Modafinil Subjectively Does Not Impair Sleep in Aviators After a Period of Extended Wakefulness

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INTRODUCTION: Modafinil is used as a countermeasure to limit the effects of fatigue in military aviation. However, literature is conflicting about its negative effects on subsequent sleep.

METHODS: This randomized placebo-controlled trial conducted by the Center of Man in Aviation of the Royal Netherlands Airforce is part of a larger study. It included 32 subjects (mean age 35 yr old, 84% male) who followed a normal daily routine and stayed awake the subsequent night. At midnight, all subjects received either 300 mg caffeine, 200 mg modafinil, or placebo. At the end of the test night, subjects were awake for a median period of 26 h. Afterwards, sleep questionnaires containing qualitative (Groningen Sleep Quality Scale) and quantitative parameters of sleep for the subsequent day (recovery sleep) and consecutive night (post-test sleep) were completed and statistically analyzed using Friedman and Wilcoxon signed rank tests.

RESULTS: A statistically significant difference in the reported recovery sleep was observed. The modafinil group slept 30% shorter than placebo, but sleep efficiency was not statistically different. Quantitatively post-test sleep did not vary statistically significantly between the three groups. However, Groningen Sleep Quality Scale scores were lower post-test than pre-test in the modafinil group, while this was not the case in the caffeine and placebo group.

DISCUSSION: This study found that modafinil subjectively does not negatively impact recovery sleep or subsequent nighttime sleep after an extended period of wakefulness and suggests it may decrease the need for recovery sleep compared to placebo or caffeine.

KEYWORDS: aerospace medicine, fatigue, work/rest cycles, vigilance, pilot/crew behavior.

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In 2020, the U.S. National Commission on Military Aviation Safety commissioned a report on military aviation losses between 2013 and 2020. One of the findings in this report was as follows: *"The pervasive sense of burnout and chronic fatigue that exists throughout the military aviation enterprise is contributing to unsafe conditions. Aircrew and maintainers cite […] the resulting fatigue and staffing shortages as the likely cause of 'the next mishap'"*.[25] Another study reported complaints of fatigue among pilots at Qatar Airways.[9] These two reports confirm that fatigue remains a problem in military and commercial aviation.

The International Civil Aviation Organization defines fatigue as *"A physiological state of reduced mental or physical performance capability resulting from sleep loss, extended wakefulness, circadian phase, and/or workload (mental and/or physical activity) that can impair a person's alertness and ability to perform safety related operational duties"*.[11] This definition indicates that fatigue may be caused by several factors, for which the best prevention measure generally is sufficient (nighttime) sleep. Regulations limiting flight times and implementing optimal rosters are known to go some way toward remediating the effects of fatigue associated with lack of sleep. However, even

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when these regulations are adhered to, it seems impossible to completely eliminate fatigue. Fatigue poses a greater challenge in military aviation, where the implementation of such regulations encounters complexity due to the diverse range of aircraft used and the multifaceted nature of operations conducted. Moreover, the tactical demands of military endeavors occasionally necessitate nocturnal operations, leading to disturbances in the conventional sleep pattern. These complexities underscore the insufficiency of relying solely on regulations to effectively address fatigue and mitigate its correlated risks. Stimulants may enhance the performance of fatigued pilots, thereby mitigating the risks associated with fatigue.[10] For stimulants to be effective, they must substantially increase vigilance and reduce fatigue, and, no less important, they must allow for good recovery sleep (i.e., the first sleep period after a period of extended wakefulness), as sleep is the best solution to reduce fatigue.

