# Should the Australian Defence Force Conduct a Drug Trial of Wakefulness-Promoting Medications?

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### Abstract

Fatigue jeopardises soldiers' lives, and despite caffeine being the approved wakefulness aid in the Australian Defence Force (ADF), its efficacy equals a placebo with unwanted side effects. The US Military uses modafinil as an alternative, but no ADF studies on modafinil exist. This article argues for exploring alternatives, ensuring consent and conducting willingness-to-participate studies before conducting ADF modafinil trials.

### Introduction

Wakefulness-promoting medications combat fatigue during prolonged missions, crucial for pilots and soldiers. Modafinil, a non-stimulant used by the US Military since 2003, may enhance soldiers' alertness during sleep-deprived operations, potentially saving lives. However, Australia lacks modafinil trials for military use. This paper discusses modafinil, its military research status and its broader health implications. It urges the Australian Defence Force (ADF) to address three key aspects before trials, emphasising exploration of wakefulness strategies, informed consent and willingness-to-participate studies.

### What is modafinil?

Modafinil acts on brain pathways like dopamine transporters (DAT) unlike addictive amphetamine-like stimulants which acts as monoamine releasers. Common side effects include headaches, diarrhoea, stuffy nose, increased blood pressure and heart rate.

### State of modafinil military research

Modafinil studies with small sample sizes pose validity concerns. A larger Singapore Air Force study using historical medical data raises issues of bias.<sup>2</sup> These concerns are exacerbated by military secrecy. To address these issues, independent public institutions running drug trials can bolster accountability, transparency and data-sharing, fostering broader studies and potential civilian applications.

### Implications of modafinil military research

Modafinil improves reaction times but its misuse by civilians raises safety concerns.<sup>3</sup> Successful military trials on modafinil could enhance its safety for mainstream civilian use under medical supervision. However, the ADF should explore non-pharmacological wakefulness management before considering modafinil.

### Alternative wakefulness-promoting strategies

As shown in Table 1, non-pharmaceutical alternatives to modafinil, such as sleep, exercise, transcranial stimulation, training, hydration and nutrition, show potential benefits.4 Adequate sleep duration significantly improves reaction times, and physical activity enhances concentration. Transcranial stimulation consistently improves attention, while adequate hydration and nutrient intake positively impact cognitive function. Despite their potential, practical limitations in conflict situations exist. Training proves effective but may be challenging during wartime demands. Caffeine, the ADF's sole approved wakefulness aid, has drawbacks. A 2009 military study on caffeine revealed inefficacy and side effects, emphasising the need for more reliable fatigue countermeasures.5

### Do soldiers even want to participate in drug trials?

Table 1. Non-pharmaceutical alternative strategies to modafinil.

Non-pharmacological strategies	Disadvantages
Sleep	Operational demands prevent sleep
Exercise	Can't exercise in cramped conditions (e.g. foxhole or cockpit)
Transcranial Magnetic stimulation	Need specialised equipment
Training	Time constraints could lead to insufficient training
Cold, citrus-flavoured drinks	Supply-chain limitations (e.g. refrigeration)
Nutrition	Supply-chain limitations (e.g. limited or intermittent supply)

sufficient participants. Altruism for country and comrades emerged as a strong motivator for study participation. Understanding these motivations is crucial for recruitment and overcoming enrolment hurdles, steering clear of undue influence. Wakefulness-promoting agents benefit soldiers, addressing battlefield casualties caused by fatigue. To understand military members' motivations, willingness-to-participate studies prove insightful, despite potential non-response bias.

## Australian Defence Force research on wakefulness-promoting strategies

The Defence Science and Technology Group aims to use science and technology for Australia's defence, with recent studies on caffeine-infused gum demonstrating improved cognitive performance.7 Another study utilised an infrared oculographybased system, reducing drowsiness in ADF Army Reservists.8 Other strategies employed by the ADF include rest and sleep management, sleep hygiene training programs, rotational policies to ensure equitable workload and rest cycles, physical fitness programs to enhance overall health and combat fatigue, nutritional support to enhance physical and mental wellbeing, the use of caffeine, efficient task management, the use of technology to improve efficiency, psychological support to provide access to mental health resources to help personnel cope with the challenges of their roles, and regular health assessments to identify issues related to fatigue and intervene as necessary. The ADF has specific, detailed policies and procedures in place tailored to the unique operational requirements of the Army, Navy or Air Force to mitigate fatigue among its members. Modafinil can prove to be a useful addition to these fatigue countermeasures after careful study.

