One of the first duties of the Physician is to educate the masses not to take medicine.
Sir William Osler [1]

Introduction

Use of stimulants in clinical settings is guided by medicine, science, and the goal of benefitting patients with defined illnesses that are known to be responsive to stimulants (e.g., narcolepsy, attention deficit hyperactivity disorder, and shift work sleep disorder – the latter is discussed in Chapter 8, this volume). At the present time, legitimate use of stimulants (specifically, the amphetamines and modafinil) in operational settings in otherwise normal, healthy adults for management of fatigue is limited to the military – and, in particular, the United States Department of Defense (DoD) [2]. Currently within the US DoD, stimulants are approved for use only under restricted circumstances in certain sectors of aviation and in some Special Forces units. In this chapter we explore some of the experience and issues surrounding this use.

The definition of “fatigue” is an issue in itself, the scope of which is beyond this chapter. The DoD uses the Human Factors Analysis and Classification System (DoD HFACS) to determine causal factors associated with accidents and mishaps [3]. DoD HFACS defines fatigue as an adverse physiological state in which:

the individual’s diminished physical or mental capability is due to an inadequate recovery, as a result of restricted or shortened sleep or physical or mental activity during prolonged wakefulness. Fatigue may additionally be described as acute, cumulative or chronic.

DoD HFACS also recognizes the contribution of circadian rhythms to degraded performance:

Circadian rhythm desynchrony is a factor when the individual’s normal, 24-hour rhythmic biological cycle (circadian rhythm) is disturbed and it degrades task performance. This is caused typically by night work or rapid movement (such as one time zone per hour) across several time zones. Referred to as “shift lag” and “jet lag.” (Time in the new time zone will lead to adaptation and recovery; the amount of time depends on the number of time zones crossed and the direction of travel. Recovery from shift lag may never occur.)

Throughout this chapter, we use “fatigue” to mean degraded cognitive/mental performance resulting from inadequate sleep, with or without circadian rhythm desynchrony.

Managing fatigue requires a comprehensive program which includes enlightened leadership, mission planning and scheduling to limit fatigue, and individual knowledge about how to appropriately implement fatigue countermeasures (to include obtaining adequate sleep). Administrative countermeasures include limiting the duration of missions and duty cycles, scheduling missions away from the circadian trough, augmenting crews with additional members, sharing duty times between individuals, providing more restful sleeping quarters, allowing and encouraging naps, and providing non-duty recovery days to allow circadian adjustment following time zone travel. Pharmacological countermeasures in the form of prescription sleep-inducing agents are also useful to promote sleep, particularly in situations where sleep is unlikely due to less than optimum sleeping quarters or timing of the sleep period at an inappropriate time within the circadian phase (e.g., daytime sleep).
In military operations, however, combining countermeasures may still leave significant unmanaged fatigue – with consequent increased risk of mission failure and mishaps. Having pre-established plans and policy for short-term use of stimulants gives line commanders an additional set of tools to manage fatigue.

**History of stimulant use in the military**

Stimulant use has been a feature of some military operations since at least the Second World War (WWII). Besides caffeine, amphetamines were used by German, British, American, and Japanese forces during WWII, both for their fatigue-ameliorating effects and for their effects on mood and morale (for a perspective on the military history of amphetamine use during WWII, see chapter 3 in [4]).

The US Air Force (USAF) officially sanctioned amphetamines to promote alertness in selected aircrew within the Strategic Air Command (SAC – dedicated primarily to long-range bombing) in 1960 and within the Tactical Air Command (TAC – predominantly fighter aircraft, light attack, and ground support) in 1962. The USAF has approved amphetamine use intermittently since then. Stimulants in military aviation are colloquially referred to as “Go-pills,” while sleep-inducing agents are referred to as “No-Go pills.”

Although records and published reports are lacking, amphetamines were used by some Army, Navy, and Air Force pilots during the Vietnam conflict to sustain alertness; however, controls over dose or frequency of use were lax and non-standardized. Pilots reported easy availability of “uppers” to maintain alertness while flying, and anecdotal reports of stimulant use during the Vietnam conflict suggest that doses of amphetamines used were higher (and related side effects more prominent) than with subsequent, more highly regulated use [5].

During Operations Desert Shield and Desert Storm in 1990–91, fatigue was considered the most significant and pervasive problem facing aircrews. Tactical (fighter aircraft) pilots faced unique challenges associated with long combat air patrols and extended flights. Particularly high-risk maneuvers included midair refueling (“tanking”) and returns to base following combat strike missions. In the lead-up to the First Gulf War (GWI), dextroamphetamine was used occasionally by USAF tactical jet pilots on transmeridian ferry flights from the Continental US to the Mideast, with flight times averaging approximately 15 hours and awake times exceeding 22 hours. In a survey of 405 responding pilots, 43% reported at least one use of a Go-pill, and several reported falling asleep without them, particularly while tanking [6]. During GWI, typical mission profiles involved flights of 6–8 hours, with crew duty days often exceeding 14 hours and sleep periods of less than 6 hours. At least two non-combat fatal mishaps during the air campaign were attributed to fatigue, although the mishap circumstances were not reported in the after-action summary. Stimulants were authorized for use by selected Air Force TAC crews, and results of voluntary surveys completed by aircrew enrolled in the program indicated that 57% reported at least one use during the air war (17% routinely, 58% occasionally, and 25% only once). Among units, per-pilot usage rates varied widely (ranging from 3% to 96%), with higher rates in those units flying sustained combat air patrol (i.e., extended duration flights protecting assets from enemy air attack). Over 60% of pilots surveyed considered the drugs “essential” to mission accomplishment, and there were no reported adverse reactions or side effects [7].

Following GWI, the Chief of Staff of the USAF released a message in March 1991 terminating the policy of in-flight stimulant use. The reason for the suspension is unclear, but Cornum et al. suggested that this decision was likely made for ethical, political, and emotional reasons not supported by the accumulated evidence of efficacy, safety, and mission necessity. Cornum et al. acknowledged that chronic use could theoretically lead to commander abuse (in which units would come to rely on the stimulant to make up for inadequate manpower or resourcing – discussed further below) and to aircrew psychological dependency, dose escalation, and abuse (arguments which, as discussed further below, are still put forth as reasons to discontinue the military’s stimulant program altogether); however they argued that no evidence existed to justify those concerns [5]. Owing to the length of ongoing air missions in Eastern Europe, the USAF did reinstitute the program in 1996 for air operations leading up to the Balkans conflict [8].

Belland and Bissell reported on the naval air challenges of flying in support of continuous operations in Operation Southern Watch (OSW) in 1992, following GWI [9]. One carrier air wing (carrier-based naval
aircraft squadrons) deployed to the Persian Gulf to fly combat missions shared flight operations with ground Air Force assets and flew around-the-clock missions for the first 18 days of OSW. Mean reported daily sleep was 5.6 hours, with average minimums and maximums of 2.6 and 7.9 hours, respectively. Combat flights ranged from 4.3 to 6.3 hours in duration, often with senior aviators flying two missions daily. Fatigue was prevalent, and aircrew reported greatest susceptibility to fatigue (1) during long missions over the area of combat operations, (2) at times when missions were routine and unchallenging, and (3) during briefs before and after flights. In general, the more senior aviators with increased collateral (non-flight) duty obligations reported higher problems with fatigue. Caffeine tablets (100–150 mg) were made available and used by 18 of the 125 aviators surveyed, and 39 relied on pre-flight coffee. After taking a caffeine tablet on an empty stomach, one pilot who was not a regular caffeine user reported feeling agitated, having difficulty with aerial refueling, and having some concerns over his carrier landing performance. Two pilots used nicotine gum while flying to substitute for their smoking habit. There were no mishaps during this initial 18-day surge, and only one mission was cancelled due to fatigue. Based on USAF experience and success with stimulants, this naval air wing had requested approval for use of dextroamphetamine; however this request was denied because at that time there was no naval aviation policy on use of stimulants.