Caffeine, a widely recognized and readily accessible stimulant, holds broad acceptance.[17] Functioning as a nonprescription central nervous system stimulant, it works by blocking adenosine receptors.[6] Typically administered within the range of 200–600 mg, caffeine demonstrates swift absorption within 15 to 40 min, yielding perceptible effects within 15–20 min.[4] With a half-life of 4–6 h, its favorable impact on vigilance tasks has been documented for up to 8 h postadministration.[14] Notably, caffeine appears to have a neutral influence on recovery sleep (17–20 h following the administration of 600 mg), likely due to its relatively concise half-life.[12,28]

Modafinil, typically administered in doses ranging from 100 to 200 mg, represents a relatively recent wakefulness-enhancing pharmaceutical compound. This drug has been approved for countering fatigue in the air forces of nations such as Singapore, the United States, India, and France.[23] Although the precise mechanisms governing its actions remain elusive, it is theorized to exert stimulatory effects by modulating various neurotransmitters, including serotonin, noradrenaline, dopamine, and gamma-aminobutyric acid.[1,13] Numerous investigations across different wakefulness periods have attested to its efficacy as a fatigue countermeasure.[7,27,29] However, modafinil possesses a comparatively extended half-life (12–15 h), a characteristic that may enable its impact to extend into recovery sleep.[24,31] Nonetheless, literature about the effect of modafinil on recovery sleep is contradictory. Modafinil has been suggested to decrease the sleep pressure, i.e., the need for sleep, that arises during sleep deprivation.[2,5] Conversely, modafinil has been reported to increase sleep latency (i.e., the time it takes to fall asleep), with or without a decreased total sleep time.[7,26] Yet other studies found no differences in recovery sleep (neither in total sleep time, nor in duration of individual sleep stages) after modafinil or placebo administration.[28]

This study is part of a larger randomized controlled trial that was designed to investigate several aspects of the implementation of modafinil and caffeine as countermeasures for fatigue in military aviation. In a previously published manuscript about this trial, we concluded that both modafinil and caffeine significantly decrease the negative effects of an extended period of continuous wakefulness on vigilance compared with a placebo.[29] The present study focuses on the second characteristic of an effective stimulant: the possible effect on subsequent recovery sleep. The median period of wakefulness at time of administration was 17 h [interquartile range (IQR) 16.5–17.5 h], and sleep quality and quantity on the successive day and night were investigated through self-reported questionnaires. We expected modafinil to have a limited negative effect on perceived quality and quantity of recovery sleep compared to that of caffeine and placebo due to the difference in their half-life.

METHODS

This study is part of a larger randomized controlled trial. A full description of the materials and methods used has been published previously in Wingelaar-Jagt et al.[29]

Subjects

The randomized controlled trial that this study was part of was conducted at the Center for Man in Aviation, Royal Netherlands Air Force (RNLAF) (Soesterberg, the Netherlands), and adhered to the principles of the Declaration of Helsinki, the International Conference on Harmonization, and the Good Clinical Practice guidelines. The protocol was approved by the Medical Ethical Committee Brabant (reference: NL62145.028.17/P1749) and the Surgeon General of the Ministry of Defense (reference: DGO100117022). The trial was registered in the Dutch Trial Register (No. NTR6922) and EU Clinical Trials Register (No. 2017-002.288-16).

Healthy employees of the RNLAF between the ages of 18 and 60 yr were eligible for inclusion. Eligible subjects were fit to fly according to the RNLAF Military Aviation Regulations or European Aviation Regulations.[8,19] Exclusion criteria were mainly based on possible side-effects or interactions with caffeine or placebo, e.g., pregnancy or breastfeeding; the use of medication that is metabolized through Cytochrome P450 (CYP) 3A4/5, CYP2C19, or CYP2C9; and/or a history of psychiatric illness, including sleep disorders.

After being informed, both verbally and in writing, about the aims, consequences, and constraints of the trial, all subjects gave written consent. This informed consent was voluntary and could be retracted at any time without any consequences. According to international privacy regulations, no study data were included in the medical files of the subjects.

Materials

An overview of the study procedures is displayed in **Table I**. For the three nights preceding each trial day subjects were requested to fill out sleep questionnaires to determine the subjective quality and self-reported quantity of pre-test sleep. Subjects were asked to complete the same sleep questionnaires on the day (recovery sleep) and consecutive night (post-test sleep) succeeding the trial day and night. These sleep questionnaires consisted of the Groningen Sleep Quality Scale (GSQS; see **Appendix A**, found online at https://doi.org/10.3357/AMHP.6390sd.2024) and

Table I. Study Outline; Three Equal Trial Days, Except for the Administered Medication.

