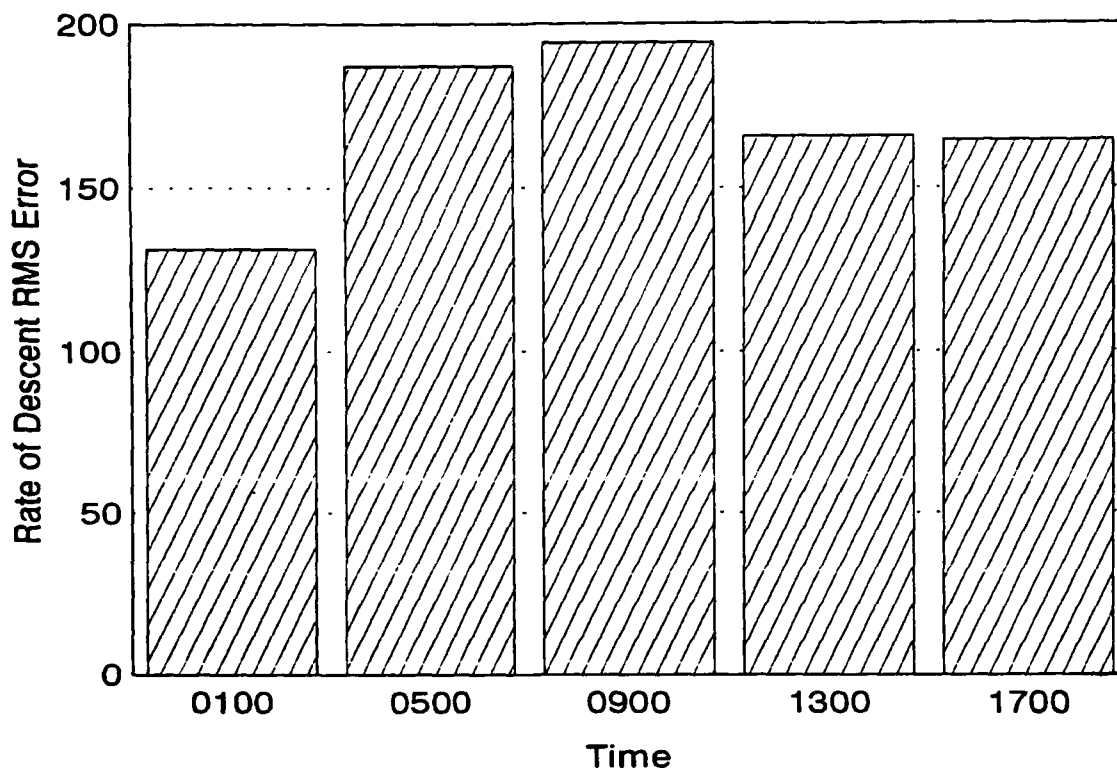


Figure 9. Rate-of-descent as a function of session during the straight descents.

In addition, there were drug main effects on how well subjects controlled airspeed ($F(1,5)=8.45$, $p=.0335$), slip ($F(1,5)=17.58$, $p=.0086$), roll ($F(1,5)=9.94$, $p=.0253$), and rate-of-descent ($F(1,5)=30.64$, $p=.0026$) during this maneuver. In every case, it was clear that Dexedrine was responsible for better performance than what was observed under placebo.

Trail formation

The 2-way ANOVA on formation angle, formation altitude, and separation from the leadship indicated no significant effects due either to drug or session. Also, there was no interaction between the two factors.

Staggered-left formation

The analysis of the staggered left portion of the formation flight also did not reveal marked differences because of drug or session. Likewise, there was no interaction between the factors.

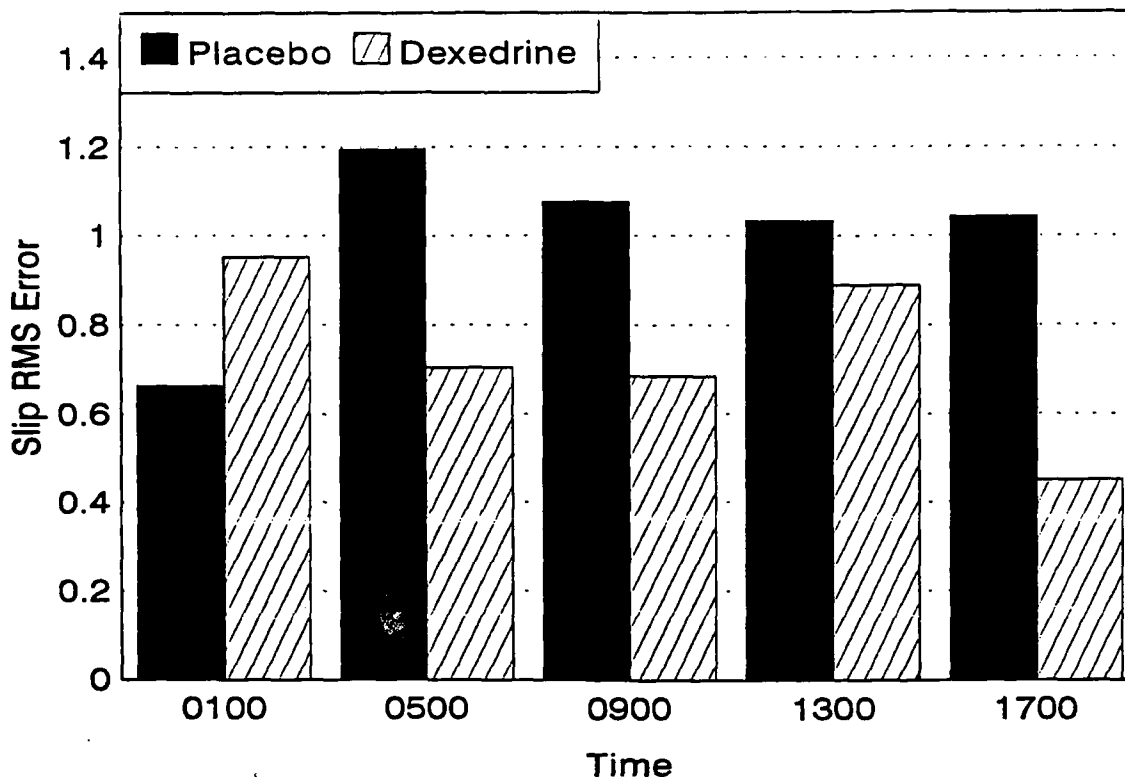


Figure 10. Slip control as a function of drug and session during the left descending turn.

Electroencephalographic data

The absolute power values from the resting EEGs were analyzed with BMDP 4V repeated measures analysis of variance (Dixon et al., 1990) to determine the effects of drug (placebo, Dexedrine), session (0220, 0620, 1020, 1420, and 1820), and eyes (closed, open). Significant effects were followed up with appropriate analyses of simple effects and/or contrasts to pinpoint the location of noteworthy differences. One subject's data was not included in the final analysis because of excessive eye-movement and muscle artifact.

Delta activity

The 3-way ANOVA on delta activity indicated there were several significant main effects and one interaction. There was a drug x eyes effect at Cz ($F(1,4)=11.67$, $p=.0269$) due to significantly greater delta activity under placebo than Dexedrine during eyes closed ($p<.05$), but not during eyes open. In addition, there were significant main effects on the eyes and

drug factors. Main effects on the eyes factor were found at Fz ($F(1,4)=39.16$, $p=.0033$), Cz ($F(1,4)=18.97$, $p=.0121$), and Pz ($F(1,4)=12.76$, $p=.0233$)--all of which were due to greater delta activity during eyes closed than eyes open. Main effects on the drug factor also were observed at Fz ($F(1,4)=38.93$, $p=.0034$), Cz ($F(1,4)=20.35$, $p=.0107$), and Pz ($F(1,4)=9.78$, $p=.0353$), and all of these were attributable to increased delta activity under placebo in comparison to Dexedrine (see Figure 11).

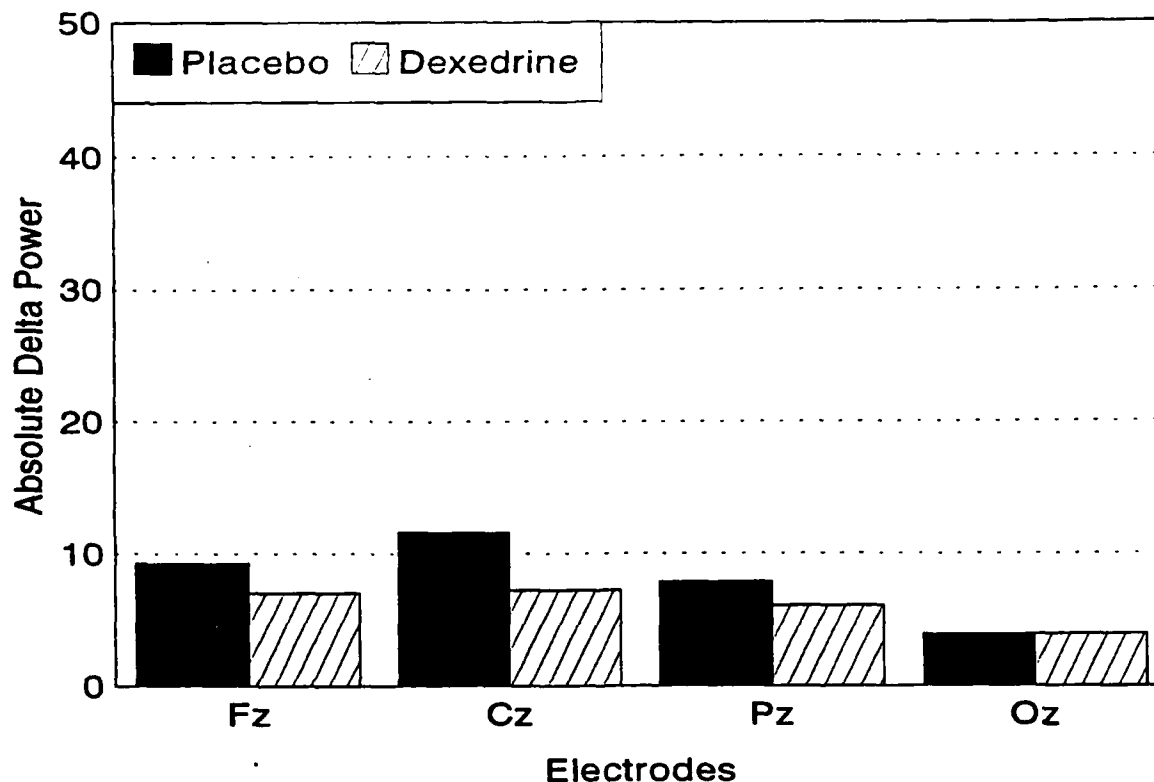


Figure 11. Delta activity as a function of drug.

