

Wake-Sleep Cycle Management during SUSOPS and CONOPS in French Military Forces: Policy and Ethics

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ABSTRACT

The consequences of sleep deprivation and of wake-sleep cycle alterations have been studied since more than 25 years in military domain. Nevertheless this point of view has only recently been taken into account by the French different headquarters. That is why the French Military Health Service has progressively built a real policy for managing the wake-sleep cycle during SUSOPS and CONOPS. This policy has two main aspects, with an educational and a pharmacological part. The consequences of sleep deprivation, and irregular sleep-wake cycle on physical and cognitive performances during SUSOPS and CONOPS have been studied extensively. Now, the different types of countermeasures are quite well defined. A policy to manage these aspects on operational field is under development in France with two distinct aspects on based on health education and on pharmacology. The educational policy is based on knowledge delivered to our forces by the mean of an interactive CD-ROM. The first version, called CYCL'OPS™, has been developed by ADSENSIO for the pilots of the French Air force. Its goal is to improve individual knowledge in this domain and to show the risk of sleepiness at the throttle according to the timing of the mission taking into account individual parameters. It may allow a better individual management of sleep – wake cycle every day. Other versions are under project for the Navy, and the Army. A light pharmacological aid is now officially approved by the French Health Service in operational field when the missions do not allow nocturnal sleep or only offer reduced possibility of sleep. Modafinil is reserved for emergency cases. It may help valid subjects to stay awake in hostile environments until the SAR means take them in charge. On the contrary, Slow-release caffeine may be used in prolonged missions (CONOPS) to fight against sleepiness for 48 hours. Finally, Z- hypnotics are also allowed to promote pre-planned sleep episodes. Nevertheless, the use of these drugs acting on the central nervous system must be supervised by the medical corps and the individual tolerance must be tested before operational use. We hope that French policy on the operational management of the sleep-wake activity combining these two aspects will be efficient to reduce the recurrent complaint of fatigue and the risk of accident, and to improve the effectiveness of our military forces. Further studies are still needed to evaluate the benefit of that policy.

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1 INTRODUCTION

Modern military operations need to maintain constant high levels of performance along the whole nycthemere (i.e. the 24-h cycle), whereas irregular work schedules, sleep deprivation and jet lag have a negative impact on human performance during sustained and continuous operations (SUSOPS and CONOPS). This topic has been studied since more than 25 years by military physiologists and physicians in our country.

Nevertheless, the fact that soldiers may be fatigued and need a minimal restorative sleep time become an increased preoccupation of French Headquarters. Military mentality progressively changes: sleeping is less considered as wasting time. On the contrary, sleeping enough at the right circadian time is more and more considered as a primordial condition of operational performance and safety.

Different types of strategies for maintaining the operational performance at its best level have been extensively studied in the past years. In that way, constant sleep hygiene for minimizing chronic sleep deprivation, optimization of work schedules taking the physiological needs into account for limiting acute sleep deprivation, napping strategies for reducing an excessive sleep pressure, and pharmacological aids to promote sleep or wakefulness in last extremity are the main available countermeasures.

2 SLEEP EDUCATIONAL PROGRAM

Daily sleep hygiene and regularity of wake-sleep cycles are fundamental to maintain cognitive performance and therefore security at a right level, to avoid mood disorders, to maintain a good well-being feeling, and to preserve long term health of our soldiers involved in military operations, which require most of the time a permanent activity all over the nycthemere.

That is why a doctrine with an official educational program dealing with sleep, vigilance and performances, emerges in France. These problems are officially recognized as key point by the French headquarters of the Army, the Air force and the Navy. The French Health Service plays an active role since many years in this settings, has decided to gather all useful information in an original modern tool, i.e. an e-learning program delivered by a CD-ROM, but also possibly by a key or by internet.

This program, called CYCL'OPS was ordered by the DGA and developed by the private French society ADSENSIO under the control of a military scientific committee. It was initially designed for the Air forces and could be adapted for the Army or the Navy in a near future.

CYCL'OPS allows the deliver of wide information about sleep challenges, using an academic way or a more interactive way, based on realistic scenarios which can be personalized with individual characteristics as the chronotype, the sleep log, and so on. A control of knowledge with a quiz is proposed for each chapter. A section is also devoted to medical knowledge dealing with sleep medicine.