TIMING	ACTIVITY
Trial day −3	Sleep questionnaire, pre-test sleep
Trial day −2	Sleep questionnaire, pre-test sleep
Trial day −1	Sleep questionnaire, pre-test sleep
Trial day 0	Wake up at normal time 16:30—Start trial day Midnight—Administration of medication
Trial day +1, early	08:30—Stop trial day Sleep questionnaire, recovery sleep (daytime)
Trial day +1, late	Sleep questionnaire, post-test sleep (nighttime)

several questions about sleep quantity. To assess sleep quantity, hours slept were derived from the answers to the aforementioned sleep questionnaires.

The quality of sleep was assessed by analyzing sleep efficiency and the scores on the GSQS. The GSQS is a self-administered 15-item questionnaire.[22] Subjects were asked not to leave any item blank and to check the most correct responses. GSQS scores range from 0–14, with scores between 0 and 2 indicating normal, refreshing sleep; 3–5 intermediate (mild) sleep disturbances; and scores ≥6 disturbed sleep.[18] Sleep efficiency was calculated as (number of hours slept/number of hours in bed)*100. Sleep quantity and quality of pre-test, recovery, and post-test sleep were compared.

Procedure

The randomized controlled trial consisted of three nonconsecutive trial days for every participant during which modafinil, caffeine, or placebo capsules were administered once just after midnight (see the previously published article[29]). The dose of modafinil was 200 mg, which is regarded as an effective countermeasure for fatigue in military aviators.[3,4] The dose of caffeine (300 mg) is the usual dose administered to RNLAF aviators nowadays; it is considered a medium range but effective dose.[4,16]

A wash-out period of at least 7 d was implemented to ensure that the drugs were completely eliminated and would not interfere with analyses on subsequent trial days. Treatments were balanced across subjects and test days using a Williams design with six treatment orders. The trial was double-blinded to ensure that both the subjects and investigators were unaware of the treatment given on trial days. The order of the treatments for each individual subject (placebo, caffeine, or modafinil) was based on a computer-generated randomization schedule organized and monitored by an external statistician. For every trial day, the researchers received a treatment kit from the pharmacist. The treatment kits were labeled with the subject number and the trial day and contained identical capsules.

Subjects remained within the time zone of the research center (daylight saving GMT +2) 1 wk prior to the start of every trial day to prevent jetlag, which can confound test results. During the trial days, no strenuous physical exercise (including sports) or sleeping was allowed, and subjects kept a log of their activities and caffeine intake. They were able to consume their normal amount of caffeine-based products until 17:00. To avoid caffeine interfering with vigilance, the subjects ceased consumption of caffeine products from 17:00 on trial days. The results of the analysis of habitual caffeine intake on the effect of caffeine administration have been published separately.[30]

Vital signs (temperature, blood pressure, and pulse) were measured four times during each trial day, two times prior to medication administration, and 2 and 8 h after administration. Additionally, on each trial day, female subjects were tested for pregnancy and all subjects were asked if they had taken any concomitant medication or unauthorized medications during the past 3 d. Subjects were asked about any adverse events multiple times during the trial days and at every visit after screening. Any adverse events that occurred during the study were recorded.

Statistical Analysis

IBM SPSS Statistics for Windows, version 27.0, was used for the statistical analyses of the outcomes of the sleep questionnaires (Armonk, NY: IBM Corp, 2020). Friedman tests were performed to analyze the main effects of treatment on the hours slept and sleep efficiency. Wilcoxon signed rank tests were carried out for pairwise comparisons between groups. Additionally, Wilcoxon signed rank tests were used to analyze within-group differences between hours slept, sleep efficiency, and GSQS scores pre- and post-test. The placebo group was included for reference. A P-value of <0.05 was considered statistically significant.