In July 1997, the US Navy (USN) conducted an air wing proof-of-concept surge exercise aboard the aircraft carrier USS NIMITZ to determine whether a forward-based carrier could carry out around-the-clock air operations for 4 continuous days. Sleep deprivation and fatigue were recognized threats to successful completion of this exercise [10]. Although the use of stimulants was considered, again the lack of USN policy obviated that possibility.

The USN first formalized a policy for stimulant use in the NAVMED P-6410 instruction, issued in January 2000 [11]. Although there are anecdotal stories of individual naval flight surgeons distributing stimulants to crews in special missions before this policy was issued, the first reported use of dextroamphetamine in naval aviation for fatigue management under this program was on 11 May 2002. A flight surgeon working with a squadron flying the EA-6B electronic countermeasures aircraft reported that an aviator deployed in the Persian Gulf took two 5 mg Dexedrine tablets in the latter half of an 8.5-hour combat mission for “degraded alertness from the extended-transit time to and from the operating area” [12]. This flight surgeon felt that use of the medication made an important difference in his aviator’s performance and improved flight safety by increasing situational awareness. A Navy carrier air wing also reported use in 2003 while involved in Operations Enduring Freedom (OEF, Afghanistan), Southern Watch (OSW, Iraq, pre-invasion), and Iraqi Freedom (OIF, Iraq Invasion 2003). This carrier was assigned as the “night carrier,” flying exclusively at night during two-carrier operations in the Persian Gulf. This group reported flying more missions, dropping more ordnance (bombs), and possessing a higher percentage of bombs on target than any other tactical unit in OIF. Of the 120 pilots eligible to enroll in the program, 85% elected to ground test (described below) and carry Go-pills in flight; however, actual use of dextroamphetamine occurred during only 54 missions. Most aviators reported taking only a single 5 mg dose. Go-pill use dropped as combat operations drew closer, reportedly because the subjective alerting effects of anticipating combat helped alleviate fatigue symptoms. Although prescription sleep-inducing agents were allowed under the program, supplies were scarce and none of the aviators chose to take sleep-inducing agents to assist with sleep or counter the action of the stimulant [13]. Subsequently, other carrier-based air wings have used both stimulants and sleep-inducing agents, with virtually all aviators approving of the program – even those electing not to take the medications. Approximately 80% of them consider fatigue management programs incorporating stimulants and sleep-inducers as “mission essential” [14].

Stimulants were used by selected USAF and USN aviation squadrons during Operation Iraqi Freedom (OIF, March – May 2003). The USAF B-2 stealth bomber crews routinely flew missions from Whiteman Air Force Base in Missouri and also from a forward operating location (FOL), with mission times averaging 35.3 and 16.9 hours, respectively. Missions were preceded by 8–9 hours of awake time for preparation and briefing. Bomber crews used a combination of fatigue countermeasures to cope with such lengthy missions, including zolpidem (Ambien®)-assisted sleep prior to missions, in-cockpit napping, caffeine, and dextroamphetamine. Pilots on the shorter flights from the FOL actually reported higher rates of dextroamphetamine use (97% reported using one or more pills) than pilots on the ultra-long flights from Whiteman AFB (57%). The longer
flights out of Whiteman AFB apparently allowed for greater use of other countermeasures such as in-cockpit napping, caffeine, and zolpidem-assisted pre-flight crew rest [15]. The crews based at Whiteman AFB possibly also gained an advantage from sleeping at home in familiar quarters compared to those operating from the FOL.

Why use stimulants in military aviation?

The military runs a 24/7 operation, and much of the flying is conducted at night. The latter forces the aviation community to operate through the early morning hours during the circadian trough in alertness and performance. The initial bombing of Baghdad as part of “Shock and Awe” during OIF started at 5:34 AM local time [16], with flight planning and prepositioning occurring during the preceding hours. The latter scenario (acute sleep deficit plus performance during the circadian trough) creates a situation that increases the likelihood of a fatigue-related mishap – and is likely compounded by an existing chronic sleep debt.

Factors contributing to fatigue may differ somewhat depending on airframe/mission. For example, bomber crews are sometimes faced with extraordinarily long missions. B-2 missions of 44 hours from Whiteman AFB to Afghanistan (described above) are the longest combat flights in recorded history [15]. In contrast, helicopter pilots face unique stresses which may increase their fatigue vulnerability: flights are usually conducted at low altitudes in close proximity to the ground, where the margin for error is marked in seconds to impact. Well-rehearsed complex verbal communication (referred to as crew resource management, or CRM) among pilot, copilot, and crew is required to share information and control the aircraft during high-risk maneuvers. Transport aircrews face the added circadian stresses which originate from multi-day missions and rapid travel across multiple time zones. Modern operational tempos frequently do not permit the one-day-per-hour of time zone travel that is generally recommended to achieve circadian adaptation.

Regardless of airframe or mission, all pilots must continually scan and integrate information from disparate gauges, displays, radio communications, and crew interactions to maintain a correct estimate of aircraft orientation, motion, and state. Poor crew resource management, spatial disorientation, and visual illusions are all prominent causes of aircraft mishaps and may be more prevalent in fatigued aircrew [17, 18, 19].

Although all three military services have policies and guidelines to limit fatigue (see below), fatigue remains a significant causal factor in military aviation mishaps. All branches of the US military follow service-specific established policies and regulations for reporting mishaps. The term “mishap” rather than “accident” implies that such events have definite causal factors which can be identified and remediated. Aviation mishaps are coded according to their seriousness and cost. Class A mishaps involve loss of life and/or aircraft or property damage of $2 million or more; Class B categorizes mishaps costing $500K up to $2M; and Class C from $50K up to $500K prior to 1 October 2009, mishap Class A, B, and C monetary thresholds had been $1M, $200K, and $20K, respectively. Instances in which a hazardous condition presents a potential for a mishap may be identified in hazard reports (also known as “HAZREPS” in the USN).

Aviation mishaps are costly in terms of both lives and assets. In the USAF, from 1972 to 2000, fatigue was a causal or contributing factor in 234 of 1837 (12.7%) Class A aircraft mishaps. No single factor ranked more detrimental to performance and safety than fatigue [20, 21]. Results from a survey of 241 Army aviators and 120 Army enlisted crew members revealed average sleep times of 6.6 and 6.2 hours/night respectively during operations, substantially below the standard 8 hours/night recommended. Of the pilots in this study, 72% indicated they had flown when they were so drowsy that they could have fallen asleep, and 45% indicated they had at some time dozed off either while flying or in the cockpit. Army Safety Center statistics indicated that 4% of Army Class A, B, and C mishaps from 1990 to 1999 were fatigue related [22]. A recent analysis of Class A naval aviation mishaps which occurred in operational squadrons (excluding training commands) during the period FY00-FY06 was conducted using DoD HFACS. In 20 out of 89 (22%) of these Class A mishaps, fatigue was identified as an HFACS “Precondition” to the mishap. Fatigue was the most frequent of the adverse physiological preconditions cited. The cost of these 20 fatigue-related mishaps was approximately $450M, and represented 70 out of 166 (42%) of the fatalities incurred during this FY00–FY06 interval. Interestingly during this same interval, aircrew had filed no HAZREPS citing fatigue, suggesting that fatigue is still underrecognized as a hazard [23].