We anticipate that CYCL'OPS will constitute a common basis in this domain for the entire military community and a first step in the knowledge of better wake-sleep cycle management in operations. CYCL'OPS is designed to help every subject to learn how to manage his wake-sleep cycle in operational to reduce the consequences of sleep deprivation and irregular work schedule. It is also designed to help our military chiefs to take the right decisions in logistic and operational settings.



Figure 1: CYCL'OPS Homepage

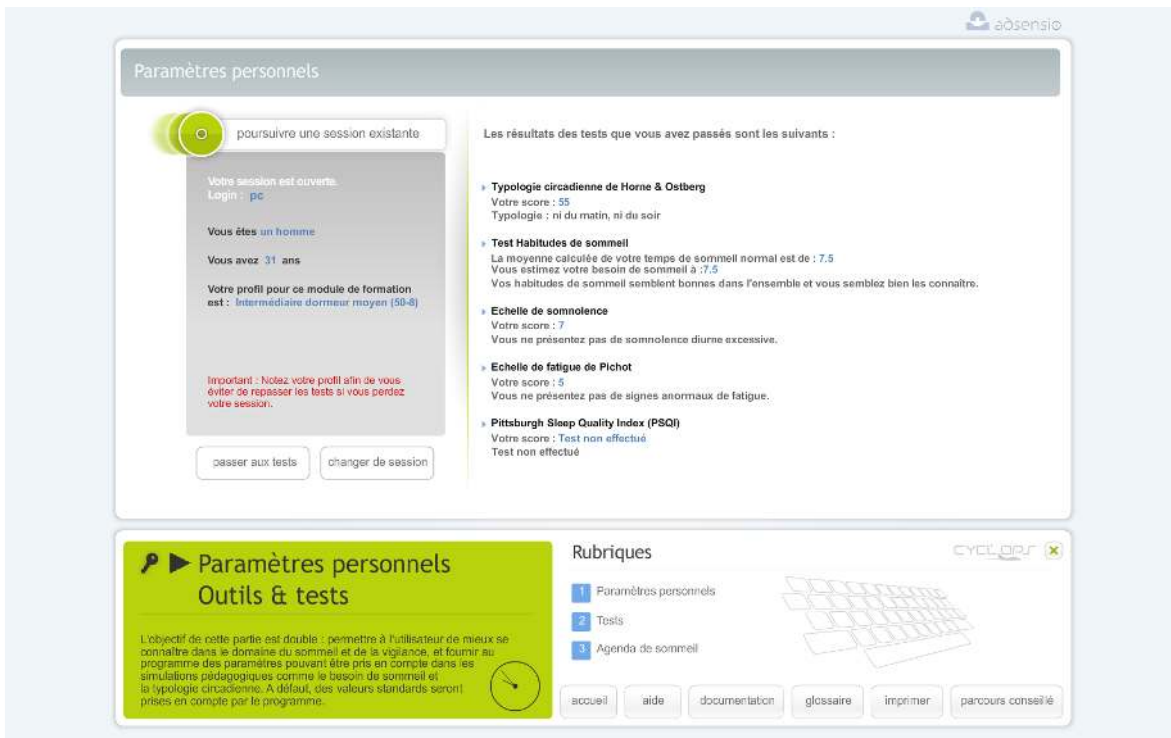


Figure 2: Individual part of CYCL'OPS (tests and questionnaires)