Theta activity

The ANOVA on the absolute power within the theta range again revealed a drug by eyes interaction at Cz ($F(1,4)=7.86$, $p=.0486$). As was the case earlier with delta activity, there was more theta observed under placebo than under Dexedrine during eyes closed ($p<.05$). There was also more theta under placebo than under Dexedrine during eyes open ($p<.05$), but the difference was smaller than what was observed during eyes closed.

There were main effects on the eyes, session, and drug factors. Increases in theta during eyes-closed in comparison to eyes-open were found at Fz ($F(1,4)=28.16$, $p=.0061$), Cz

($F(1,4)=24.22$, $p=.0079$), and Pz ($F(1,4)=13.45$, $p=.0214$), but changes in the amount of theta across testing sessions were observed only at Fz ($F(4,16)=6.16$, $p=.0034$). Here, theta gradually increased until 1420 and then dropped at 1820 (see Figure 12). Contrasts showed there was less theta at 0220 than at 1020 and 1420 ($p<.05$), and a tendency toward less theta at 0220 than at 1820 ($p<.06$). Also, there was less theta at 0620 than at 1420 while there was more theta at 1420 than at 1820.

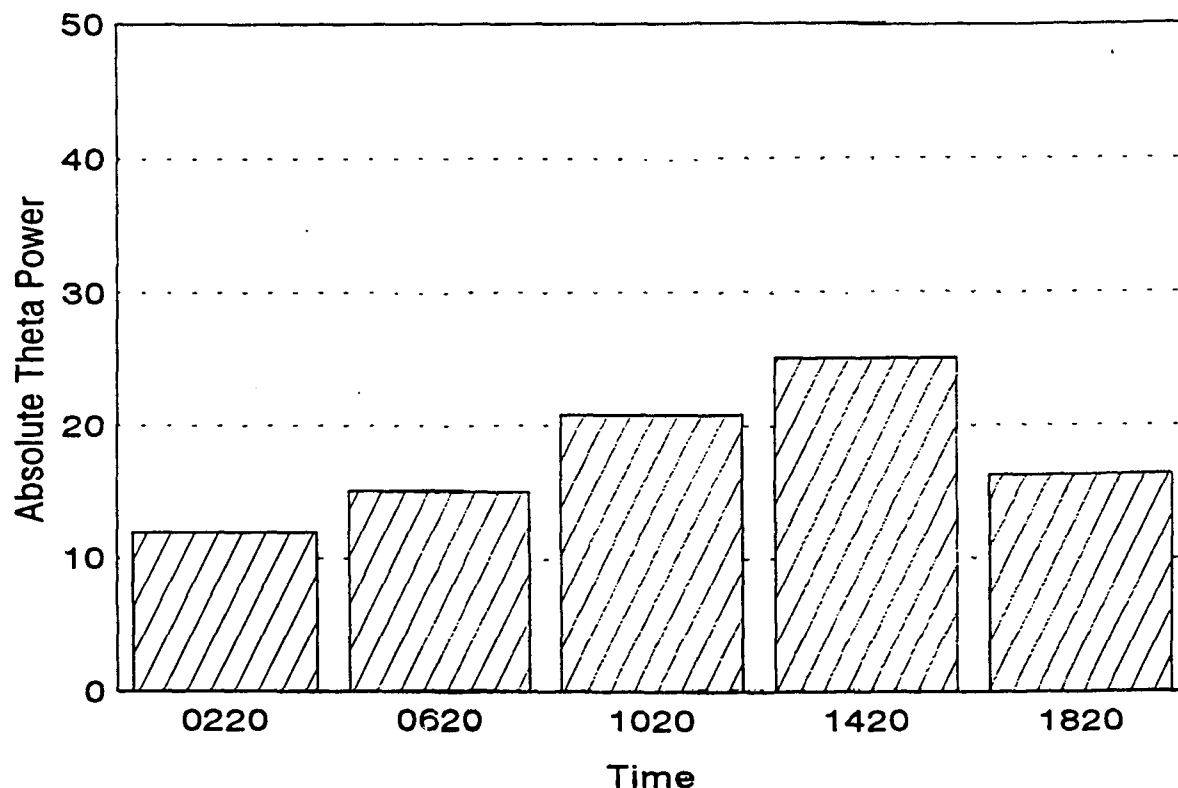


Figure 12. Theta activity at Fz as a function of testing session.

The main effects on the drug factor were observed at Cz ($F(1,4)=17.52$, $p=.0139$) and Pz ($F(1,4)=15.16$, $p=.0176$). Both were due to reduced theta under Dexedrine in comparison to placebo (see Figure 13).

Alpha activity

The ANOVA on the absolute power within the alpha band revealed a 3-way interaction (drug x session x eyes) and several main effects on the eyes factor. The interactions were found

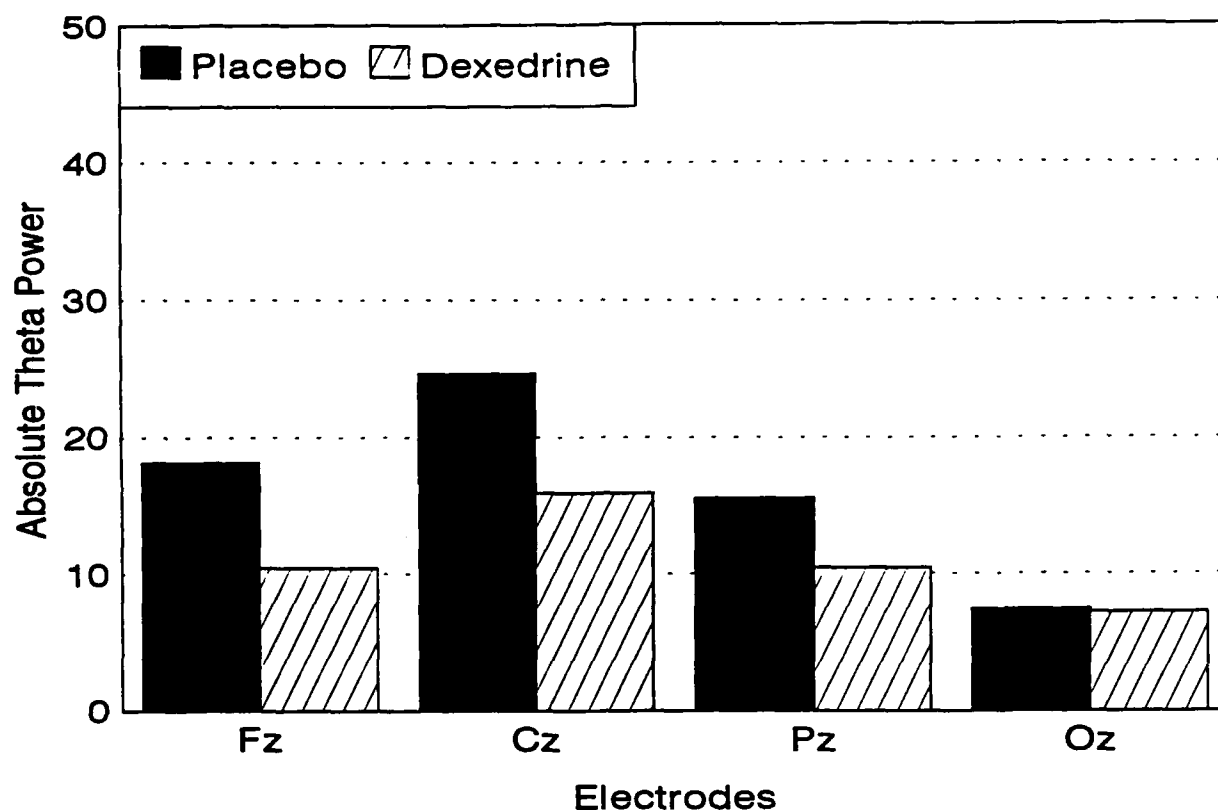


Figure 13. Theta activity as a function of drug.

at Cz ($F(4,16)=4.59$, $p=.0116$) and at Pz ($F(4,16)=4.03$, $p=.0191$), where the followup analyses of simple effects showed there were session-by-eyes interactions at both electrode locations under Dexedrine, but not placebo ($p<.05$). Subsequent examinations of these data revealed that at Cz under Dexedrine, there was substantially more alpha under eyes-closed in comparison to eyes-open during the 0202 and 1020 sessions while the opposite was true (more alpha under eyes-open than eyes-closed) at the 1820 session. At Pz, there was a similar effect of more alpha at eyes-closed than eyes-open at 0220 and 1020, while there was a tendency ($p<.08$) for a reversal at 1820. Conversely, under placebo at both Cz and Pz, there appeared to be more alpha under eyes-closed than eyes-open regardless of the testing session (see Figure 14).

In addition to the 3-way interaction, there were also main effects on the eyes factor at Cz ($F(1,4)=12.65$, $p=.0236$), Pz ($F(1,4)=10.66$, $p=.0309$), and Oz ($F(1,4)=19.78$, $p=.0113$). All of these were due to the expected elevations in alpha activity when subjects closed their eyes.

