Differential effects of modafinil on performance of low-performing and high-performing individuals during total sleep deprivation

J. Lynn Caldwella,⁎, Valarie M. Schroederb, Christina L. Kunkleb, Henry G. Stephensonb

a Naval Medical Research Unit Dayton, United States of America
b The Henry M. Jackson Foundation for the Advancement of Military Medicine, United States of America

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ABSTRACT

Background: Individual responses to the effects of inadequate sleep have been well documented: some people are more vulnerable to the effects of sleep loss than others. Fatigue-vulnerable individuals generally require access to effective fatigue countermeasures; however, the question arises as to whether these fatigue-vulnerable individuals receive the same benefits shown in group efficacy data. The present study administered modafinil to individuals to determine its differential effects on performance of best and worst performers during sleep deprivation.

Methods: A sample of 22 men, age 21–40 yrs., was tested on 2 separate occasions during which they were kept awake for 36 h. During one period they received 200 mg modafinil; during the other they received placebo. Participants were tested on a variety of tasks while rested and at 5-hr intervals across the continuous wakefulness period. Performance for each cognitive task and subjective measure of fatigue from the placebo period was used to group individuals into high (HP) or low performance (LP) groups to indicate fatigue vulnerability for each task.

Results: Results indicated that on the MTS task, the HP group performed the same throughout the testing period, regardless of whether they received modafinil or not. However, the LP group significantly improved after receiving modafinil compared to placebo. Performance on the PVT showed the HP group had a small decrease in the number of lapses after receiving modafinil compared to placebo, whereas the LP group had a large decrease in lapses after receiving modafinil compared to placebo. Performance on the RDM showed no difference between groups, regardless of drug condition. Groups did not differ after receiving modafinil on subjective fatigue measured by the POMS.

Conclusions: Depending on the task, HP individuals did not benefit substantially when administered modafinil compared to placebo. However, the LP individuals improved after receiving modafinil compared to placebo.

1. Introduction

Sufficient sleep has been recognized as one of the most important factors in practically all operations, including industrial, transportation, and military (Caldwell et al., 2019). Despite these facts, it is generally the case that insufficient sleep (acute sleep deprivation and/or sleep restriction) is commonplace (Dawson and McCulloch, 2005; Giam, 1997; Krueger, 1989; Lerman et al., 2012; Lindsay and Dyche, 2012; Miller et al., 2007). As a result, fatigue-related problems such as involuntary microsleeps, attentional instability, judgment errors, delayed reaction times, accuracy losses, learning difficulties, time-sharing problems, and impaired situational awareness are likely to occur (Balkin et al., 2008; Banks and Dinges, 2011; Killgore, 2010; Lim and Dinges, 2010). These deficits are compounded by high workload situations, circadian disruptions, and insufficient recovery time between work periods (Caldwell et al., 2009; Neville et al., 1994; Samel et al., 1995). Needless to say, these factors have made fatigue from sleep loss and circadian misalignments a serious problem for workers, especially those who, because of innate factors, are most physiologically predisposed to fatigue’s insidious negative effects.

Individual differences in fatigue vulnerability have been a matter of academic interest for quite some time, but have become even more important since technological advances have placed greater responsibilities on fewer and fewer personnel. Successful accomplishment of many tasks is now often a function of the capacity of only one or a handful of key personnel rather than a group of individuals where the failure of any one worker can be overcome by other less-affected members of the group. For example, in the realm of military aviation, a
single B-2 bomber operated by only two crewmembers is now relied upon to accomplish the same mission that was once expected of a thousand fully-manned B-17’s in World War II (Robb and Ortega, 2012). Similarly, in the civilian world, a single factory worker is now often responsible for jobs that once relied on twelve or more skilled employees (Emont, 2018).