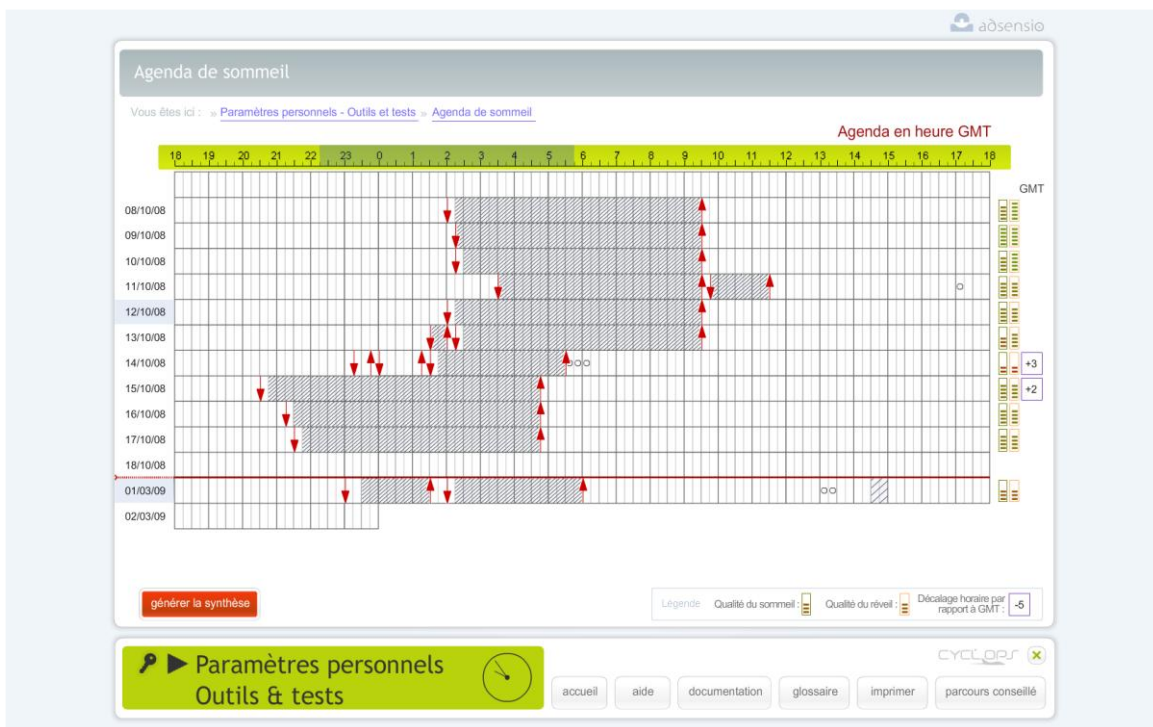
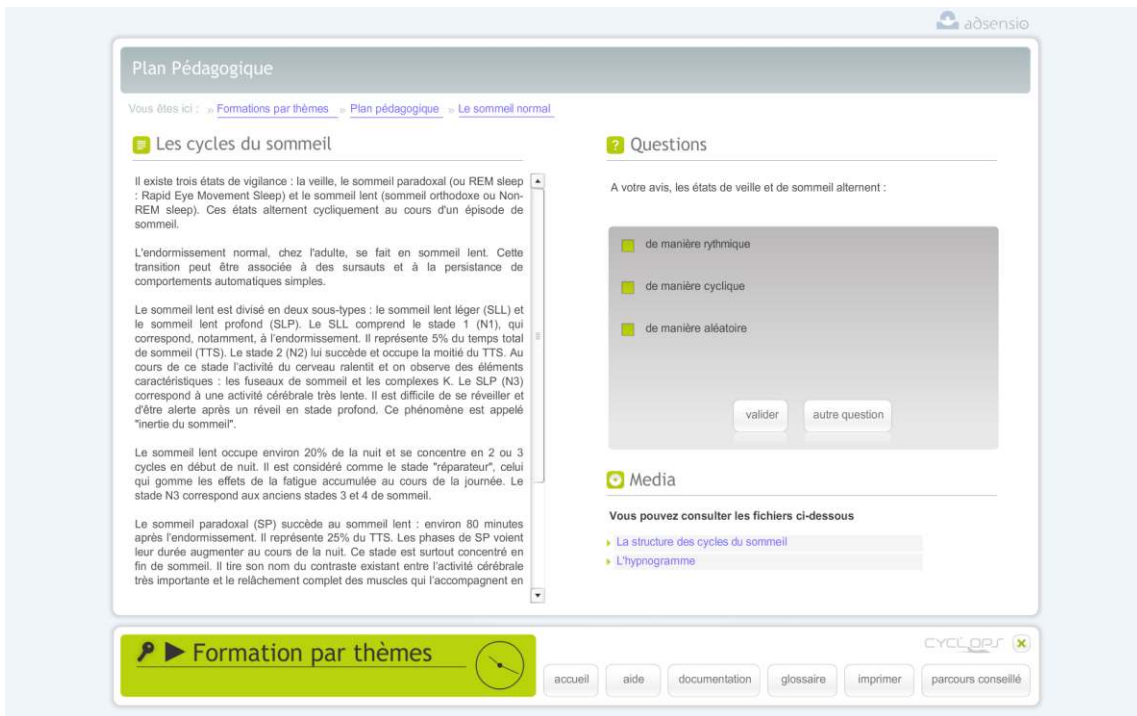


Figure 3: Individual part of CYCL'OPS (Sleep logs)



Plan Pédagogique

Vous êtes ici : » Formations par thèmes » Plan pédagogique » Le sommeil normal

Les cycles du sommeil

Il existe trois états de vigilance : la veille, le sommeil paradoxal (ou REM sleep : Rapid Eye Movement Sleep) et le sommeil lent (sommeil orthodoxe ou Non-REM sleep). Ces états alternent cycliquement au cours d'un épisode de sommeil.