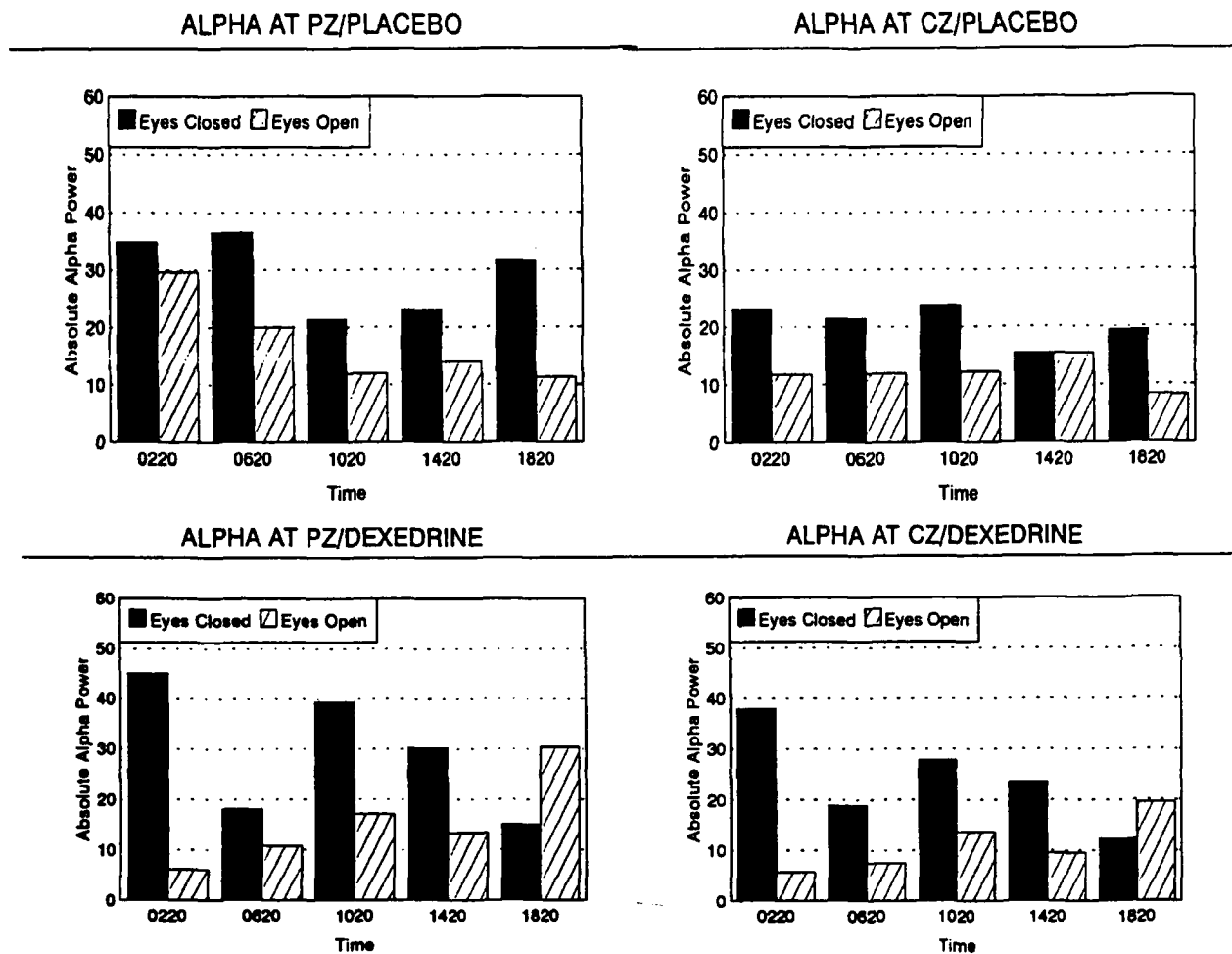


Figure 14. Alpha activity as a function of drug, session, and eyes.

Beta activity

The analysis of EEG activity within the beta range revealed several marginal main effects and interactions; however, the only significant effect was attributable to changes in beta as a function of eyes-closed versus eyes-open at Cz ($F(1,4)=13.22$, $p=.0220$). At this electrode location, there was more beta during the eyes-closed condition than during eyes open.

Desktop flight simulation task

The scores from the desktop flight simulation task (Microsoft flight simulator) were analyzed with BMDP 4V (Dixon et al., 1990) to determine the effects of drug (Dexedrine versus placebo) and session (0305, 0705, 1105, 1505, and 1905).

The ANOVA indicated an interaction between drug and session ($F(2.34, 11.72) = 4.26$, $p = .0361$), but there were no main effects. Although corrections for sphericity violations yielded non-significant simple effects, the interaction tended to be due to an overall difference among the various sessions at placebo ($p < .12$), but not Dexedrine. Subsequent contrasts showed this effect at placebo was due to better performance at 1900 than at either 1100 or 1500 ($p < .05$). Although the performance at 0700 appears to be worse than 1900 as well, the difference was not significant (see Figure 15).

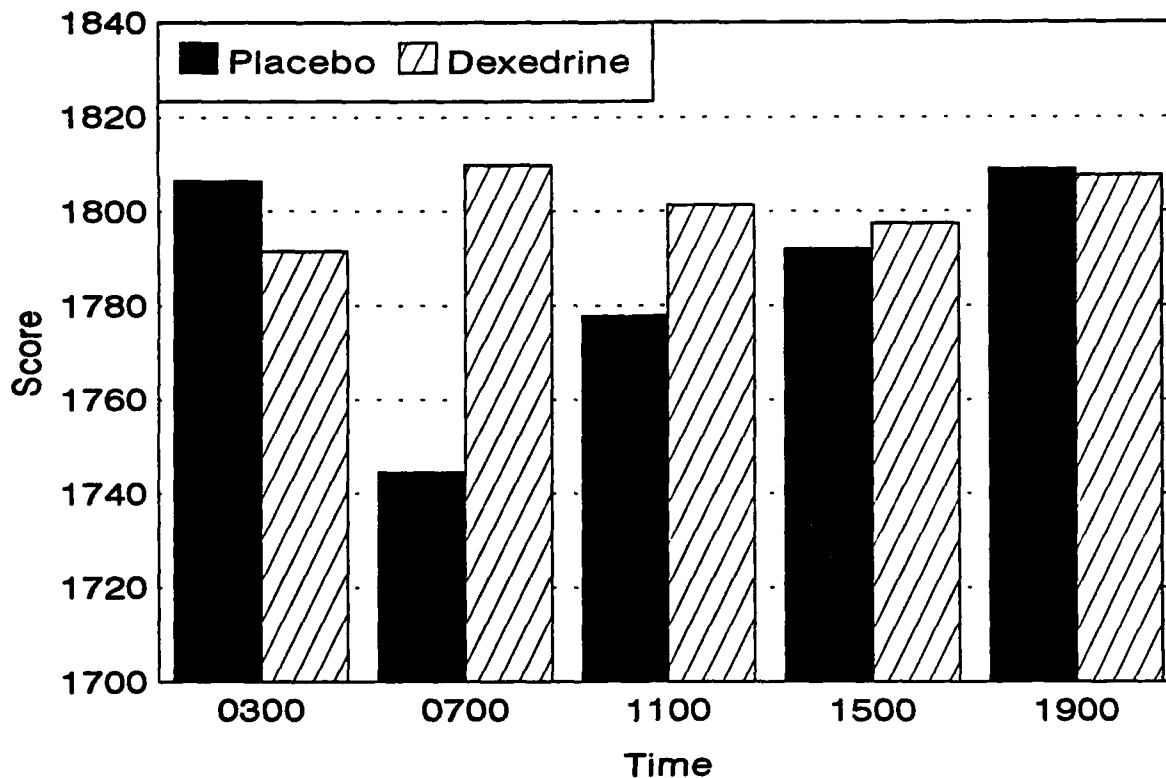


Figure 15. Microsoft flight simulator scores as a function of drug and testing session.

Profile of Mood States

Data from each of the six scales of the Profile of Mood States (POMS) were analyzed with BMDP 4V (Dixon et al., 1990). The two within-subjects factors were drug (placebo, Dexedrine) and session (0340, 0740, 1140, 1540, 1940, and 2225). Significant main effects and interactions were followed by appropriate posthoc analyses consisting of simple effects and/or contrasts to pinpoint the location of noteworthy differences.

Tension-anxiety

The 2-way analysis of variance on the tension-anxiety scale, which reflects heightened musculoskeletal tension, indicated there was no drug x session interaction and no drug main effect. However, there was a main effect on the session factor ($F(5,25)=3.25$, $p=.0214$). This was because tension-anxiety was significantly lower at the 2225 session (immediately prior to bedtime) than it was at any session from 0740 to 1940 ($p<.05$). Although the score at 2225 also appears lower than the score at 0340, this difference was not significant (see Figure 16).

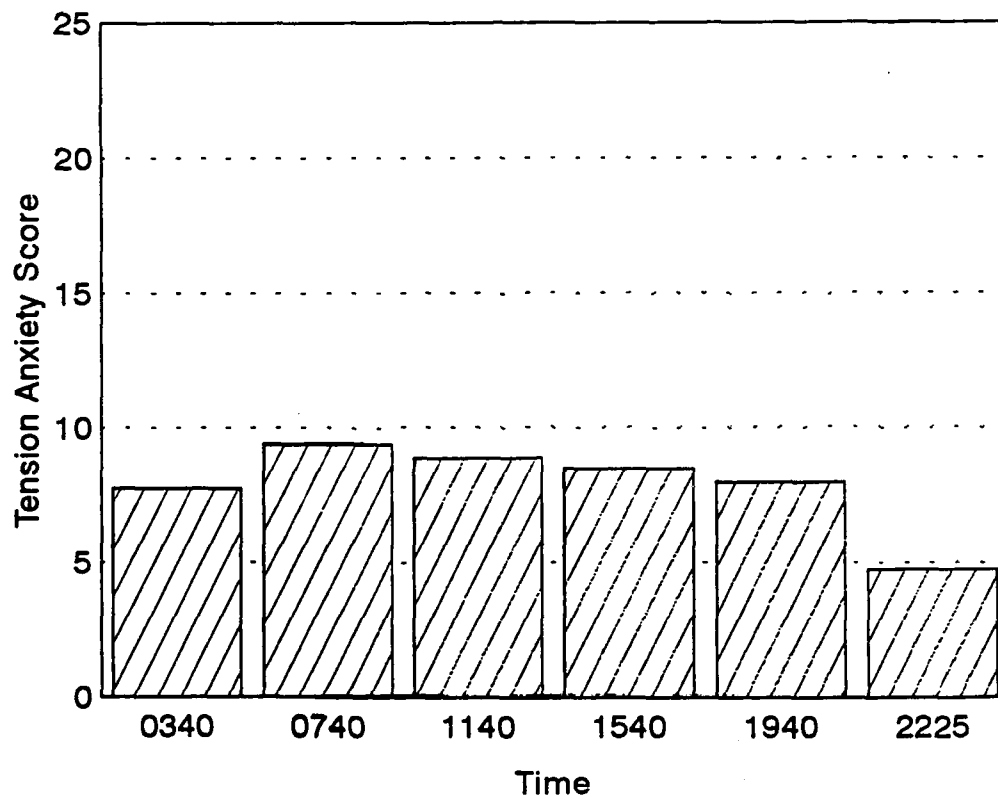


Figure 16. Tension-anxiety scores as a function of testing session.