From an efficiency standpoint, “doing more with less” is a favorable development, but the increased role of individuals (rather than groups) has dramatically increased the importance of ensuring the fitness of each individual. This comes at a time in which the 24/7 pace of the modern world challenges human physiological capacity more than ever before in history. Long duty days, rotating work shifts, and a number of other factors can substantially increase the risk of fatigue-related decrements in the workplace, and these risks pose serious challenges for safety-sensitive jobs (Lerman et al., 2012). These risks will be significantly exacerbated when fatigue-vulnerable versus fatigue-resistant personnel are involved.

Fatigue-vulnerable individuals suffer marked performance decrements after only a short period of sleep deprivation, while their fatigue-resistant peers are far less impacted (Rusterholz et al., 2017; Van Dongen et al., 2012; Xu et al., 2016). This difference is a trait-like response to both acute, total sleep deprivation (Leproult et al., 2003; Rupp et al., 2012; Van Dongen et al., 2004) as well as chronic sleep restriction (Dennis et al., 2017). An individual who is fatigue resistant on one occasion will be consistently fatigue resistant on other occasions even when tested after several months; one who is fatigue vulnerable in one situation will display this vulnerability in other circumstances as well. However, performance on various tasks will differ during sleep deprivation; individuals whose performance declines on one task may perform better on another task (Sprich et al., 2019; Van Dongen et al., 2004). From a fatigue management standpoint, it is clear that fatigue-vulnerable personnel will need increased access to effective fatigue countermeasures in order to safeguard their alertness and performance; however, a question arises as to whether or not these fatigue-vulnerable individuals, once administered an alertness aid, can receive the same benefits shown in group efficacy data and whether benefits are sustained.

A case in point is the fatigue-countermeasure modafinil which is widely used to treat excessive daytime sleepiness associated with shift work sleepiness disorder, narcolepsy, or obstructive sleep apnea (Czeisler et al., 2005, 2009; Roth et al., 2007; Schwartz, 2005). It is also highly effective for alertness maintenance when sleep and circadian factors degrade performance (Caldwell et al., 2008). This and other prescription alertness aids have proven generally effective in terms of enhancing or sustaining average group performance in both laboratory simulations and real-world operational environments; however, little is known about whether or not individual variations in the responses to these alertness aids may arise out of individual variations in fatigue vulnerability.

The present study addressed whether the efficacy of modafinil was influenced by fatigue vulnerability. Although none of the participants in the present investigation were completely resistant to the effects of sleep loss, those who were the most resistant were grouped, per task, as high performers (HP) and those who were the least resistant were grouped as low performers (LP). It was hypothesized that the LPs would benefit the most from administration of modafinil.

2.2. Participants

A sample of 29 individuals enrolled in the protocol, with 22 successfully completing both data collection periods. The 7 participants who dropped out of the study discontinued for various reasons, mainly due to discomfort associated with sleep deprivation. All participants were male active duty military between the ages of 21 and 40 (M = 28.50, SD = 5.59). Exclusion criteria included daily consumption of more than 250 mg of caffeine; a history of significant psychiatric, neurological, or sleep-related problems; tobacco use within the last 6 months; and any medication use. Participants were required to obtain a minimum of 7.5 h of sleep for the 3 days prior to the study days in order to minimize sleep debt; compliance was checked by actigraphy. Participants were compensated for their time and effort.

2.3. Measures

A series of cognitive evaluations were collected during the training, baseline, and continuous wakefulness periods. Tests measured a variety of cognitive functioning, including attention, reaction time, memory, and psychomotor tracking. Most of the tests were presented from the NTI Armony Test System (ATS™) battery of tests (NTI, Inc., Fairborn, OH) and will be indicated as such. Considering that the primary aim of this study was to examine individual differences on tasks impacted by sleep deprivation, only a subset of tests was selected for analysis, specifically those tests that proved sensitive to the effects of continuous wakefulness. Tasks that participants performed but which did not show sensitivity to continuous wakefulness include: the Stroop task, a measure of cognitive interference, control, and processing speed; the Wisconsin Card Sorting Task, a measure of reasoning and attentional shifting, and the Tumbling E task, a measure of visual acuity. These tasks were not further examined. In addition to the cognitive tasks, the Fatigue factor from the Profile of Mood States (POMS) questionnaire was examined for individual differences in order to assess subjective responses associated with fatigue vulnerability and response to modafinil.