RESULTS

The trial included 32 subjects: 2 subjects did not participate in the caffeine condition due to operational reasons. Of the 32 subjects, 1 subject failed to provide information about sleep duration on the pre-test questionnaire (prior to placebo administration), and 8 subjects did not complete the recovery sleep questionnaire as they did not sleep during the day. The number of respondents per sleep period and condition are visualized in **Table II**. The subjects' characteristics are equal to those described in the article about the comparison between the effects of modafinil and caffeine with placebo on nighttime vigilance[29]: Subjects' ages ranged from 25–59 yr (median age: 30.9 yr, IQR: 28.9–39.3 yr). Among the 32 subjects, 5 (16%) were women and a majority of 21 (66%) were pilots. Throughout the trial, no adverse events were reported. The administration of the drugs did not exert any discernible impact on the subjects' vital parameters. The trial concluded in alignment with the protocol.

The median time subjects reported falling asleep in the nights immediately prior to the trial days was similar between the three conditions (modafinil, caffeine, and placebo) (see

Table II. Number of Respondents per Condition and Sleep Period.

CONDITION	PRE	RECOVERY	POST
Caffeine	30	26	30
Modafinil	32	30	32
Placebo	31	30	32

Table III. Median Sleep Times on the Pre-Test Nights

CONDITION	NIGHT PRIOR TO TEST NIGHT	ALL THREE PRE-TEST NIGHTS
Caffeine	23:15 (IQR 22:36–23:43)	23:20 p.m. (IQR 22:40–00:00)
Modafinil	23:12 (IQR 22:30–23:41)	23:15 (IQR 22:40–23:51)
Placebo	23:12 (IQR 22:44–23:42)	23:15 (IQR 22:45–23:58)

Table III). After the trial days, in all but eight instances, subjects had their recovery sleep during the day. The median reported time subjects fell asleep during the day was similar in all conditions [caffeine 10:00 (IQR 09:35–10:35), modafinil 10:05 (IQR 09:20–10:34), placebo 10:02 (IQR 09:17–10:31)]. Consequently, recovery sleep onset was generally 10 h after medication administration. The total period of wakefulness before the recovery sleep was also comparable for all conditions [caffeine 27.1 h (IQR 26.7–28.0), modafinil 27.6 h (IQR 26.6–28.3), placebo 27.5 h (IQR 26.6–28.3)].

The eight instances in which subjects did not have their recovery sleep during the day were attributed to six subjects. Among these, three instances occurred in one individual who failed to sleep after any of the three administrations. The other five instances occurred independently in five individual subjects (three who did not sleep after caffeine administration, one who did not sleep after modafinil administration, and one who did not sleep after placebo administration). In these eight instances, the subjects stayed awake during the entire day and the median time they fell asleep was 22:47, meaning they had a median period of wakefulness of 40.9 h (IQR 40.1–41.5). In the other 86 instances, the median time subjects fell asleep was 23:03 (IQR 22:26–00:00) and the median period of wakefulness was 10.0 h (IQR 8.6–11.2).

Table IV shows the results of analyses of the reported hours slept. The Friedman tests showed a statistically significant difference in the hours slept during the recovery sleep [$\chi^2(2) = 7.600$, $P = 0.022$]. Pairwise comparisons (Wilcoxon signed rank test) showed that recovery sleep was statistically significantly shorter by 30% in the modafinil condition than in the placebo condition ($Z = -2.365$, $P = 0.018$). There was no statistically significant difference between caffeine and modafinil or between caffeine and placebo ($Z = 0.745$, $P = 0.456$ and $Z = -1.127$, $P = 0.201$, respectively).

Pairwise comparisons using the Wilcoxon signed rank test showed that post-test sleep was statistically significantly longer than pre-test sleep in all three conditions (caffeine 13.6% longer, $Z = 2.688$, $P = 0.007$; modafinil 11.1% longer, $Z = 3.090$, $P = 0.002$; and placebo 25.4% longer, $Z = 3.976$, $P < 0.001$). **Table V** shows the results of the analyses of reported sleep efficiency. The Friedman tests showed no statistically significant difference in sleep efficiency between the different conditions for pre-test, recovery, or post-test sleep. Pairwise comparisons using the Wilcoxon signed rank test showed that post-test sleep efficiency was statistically significantly higher in the modafinil condition ($Z = 2.968$, $P = 0.003$) and placebo condition ($Z = 3.290$, $P = 0.001$) when compared with pre-test sleep. In the caffeine condition, this difference was not statistically significant ($Z = 0.051$, $P = 0.959$).