Depression-dejection

The ANOVA on the depression-dejection scores indicated there were no significant main effects or interactions on this POMS scale.

Anger-hostility

The ANOVA on the anger-hostility scores, which reflect anger and antipathy towards others, revealed only a single significant effect. Overall, there was more anger-hostility under placebo than Dexedrine ($F(1,5)=7.43$, $p=.0415$), regardless of the testing session under consideration. It should be noted that one subject's data on this scale were slightly confounded because he interpreted the mood state "ready to fight" in a positive light (i.e., meaning ready to perform combat aviation duties). The other subjects were advised as to the correct interpretation of this item.

Vigor-activity

The ANOVA on the vigor-activity scale, which reflects vigorousness and high energy, revealed a significant 2-way interaction between drug and session ($F(5,25)=11.62$, $p<.0001$) and significant main effects on both drug ($F(1,5)=16.69$, $p=.0095$) and session ($F(5,25)=5.80$, $p=.0011$). The interaction resulted because Dexedrine produced higher vigor scores than placebo at every session ($p<.05$) with the exception of the ones at 1540 and 1940 as can be seen in Figure 17. The main effect on the drug factor was supportive of this observation (Dexedrine was higher than placebo overall). The session effect was because vigor tended to decline throughout the day. It was higher at 0340 than at 0740, 1940, or 2225, higher at 0740 and 1140 than at 2250, and higher at 1540 than at 1940 ($p<.05$). These data are depicted in Figure 18.

Fatigue-inertia

The analysis of the fatigue-inertia scale, which reflects a mood of weariness, inertia, and low energy, revealed a variety of effects. There was a significant drug by session interaction ($F(5,25)=3.68$, $p=.0124$) which was due to substantial reductions in fatigue under Dexedrine in comparison to placebo at every session with the exception of the one at 1940 (see Figure 19). The drug main effect ($F(1,5)=18.96$, $p=.0073$) corroborated this finding (overall reductions in fatigue under Dexedrine). The session main effect revealed that fatigue-inertia tended to increase throughout the testing days, with significant differences between 0340 and both 1140 and 2225 ($p<.05$) as well as tendencies between 0740 and 2225 ($p=.06$) and 1140 and 2225 ($p<.06$). The means are depicted in Figure 20.

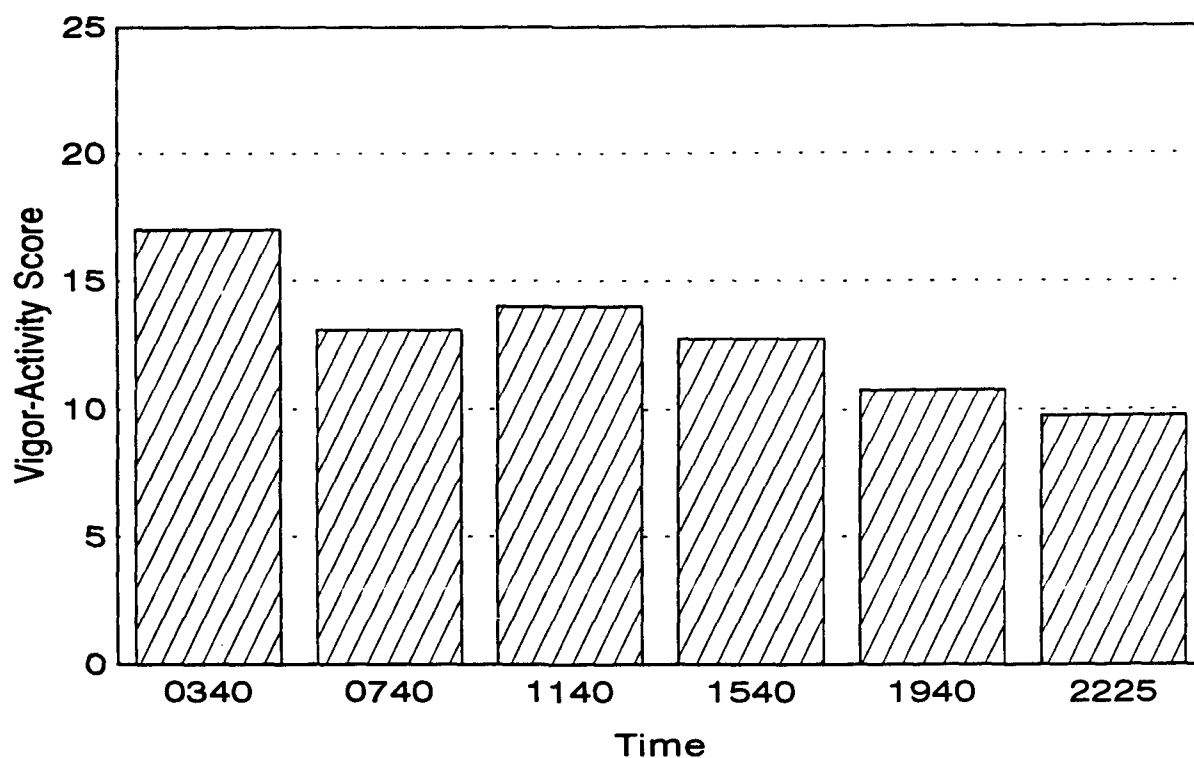


Figure 17. Vigor-activity scores as a function of drug and session.

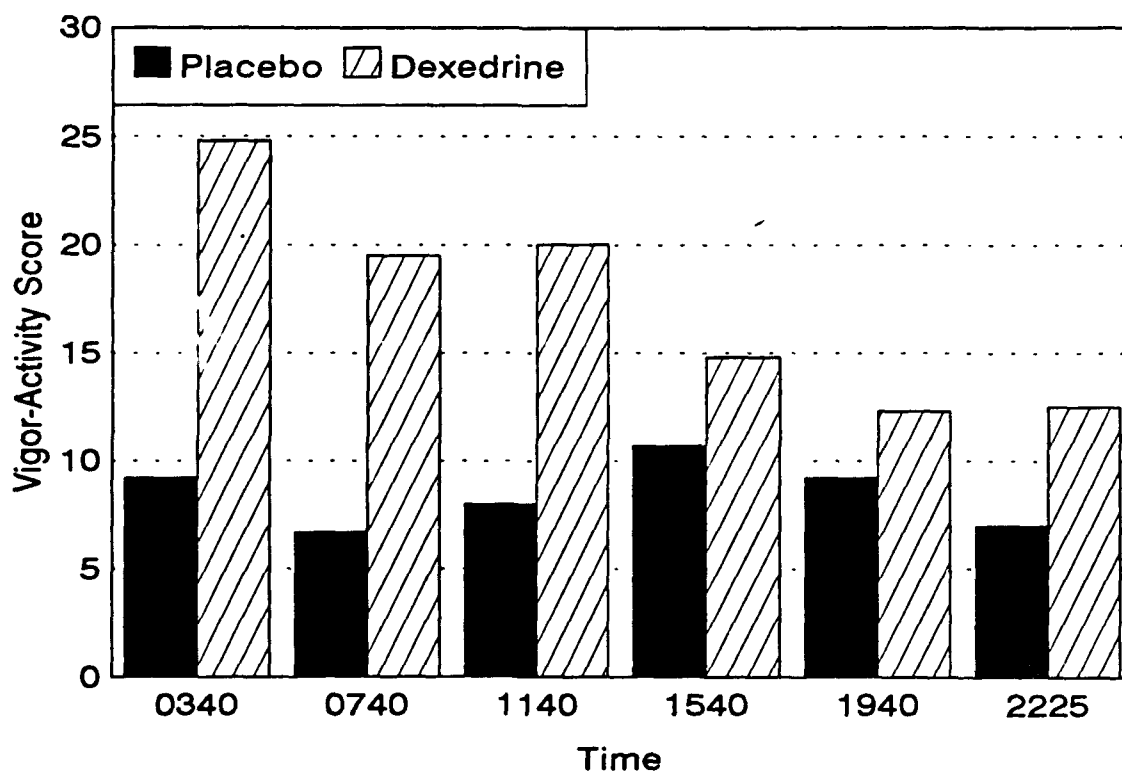


Figure 18. Vigor-activity scores as a function of testing session.