L'endormissement normal, chez l'adulte, se fait en sommeil lent. Cette transition peut être associée à des sursauts et à la persistance de comportements automatiques simples.

Le sommeil lent est divisé en deux sous-types : le sommeil lent léger (SLL) et le sommeil lent profond (SLP). Le SLL comprend le stade 1 (N1), qui correspond, notamment, à l'endormissement. Il représente 5% du temps total de sommeil (TTS). Le stade 2 (N2) lui succède et occupe la moitié du TTS. Au cours de ce stade l'activité du cerveau ralentit et on observe des éléments caractéristiques : les fuseaux de sommeil et les complexes K. Le SLP (N3) correspond à une activité cérébrale très lente. Il est difficile de se réveiller et d'être alerte après un réveil en stade profond. Ce phénomène est appelé "inertie du sommeil".

Le sommeil lent occupe environ 20% de la nuit et se concentre en 2 ou 3 cycles en début de nuit. Il est considéré comme le stade "réparateur", celui qui gomme les effets de la fatigue accumulée au cours de la journée. Le stade N3 correspond aux anciens stades 3 et 4 de sommeil.

Le sommeil paradoxal (SP) succède au sommeil lent : environ 80 minutes après l'endormissement. Il représente 25% du TTS. Les phases de SP voient leur durée augmenter au cours de la nuit. Ce stade est surtout concentré en fin de sommeil. Il tire son nom du contraste existant entre l'activité cérébrale très importante et le relâchement complet des muscles qui l'accompagnent en

Questions

A votre avis, les états de veille et de sommeil alternent :

- de manière rythmique
- de manière cyclique
- de manière aléatoire

valider autre question

Media

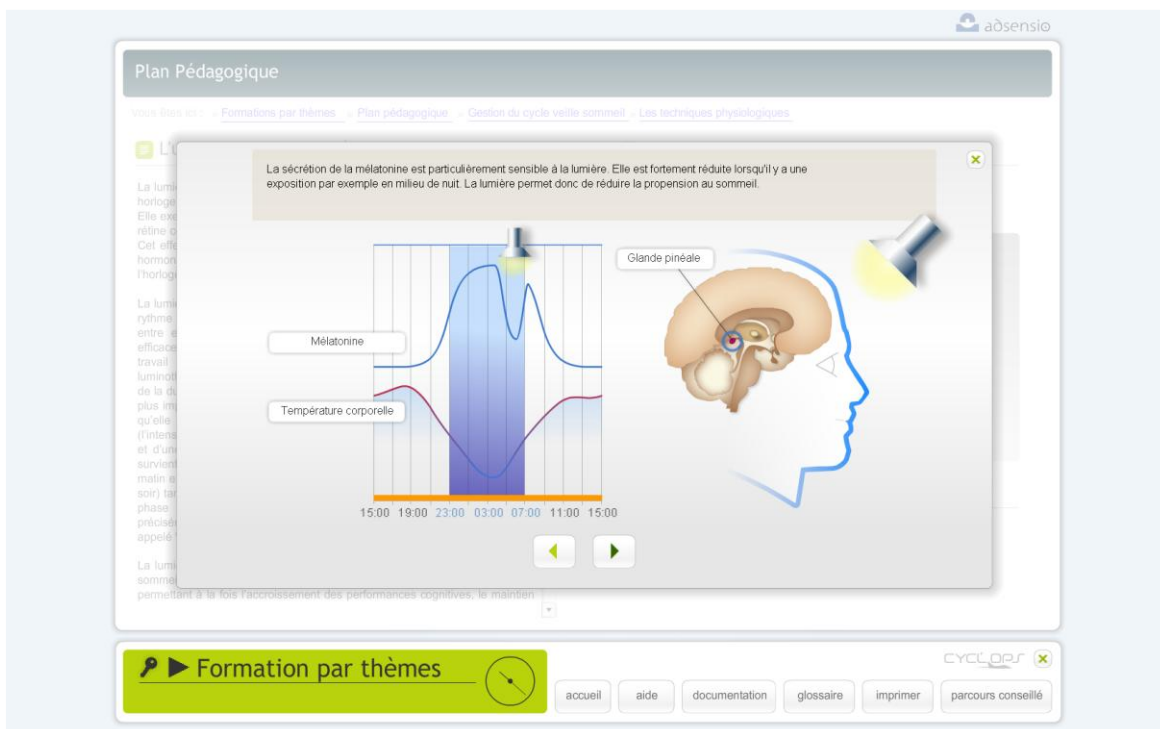
Vous pouvez consulter les fichiers ci-dessous