Why not use stimulants in civilian aircrew?

While the US military has chosen to employ stimulants in certain flight operations, the United States
Federal Aviation Administration (FAA) specifically forbids use of psychoactive drugs (including amphetamines) in civilian aircrew. Why is the military pilot a more likely candidate for stimulants than his civilian counterpart? Caldwell argues several points, the most persuasive of which is that military flights are often conducted under the most arduous of conditions to sustain the operational tempo (as noted above) – to include unpredictable flight operations. As a result, waivers from crew rest guidelines are often required, and granted. In contrast, civilian pilots are constrained by FAA crew rest regulations and are not allowed waivers from these regulations [2]. The military also has the benefit of integrated medical support and oversight of stimulant use not usually available to commercial ventures, making prescribing, dispensing, and safety monitoring much easier.

International military guidance on pharmacological management of fatigue

The US military maintains a stimulant policy while most of its allies do not allow use of stimulants (other than perhaps caffeine) to maintain/restore performance and manage fatigue. A review of international military service policies [24] reveals a variety of policies on pharmacological fatigue management. In Australia, zolpidem and temazepam (Restoril®) to assist with sleep are permitted, but no stimulants other than caffeine are authorized. In Canada and New Zealand no national doctrine for fatigue management exists, but short-acting prescription sleep-inducing agents are permitted under special circumstances; stimulants are not allowed. In the United Kingdom, short-term use of temazepam to aid sleep is permitted but stimulants are not allowed. In Germany, Denmark, and The Netherlands, use of stimulants other than caffeine is not allowed by their national laws, which do not permit off-label prescribing [25, 26, 27, 28].

Current US service policies on stimulant use

Force Health Protection

All US military services fall under the provisions of Title 10 U.S.C. 1107 [29], and the DoD Instruction 6200.02 [30], which specify procedures for FDA-approved drugs to be prescribed and used “off-label” (i.e., for a non-indicated purpose) for Force Health Protection (FHP). FHP is defined specifically as “an organized program of healthcare preventive or therapeutic treatment, or preparations for such treatment, designed to meet the actual, anticipated, or potential needs of a group of military personnel in relation to military missions” [31]. Use of pharmacological agents in fatigue management programs to alleviate performance degradation resulting from military mission demands and sleep deprivation fall under the FHP definition. By these policies, a drug being used off-label is considered equivalent to an Investigational New Drug (IND), and several conditions must be met in order to implement them. Since neither dextroamphetamine nor modafinil are FDA-approved for use in management of fatigue in otherwise healthy individuals, their use also is bounded by these instructions. Of particular note, the policy requires that:

1. Service members participate voluntarily and provide written informed consent to use the drug, and that this informed consent be documented in their military medical record;
2. Service members receive training and risk communication that includes warnings that the drug is not FDA-approved for this application, the reasons the military wishes to use the drug, and possible side effects that the drug may cause;
3. Detailed records be kept regarding distribution of the drug to service members.

Military service branch–specific policies

As noted above, the USAF allows use of both dextroamphetamine and modafinil. Currently, the US Army and Navy allow only dextroamphetamine but as of this writing both services are in the process of approving modafinil as an alternative to dextroamphetamine. US Marine Corps aviation is conducted under Naval Aviation rules and operates under Navy medical policy guidance. The US Coast Guard does not allow stimulants.

Official USAF policy is contained in a series of Policy Letters originating from the Air Force Medical Operations Agency (AFMOA) and the Official Air Force Approved Aircrew Medications List [32, 33, 34]. These policies specify the dose and frequency of stimulants (and sleep-inducing agents, described further below) authorized along with program requirements.
and forms. Dextroamphetamine in 5–10 mg doses is approved for use in selected fighter and bomber aircrews. Modafinil 200 mg was also approved for all aircrews in June 2006 after operational experience indicated that it was safe and without nausea and vestibular side effects that had earlier been reported in the literature at accumulated doses higher than 400 mg/day [35, 36].

The US Navy first issued guidance in January 2000 for use of dextroamphetamine (and sleep-inducing agents – see below) in flight operations for selected missions involving combat or exceptional circumstances of operational necessity, in the instruction “Performance Maintenance During Continuous Flight Operations: A Guide for Flight Surgeons” [11]. In 2003, the approval authority for use was raised from the squadron commander to the next higher level wing commander or equivalent, possibly in response to public concerns raised in the Tarnak Farms incident (discussed below) [37]. Further guidance on minimum mission durations and maximum continuous days of use, which had not been specified in the original instruction, was issued in a message from Commander, Naval Air Forces, in January 2010.

US Army guidance and policy is contained in a Leader’s Guide to Crew Endurance and an Aeromedical Policy Letter from February 2003 [38, 39], which authorizes use of dextroamphetamine 5 mg (up to 30 mg per day) in some Army aviation missions (albeit to date, with the exception of some Special Forces units, no Army aviation units are known to have requested use of the program) [40].

US Special Forces operate jointly but are governed by their respective service policies regarding use of stimulants and sleep-inducing agents. Guidelines are similar to those used in DoD aviation. Some ground units may be authorized dextroamphetamine or modafinil for fatigue management, to be used only after 18 or more hours of wakefulness.

The above-indicated individual service policies continue to evolve, and they clearly differ regarding such variables as level of approval authority required, which medications are approved for use, which units and missions may be approved, maximum time period approval lasts, and minimum mission duration thresholds for use. For instance, Air Force tactical jet mission minimum durations for stimulant approval are nominally at least 8 hours, whereas the Navy specifies a minimum of 6.5 hours (although both services recognize that in certain circumstances medications may be indicated for shorter missions).

Table 17.1 summarizes the currently allowed stimulants and doses in the US military branches.

### Table 17.1. Current US military policies on stimulant use

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Use guidance</th>
<th>Max use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextroamphetamine</td>
<td>5–10 mg</td>
<td>Not in policy; generally every 4 hrs</td>
<td>USAF: no more than 60 mg per 24 hrs</td>
</tr>
<tr>
<td></td>
<td>5–10 mg</td>
<td>Recommended: 5 mg every 2–3 hrs; max 30 mg per 24 hrs</td>
<td>US Navy: no more than 30 mg per 24 hrs</td>
</tr>
<tr>
<td></td>
<td>5 mg</td>
<td>No more than 30 mg</td>
<td>US Army: no more than 400 mg before crew rest is required</td>
</tr>
<tr>
<td>Modafinil</td>
<td>200 mg</td>
<td>Every 8 hrs</td>
<td>400 mg before crew rest is required</td>
</tr>
<tr>
<td></td>
<td>200 mg*</td>
<td>Every 8 hrs</td>
<td>400 mg before crew rest is required</td>
</tr>
<tr>
<td></td>
<td>100–200 mg*</td>
<td>Every 4–8 hrs</td>
<td>400 mg before crew rest is required</td>
</tr>
</tbody>
</table>

*Implementation pending as of this date.