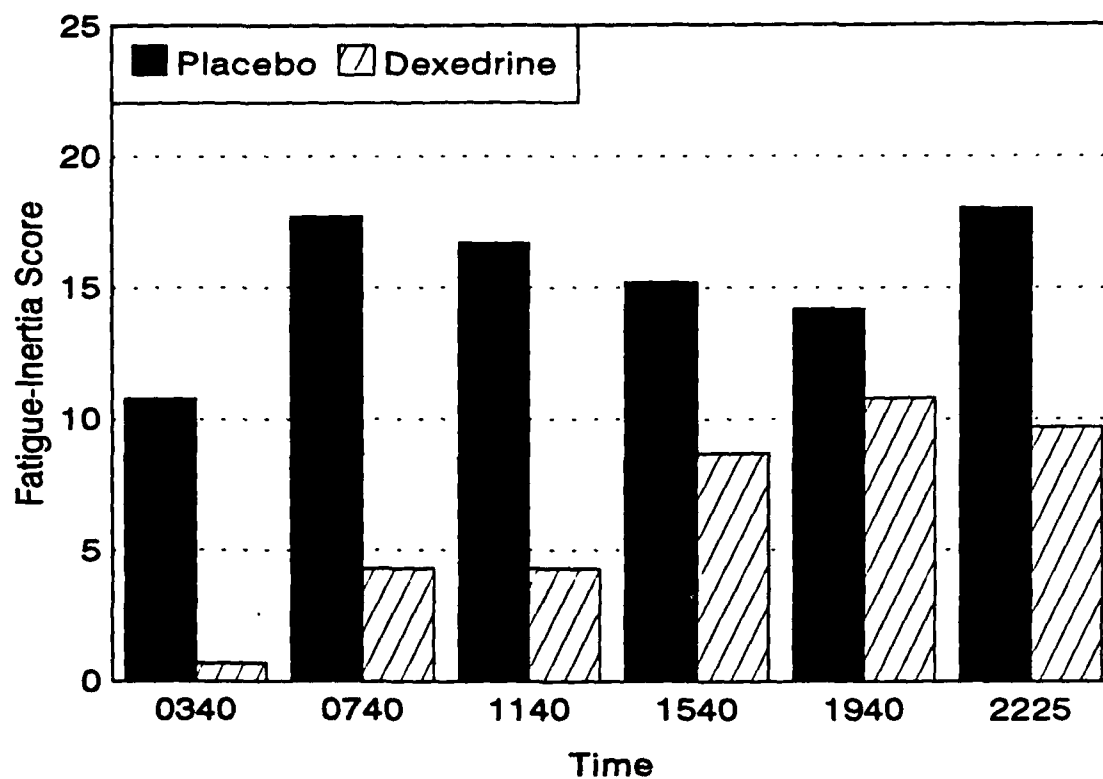


Figure 19. Fatigue-inertia scores as a function of drug and session.

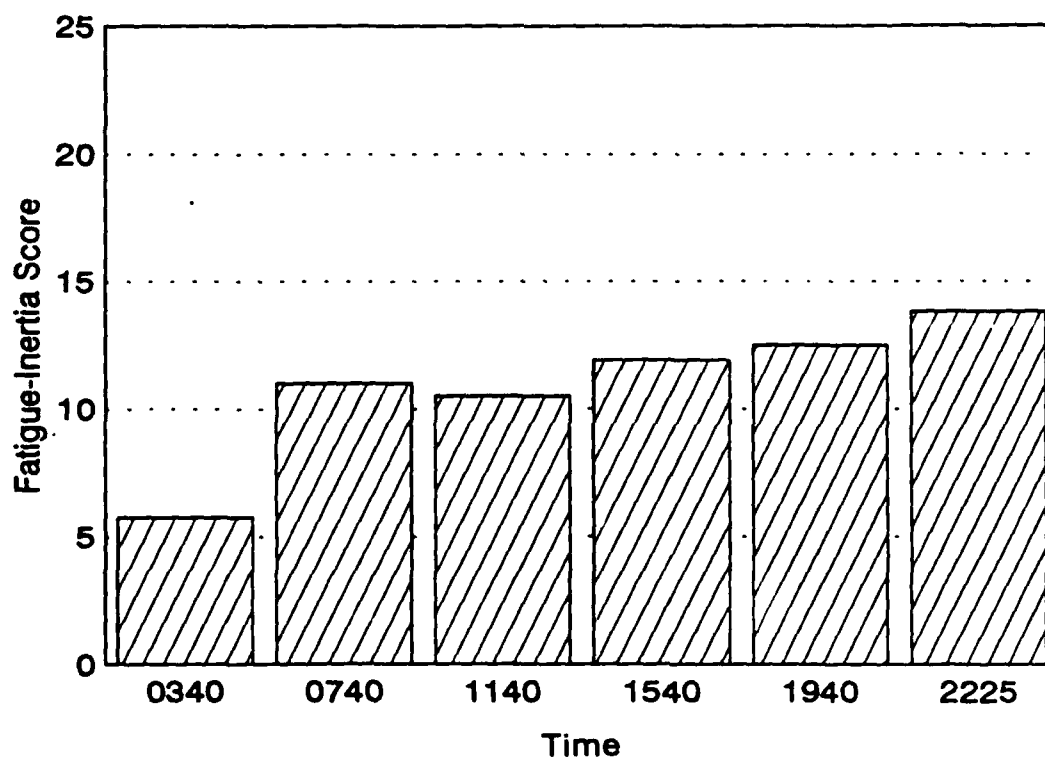


Figure 20. Fatigue-inertia scores as a function of testing session.

Confusion-bewilderment

The ANOVA on the confusion-bewilderment scale, which reflects bewilderment and muddleheadedness, also indicated a variety of significant effects. There was an interaction between drug and session ($F(5,25)=3.62$, $p=.0133$) which was due to lower scores under Dexedrine than placebo during the 0340, 0740, and 1140 sessions (see Figure 21), while there were no differences during the later sessions. The drug main effect ($F(1,5)=6.48$, $p=.0515$) was because of overall reductions in confusion-bewilderment under Dexedrine, and the session effect ($F(5,25)=3.47$, $p=.0162$) was due to lower scores at 0340 than at 0740; however, none of the other sessions differed from one another.

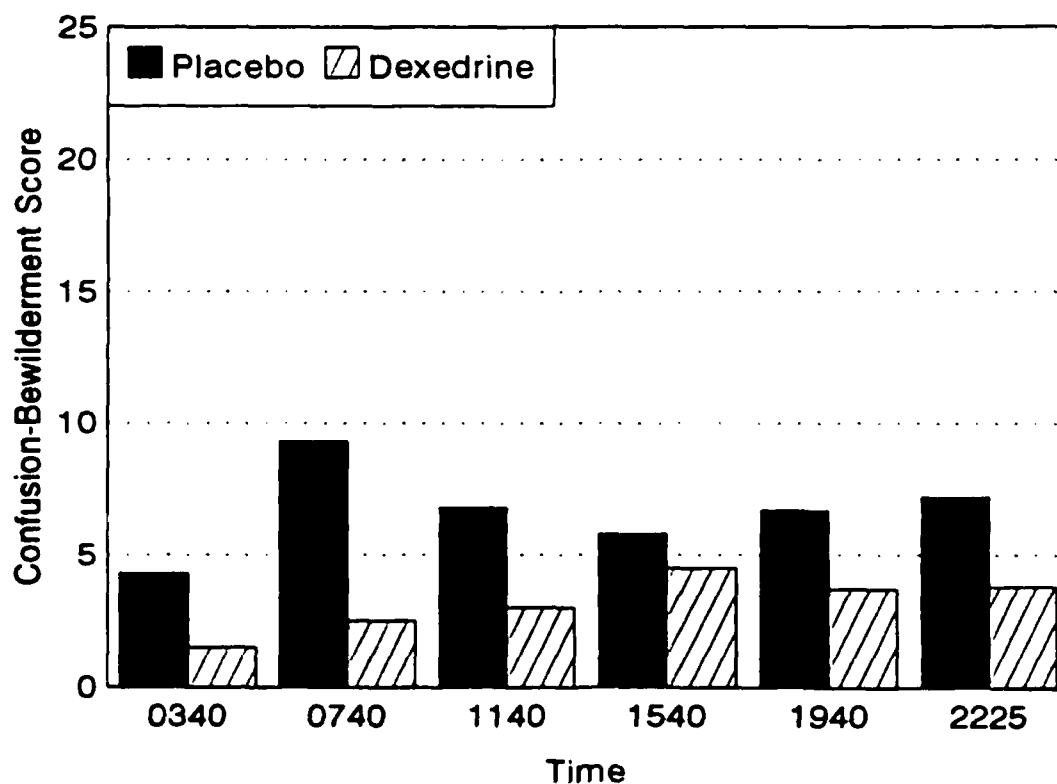


Figure 21. Confusion-bewilderment as a function drug and session.

Synthetic work battery

All six subjects contributed data for the analysis of each task with the exception of visual monitoring. In this case, one subject's scores were dropped because, on the 5th day of testing (after the subject asked several questions of a staff member), he changed his test-taking strategy. Thus, the changes on that particular drug-administration day were not due to drug effects.

The data were analyzed with BMDP 4V repeated measures analysis of variance (Dixon et al., 1990) to determine the effects of drug (Dexedrine, placebo) and session (0345, 0745, 1145, 1545, and 1945), as well as interactions between these two factors.

Sternberg task

To examine the potential impact of drug and session on this task, the percentage of correct responses, the latency to correct responses, and the number of memory-set retrievals were analyzed. The ANOVA indicated there were no significant main effects or interactions on any of these variates.

Arithmetic task

Performance on the arithmetic task was examined in terms of the percentage of correct responses and the amount of time it took to correctly answer problems. The ANOVA indicated there were no significant interactions or drug main effects on either variate. However, there was a session effect on the amount of time it took to reach a correct answer ($F(4,20)=4.36$, $p=.0107$). Contrasts showed this was because it took longer to correctly perform mathematical calculations at 0745 than at any of the subsequent sessions (1145, 1545, or 1945).

Visual monitoring task

Performance on the visual monitoring task was examined in terms of how far the subjects allowed the pointer to move before resetting it to the center and the average inter-reset time. Also, the number of times the subjects failed to reset the pointer before it reached the end of the scale was examined. The analysis indicated there were no significant main effects or interactions on any of these variates.

Auditory monitoring task

Performance on this task was evaluated with regard to the percentage of correct responses, the percentage of signals detected, and the detection latency. The ANOVA indicated there were no significant interactions or main effects on any of these variates.

Physiological data

The vital signs data were collected primarily for safety reasons as opposed to testing any hypothesis. However, these data were analyzed with BMDP 4V repeated measures analysis of variance (Dixon et al., 1990). The two within-subjects factors were drug (Dexedrine, placebo) and time (time 1 through time 24).

Oral temperature

Analysis of the oral temperatures indicated there were significant drug ($F(1,5)=7.00$, $p=.0457$) and time ($F(23,115)=1.94$, $p=.0116$) effects, but no significant interaction between drug and time. The time effect was not followed up further with pairwise contrasts because of the excessive number of comparisons that would have been necessary, and because this effect is not particularly important for the purposes of this study. However, the means are depicted in Figure 22. The main effect on the drug factor was due to a slight elevation in oral temperature under the Dexedrine condition (Dexedrine= 97.6° F, placebo= 97.3° F). The ranges were $94-101^{\circ}$ under placebo and $95-99^{\circ}$ under Dexedrine. It should be noted that these data are somewhat confounded because oral temperatures were collected during the noon and evening meal times. Thus, some of the temperature elevations were artifacts attributable to eating hot food (as was the case for the 101° temperature mentioned above).