- La structure des cycles du sommeil
- L'hypogramme

Formation par thèmes

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Figure 4: Pedagogic part of CYCLOP'S (example of text)



Plan Pédagogique

Vous êtes ici : » Formations par thèmes » Plan pédagogique » Gestion du cycle veille sommeil » Les techniques physiologiques

La sécrétion de la mélatonine est particulièrement sensible à la lumière. Elle est fortement réduite lorsqu'il y a une exposition par exemple en milieu de nuit. La lumière permet donc de réduire la propension au sommeil.

Mélatonine

Température corporelle

Glande pinéale

15:00 19:00 23:00 03:00 07:00 11:00 15:00

Formation par thèmes

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Figure 5: Pedagogic part of CYCLOP'S (example of illustration)

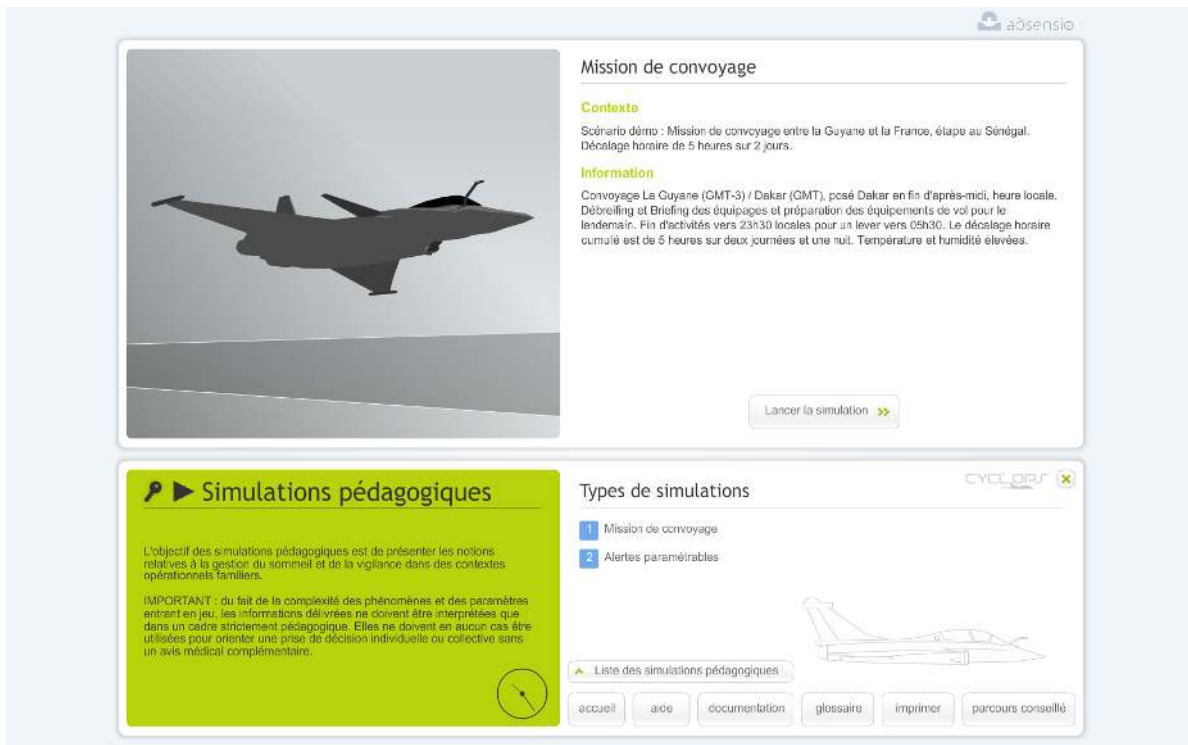


Figure 6: Simulation part of CYCL'OPS



Figure 7: Simulation part of CYCL'OPS (zone of vulnerability with increased propensity to sleepiness)