2.3.1. Psychomotor vigilance test (PVT)

Reaction time was assessed using the 10-minute PVT, a simple reaction time test known to be sensitive to sleep loss (Dinges et al., 1997). The PVT requires sustained attention and discrete motor responses. The portable, battery-operated device visually displays numbers counted up by milliseconds in a window. The stimulus is presented for up to 1 min (60,000 msec), allowing the participant to respond. The participant is asked to press a microswitch as quickly as possible once the numbers are displayed, and the device records reaction time. The interstimulus interval ranges randomly from 2 to 12 s. The data were downloaded from the device, stored on a computer, and reduced using custom software for future analysis.

2.3.2. Rapid decision making task (RDM) (NTI ATS™)

This test measured the participants’ ability to examine visual stimuli in the context of the task’s stated rules. Participants were shown several levels represented by overlapping ring sections with each level equating to a different threat level (red = critical, yellow = danger, green = alert). At various intervals, different “vehicles” were indicated somewhere on the display and the possible danger posed by that vehicle was evident by the symbol representing it (i.e. “?” = minimal danger, “O” = medium danger, and “X” = high danger). Participants were
instructed to assess the threat posed by a given vehicle based on its location as well as the danger rating using the vehicle’s symbol, and indicate which vehicle was the greatest threat. Participants were instructed to weigh the vehicle’s location more heavily than the classification. For example, in the first panel in Fig. 1 below, the “X” is the greatest threat. In the middle panel, the “X” is again the greatest threat while in the third panel, the “O” is the greatest threat.

2.2.3 Delayed Match to Sample (MTS) (NTI ATS™). This task is designed to assess the participant’s short-term spatial memory and pattern recognition skills by quickly and accurately choosing a test stimulus which is identical to a standard stimulus presented previously. Participants were initially presented with a 4 × 4 checkerboard matrix design. After viewing the sample matrix stimulus for a time adequate for committing the stimulus to memory (maximum view time was 60 s), the participant pressed a mouse key to clear the screen and initiate the interference stimulus. The interference stimuli consisted of 4 alphabet characters presented for 4 s when a vowel was present and 25 s when a vowel was not present. The participant was required to determine if the letter string contained a vowel by pressing the left mouse button if a vowel was present, and the right mouse button if no vowel was present. Afterward, the test trial was presented which consisted of two matrices side by side on the screen. One of the matrices was identical to the initial sample matrix while the other was different. The participant responded with the mouse button which corresponded to the test matrix which was identical to the initial sample matrix with a maximum viewing time of 30 s. The sequence of stimuli are shown in Fig. 2.

2.3.3. Profile of mood states (POMS)

This questionnaire (McNair et al., 1981) consists of 65 items which measure affect on 6 scales: tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment.

3. Study procedures

All participants were tested in the NAMRU – D Cognitive Readiness and Resilience (CRR) lab. Participants were required to rise at 0600 the morning of their scheduled visit and arrived at the CRR lab at 0800 on Day 1. They wore actigraphy monitors to track of sleep/wake episodes, and were required to have at least 7.5 h in bed with at least 7 h of sleep for 3 consecutive nights immediately preceding the in-house portion of the study. If the sleep requirements were not met, the participant was given the option to reschedule or was not enrolled in the in-house portion of the study.

After finishing intake procedures, participants completed two training sessions and one baseline session. The training sessions were intended to ensure that participants reached steady performance prior to the actual start of the experiment, and that practice effects did not interfere with the results. All test sessions were scheduled to begin every 4 h, with short breaks scheduled within the sessions and a longer break scheduled between sessions. Each testing session was identical and included neurobehavioral measures common in fatigue research.