The median GSQS scores of pre- and post-test sleep indicated normal sleep. Nonetheless, in all conditions, some subjects reported mild to severely disturbed sleep (See **Table VI**). The median GSQS score of recovery sleep indicated mild sleep disturbance. However, the number of subjects reporting severely disturbed recovery sleep was comparable to the number reporting severely disturbed pre-test sleep, and lower than the number reporting severely disturbed post-test sleep. Friedman tests showed no statistically significant differences in the GSQS score between the different conditions. Comparison of pre-test and post-test GSQS scores using Wilcoxon signed rank tests showed that GSQS scores were statistically significantly lower post-test than pre-test in the modafinil condition ($Z = -2.236$, $P = 0.020$). In the caffeine and placebo conditions, this difference was not statistically significant ($Z = -1.453$, $P = 0.146$ and $Z = -0.206$, $P = 0.206$, respectively).

DISCUSSION

This study demonstrates that previously administered modafinil does not interfere with subjective quality and quantity of

Table IV. Analyses of Hours Slept.

CONDITION	PRE ($N = 30$)	RECOVERY ($N = 22$)	POST ($N = 30$)
Caffeine	7:35 (IQR 7:02–8:25)	3:03 (IQR 2:28–3:55)	8:39 (IQR 7:37–9:55)‡
Modafinil	7:25 (IQR 6:37–7:55)	2:47 (IQR 1:55–3:51)†	8:16 (IQR 7:30–9:04)‡
Placebo	7:00 (IQR 6:02–7:37)	3:58 (IQR 2:26–4:54)†	8:47 (IQR 7:13–9:12)‡
P (Friedman tests)	0.215	0.022*	0.897

*Statistically significant results ($P < 0.05$) from the Friedman test; †pairwise comparison using a Wilcoxon signed rank test showed that the recovery sleep differed statistically significantly between modafinil and placebo ($P < 0.05$); ‡statistically significant results ($P < 0.05$) from the Wilcoxon signed rank test comparing hours slept pre- vs post-trial days.

Table V. Analyses of Sleep Efficiency.

CONDITION	PRE ($N = 30$)	RECOVERY ($N = 22$)	POST ($N = 30$)
Caffeine	95.9 (IQR 89.6–98.0)	99.2 (IQR 98.4–99.5)	96.8 (IQR 91.2–97.7)
Modafinil	93.4 (IQR 87.4–97.4)	99.0 (IQR 98.1–99.6)	96.8 (IQR 91.0–98.4)*
Placebo	91.5 (IQR 82.5–97.4)	99.1 (IQR 97.9–99.6)	97.3 (IQR 94.1–98.4)*
P (Friedman tests)	0.218	0.873	0.301

*Statistically significant results ($P < 0.05$) from the Wilcoxon signed rank test comparing sleep efficiency pre- vs post-trial days.

Table VI. Analyses of Groningen Sleep Quality Scale (GSQS) Scores.

SLEEP QUALITY PER CONDITION	PRE	RECOVERY	POST
Caffeine	2.00 (IQR 0.00–4.25)	4.00 (IQR 2.00–5.00)	2.00 (IQR 0.00–3.00)
Normal (0–2)	*N* = 19	*N* = 9	*N* = 22
Mildly disturbed (3–5)	*N* = 7	*N* = 13	*N* = 7
Severely disturbed (≥6)	*N* = 4	*N* = 4	*N* = 1
Modafinil	3.00 (IQR 0.00–4.25)	4.00 (IQR 2.00–5.00)	2.00 (IQR 0.00–3.00)*
Normal (0–2)	*N* = 15	*N* = 6	*N* = 22
Mildly disturbed (3–5)	*N* = 12	*N* = 20	*N* = 10
Severely disturbed (≥6)	*N* = 5	*N* = 4	*N* = 0
Placebo	2.50 (IQR 0.00–6.00)	4.00 (IQR 3.00–6.00)	2.00 (IQR 0.00–3.25)
Normal (0–2)	*N* = 15	*N* = 6	*N* = 21
Mildly disturbed (3–5)	*N* = 7	*N* = 17	*N* = 8
Severely disturbed (≥6)	*N* = 9	*N* = 7	*N* = 3
P (Friedman tests)	0.816	0.798	0.682