Role of the flight surgeon in stimulant-based fatigue management

Use of stimulants in aviation operations is overseen by a flight surgeon (a military medical officer – medical doctor or doctor of osteopathy – who has...
received additional training in aerospace medicine). The flight surgeon’s main role is promotion of crew safety by actively assessing risk factors that may compromise crew health and by mitigating risk associated with these factors. The latter is in contrast to the traditional medical relationship, in which the physician’s role is to treat the patient’s ailment. In the operational environment, the flight surgeon is usually dealing with an exceptionally fit and healthy individual and monitoring that person to protect him/her from the challenging and stressful environment of flight operations. The flight surgeon can ground the aviator (prohibit flying) if there is any doubt regarding safety.

General principles for stimulant use

The following general principles apply across all US military services:

1. Stimulants are used to maintain performance or attempt to restore fatigue-degraded performance to a baseline condition. They are specifically not intended to enhance performance beyond the well-rested state.

2. Conditions under which stimulants may be considered are limited to combat and other exceptional circumstances of operational necessity. The use of drugs is considered a last resort, after all other fatigue countermeasures have been used and shown to be inadequate in controlling fatigue.

3. The use of drugs does not replace the requirement to adhere to established guidance on other fatigue countermeasures, such as maximum daily, weekly, and quarterly flight times, nor does it allow altering procedures to obtain waivers of flight limits.

4. Use of stimulants is purely voluntary, and always at the discretion of the individual service member. Written informed consent from the service member is required.

5. Ground testing (pre-testing prior to actual operational use) is required to rule out adverse reactions or side effects from the medication before authorizing use.

6. Standardized doses and dosing recommendations are established, and maximum limits are usually specified by day, mission, and maximum number of continuous days allowed.

7. Adverse reactions to drugs must be recorded in the individual’s medical record and reported to a higher authority.

In addition, individuals are prohibited from using prescription stimulants outside formally approved programs and without command and medical officer approval.

Implementation of stimulant use

As an example, Figures 17.1 and 17.2 show sample flow sheets of the two phases and intermediate steps involved in approval, ground testing, implementation, tracking, and reporting of modafinil use in USAF aircrews. The first phase is modafinil ground testing (Figure 17.1). Airmen who are eligible for stimulant use and wish to use modafinil are required to ground test modafinil prior to operational use. The flight surgeon responsible for the crew educates prospective aircrew members who volunteer for the program, and places signed copies of a patient consent form in the individual’s military medical record. A “clearance for ground test” form is then completed, and the flight surgeon issues the airman a specified dose (currently, two modafinil 200 mg tablets) along with an instruction sheet for ground testing. The airman takes the medication as prescribed, notes the effects, and returns to the flight surgeon the following duty day (or as soon as possible if any adverse reactions occur). The flight surgeon confirms that the correct dose was taken, that no adverse outcomes resulted, and that the airman was satisfied with the effect of the medication. The airman is then considered “cleared” for operational use of modafinil, and the results are documented in his or her military medical record.

The second phase involves modafinil use operationally (Figure 17.2). If significant fatigue is anticipated in a planned operation and fatigue cannot be controlled with standard non-pharmacological countermeasures, and if missions are expected to exceed 8 hours for fighter crews or 12 hours for bomber crews, a squadron commander may submit a stimulant approval form to the wing commander for consideration. If the wing commander approves, the major command (MAJCOM) Director of Operations (DO) and Command Surgeon (SG) over the wing and squadron are notified. If the ground-tested aircrew member requests medication, the flight surgeon verifies his/her ground test status, then issues a limited
Modafinil ground testing

Airman eligible for stimulants? yes
Airman volunteers for ground test? yes
FS Explains test instructions, side effects, usage
Airman signs informed consent, receives meds & instructions
Airman completes ground test & reports back to FS
Unanticipated or adverse side effect?
    yes
    Unexpected result filed in Health Record
    Adverse result filed in Health Record
    Clearance filed in Health Record
    Airman completes Health Record, “cleared” for modafinil use
    Airman is now QUALIFIED for modafinil use
    Aircrew not previously ground tested can choose to test prior to mission, if time allows. No Ground Test = NOT CLEARED
    Monkeying not issued
    Monkeying not issued

Wing commander approves operational use of modafinil
Airman wants modafinil available for mission? yes
FS checks health record for Ground Test results:
    Informed Consent filed in Health Record
    Clearance for use filed?
    Unexpected or adverse reaction?
    yes
    Airman completes ground test & reports back to MAJCOM SG
    Airman signs informed consent, receives meds & instructions
    FS Explains test instructions, side effects, usage
    Airman volunteers for ground test?
    yes
    Airman eligible for stimulants?
    yes
    Monkeying not issued
    Monkeying not issued

Meds not issued
Meds not issued

Airman uses modafinil as needed, in accordance with instructions and limitations

FS completes daily usage documentation
Adverse reaction to modafinil? no
FS completes weekly usage documentation
Use until mission complete or no longer needed
Mission complete; surveys given to participants
FS completes usage summary for mission

Anomalies report back to MAJCOM SG
FS completes adverse reaction report; files in Health Record
Weekly use filed in Health Record
Individual summary use filed in Health Record

Figure 17.1. Sample flow-sheet illustrating US Air Force guidance for Ground Testing and Approval of aircrew for modafinil use.

Modafinil usage

Mission fatigue anticipated?
    yes
    Bomber > 12 hrs?
    yes
    Fighter > 8 hrs?
    yes
    Use modafinil?
    yes
    Airman signs informed consent, receives meds & instructions
    Airman completes ground test & reports back to FS
    Unexpected or adverse side effect?
    yes
    Airman completes ground test & reports back to MAJCOM SG
    Airman signs informed consent, receives meds & instructions
    FS Explains test instructions, side effects, usage
    Airman volunteers for ground test?
    yes
    Airman eligible for stimulants?
    yes
    Monkeying not issued
    Monkeying not issued

FS completes daily usage documentation
Adverse reaction to modafinil? no
FS completes weekly usage documentation
Use until mission complete or no longer needed
Mission complete; surveys given to participants
FS completes usage summary for mission

Anomalies report back to MAJCOM SG
FS completes adverse reaction report; files in Health Record
Weekly use filed in Health Record
Individual summary use filed in Health Record

Figure 17.2. Sample flow-sheet illustrating US Air Force guidance for operational Dispensing, Tracking, and Documentation of aircrew modafinil use.
The documentation-intensive. The difficulties in implementing them could be a deterrent to using the drugs in situations in which they might be indicated. However, these tight controls are intended to promote close command and flight surgeon oversight of stimulant use and to minimize the chance for misuse, diversion, or abuse.