3 PHARMACOLOGIC AID

The use of pharmacological drugs interfering with sleep, wakefulness, and sustained vigilance in military settings is now officially approved by the «MD Instruction n° 744/DEF/DCSSA/AST/TEC, 2008 March 31. This text closes a long ethical debate in France about pharmacological aids interfering with the wake-sleep cycle. This type of aids has been considered as doping methods and therefore unethical for a long time. But, in fact, a pharmacological aid, provided in exceptional circumstances, is not able to improve performances like a doping substance. It only maintains these performances at usual daytime level during prolonged sleep deprivation in the best case. On the contrary, it would be now considered as a fault, not giving all chances to our soldiers to achieve long duration missions including an important sleep deprivation.

The principles of this pharmacological aid are simple and respond to the criteria of a light pharmacological aid, a concept developed by Lagarde. This aid must be simple (simplicity of the protocol and of the administration), innocuous, but efficient on the wake-sleep cycle. Its efficiency is limited to **48-72 hours of continuous use**. Moreover it requires a medical supervision. Although previous laboratory studies do not detect any major problem of clinical tolerance, a problem of individual variability and susceptibility encountered with these drugs acting on the central nervous system cannot be excluded. That is why a **systematic individual trial** of these drugs is recommended **before operational use** and **under medical control** in order to detect unexpected individual side effects and also to adapt the dose if necessary, particularly taking gender into account.

Modafinil, slow release caffeine and Z-hypnotics are only authorized. Other psychostimulant drugs are not officially approved or simply forbidden.

3.1 Modafinil

3.1.1 Presentation of the molecule

Modafinil (diphenylmethylsulfinil-2-acetamide) has been synthesized in 1981 by a French pharmaceutical laboratory (Lafon), bought a few years by an American laboratory (Cephalon).

It is an awakening drug, used in human therapeutics against the excessive daytime sleepiness encountered in narcolepsia, idiopathic hypersomnia, and sometimes in treated obstructive sleep apnea syndrome.

From a pharmacologic point of view, plasmatic peak of modafinil is reached 2 hours after an oral intake and the duration of its awakening effect is about 8 hours. The effect is dependent of the dose with a linear dose-effect relation. Modafinil probably acts on several targets in the Central Nervous System (CNS). Modafinil interacts with noradrenergic and dopaminergic systems, via an action on specific carrier proteins [1, 2]. It also modifies the GABA/Glutamate balance, leading in turn to an increased thalamo-cortical electrotonic coupling which has been recently identified as an important mechanism to maintain wakefulness [3-5]

Modafinil's use in military field during SUSOPS and CONOPS was widely studied by physicians and researchers of French Health Service. Field and laboratory studies in healthy subjects during sleep deprivation experiments showed that modafinil is able to maintain wakefulness and cognitive performances at a sufficient level for 48 hours continuously [6].

3.1.2 In practice

Modafinil should be reserved for exceptional and critical circumstances (surviving), for example after ejection over a hostile territory. In these situations, maintaining wakefulness for a short period (48 hours) could be a main goal for a valid subject in order to help him to survive.

Two protocols are provided. An oral 100 mG dose of modafinil (1 pill) every 8 hours is sufficient for maintaining wakefulness, vigilance, and cognitive performances for 24 hours or less. A 200 mG dose (2 pills) every 8 hours is adapted for missions lasting 24 hours or more. In this case, the first intake of modafinil is recommended at 22:00 h, i.e. one or two hours before the usual nocturnal decline of cognitive performances. In each case, the total duration of modafinil intake should not exceed 48 hours.

3.1.3 Possible side effects

Neither major side effect, nor addictive behaviour have been reported with modafinil in healthy subjects, like with amphetamines.

Nevertheless, a few patients suffering of hypersomnia and treated with modafinil sometimes complain of headaches, nausea, and increased anxiety. Those adverse effects are quite seldom observed and mainly occur at the beginning of the treatment. That is why the individual test of tolerance, planned in the MD instruction, seems to be particularly important for modafinil before operational use.