At 2400 on Day 2, after being awake for 18 h, each participant was given either 200 mg modafinil or placebo (counterbalanced between visits). Participants then continued the remaining testing sessions throughout the night and next day until they completed 4 testing sessions, 1 every 4 h with a total continuous wakefulness period of 36 h. The testing schedule is outlined in Table 1. The individual session schedule is outlined in Table 2. At the end of the last session on Day 2, participants were debriefed and dismissed. Participants were not allowed to drive themselves home.

4. Results

Only one metric from each of three cognitive tests was analyzed using the SPSS statistical software package Version 25 (International Business Machines Corporation, Armonk NY). Data were screened for outliers; a participant was excluded from the analysis of a particular test if his baseline score was 3 or more standard deviations from that test’s baseline mean. For the measures used in this analysis, no outliers were identified; therefore, all participants’ data were included in the analyses. The three nights sleep data prior to each participant’s placebo
night were analyzed for each task grouping to determine if the groups differed in the amount of sleep obtained. The nights before the placebo condition were analyzed since the groups were assigned based on the night and session. The effects are illustrated in Fig. 3.

For the group by session interaction, the two groups were significantly different as the test sessions progressed, with the HP group having fewer lapses during the modafinil condition than during the placebo condition (Fig. 3, bottom right panel).

For the drug by session interaction, performance was better during the modafinil condition at sessions 2 and 3 than during the placebo condition. Additionally, during the modafinil condition, the baseline session was significantly better than sessions 2 through 4, and session 1 was better than sessions 2 and 4. Within the LP group, the baseline session was significantly better than all other sessions, and session 1 was significantly better than sessions 2 through 4 (Fig. 3, top right panel).

For the drug by session interaction, performance was better during the modafinil condition at sessions 2 and 3 than during the placebo condition. Additionally, during the modafinil condition, the baseline session was significantly better than all other sessions, and sessions 1 and 2 were better than session 4; during the placebo condition, the baseline session was significantly better than all other sessions, and session 1 was significantly better than sessions 2 through 4 (Fig. 3, bottom left panel).

4.2. Rapid decision making task

The metric analyzed for the RDM task was reaction time for the number of correct responses. The two groups were formed with 11 participants in each group. The mean (SD) amount of sleep obtained the HP and LP, and drug (modafinil and placebo) and session (baseline and sessions 1 through 4) as the repeated factors. Levine’s Test for Equality of Variances was used to test the assumption of equal variance between the two groups. Mauchly’s Test of Sphericity was used to test the assumption of sphericity within drugs and sessions. When the sphericity assumption was violated, the Huynh-Feldt adjusted degrees of freedom were used to calculate the F statistic. The results of both the Levine’s Test for Equality of Variances and Mauchly’s Test of Sphericity are reported only when the assumptions are violated. Significant interactions were followed with analyses of simple effects and Fisher’s Least Significant Difference (LSD) tests. Significant main effects for session were further analyzed with LSD tests. The alpha level for statistical significance was set to 0.05. Only metrics proven to show an effect from fatigue due to continuous wakefulness were analyzed in order to examine individual differences resulting from fatigue. All analysis results by test are shown in Table 3.

4.1. Psychomotor vigilance task

Unlike the other tests which were administered once each test session, the PVT was administered every hour starting at 1200 on Day 1. However, only the first PVT administered at the beginning of each test session was analyzed to remain consistent with the timing of the other tests. The metric analyzed for this task was the number of lapses (RTs > 500 msec). The two groups were formed with 10 participants in the HP group and 12 participants in the LP group. The average (SD) hours of sleep obtained the 3 nights before the placebo visit to the lab was 7.90 h (0.36) for the HP group and 8.24 h (0.64) for the LP group. The group by night interaction and the group main effect were not statistically significant.

Mauchly’s Test of Sphericity was violated for the drug by session interaction ($\chi^2(9) = 21.896, p = .009; \epsilon = 0.903$) and the session main effect ($\chi^2(9) = 25.490, p = .003; \epsilon = 0.781$). The ANOVA did not reveal a statistically significant three-way interaction among drug, group, and session, but did show statistically significant two-way interactions between group and drug, group and session, and drug and session. There were statistically significant main effects for group, drug, and session. The effects are illustrated in Fig. 3.