*Statistically significant results ($P < 0.05$) from the Wilcoxon signed rank test comparing GSQS score pre- vs post-trial days.

recovery sleep (daytime sleep period after the trial) after an extended period of continuous wakefulness (median 27.0 h) compared with placebo or caffeine. Additionally, post-test sleep (sleep on the night following the trial) after modafinil administration was reported to be longer, more efficient, and had better GSQS scores than pre-test sleep. In order for stimulants to be effective, they must substantially increase vigilance and reduce fatigue and, secondly and no less importantly, they must allow for good recovery sleep, as sleep is the best solution to reduce fatigue. In a previously published manuscript about this trial, we concluded that subjects, when administered modafinil or caffeine, showed greater vigilance after an extended period of continuous wakefulness than those administered a placebo.[29] As the presented data suggests that the subjective perception of recovery sleep is not impaired by modafinil, it provides further evidence toward the aforementioned second criteria for its usage as a stimulant in military aviation.

In the present study the reported recovery sleep in the modafinil condition was statistically significantly shorter by 30% than in the placebo condition. However, subjectively reported sleep efficiency and GSQS scores were similar between the conditions, suggesting the shorter sleep time did not cause a negative impact on subjective perception of sleep quantity and quality. A decrease in recovery sleep after modafinil administration compared to placebo has also been reported in previous studies.[2,7,15] Using polysomnography, Buguet et al. found a shorter sleep period after modafinil administration, with sleep patterns close to that of placebo, and attributed this decrease to a reduced need for recovery sleep.[2] In the later study of Estrada et al., a similar shorter sleep period after modafinil administration was found using actigraphy. However, this was hypothesized to be due to an increase in sleep onset latency rather than a decrease in need for recovery sleep, even though performance after the shorter recovery sleep was similar.[7] In the current study subjects did not perceive an increase in sleep onset latency after modafinil administration. This provides additional, though subjective, evidence for the hypothesis that modafinil indeed decreases sleep pressure in periods of extended wakefulness.[5] This effect was not seen after caffeine administration in this study, with the notable observation that four subjects did not have a recovery sleep during the day, compared to two subjects in both the modafinil and placebo conditions. However, due to the small number of subjects in the test conditions, conclusions based on this observation must be drawn carefully.

Median reported onset of post-test sleep was 23:03, which was comparable to the sleep onset on pre-test nights. However, at the start of post-test sleep, the median period since the subjects' last normal nighttime sleep was 40.0 h (IQR 39.5–40.0). Even though most subjects did enjoy a recovery sleep, this recovery sleep period was shorter and more disturbed than normal nighttime sleep, most probably resulting in a higher level of fatigue than usual.[11] Possibly due to this residual sleep loss, the reported quantity of post-test sleep was better than those of pre-test sleep in all three conditions. The placebo group slept 25.4% longer post-test than pre-test, compared with 13.6% and 11.1% in the caffeine and modafinil group, respectively, but the differences between the conditions were not statistically significant. Reported sleep efficiency increased statistically significantly in both the modafinil and placebo conditions. The absence of a statistically significant difference in the caffeine condition may be explained by the very high pre-test sleep efficiency, i.e., a relative ceiling effect. GSQS scores only improved statistically significantly in the modafinil condition post-test compared to pre-test, which is in line with previous literature reporting that modafinil improves sleep quality in other circumstances.[20,21]