3.2 Slow release Caffeine

3.2.1 Presentation of the molecule

Coffee is the stimulant beverage the most ingested in the world. Coffee consumption varies from one to ten cups per day with ~ 100 mG of caffeine per cup. Caffeine intake should not exceed 1000 mG per 24 h.

Caffeine has psychostimulant properties. It stimulates wakefulness, acting through an anti-adenosinergic effect in the central nervous system. Indeed, the accumulation of adenosine in the CNS during the awakening time, as a product of ATP degradation, contributes at least in part to the mechanisms of sleepiness.

Caffeine intake allows maintaining cognitive and psychomotor performances in sleep deprived subjects. But caffeine is quickly eliminated. The psychostimulant effect expected after a single intake of caffeine is therefore transient. Finally, the clinical tolerance of caffeine is generally excellent. Only, minor effects, i.e. diuretic effect, palpitations or slight tremor, are observed with high plasma concentrations of caffeine.

The brief pharmacologic effect of caffeine led a few years ago to a new galenic formulation by the research centre of Nestle (NESTEC), i.e. a slow release caffeine form (SR-caffeine).

Several pharmacological studies performed by the former Aerospace medicine institute showed that a 300 mG dose of SR-caffeine was able to produce an efficient psychostimulant effect lasting 10 hours at least, without reaching the trouble threshold [7-10]. Laboratory and field studies showed thereafter that this dose of SR-Caffeine was able to maintain cognitive performances at a physiologic level comparable to the level observed before sleep deprivation. A

300 mG dose of SR-caffeine has the same efficiency that a 200 mG dose of modafinil during a 18-hr continuous work. This dose of SR-caffeine also adapted for women most of the time, although females are often more sensitive to caffeine than males subjects [11].

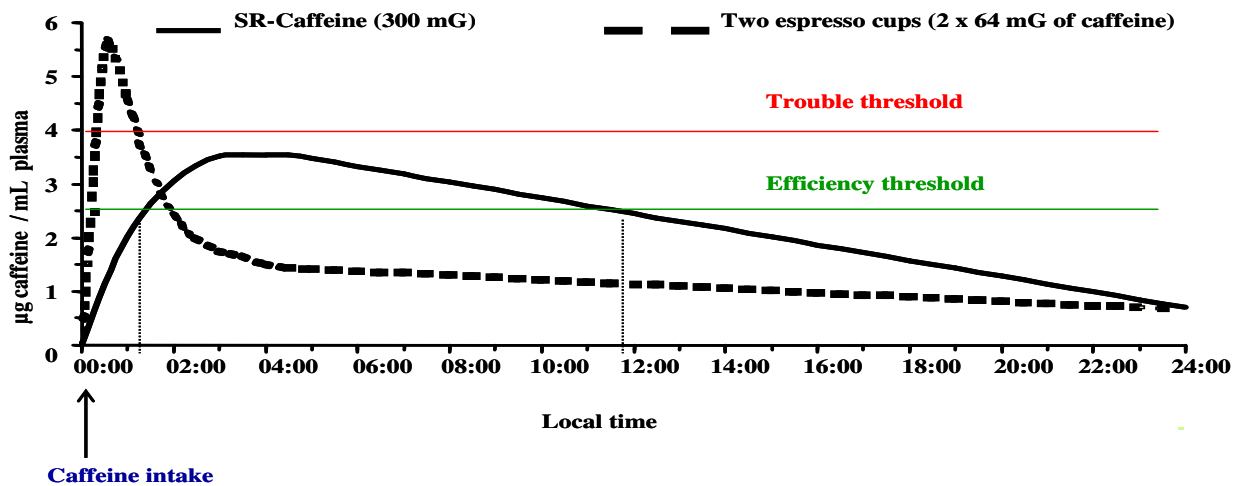


Figure 8: Pharmacokinetic profiles of SR-Caffeine vs. Coffee

3.2.2 In practice

SR-Caffeine will be very soon available in our military operational forces. This form of caffeine is very interesting during CONOPS to sustain wakefulness and vigilance during several days. **Two intakes per day are sufficient to produce a continuous psychostimulant effect for 24 hours.** Moreover, its efficiency seems to be more important when the level of physical activity is not high. In other words SR-caffeine may be particularly valuable in subjects affected in operational centres and operational headquarters and involved in supervision and decision making tasks.