For the group by drug interaction, post hoc analyses indicated differences between the two groups during the placebo condition ($p < .001$). Additionally, the HP group did not show a significant difference between the two conditions, but the LP group had fewer lapses during the modafinil condition than during the placebo condition (Fig. 3, bottom right panel).

Table 2

Testing session schedule (Bold indicates tests analyzed in this effort).

| Minutes from start of session | Task                                      |
|------------------------------|-------------------------------------------|
| 00                           | PVT                                       |
| 15                           | Vision (acuity)                           |
| 30                           | Vision (PMI)                              |
| 35                           | NTI Battery: Stroop                       |
| 40                           | RDM Task                                  |
| 60                           | Wisconsin Card Sorting Task               |
| 90                           | MTS Task                                  |
| 95                           | PVT                                       |
| 120                          | Resting EEG                               |
| 130                          | ERP                                       |
| 180                          | POMS/VAS/SE                               |

Table 1

Daily testing schedule.

| Time  | Day 1  | Day 2  |
|-------|--------|--------|
| 0000  | DRUG DOSE | Depreciation |
| 0100  | Session 1  |
| 0200  |          |
| 0300  |          |
| 0400  |          |
| 0500  |          |
| 0600  |          |
| 0700  | Wake-up  |
| 0800  | Session 2  |
| 0900  |          |
| 1000  |          |
| 1100  |          |
| 1200  |          |
| 1300  | Session 3  |
| 1400  |          |
| 1500  |          |
| 1600  |          |
| 1700  | Training 2; Debrief/Dismiss |
| 1800  |          |
| 1900  |          |
| 2000  |          |
| 2100  | Baseline  |
| 2200  |          |
| 2300  |          |

Testing session schedule (Bold indicates tests analyzed in this effort).
3 nights before the placebo visit to the lab was 8.23 (0.53) for the HP group and 8.33 (0.79) for the LP group. The group by night interaction and the group main effect were not statistically significant.

Mauchly’s Test of Sphericity was violated for the drug by session interaction ($\chi^2(9) = 22.849$, $p = .016$; $\varepsilon = 0.879$) and the session main effect ($\chi^2(9) = 20.464$, $p = .003$; $\varepsilon = 0.878$). The ANOVA did not show a statistically-significant three-way interaction among drug, group, and session, nor a two-way interaction between group and drug. However, there were statistically significant two-way interactions between group and session as well as between drug and session. There were statistically significant main effects for group, drug, and session. The effects are illustrated in Fig. 4.

For the group by session interaction, the two groups were significantly different at all sessions, with the HP group having shorter reaction times than the LP group. Within the HP group, reaction time was significantly shorter at the baseline session than at sessions 2 and 4; reaction time at session 1 was significantly faster than at session 2. However, within the LP group, the baseline session was significantly faster than all other sessions; the first session was significantly faster than sessions 2 through 4; and session 2 was significantly slower than sessions 3 and 4 (Fig. 4, top right panel).

For the drug by session interaction, performance was faster during the modafinil condition at sessions 1 through 4 compared to the placebo condition, and better than the LP group during the placebo condition at sessions 1 through 3 (Fig. 5).

The effect analyzed for the POMS questionnaire was Fatigue. The two groups were formed with 10 participants in the HP group and 11 participants in the LP group. One participant had data missing due to a technical difficulty, leaving a total sample size of 21. The average (SD) hours of sleep obtained the 3 nights before the placebo visit to the lab was 8.50 h (0.81) for the HP group and 8.08 h (0.48) for the LP group. The group by night interaction was statistically significant, with the HP group receiving more sleep than the LP group on nights 1 and 2, but not on night 3. The means and standard deviations are shown in Table 4. The group main effect was not statistically significant.