**Current operational experience**

Aside from the results reported above [6–13], surprisingly few studies have addressed how pharmacological fatigue management programs are implemented under actual operational conditions. In one recent survey of 29 deployed F-15E Air Force fighter pilots, Gore et al. [41] found that stimulant use was occurring earlier in missions, at lower doses, and on shorter flights than was previously thought: the average sortie (flight) length across 111 missions was 7.6 hours, with 60 (54%) being less than 8 hours in duration, the nominal USAF minimum mission length in tactical aviation for stimulant use. Of these 60 sorties, stimulants were used on 15. At the beginning of flights, sleepiness scores, as measured by the Stanford Sleepiness Scale (SSS), were similar between users and non-users (2.2 vs. 1.9, respectively); however, scores for users were significantly higher by the first hour of flight, which then declined (indicating less sleepiness) as the sortie progressed, whereas scores for non-users steadily increased. Overall, stimulants were used on 39 (35.1%) of the sorties and usage was significantly more prevalent in missions exceeding the 8-hour duration (odds ratio (OR) 2.77), in flights extending through the night circadian trough (OR 3.39), and in aircrew who had previously used a sleep-inducer (OR 2.38). Gore et al. suggested that these findings indicated that rules based on mission length might be too restrictive and that use of sedatives, flight scheduling inconsistency, and circadian disruption should also be considered when authorizing use of stimulants.

In our experience, Go-pill use varies widely by individual aircrew members; i.e., some never take a pill while others take at least one pill on most missions. The individual differences in fatigue susceptibility, expectations of the benefits of Go-pill use, and psychological factors which may be driving this variability are largely unknown. Figure 17.3 shows the frequency distribution of Go-pill usage during one Navy carrier air wing combat deployment. Results represent the number of aircrew members (naval aviators and naval flight officers) and the percentage of the combat sorties they flew in which they used at least one Go-pill. Of 108 aircrew members eligible, 12 chose to not enroll in the stimulant program. Of the remaining 96 who enrolled and completed the drug ground test, 9 chose to never carry Go-pills with them on sorties, and another 11 never took a pill although they carried pills with them during flight; thus 20 never used them on any sorties (i.e., 0% of sorties). At the other extreme, three individuals used at least one Go-pill on over 90% of their sorties. Between these extremes, individual frequency of Go-pill use was distributed over the 1463 combat sorties flown as shown. Forty two aircrew members used Go-pills on over half their flights, and the most common experience during this cruise (mode of the distribution) was aircrew using Go-pills on 61–70% of the sorties (13 aircrew).

Not illustrated in Figure 17.3, however, is the fact that overall, the total number of pills taken per aircrew member per sortie was low: of those flights during which an individual used Go-pills, in 58% of the occasions he/she took only one 5 mg Dexedrine pill, in 37% of the occasions two pills were required, and on only 5% of occasions did individuals require three or more pills. The maximum number of pills used by a single aircrew member on a given sortie was four pills.
(20 mg), which occurred on two occasions [14]. Two other individuals routinely took one-half tablet (2.5 mg Dextedrine) for dosing. These results suggest that when used under the currently implemented programs in US military aviation, stimulants are used relatively infrequently and at low dosages. Notably, no adverse outcomes have been identified or reported to date.

**Combined stimulant/sleep-inducing agent use**

Within performance maintenance programs, sleep-inducing agents are invariably authorized in addition to stimulants. Fatigue management also involves managing sleep as well as wakefulness, and all service policies involving stimulants include guidance and dosage recommendations for sleep-inducing agents to aid sleep. Furthermore, modafinil and dextroamphetamine possess long half-lives and can interfere with sleep up to 15 hours after dosing [42]. During one air wing deployment, a third of naval aviators reported use of zolpidem to help with sleep and counter the effects of dextroamphetamine taken earlier during flights [43]. Schultz and Miller also reported that 7 of 16 pilots (44%) noted difficulty obtaining adequate sleep following use of dextroamphetamine [44]. As noted above, Gore et al. reported an association of stimulant use after using sleep-inducing agents, raising the question of whether pilots were using stimulants to counter the effect of the sleep-inducer, were using sleep-inducing agents to manage schedule variations, or were simply more likely to employ both drugs [41]. It should be noted that the extent to which sleep-inducing agents reverse the effects of stimulants – and vice versa – has not been determined [36].

Even if not explicitly stated, within most military policies pharmaceutically based fatigue management is viewed as a two-staged process, with use of sleep-inducing agents to be tried alone before employing stimulants. Although not as rigidly controlled as stimulants, use of sleep-inducing agents in fatigue management programs is still subject to the same DoD FHP provisions regulating off-label use, including ground testing, tracking, and military medical record documentation. In contrast, the therapeutic use of sedative-hypnotics to treat insomnia in aircrew falls within traditional clinical practice standards and is not governed by these programs – in these instances, aircrew must be grounded until the insomnia is resolved.

**Practical challenges with stimulant policy implementation**

Although the policy and procedures listed above are based on sound principles, and experience to date indicates that stimulants have been used with good
success and with no adverse consequences, challenges in appropriately implementing these programs exist.

First and perhaps foremost, taking a stimulant or sleep-inducing agent is easy compared to implementing the other non-pharmacological fatigue countermeasures which are required first and which require scheduling sleep and prioritizing it over competing duties or personal downtime. Therefore, fatigue management programs employing stimulants must be comprehensive, and continual attention must be paid to overall utilization of non-pharmacological countermeasures to justify use of the drugs.

Second, stimulant use programs require substantial documentation, oversight, tracking, and intrusive leadership. As noted above, the flight surgeon is responsible for prescribing and distributing stimulants to restore or maintain performance. The aviator may not appreciate the need for the flight surgeon to regulate and limit distribution of prescription stimulants. The flight surgeon may be viewed as the gatekeeper to the aviator’s success, and the flight surgeon must balance the demand for stimulants against the actual benefit and the potential for harm. Pilots sometimes complain about having to check out and check in medications, account for each pill they take, and fill out documentation on each use. A complaint sometimes voiced is that if a highly educated professional pilot can be trusted to fly a $50M aircraft and employ lethal weaponry in combat, he or she should be entrusted to manage his or her own set of Go- and No-Go pills. However, the flight surgeon is required to abide by the legal requirements for dispensing controlled substances. Also, it is perhaps worth observing that physicians too are highly educated professionals who are knowledgeable about drug effects, yet neither the FDA nor medical licensing boards entrust physicians to self-prescribe and manage their own controlled substances.

Third, prescribing and dispensing drugs with opposite effects is not without the possibility of making mistakes. The aviator-applied use of the terms “Go-pill” and “No-Go pill” is consistent with other aviation procedures in which the attempt is to simplify nomenclature, standardize language, and minimize the possibility of confusion during flight operations. Flight surgeons will usually further color-code the pill packages: green for “Go” (go flying) and red for “No-Go” (not go flying). Despite this added precaution, there have been anecdotal reports of aviators taking dextroamphetamine when intending to ground test a sleep-inducing agent. The night of poor sleep which likely resulted would be of minimal consequence while ground testing; however if the opposite were to occur (i.e., were an aviator to inadvertently take a sleep-inducer to counter the effects of fatigue during actual flight), the result could be disastrous. Sedative use has been associated with at least one military aviation mishap [45], and sedating antihistamines have been associated with both military and civilian aviation mishaps [46, 47]. Strict rules forbidding aviators to carry sleep-inducing agents in flight must be enforced, and many squadrons make it a pre-flight checklist item to ensure that no aviator inadvertently includes No-Go pills in his/her flight equipment.