Pulse

Analysis of the pulse data showed there was an interaction between drug and time ($F(23,115)=1.91$, $p=.0137$) and main effects on the drug factor ($F(1,5)=6.88$, $p=.0469$) and the session factor ($F(23,115)=5.17$, $p<.0001$). The interaction was due to a time effect under Dexedrine ($p<.05$) which was not present under placebo. Examined in another way, differences were found between Dexedrine and placebo at 1140, 1220, 1410, 1540, 2050, and 2220 ($p<.05$). In every case, the mean pulses were higher under Dexedrine than under placebo (see Figure 23).

Effect of Dexedrine on Oral Temperature

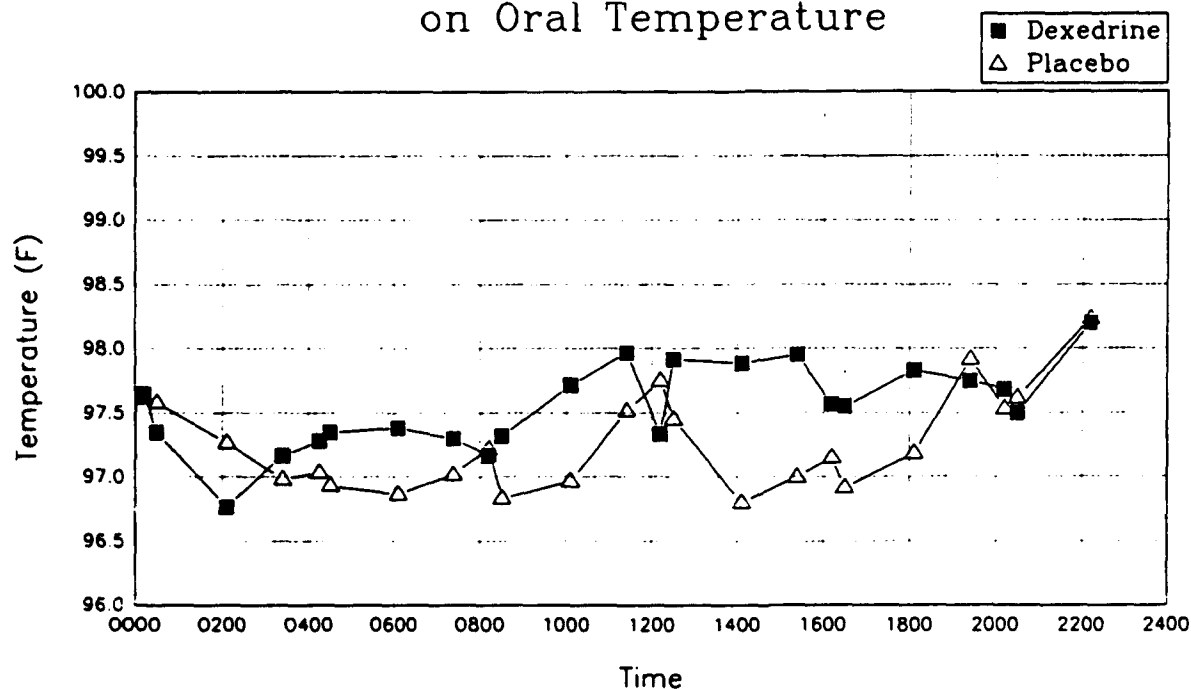


Figure 22. Oral temperature as a function of drug and time of day.

Effect of Dexedrine on Heart Rate

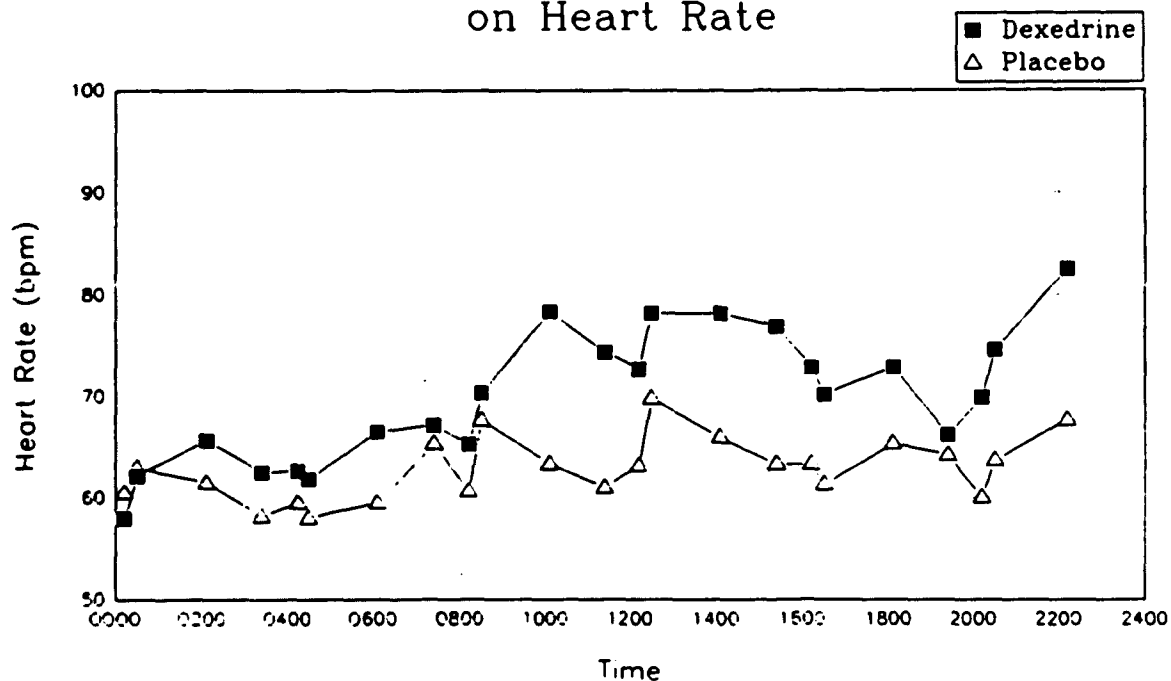


Figure 23. Heart rate as a function of drug and time of day.

The main effect on the drug factor supported what was observed in the interaction by showing that overall the mean pulse was higher under Dexedrine (69.5 beats per minute) than under placebo (62.8 beats per minute). The ranges were 43-96 beats per minute under placebo and 46-111 beats per minute under Dexedrine. The main effect on the time factor was not pursued further because of its lack of importance in the present context.

Systolic blood pressure

Systolic blood pressure was significantly affected by the combination of drug and time ($F(23,115)=1.74$, $p=.0301$), and there were main effects on the drug factor ($F(1,5)=21.61$, $p=.0056$) and the time factor ($F(23,115)=1.69$, $p=.0370$). The interaction was attributable to a time effect under Dexedrine ($p<.05$) which was not present under placebo. Also, there were differences between Dexedrine and placebo at 0050, 0210, 0420, 0850, 1140, and 1250 ($p<.05$)--systolic blood pressure was higher under Dexedrine in every case (see Figure 24).

The main effect on the drug factor was due to an overall elevation in systolic pressure under Dexedrine in comparison to placebo (129 versus 121). The ranges were 97-163 mmHg under placebo and 107-163 mmHg under Dexedrine. The main effect on the time factor (without considering the impact of drug) was not examined further.

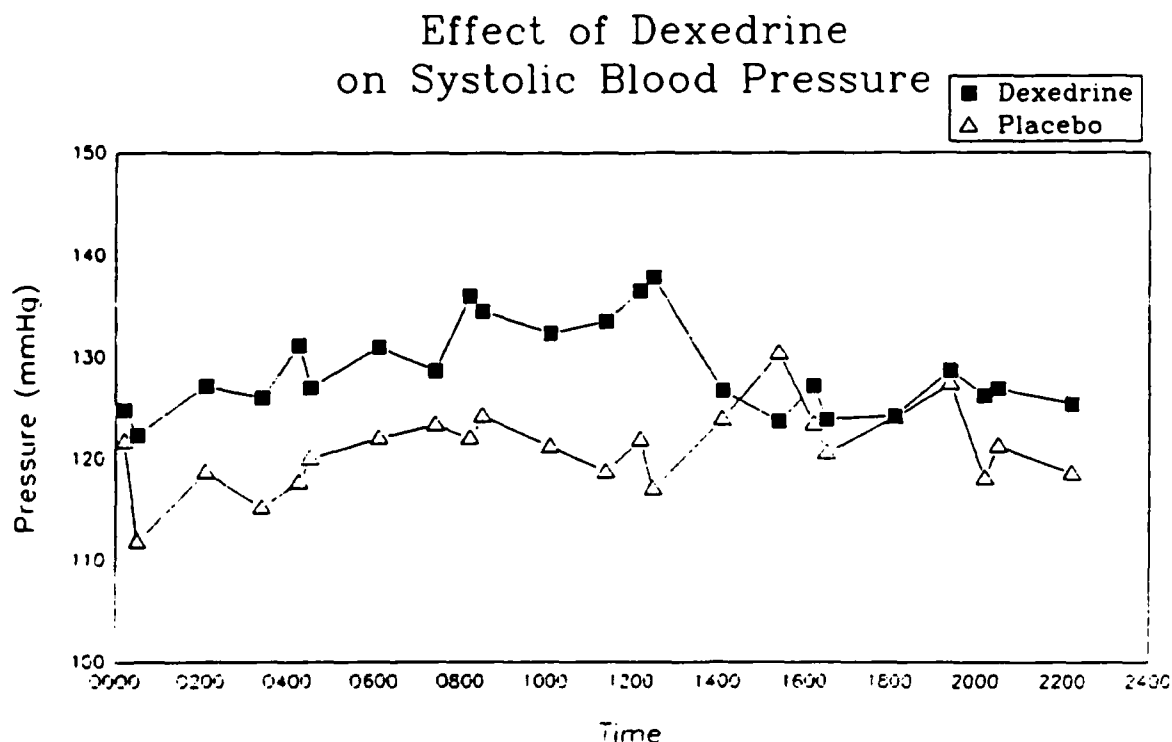


Figure 24. Systolic blood pressure as a function of drug and time of day.