Mauchly’s Test of Sphericity was violated for the drug by session interaction ($\chi^2(9) = 22.849$, $p = .010$; $\varepsilon = 0.859$). The ANOVA revealed a statistically-significant three-way interaction between drug, group, and session. There also were statistically significant two-way interactions between group and drug, group and session, and drug and session. There were statistically significant main effects for group, drug, and session. The three-way interaction is illustrated in Fig. 5.

For the group by drug by session interaction, post hoc analyses indicated that the HP group performed better than the LP group during the modafinil condition at the baseline session, and better than the LP group during the placebo condition at sessions 1 through 3 (Fig. 5).

### 4.4. Profile of mood states questionnaire

The factor analyzed for the POMS questionnaire was Fatigue. The two groups were formed with 10 participants in the HP group and 11 participants in the LP group. One participant had data missing due to a technical difficulty, leaving a total sample size of 21. The average (SD) hours of sleep obtained the 3 nights before the placebo visit to the lab was 8.50 h (0.81) for the HP group and 8.08 h (0.48) for the LP group. The group by night interaction was statistically significant, with the HP group receiving more sleep than the LP group on nights 1 and 2, but not on night 3. The means and standard deviations are shown in Table 4. The group main effect was not statistically significant.

Mauchly’s Test of Sphericity was violated for the drug by session interaction ($\chi^2(9) = 22.849$, $p = .007$; $\varepsilon = 0.752$) and the session main effect ($\chi^2(9) = 20.332$, $p = .016$; $\varepsilon = 0.812$). There was not a significant group by drug by session interaction nor a significant group by drug interaction. There were statistically-significant two-way interactions between group and session and drug and session. These effects are illustrated in Fig. 6.

For the group by session interaction, post hoc analyses indicated the HP group reported feeling less fatigue than the LP group at all sessions.
Fig. 3. Means (± standard error of the mean) of PVT Lapses. HPn = 10; LPn = 12. Top left panel: Group by drug by session interaction; Top right panel: Group by session interaction; Bottom left panel: Drug by session interaction; Bottom right panel: Drug by session interaction.
Fig. 4. Means (± standard error of the mean) of RDM Task Correct RT. HP n = 11; LP n = 11. Top left panel: Group by drug by session interaction; Top right panel: Group by session interaction; Bottom panel: Drug by session interaction.
Within the HP group, the baseline session and session 1 were significantly lower than sessions 2 and 3. Within the LP group, the baseline session and session 1 were significantly lower than sessions 2 through 4. These effects are illustrated in Fig. 6, top right panel.

For the drug and session interaction, post hoc analyses indicated differences between the two drugs at sessions 1 through 3. Within the modafinil condition, the baseline session and session 1 were significantly lower than sessions 2 through 4. Within the placebo condition, the baseline session was significantly lower than all sessions; session 1 was significantly lower than sessions 2 and 3. These effects are illustrated in Fig. 6, bottom panel.

5. Discussion

The present study indicated, as expected, that individuals responded differently to the effects of long hours of wakefulness. In addition to individual differences in response to fatigue, it was found that modafinil tended to benefit lower performing subjects more than higher performing subjects. However, classification into fatigue-response group depended on the task performed. Of the three cognitive tasks analyzed in this study, a task of working memory showed significant differences between the sleep-deprived LP versus the HP groups. Specifically, in the MTS task, the HP group showed stable performance throughout the testing period, regardless of whether they received modafinil or not; however, the LP group significantly improved only after receiving modafinil (compared to their performance after receiving placebo). Performance on the PVT also differed between groups. The HP group had a small decrease in the number of lapses on average after receiving modafinil compared to when they received placebo, whereas the LP group had a large decrease in lapses after receiving modafinil compared to when they received placebo. Performance on the RDM task showed no difference between the group responses, regardless of drug condition. In many cases for all tasks, the declines in performance and self-rated fatigue were significant at the 0500 session when the circadian dip in alertness and performance affected task scores the most, particularly in the LP group. Modafinil was effective at attenuating this effect in both groups.