Finally, the aviation service policies are written with the philosophy that stimulants are intended to restore performance to a well-rested state rather than to enhance performance. However, a number of hypothetical scenarios might influence stimulant use. For example, making the distinction between “return to well-rested” and “enhance performance” may be difficult to accomplish. Aviators are competitive, and if they feel they are performing better, scoring better landing grades, or flying more safely as a result of taking the Go-pill, then it is possible that they would be more likely to choose to take the pill. Command climate and leadership could also potentially influence stimulant use within a squadron. Although the approval level for authorizing stimulants rests above the squadron commander, the squadron commander makes the final decision as to whether to employ the drugs. Commanders who are enthusiastic about using stimulants to counter fatigue may instill that culture in their subordinates. Conversely commanders who decide not to use stimulants at all deprive their pilots of the option to choose the drugs if they feel they need them.

**The Tarnak Farms incident**

An examination of an event which has become known as the Tarnak Farms incident illustrates some of the practical challenges (discussed above) associated with use of stimulants in the operational environment. This friendly fire incident reignited the public debate over stimulant use within the US military.

In the early morning hours of 18 April 2002, two Air National Guard F-16s (referred to as “Coffee 51” [lead pilot] and “Coffee 52” [wingman]) were returning to base from a combat air patrol in Afghanistan. Near the city of Kandahar, transiting toward a
scheduled aerial refueling, the pilots spotted what they perceived to be surface-to-air fire (SAFIRE) from enemies located on the ground. They received permission from Combat Air Controllers to return to the area and locate the perceived threat from a safe distance for further evaluation. In the process, Coffee 52, the wingman, descended below the altitude considered safe within procedural guidance for evaluating a surface-to-air threat. He ignored “standby” and “hold fire” calls from mission controllers and dropped a 500-pound laser-guided bomb on what turned out to be friendly Canadian forces engaged in a ground-based live-fire exercise. Four Canadian soldiers were killed and another eight were injured. Approximately 2 hours prior to the incident, both pilots had taken Go-pills; the wingman had taken two 5 mg dextroamphetamine tablets, and the lead pilot had taken one 5 mg tablet.

During the subsequent investigations conducted by the USA and Canada, several incidental factors were found, among them were shortcomings in the operational and medical administration of the Air Force fatigue management program under which stimulants and sleep-inducing agents were dispensed. Specifically, the Coalition Investigation Board (CIB) [48] found that:

1. There did not appear to have been a significant effort to apply non-pharmacological fatigue management measures before employing Go-pills;
2. Aircrew were inconsistently briefed individually on the use of Go/No-Go pills by the prescribing physician, who was often not a flight surgeon;
3. The application of non-pharmacological measures did not appear to have been formally briefed to commanders or flight schedulers;
4. Although the deployed flight surgeon and commander had authorization to use Go-pills as required by their unit’s parent command, the coordination and approval process was not documented as required; and
5. Required weekly Go-pill use reports were not being forwarded to the parent command.

Although these and other command oversight and administrative issues were uncovered, both the Canadian Board of Inquiry (BOI) [49] and the CIB found that the pilots themselves were to blame for the incident.

Initially responding to the Air Force’s charges, the wingman’s defense attorney cited poor planning by the pilot’s commander as well as USAF-issued dextroamphetamine to combat fatigue as two potential contributing factors [50]. At the time of the incident, the wingman had been awake for over 15 hours and was over five and a half hours into the mission when he took dextroamphetamine. His defense attorney argued that impaired judgment from the amphetamine was contributory: “... (the pilots) exercised poor judgment, they reacted too quickly, and didn’t wait long enough. Well, when the drug manufacturer says these are the hazards, how dare you give them the drugs that say this can cause these effects, and then you charge them with doing those things?” [51] He also asserted that the pilots’ use of amphetamines was not voluntary, stating that the Air Force pushed them on their pilots as a “counter fatigue measure” – an off-label use of the drug not approved by the FDA [52]. Nevertheless, the assessment of the CIB’s Medical Advisor was that the operational use of the “Go-Pill” had no adverse effect on the Coffee Flight aircrew. The argument that the wingman’s use was not voluntary also was not substantiated. Rosenow, the Article 32 administrative hearing judge, stated “Their (the pilots) use (of Dexedrine) was certainly sanctioned, if not strongly encouraged ... It would seem unfair to order pilots to fly long missions, provide them with stimulants to fend off fatigue, and then hold them responsible if the stimulant affected their judgment ... Ultimately, I believe the Go-pills had no effect on Coffee Flight’s judgment” [53]. Based on the investigation boards’ results and the administrative “Article 32” hearing that followed, the 8th Air Force Commander found that Coffee 52 (wingman) was individually guilty of dereliction of duty and fully in control of and responsible for his actions.

When it became known that the wingman had taken dextroamphetamine prior to the incident, a heated public debate on stimulant use in the military ensued. For example, Dr. Robert DuPont, a former White House drug czar, reported he was stunned to learn about the Air Force’s use of amphetamines and in his statement drew (perhaps erroneous) parallels between the Air Force’s use of stimulants and individuals addicted to amphetamines [54]. A more realistic counterpoint was made by military analyst Major General (Ret.) Don Shepperd, who himself had served as a combat pilot and had used stimulants to execute his mission [55]. When asked if the public should be concerned about a pilot fatigued enough to need a pill, he stated that the concern was more with a pilot asleep...
at the controls than a pilot using stimulants to manage wakefulness (something he indicated he had done himself).

In addition to the challenges of administering stimulant programs, the Tarnak Farms incident also illustrates some of the ethical issues (both legitimate and otherwise) that may later be considered relevant if an adverse event or mishap occurs, which are considered next.

The ethics of pharmacological management of fatigue in the military

The US Department of Defense has chosen to allow off-label use of stimulants with the justification that sometimes this use is a military necessity. Some have questioned whether such use is ethical, and as noted above, most other Western military allies do not use stimulants. Those arguing against stimulant use may contend that using such drugs invites the risk of psychological dependency and addiction, causes altered cognitive function leading to impulsive actions outside their complete control, or leads to undesirable organizational behavior (e.g., “commander abuse”), among other adverse effects. The arguments often imply that to use such drugs invites one to descend a “slippery slope” and cite historical precedents such as are enumerated by Rasmussen [4]. Others have argued that current policy guidelines in the US military are adequate to ensure that stimulant use is ethically and morally correct, and that any perceived risks with stimulant use are more than countered by the hazards of unmanaged fatigue in military flight operations [2].

Fatigue also affects mood, judgment, and risk-taking behavior. Echoing statements noted above that were made by military analyst Major General (Ret.) Don Shepperd, Caldwell states that the true choice in many military situations is not between a well-rested, non-medicated pilot versus a fatigued pilot on stimulants, but between sleep-deprived pilots flying the mission with the aid of proven alertness-enhancing drugs versus sleep-deprived pilots flying without stimulants and struggling to stay awake. To accept the position that any use of stimulants to counter fatigue is fundamentally unethical is to abandon pharmacological countermeasures that have been shown to be effective, and accept degradation in mission capability and continuing loss of lives and assets to fatigue mishaps. As Caldwell and others have correctly observed, there are many instances of mishaps and lives lost to fatigue in the military, but to date, there are no known cases of stimulant use being causal to a mishap, or pilots becoming dependent on these medications. Perhaps a better analogy of the risk–benefit calculus of stimulant use would envision a multi-dimensional “slippery dome” where one attempts to maintain a central position between undertreatment and excessive use, judiciously employing stimulants to treat fatigue, optimizing performance, mission capability, and safety, while avoiding the many risks which those opposed to stimulants have raised.