Diastolic blood pressure

The analysis of diastolic blood pressure indicated fewer effects than the number observed with systolic pressure. Specifically, there was no interaction between drug and time, and there was no main effect due to the time factor. However, there was an overall drug effect ($F(1,5)=6.31$, $p=.0537$) which was due to higher diastolic pressure under Dexedrine (72 mmHg) than under placebo (69 mmHg). The ranges were 54-80 mmHg under placebo and 58-90 mmHg under Dexedrine. These data are depicted in Figure 25.

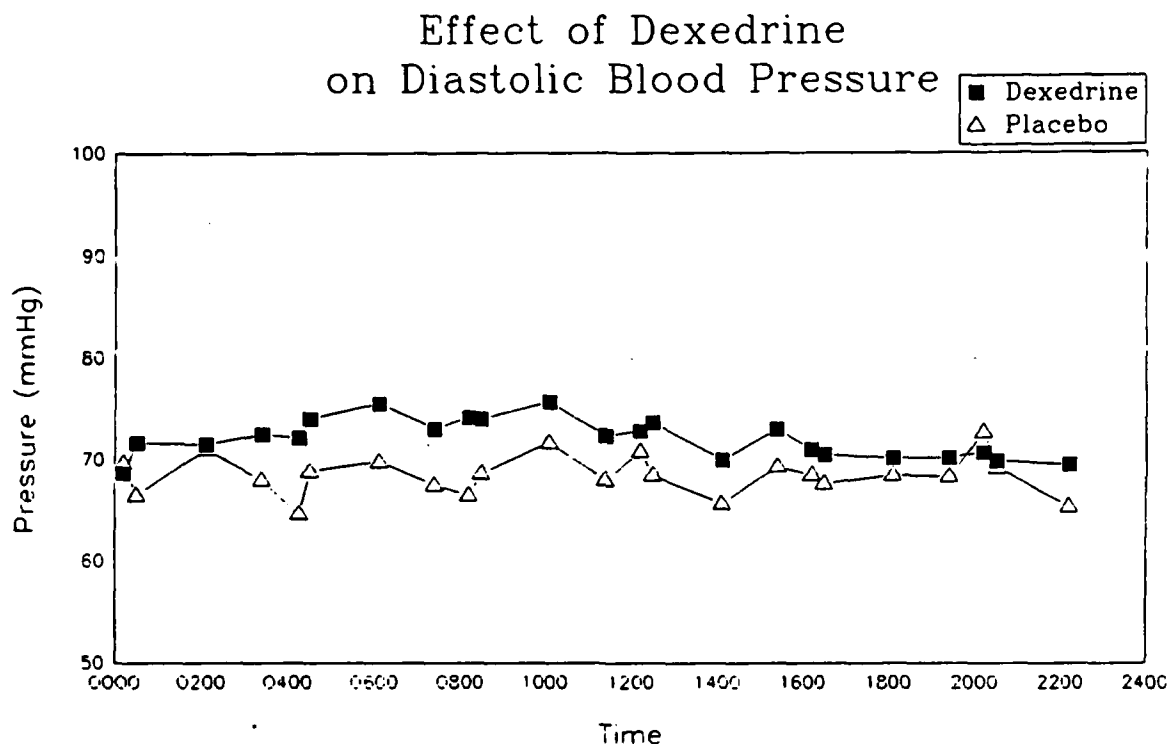


Figure 25. Diastolic blood pressure as a function of drug and time of day.

Polysomnographic data

The number of minutes from lights out to the appearance of stage 2 sleep (sleep onset), the percentage of time subjects spent in stages 1-4 and rapid eye movement (REM), the percentage of time subjects were awake, and the movement time during their sleep periods were analyzed with one-way ANOVAs for the 2 recovery days (Dexedrine recovery, placebo recovery). Prior to analysis, the percent data was transformed using the two arcsine square-root transformation to stabilize the variances.

These analyses revealed significant increases in the percentage of stage 1 ($F(1,5)=25.94$, $p=.0038$) and stage 2 sleep ($F(1,5)=7.60$, $p=.0400$) on the night after Dexedrine administration in comparison to the night after placebo. The amounts of stages 1 and 2 sleep after Dexedrine were respectively 7.6 percent and 58.3 percent, whereas these amounts were 4.7 percent and 53 percent after placebo.

The percentage of time subjects were awake during the sleep period ($F(1,5)=7.55$, $p=.0404$) and the movement time ($F(1,5)=6.80$, $p=.0478$) also were greater after Dexedrine than after placebo. The percentage of awake time was 0.2 after Dexedrine and 0.0 after placebo, while the movement time was 11.7 after Dexedrine and 6.2 after placebo.

Sleep onset was not significantly affected by either dose condition--it took subjects 4.2 minutes to reach stage 2 after Dexedrine and 3.5 minutes after placebo. The amount of slow-wave and REM sleep were not altered.

Discussion

Flight performance

Drug-related changes were observed on at least one measure of aviator skill during every flight maneuver with the exception of the hovering turns and the formation flight. Dexedrine enhanced overall heading control during the straight hover and the straight climb as well as heading, altitude, and air speed control during the straight and levels. Dexedrine improved altitude control during the low-level navigation and both standard-rate turns while concurrently enhancing slip control during the navigation portion, roll control during the left turn, and air speed control during the right turn. In addition, Dexedrine improved the ability of subjects to maintain precise air speeds and rates of descent during both the straight descent and the left descending turn, while also facilitating slip and roll control during the latter maneuver.

Dexedrine did not appear to affect performance in the hovering turns or the formation flight segments. The reason for the lack of effect on the hovering turns is not readily apparent at this point, but the lack of effects on the formation flight may have been due to the nature of the task. On virtually every other flight maneuver examined in this study, the subjects were required to maintain precise control of the aircraft by focusing on instruments inside of the cockpit. However, during the formation flight, subjects had to rely on outside visual cues to follow the lead ship accurately. In all likelihood, this heavy reliance on outside cues in the performance of a task that is not

frequently performed in many operational settings increased the overall variance and made it more difficult to detect drug-related differences. Also, it is well known that depth perception is limited in the simulator environment.

With regard to the effects of the automatic flight control system (AFCS), analyses of the maneuvers flown with the AFCS trim on and then off revealed, as expected, an overall increase in control errors when the trim system was not used. In several cases, the maneuver iterations most sensitive to drug effects were the ones in which the AFCS trim was turned off. During the straight and levels, this was evident from the significant differences in altitude control between the Dexedrine and placebo conditions at three sessions (0500, 0900, and 1300) when the AFCS was not engaged, while there were either no differences at any sessions or intermediate effects (i.e., only two sessions affected) when the AFCS trim was used. This heightened sensitivity of the non-AFCS iterations was evident further in the left standard-rate turns where control of roll, air speed, and turn-rate were enhanced primarily by Dexedrine when the AFCS trim was off. Likewise, during the straight descents, there were marked differences in the maintenance of a precise rate of descent at three sessions (0500, 0900, and 1700) when the AFCS trim was not used, whereas only two sessions revealed drug effects when the AFCS trim was used. Thus, as expected, the additional workload of flying the aircraft without computerized trim stabilization taxed subjects to the point where sleep deprivation induced clearer decrements under the placebo condition.

In addition to the performance effects of flying maneuvers with and without AFCS trim, there were several differential drug effects depending on the time of day at which testing was conducted. The majority of these effects (where Dexedrine enhanced performance in comparison to placebo) occurred at 0900 with the next most frequent effects occurring at 0500 or 1700. The fewest drug-induced changes were observed at the first testing session of the day (at 0100) where only one drug-related difference was observed. This might have been expected since subjects were not significantly sleep deprived at 0100. However, there were only two drug-related effects at 1300, possibly because the circadian cycle tended to mitigate the effects of sleep loss during the middle of the day. Taken together, these results suggest that sleep-deprived subjects received the most benefit from Dexedrine during the early parts of the day (after 0400) and during the evening, whereas there were few differences attributable to Dexedrine versus placebo in the middle of the day. The fact that Dexedrine diminished the decrement seen under placebo at the 1700 session is noteworthy since subjects received their final drug dose 9 hours earlier.

These data provide experimental support for the recently reported findings of Cornum (1993) and Senechal (1988), both of whom found that dextroamphetamine was helpful in terms of overcoming pilot fatigue during extended flight missions. In addition, they indicated that d-amphetamine did not produce erratic performance or other side effects which would have compromised mission success or safety.

Electroencephalographic data

The resting eyes-closed/eyes-open EEGs indicated that Dexedrine moderated the reductions in central nervous system arousal normally associated with sleep deprivation. There were noteworthy drug main effects on both delta and theta activity, and there was a drug x session x eyes interaction involving alpha.

The 3-way interaction in the alpha range was because under placebo, there typically was more alpha under eyes-closed than eyes-open at every session, but while under Dexedrine, this relationship was not maintained. Here, there was more alpha during eyes-closed than eyes-open early in the day, but the opposite was true at the last testing session. At first, it appeared that the reversal could have been occurring because subjects were falling asleep at the last session of the day; however, there was no corroborating evidence in terms of consistent changes in the theta band. Thus, these rather peculiar findings with regard to alpha activity cannot be explained yet.

However, the overall drug effects which were observed in the delta (1-3.5 Hz) and theta (3.5-7.5 Hz) activity bands at Fz (delta only), Cz, and Pz were straightforward. In every case under placebo, there were marked increases in slow-wave EEG activity (indicative of decreased alertness), whereas Dexedrine diminished these effects. The fact that alertness was reduced under placebo corroborates earlier reports that sleep deprivation produces elevations in delta and/or theta (Pigeau, Heslegrave, and Angus, 1987; Comperatore et al., 1993). The fact that Dexedrine diminished these effects generally supports the findings of Newhouse et al., (1992) who observed that dextroamphetamine substantially increased alertness in sleep-deprived subjects (as measured by a sleep-latency test).