SR-caffeine could also be interesting after a transmeridian flight as a countermeasure of sleepiness induced by a sleep deprivation frequently associated to jet lag from the one hand and as chronobiotic drug facilitating the resynchronization of biological rhythms to the other hand [12].

Nevertheless, SR-Caffeine intake should be avoided in the two hours preceding a planned rest span, particularly if sleep debt is not very high. In this case, SR-caffeine will counteract sleepiness and may delay sleep occurrence.

Finally, we don't recommend a continuous SR-caffeine intake for more than 48 hours without sleeping.

3.2.3 Possible side effects

Cardiovascular effects (palpitations and tachycardia), neurologic effects (tremor) and diuretic effects, which are well known after a caffeine abuse, have been rarely reported with the 300 mG dose of SR-caffeine, probably due to the galenic form.

3.3 Hypnotics

Many drugs have hypnotic properties, as anti-histaminic drug (anti-H1) and benzodiazepines (BZD). They can be ordered by the military physician for precise reasons. For example, BZD may be ordered as a treatment of acute anxious state in association acute insomnia [13]. But it is not the purpose of the present Instruction.

BZD have not been chosen to promote planned sleep for operational use, because of their frequent side-effects (residual sleepiness, mnesic troubles, locomotor ataxia). We propose to use only Z-hypnotics in the field. Although their mechanisms of action via the GABA-A receptors are very close from those of BZD, Z-hypnotics have less side-effects than BZD.

3.3.1 Presentation of Z-hypnotics

Z-hypnotics constitute a heterogeneous chemical family, including Zolpidem (Stilnox^R), Zopiclone (Imovane^R), and Zaleplon (Sonata^R not sold in France).

Zolpidem belongs to the Imidazopyridine family. From a pharmacokinetic point of view, Zolpidem absorption is fast with a T max between 0.5 and 3 hours. Zolpidem plasma half-life is about 3 hours. It acts as a specific agonist of Ω_1 receptors belonging to the macromolecular complex GABA-A. At a 10 mG dose, a decrease of sleep onset latency and intra-sleep awakenings, and an increase of sleep duration with an improved sleep quality are generally observed. Its hypnotic effect lasts about 6 hours

Zopiclone belongs to the cyclopyrrolone family. Its plasma half-life is longer than for Zolpidem, i.e. 4 à 6 hours. Its mechanism of action is similar, which a longer hypnotic effect of about 8 hours.

Zaleplon is a novel hypnotic drug belonging to the pyrazolopyrimidine family. This drug selectively acts on GABA-A (type I) receptors. Pharmacokinetics studies showed a T max and a plasma half-life of about one hour. Its hypnotic effect mainly consists in a rapid induction of sleep for a short duration (3 hours) after 2 to 10 mG Zaleplon intake.

3.3.2 In practice

Z-hypnotics » could be employed during CONOPS to promote pre-planned sleep episodes, even during daytime. We recommend an administration for a short time, i.e. a few days, with the minimal effective dose, which can be also determined by an individual trial under medical control before operational use.

The choice of the molecule may be guided by the duration of the pre-planned sleep episode and by the pharmacological properties of the drugs. For a 6-hr sleep episode, Zolpidem seems to be a good choice. For a longer episode (8 hours at least), Zopiclone may be more adapted. For a shorter episode of about 3 hours, the choice of Zaleplon may be more judicious.

Zolpidem appears as a median choice, acceptable in most of operational situations. Its use is quite safe. There are no residual effects on vigilance six hours after intake. It can be also used in altitude to promote sleep without increasing the effect of altitude on ventilation [14]. Finally, it can be combined to psychostimulants during CONOPS [15].

3.2.3 Possible side effects

Side effects are less frequent with Z-hypnotics than with BZD, although they have quite the same pharmacological target, i.e. the GABA-A receptor. It is due to a shorter plasma half-life at least I part. Moreover, addiction risk is also considered lower with Z-hypnotics than with BZD. A rebound of insomnia is nevertheless reported the third day of use by a few subjects. Finally, Z-hypnotics are counter-indicated in case of suspicion of obstructive sleep apnea syndrome.

4 CONCLUSIONS

We hope that French policy on the operational management of the sleep-wake activity combining an educational aspect and a pharmacological one will be efficient to reduce the recurrent complaint of fatigue and the risk of accident, and to improve the effectiveness of our military forces during SUSOPS and CONOPS. Further studies are obviously still needed to evaluate the benefit of that policy.

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