Russo has suggested that using stimulants in the military may be considered ethical if the following five questions are answered affirmatively [56, 57], and regardless of opinion, these questions serve as a useful framework for exploring issues related to use of stimulants in military operations and describing methods already in place to reduce risk:

1. Is the medication safe for use in this individual, and safe within the context of the operational environment?
2. Is use truly voluntary – is an individual requesting the medication with a full understanding of its primary effects and side effects?
3. Is the use of the medication consistent with its dosage and pharmacological function?
4. Is the medication used with appropriate medical supervision?
5. Have available non-pharmacological alternatives been fully utilized?

Is the medication safe for use in this individual and safe within the context of the operational environment?

Safety considerations include (1) drug physiological side effects, (2) risk of abuse and addiction with drug use, and (3) drug effects on cognition and behavior.

Drug physiological side effects

All drugs possess the potential to cause unwanted side effects. Although rare and generally seen only at very high doses, dextroamphetamine can have serious cardiovascular effects, including death. Modafinil has been associated with headache, anxiety, nausea, and other GI symptoms, and rarely with anaphylactic reactions. To minimize these risks, all aircrew are required
to undergo ground testing under the supervision of a flight surgeon to guard against problematic idiosyncratic reactions. Military pilots are a pre-screened population in excellent health, and are likely free of medical complications that would contraindicate use of stimulants. Furthermore, allowable doses of dextroamphetamine and modafinil are within the range of doses already approved by the FDA for indicated uses.

Risk of abuse and addiction

The abuse liability associated with dextroamphetamine, modafinil, and caffeine is reviewed in Chapter 9, this volume. Briefly, dextroamphetamine exhibits a higher abuse liability than modafinil. It has been argued that the potential for abuse and addiction under controlled military use of amphetamines is much less than that found in the private sector (and that experience from the post-Vietnam era to the present bears this out) because appropriate procedures and safeguards are already in place [5]. Specifically:

1. Military pilots are a well-screened, intelligent, motivated, and mentally healthy population, with a remarkably low incidence of addictive behavior or mental pathology.
2. Medication is administered on a case-by-case basis by a flight surgeon working closely with the pilots and under the direction of the squadron commander.
3. Doses are typically small, are issued before missions commence, the amount of drug taken is documented, and any remaining drug is collected after the mission is completed.
4. The pilot receives education on the effects, ground testing, and guidance on planning dosages in accordance with mission demands.
5. Medication is obtained from a military pharmacy and dispensed by a military provider; thus, the pilot is not exposed to an illegal drug counterculture.

Drug effects on cognition and behavior

It has been widely documented that both dextroamphetamine and modafinil improve or restore aspects of cognitive functioning that are degraded by sleep loss. As reviewed in Chapter 5 (this volume), there is some evidence that modafinil causes an overestimation of performance; however, this effect is seen only at doses of 300 mg or higher – and the bulk of the evidence shows that both modafinil and dextroamphetamine improve objectively measured cognitive performance.

The issue raised with regard to use in the military is the extent to which stimulants interfere with rational behavior, produce increased aggression or result in less regard for personal survival (effects of dextroamphetamine which were implied by the defense attorney for the wingman from the Tarnak Farms incident but otherwise unsubstantiated in the open, scientific literature). Because few studies have addressed these mental functions (which fall under the category of “executive functions” – see Chapters 5 and 6, this volume), the effects of stimulants on these functions is largely unknown. However, available published evidence indicates that at the doses used operationally, there is no negative effect of stimulants on these types of mental capabilities nor are these stimulants’ subjective effects consistent with these types of behaviors at the doses used – and perhaps most relevant, no such adverse effects have been reported by the operational community.

Is use truly voluntary – is an individual requesting the medication with a full understanding of its primary effects and side effects?

Is use truly voluntary?

The decision to employ stimulants for an operational mission is made jointly by the commanding officer, the medical officer (flight surgeon), and the individual pilot. The decision whether to use a stimulant is voluntary, and at the time that decision is made, the pilot is alone without medical or command oversight [2]. “Involuntary use” was alleged by the Tarnak Farms defense attorney and has been cited as a potential result of the USAF informed consent policy which allows the commander and flight surgeon to determine the crew-member to be unfit if he/she is too fatigued to fly and elects to not use stimulants. However, the commander and flight surgeon have the same decision power (grounding a pilot) even if the pilot elects to use stimulants. Furthermore, the extent to which use is voluntary is continuously monitored by the flight surgeon.

A related issue is whether use is being “coerced” (either implicitly or explicitly) at the commander
level. Drugs which enhance individual pilot mission capability also extend the commander’s warfighting capability. The possibility exists that constraints on manpower and resources may lead to dependence on stimulants to complete missions which, with better resourcing, could be accomplished without them. If the commander were to depend on the stimulant to make up for the shortfall (rather than insisting on adequate resources or rejecting the mission), the individual pilot may no longer feel free to refuse stimulants. The extent to which competitive pressures or mission demands influence medication use was examined directly by Kenagy, who reported that out of 94 B-2 pilots, only 5% reported feeling pressured to take Go-pills (interestingly, just over 5% reported feeling pressured to not take Go-pills). These results indicate that in most pilots, Go-pill usage is perceived as voluntary.

**Is use truly informed?**

Flight surgeons are responsible for educating pilots about the limitations of stimulants, the expected benefits, the side effect profiles, and the risks. This is accomplished at the time pilots review and sign informed consent statements. At the time of ground testing, they are again educated regarding the purpose and effects of the medications. Flight surgeons also provide briefings to squadron personnel prior to implementing performance maintenance programs, covering topics including: basic sleep, circadian rhythms, and performance information, USAF experience with stimulants, and guidelines for stimulant use [11].

**Is the use of the medication consistent with its dosage and pharmacological function?**

Although as noted earlier, stimulants used in performance maintenance programs fall outside FDA-approved indications, an extensive literature supports the benefits of stimulants in countering fatigue in laboratory and simulator studies. These include flight simulator performance in experienced pilots [36, 58] (also reviewed in Chapters 5–7, this volume); subjective improvements in fatigue and perceived benefits of stimulants have also been reported in survey studies [6, 15]. Furthermore, as outlined in Table 17.1, allowable stimulant doses are consistent with those used in SWSD.

However, there are no studies of stimulant effects on objective in-flight performance during actual operations. That is, although it is widely believed that military operational use is supported by actual operational experience, there is no evidence that stimulants are measurably improving mission success or minimizing mishap risk. Roedig implied that properly evaluating the effects of stimulants in the operational environment would be difficult and had not yet been proven [28]. Meijer argued that if medications used in manned weapons systems cause only subjective improvements in performance, “their use should be stopped immediately, as overestimating one’s own performance leads to unacceptable risks, both for personal safety and operational performance” [26]. Jaeger also cited the relative paucity of data on the efficacy of stimulants employed in the operational setting and feels the line commander will likely make decisions based on supposition rather than the missing objective data [25]. Although it is true that there are no objective data from actual operations that prove that stimulants maintain operationally relevant aspects of performance during sleep loss, as already noted the bulk of laboratory data support their use.