### Dual-use and wakefulness-promoting medications

Dual-use ethics addresses the potential misuse of military technology in civilian applications.<sup>9</sup>

Concerns over wakefulness-promoting medications, like modafinil, focus on potential permanent effects, raising fairness and safety issues. Studies show short-lived, dose-dependent effects, limiting its applicability beyond defined military mission parameters.<sup>3</sup>

### Conclusion

The ADF hasn't investigated wakefulness-promoting agents like modafinil in a drug trial, which, if successful, could save soldiers' lives and benefit civilians like shift workers. While alternative strategies like hydration, nutrition and exercise have limitations, caffeine remains the only approved fatigue countermeasure, but has its own efficacy concerns. Willingness-to-participate studies and a well-designed consent process ensure participant autonomy. Addressing these considerations is crucial before conducting modafinil drug trials for military use. Given the promise that modafinil holds in improving safety for soldiers and civilians alike, it is imperative that the ADF conduct a drug trial to explore its safety and effectiveness.

### Acknowledgements

The author would like to thank Dr Rebekah McWhirter for her expert assistance in all aspects of writing this paper as the author's Research Scholar Program Advisor at Deakin University. I would also like to extend my gratitude to Dr Cynthia Forlini for her valuable input. This paper did not receive funding from any source and does not represent the views of the Australian Defence Force or Deakin University. These views are my own.

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#### References

- Costa R, Oliveira NG, Dinis-Oliveira RJ. Pharmacokinetic and pharmacodynamic of bupropion: Integrative overview of relevant clinical and forensic aspects. Drug Metabolism Reviews. 2019;51(3):293–313. doi:10.1080/03602532.2019.1620763
- 2. Ooi T, Wong S, See B. Modafinil as a stimulant for military aviators. Aerospace Medicine and Human Performance. 2019;90(5):480-33.
- 3. Wingelaar-Jagt YQ, Bottenheft C, Riedel WJ, Ramaekers JG. Effects of modafinil and caffeine on night-time vigilance of Air Force crewmembers: A randomized controlled trial. Journal of Psychopharmacology. 2022;37(2):172–80. doi:10.1177/02698811221142568
- 4. Defense Technical Information Centre. A systematic review of cognitive enhancement interventions for use in military operations [Internet]. 2016 [cited 2023 Feb 1]. Army Aeromedical Research Lab. Available from: <a href="https://apps.dtic.mil/sti/citations/AD1083490">https://apps.dtic.mil/sti/citations/AD1083490</a>
- Defense Technical Information Centre. Performance sustainment of two man crews during 87 hours of extended wakefulness with stimulants and napping [Internet]. 2009 [cited 2023 Feb 3]. Army Aeromedical Research Lab. Available from: <a href="https://apps.dtic.mil/sti/citations/ADA498120">https://apps.dtic.mil/sti/citations/ADA498120</a>
- 6. Cook W, Doorenbos A. Indications of recruitment challenges in research with U.S. Military service members: A <u>ClinicalTrials.gov</u> Review. Military Medicine. 2017;182(3):1580-7.
- 7. Aidman E, Balin M, Johnson K, Jackson S, Paech GM, Pajcin M, et al. Caffeine may disrupt the impact of real-time drowsiness on cognitive performance: A double-blind, placebo-controlled small-sample study. Scientific Reports. 2021;11(1). doi:10.1038/s41598-021-83504-6
- 8. Aidman E, Chadunow C, Johnson K, Reece J. Real-time driver drowsiness feedback improves driver alertness and self-reported driving performance. Accident Analysis & Prevention. 2015;81:8–13. doi:10.1016/j.aap.2015.03.041
- 9. Sattler S, Jacobs E, Singh I, Whetham D, Bárd I, Moreno J, et al. Neuroenhancements in the military: A mixed-method pilot study on attitudes of staff officers to ethics and rules. Neuroethics. 2022;15(1). doi:10.1007/s12152-022-09490-2