In addition to cognitive performance, self-reported fatigue was greater in the LP group compared to the HP group, regardless of the drug administered. This may have resulted from the amount of sleep obtained prior to study participation; the LP group reported less sleep than the HP group, perhaps leading to a higher subjective rating of fatigue for the LP group.

Past research into individual differences in response to sleep deprivation has shown that people respond differently based on the task performed (Sprecher et al., 2019; Van Dongen et al., 2004). This study’s data support these previous findings; very few individuals remained in either the HP or LP group across tasks. This is illustrated in Fig. 7 where each individual’s modafinil and placebo scores are plotted by task. Each task is plotted by each individual’s modafinil and placebo performance.

Identification of those who perform poorly while deprived of sufficient sleep would be beneficial when deciding whether to administer an alertness aid such as modafinil. In the present study, for some metrics, modafinil was able to help the LP individuals more than the HP individuals. HP individuals did not benefit substantially when administered modafinil compared to no intervention. However, modafinil did improve performance of the LP individuals compared to no intervention.

Identification of fatigue vulnerability is important in many sectors of society where inadequate sleep is common, but work must continue in fields such as in military and emergency operations. However, an a priori way to identify those individuals who are particularly vulnerable to the effects of sleep deprivation is still not available, despite efforts to do so. The PVT which is the “gold standard” for assessing performance deficits associated with sleep deprivation (Abe et al., 2014) has often been suggested as a real-world measure of fatigue vulnerability, but it should be kept in mind that while this test is highly sensitive to the effects of sleep loss, it may not capture instances of fatigue vulnerability across all cognitive tasks. Some individuals who perform best on the PVT may not perform the best on higher level cognitive tasks, while those who perform the worst on the PVT may not necessarily perform worse on other cognitive tasks (Frey et al., 2004). The present study found that individuals classified as low performers on the PVT may not have been placed in the same group on another task. The question of establishing the general level of fatigue vulnerability remains difficult.

Table 4

| Group | Night 1  | Night 2  | Night 3  |
|-------|---------|---------|---------|
| HP    | 8.85 (0.82) | 8.75 (0.64) | 7.90 (0.58) |
| LP    | 8.17 (0.44) | 7.96 (0.46) | 8.13 (0.49) |

Fig. 5. Means (± standard error of the mean) of MTS Number Correct group by drug by session interaction. HP n = 10; LP n = 12.
Fig. 6. Means (± standard error of the mean) of POMS Fatigue factor. HP n = 10; LP n = 11. Top left panel: Group by drug by session interaction; Top right panel: Group by session interaction; Bottom panel: Drug by session interaction.
Fig. 7. Individual placebo and modafinil scores plotted by task.
to answer. Nevertheless, once individuals are identified as fatigue vulnerable or resistant (typically based on their observed responses to sleep loss), decisions can be made regarding the need for countermeasures to improve performance which would otherwise degrade due to the effects of inadequate sleep. As shown by the present study, those most impacted by sleep loss will likely benefit the most from an alertness-enhancing intervention, but the exact extent of the benefit across a variety of tasks appears to be uncertain.

Some limitations to the present study could be addressed in future research to help answer remaining issues. The small sample size may have led to non-significant results due to the lack of power. A larger sample may also capture more fatigue-vulnerable individuals. Generally, individuals who have difficulty performing tasks when sleep deprived may not volunteer for a sleep deprivation study, therefore, a true sample of fatigue-vulnerable individuals may not have been included in the present study. Additionally, some of the test score ranges were very narrow, so the scores separating low performers from high performers were minor. Additionally, performance on these tests may not equate to similar performance on occupationally-relevant tasks. Furthermore, total sleep deprivation is not as common as long-term sleep restriction in real-world operations. More research is needed to determine if these results apply to performance during sleep restriction. Finally, the sample tested in this study consisted of young men which limits the generalizability of the study.

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