A related issue concerns what operational metrics should be used to determine stimulant efficacy: Kenagy et al. suggested that aerial refueling performance, accuracy of bombing, and percentage of targets hit may be good measures [15]. However, the latter may be difficult to quantify objectively (e.g., what constitutes bombing accuracy? A direct hit?). Carrier landing grade is another operational metric; however, grading is performed by a Landing Signal Officer (LSO) and thus has a subjective component. Mission completion rates are generally subject to ceiling effects (i.e., are generally near 100%) and avoidance of mishaps is difficult to objectify because mishaps are rare events. Thus, the question of what operational metrics could be used to determine stimulant efficacy also is a matter of debate. Whether a pilot is actually performing better or more safely while using stimulants is based almost solely on the pilot’s subjective self-assessment. The reasons pilots choose to take (or refrain from) Go-pills and the extent to which objective improvement in performance and safety is gained are largely unknown and deserving of further study.

**Is the medication used with appropriate medical supervision?**

Stimulant use programs in US military aviation are closely supervised by flight surgeons who prescribe,
track, and document individual medication use, and who have the power to recommend suspension from use for any individual suspected of misusing medications. The flight surgeon is guided by the existing regulations, but with each act of prescribing and dispensing medication to an aircrew member, he or she is also making value judgments regarding the appropriateness of use. The judgment of the flight surgeon may be subtly influenced by several factors which he or she should be aware of. Two of these – “mixed agency” and “medicalization” – are mentioned now.

Mixed agency
The military physician and flight surgeon serves not just the individual military member but also the military organization. That is, although the military flight surgeon ensures that the aviator is capable of performing the mission, the flight surgeon also advises the commander on the health of his aviators and their ability to perform – this dual role is referred to as “mixed agency.” Although the flight surgeon will protect the individual’s privacy by not volunteering more intimate details of an aviator’s health than are necessary for the commander to determine the aviator’s mission capability, there is no expectation of patient–physician confidentiality in the military such as exists in the civilian community. The commander requires information in order to ensure operational readiness and mission success, and he or she may have to place this requirement above safety considerations and individual health in combat. With use of stimulants to fight fatigue in situations of exceptional operational necessity, the flight surgeon may be expected – or ordered – to provide medications to a pilot who requests them, when in his medical judgment, grounding and rest may be more appropriate. This dual loyalty conflict is not unique to medical practice in the military: physicians employed in specialties such as sports medicine, occupational medicine, and correctional medicine also have to balance the needs and desires of their patients against the competing demands of the team, the corporation, or the penal system. However, it could be argued that the stakes of these competing demands are much higher in the military.

Military members recognize that military physicians may be expected, when the military interests override those of the individual, to sacrifice the member’s individual interest in support of the mission or greater numbers of individuals. Howe [59] counsels that in those situations, military physicians must recognize their duty not only to voice their view and educate the commander in the best way possible to the medical implications of their decisions, but also to assume a military role-specific ethic, and allow the commander – who should have a broader view and has been authorized to make these judgments – to prevail. He also observes that these situations in which military role-specific ethical decisions should prevail are rare and that the vast majority of these mixed agency ethical dilemmas should be resolved in the patient’s best interest.

Medicalization
Schermer [60] discusses the social process termed “medicalization” in which a condition previously considered to be non-medical comes to be seen as a medical problem. A consequence of medicalization is that a shift occurs in perceived risk–benefit ratios of using drugs to treat these conditions: drugs are used for less serious or questionable medical conditions for which the risks of treating with a drug are considered to be low, unknown, or likely to occur only in the distant future [60]. An example of this phenomenon is shift work sleep disorder (SWSD—discussed in Chapter 8, this volume). Shift work sleep disorder is characterized by the inability to stay awake during night shift work and inability to sleep during subsequent daytime sleep. It is considered a disorder of the circadian rhythm. However, SWSD could actually be viewed as reflecting an appropriately functioning circadian rhythm in that sleepiness would be expected during the night and problems sleeping would be expected during the day (the circadian rhythm is slow to re-entrain to changes in work/sleep schedules). Classification of this problem as a medical illness enabled Cephalon to seek FDA approval to extend the use of modafinil (originally approved to treat daytime sleepiness associated with narcolepsy) to treat the excessive sleepiness associated with SWSD. Medicalization may influence aircrew and flight surgeons to view a drug as the preferred fatigue countermeasure rather than other non-pharmacological measures which may be more appropriate, more effective, and/or with fewer side effects. As discussed earlier, within DoD performance maintenance programs, stimulants are the last measure to be employed, and it remains the commander’s and physician’s responsibility to enforce policies that require all other fatigue countermeasures to be fully implemented before employing pharmaceutical agents.
Have available non-pharmacological alternatives been fully utilized?

Traditional fatigue countermeasures tend to be difficult to implement compared to taking a pill. As noted above, deficiencies in educating commanders, schedulers, and aircrew to traditional fatigue countermeasures, and a lack of emphasis of those over medication use, were cited in the Tarnak Farms investigation.

Sleeping spaces in combat theaters may be in tents or temporary living spaces subject to flight line noise and poor control over light and environmental temperatures. Improving sleeping quarters aboard ship is constrained by limited space, the noise of machinery and flight operations, ship’s motion, and the necessity of emergency announcements, drills and other interruptions to sleep. Administrative requirements for pilots for night currency and proficiency with night vision devices require regular shifts between day and night flight schedules. Rotating schedules combined with shared sleeping quarters increase the chance of individuals disturbing each other during sleep. Training and administrative duties also compete with sleep. And all are subject to sudden changes in plans which may be dictated by operational necessity. The availability of pharmacological solutions may lessen the attention and urgency to continually attempt to improve these conditions.

Using stimulants during planned operations is difficult to justify (for example, using Go-pills in transport crews to bypass non-pharmacological aircrew rest scheduling alternatives) [56]. Likewise, in planned and routine loitering missions (during which pilots remain within the vicinity of possible target zones for an extended duration of time), crew rest should be adequately scheduled and mission length adjusted so that pilots do not have to consider the option of routinely using stimulants [56].

Summary and conclusions

Like many other tools available to military planners, strategists, commanders, and physicians, stimulants appear to be a two-edged sword. Used under the right circumstances, with clearly defined policies, and with rigorous oversight, stimulants can temporarily maintain warfighter capabilities and maintain mission success rates, thereby preserving lives and assets. Available evidence and experience suggest that stimulants can be safely implemented to maintain operational capabilities. An alternative question to the issue of whether use of stimulants poses an ethical dilemma is whether it is ethical to withhold such tools from the warfighting community.

Performance maintenance programs were developed to include stimulants as an operational tool of last resort – and if stimulants are used, they are intended to be used as part of a balanced fatigue countermeasures/performance sustainment program. Future iterations of performance maintenance programs will likely include the use of fatigue modeling for mission planning and to determine when medication dosing may be required.

Finally, no stimulant substitutes for adequate sleep. In the short run, stimulants could be used as a substitute for adequate staffing and manpower, or integral to carrying out routine operations, but in the long run replacing adequate sleep with stimulants is unsustainable and will be placing warfighters in even greater jeopardy of fatigue-related mishaps and unintended health-related consequences.

Disclaimer

The views expressed in this chapter are those of the authors and do not necessarily reflect the official policy or position of the US Navy, US Air Force, the Department of Defense, or the US Government.

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References


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[29] Title 10 U.S.C 1107. (Military medical care) “Notice of use of an investigational new drug or a drug unapproved for its applied use.”


[31] DoD Instruction 6200.02, encl. 2, p 6, para. E2.2.


[40] Personal communication with Director, US Army Aeromedical Activity, Jul 2010.


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