These EEG changes are also consistent with the flight performance effects presented earlier. The reductions in CNS activation under the placebo condition no doubt contributed to increases in flight-control errors during the sleep-deprivation periods. The fact that Dexedrine administration mitigated the

performance losses agrees well with the finding that the drug also resulted in higher levels of overall CNS alertness.

Desktop flight simulation task

The Microsoft flight simulation task was used in the present study to determine its utility for studying the effects of various stressors in an aviation research context and to examine the impact of Dexedrine and/or sleep deprivation on basic psychomotor skills. Although the task had not been used in this type of context previously, it indicated sensitivity to the independent variables under investigation. There were drug effects on how quickly and accurately subjects flew a timed course consisting of 21 "gates." The analysis showed that performance during the sleep-deprivation period tended to decline in the middle of the day under placebo (both the 1100 and 1500 sessions were worse than the one at 1900); but, when Dexedrine was administered, none of the sessions differed from one another. Although there were not pair-wise differences between Dexedrine and placebo at any of the testing times (as were observed in the UH-60 simulator), it is interesting to note that Dexedrine prevented the overall trough in performance which occurred under placebo.

Profile of Mood States

The overall reductions in tension-anxiety scores immediately before bedtime suggested that subjects felt more relaxed knowing the sleep-deprivation/continuous-performance period was about to end. The reduced anger-hostility scores under Dexedrine in comparison to placebo was consistent with staff observations that subjects were less irritable after sleep deprivation when their alertness was maintained by Dexedrine.

The vigor-activity scores and the fatigue-inertia scores presented congruous evidence that Dexedrine enhanced the subjects' energy levels and diminished the onset of weariness or fatigue in comparison to placebo. There were overall improvements (more vigor and less fatigue) on both of these scales when Dexedrine was administered. Fatigue was significantly diminished by Dexedrine at every session with the exception of the one at 1940 despite the fact that the last drug administration occurred at 0800 in the morning. However, visual inspection of these data showed Dexedrine's effects tended to subside later in the afternoon. Analysis of the vigor scale substantiated this conclusion by showing that vigor was enhanced by Dexedrine at every session except for the ones at 1540 and 1940. Interestingly, subjects reported less fatigue and more vigor immediately before bedtime on the Dexedrine days than on

the placebo days. Since the polysomnography data showed there were slight differences in sleep quality after the Dexedrine versus the placebo day, perhaps this effect was because subjects continued to experience small Dexedrine effects even several hours after the final dose.

The confusion-bewilderment scale indicated that subjects also were able to think more clearly under the influence of Dexedrine in comparison to placebo. This was especially evident during the mornings (0340, 0740, and 1140); however, as was the case with the vigor scores, subjects perceived the effects of Dexedrine subsiding in the afternoon and evening.

Taken together, the POMS data are reasonably consistent with the flight performance data discussed earlier. Overall, during the sleep-deprivation periods, subjects were less irritable, more energetic, and more clear-minded under the influence of Dexedrine than placebo. With regard to the fatigue, vigor, and confusion-bewilderment scores, Dexedrine was shown to be especially useful for sustaining subjects' positive appraisals of their own well-being during the morning (0340, 0740, and 1140) as opposed to the afternoon and evening. It is interesting to note that while the POMS data indicated Dexedrine's effects were subsiding in the afternoon, the flight data suggested Dexedrine was responsible for continued sustainment of flight performance as late as the last simulator session (at 1700 hours). These findings corroborate those of Newhouse et al., (1989) who reported that the cognitive performance of sleep-deprived subjects was sustained by a 20 mg dose of amphetamine beyond the time at which vigor scores declined.

Synthetic Work Environment

The scores from the Synthetic Work Environment failed to show the robust drug effects seen on the other dependent variables examined in this study. There were no significant differences on the scores from the Sternberg memory task, the auditory monitoring task, or the visual or auditory monitoring tasks attributable to whether subjects received Dexedrine or placebo, and there were no interactions between drug and session. However, there was a session effect on the arithmetic task which was due to slower overall performance at 0745 than at 1145, 1545, or 1945.

Because there were no effects on the cognitive testing an inconsistency exists in comparison to the flight performance, EEG, and POMS data. One possible explanation is that the relatively short testing period (10 minutes) may have been insufficient to reveal the performance losses expected to have been associated with sleep deprivation under the placebo

condition. This explanation seems credible when considered in light of the iteration effects from the flight profile, where it was found that later iterations of maneuvers often were worse than earlier iterations. Perhaps subjects are able to summon sufficient resources to accurately complete tasks for short time periods, whereas the maintenance of such performance during prolonged tasks tends to suffer.

Another possibility is that the synthetic work battery is not sensitive to the effects of only 36 hours of sleep deprivation. This explanation would be consistent with earlier findings on another cognitive performance test after sleep deprivation. Newhouse et al., (1989) stated that the Walter Reed performance assessment battery (PAB), which examines arithmetic skills, logical reasoning, spatial rotation, and reaction time, is not typically affected by less than 48 hours of sleep deprivation. Although the synthetic work battery is a different type of test, it is possible that it may suffer from a similar lack of sensitivity. In the future, it would be interesting to extend the duration of the synthetic work battery and to test subjects during more prolonged periods of sleep deprivation in order to explore these issues further.

Physiological data

Analysis of the 23 sets of vitals signs data collected on each drug-administration day showed that Dexedrine produced slight overall elevations in oral temperature of approximately 0.3°F. Dexedrine also produced a time-dependent increase in pulse. The subjects' heart rates were found to be accelerated 13 beats per minute (bpm) by Dexedrine beginning about 4 hours after the third drug administration, and this effect persisted during three of the afternoon times (10-14 bpm increases) and two of the evening times (11-18 bpm increases).

In addition, Dexedrine caused a time-dependent elevation in systolic blood pressure and an overall increase in diastolic blood pressure. Systolic pressure was 10 mmHg higher under Dexedrine than placebo as early as 50 minutes after the first dose and there were statistically significant increases at 0210, 0420, 0850, 1140, and 1250 ($p < .05$) (ranging from 8-21 mmHg). However, after 1250, there were no differences between the drug conditions. The overall effect of Dexedrine on diastolic pressure was less dramatic (3 mmHg increase) and did not show a clear-cut time relationship. Instead, visual inspection of the data showed the Dexedrine and placebo curves tended to separate about 3.5 hours after the first dose (Dexedrine producing higher values), and this separation seemed to diminish about 7.5 hours after the last dose.

Although some of the temperature data collected in this study were contaminated because they were gathered during meal times, the complete set of vital signs results taken together support the findings of Newhouse et al., (1989) who observed elevations in oral temperature, pulse, and blood pressure after dextroamphetamine administration. Newhouse and coauthors noted that systolic blood pressure increased within 1 hour of the 20-mg dose and remained elevated for approximately 5 hours. Also, they reported a delayed increase in pulse which was thought to be secondary to the drop in blood pressure several hours after the dose. Similar effects were observed here. However, the time-course effects on diastolic pressure (noted by Newhouse et al. (1989)) were not confirmed in this study even though an overall increase in diastolic blood pressure was observed under Dexedrine.

Polysomnographic data

The evaluations of sleep architecture on the recovery nights following Dexedrine and placebo administration revealed that sleep quality was degraded slightly by amphetamine, but there was no insomnia, and sleep onset was not delayed. However, Dexedrine did increase stages 1 and 2 sleep, the amount of movement time, and the amount of awake time during the night. In addition, there was a tendency toward reductions in rapid eye movement sleep, although this was not significant.

The effects of amphetamines on recovery sleep (after deprivation) have not been well studied, but our results were predictable based on other research in which amphetamines were given immediately prior to bedtime. The increases in awakenings and stages 1 and 2 sleep accompanied by decreases in stage 4 and REM sleep reported by Maggini et al., (1988), were partially confirmed here. However, the sleep disturbances seen in the present study were not identical. This is understandable since the opportunity to sleep occurred 15 hours after the last dose and 40 hours after the last sleep period.

Although subjects continued to experience Dexedrine effects well into the night (because of the drug's long half life), the pressure to sleep (from sleep deprivation and continuous task demands) ensured rapid sleep onset without subsequent insomnia. Also, while the overall quality of sleep was reduced, there were no subjective complaints of inadequate recovery sleep.

Conclusions

This study is the first placebo-controlled investigation of the use of Dexedrine to maintain helicopter pilot performance

despite sleep deprivation. The results indicate that Dexedrine is clearly effective for this purpose. Dexedrine also prevented reductions in central nervous system arousal and mitigated fatigue following sleep loss. Of substantial importance is that these positive effects were obtained without complications. No adverse psychological or physiological reactions were observed in this study.

These data support the general conclusions from earlier controlled studies with nonaviators (Weiss and Laties, 1967; Newhouse et al., 1989) and anecdotal reports from aviation contexts (Babkoff and Krueger, 1992; Senechal, 1988; Cornum, 1993), that amphetamines are effective in overcoming the effects of fatigue. The major finding of this investigation is that Dexedrine was efficacious when given prophylactically to helicopter pilots for the prevention of performance decrements associated with sleep deprivation during simulated helicopter flight missions. This is a useful addition to the results from several of the previous nonaviation investigations which have focused more on the ability of amphetamines to recover performance which has already degraded.

Although these findings support Dexedrine administration as an effective way to sustain aviator performance, caution should be exercised. There is need for further research to: 1) determine whether or not these beneficial short-term effects of Dexedrine are followed by any rebound negative effects on subsequent days, 2) determine whether Dexedrine can be used safely for longer periods of time (i.e., 2-3 days), 3) establish how these findings in the UH-60 simulator apply to the actual in-flight environment, and 4) replicate the results of this investigation on a larger sample of subjects which includes females, a growing minority in the Army aviator population.

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Appendix A.

List of manufacturers.

List of manufacturers

Cadwell Laboratories
909 North Kellogg Street
Kennewick, WA 99336

CH Products
970 Park Center Drive
Vista, CA 92083

Critikon
4110-T George Road
Tampa, FL 33614

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10300 Campus Point Drive
San Diego, CA 92121-1579

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Milwaukee, WI 53223

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