Although the present study is, to our knowledge, the first to examine the effects of caffeine and modafinil on sleep quality and quantity in this manner after a moderate period of wakefulness, it has certain shortcomings that need to be addressed. The most apparent shortcoming is that no objective measurements of sleep (e.g., polysomnography) were included in our study. Consequently, time slept, sleep patterns, and sleep disruptions were not objectively measured, but were instead deduced from questionnaire responses. This may have resulted in recall bias, which might influence the findings in this study. As a result, this limits the strength of the conclusions that can be drawn from this study, as subjective data is not sufficient to definitely rule out sleep impairment after modafinil use. However, previous studies did include

polysomnography and found no significant differences in sleep patterns after modafinil administration compared to placebo administration.[2,28] Additionally, the double-blinded nature of the study should have minimized the impact of possible recall bias. Even so, additional studies with polysomnography are necessary to confirm our findings and provide more insight into the hypothesized decrease in sleep pressure after modafinil administration and its possible effect on sleep patterns and quality. And perhaps even more importantly, studies should investigate if there is a difference in performance after this shorter period of recovery sleep (which was not found in the actigraphy study).

Another limitation of this study is that not all subjects had recovery sleep, even though they were instructed to do so. Six subjects did not sleep in a total of eight instances during the day. However, because the eight instances were distributed across the three groups (four in the caffeine condition, two in the modafinil condition, and two in the placebo condition; one subject did not sleep in any condition), the impact on the analyses was deemed to be small. Thirdly, the bedtimes and waking times of the subjects were not imposed; consequently, there was variability among subjects in terms of both the duration of their most recent nocturnal sleep and the time elapsed since that sleep episode. Nevertheless, owing to the crossover design of our study, we hold the viewpoint that these differences are unlikely to exert any significant influence on the interpretations drawn from our study findings. Additionally, both the timings of sleep onset and subsequent awakening were similar between the different groups, which increased the reliability of these timings. Moreover, the slight fluctuations in timings are more representative of the circumstances of operational military aviation, and daily life in general, than those of a controlled laboratory setup. We therefore think the fluctuations in timings increase the practical validity of the study. Fourthly, habitual caffeine consumption was allowed until 17:00 on the trial day; afterwards subjects ceased all caffeine intake. This resulted in different caffeine intakes during the trial days by the subjects. Due to the short half-life of caffeine (4–6 h) we do not believe this would influence sleep parameters approximately 17 h later. Additionally, a separately published article shows that this habitual caffeine intake until 7 h prior to caffeine administration did not influence the effect of caffeine administration.[30] And again, allowing for daytime caffeine consumption enhances the practical validity of the study. Lastly, our study population was limited to military personnel. While this accurately represents the military aviator population, the results might not be applicable to nonmilitary aviators or the general population. Thus, interpretation of these results for nonmilitary groups should be done carefully.

In conclusion, modafinil administration did not negatively affect the subjective efficiency and quality of recovery sleep, although it shortened its duration. The current study suggests modafinil might decrease sleep pressure, i.e., the need for recovery sleep, resulting in a shorter reported recovery sleep with no negative impact on subjective sleep quality. Additionally, the reported quantity and quality of post-test sleep were higher than those of pre-test sleep after modafinil administration. These effects were not seen after caffeine administration. To further investigate the use and value of modafinil for military aviation, research should aim to evaluate the cognitive performances of pilots during the recovery day and days thereafter. Additionally, polysomnography might provide more insight into the hypothesized decrease in sleep pressure and its effect on sleep patterns after modafinil administration.

The importance of fatigue and its negative effects on performance is not limited to military aviation. In industries such as healthcare and logistics, in which peak performance is required during nighttime or after periods of sleep deprivation, it is equally important to be able to counteract the adverse effects of fatigue. The present study confirms that modafinil subjectively does not negatively impact daytime recovery sleep quality, efficiency, or subsequent nighttime sleep. Therefore, modafinil appears to subjectively support recovery after extended wakefulness, which is an important aspect for application as a fatigue countermeasure in operational settings.

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