

# THE USE OF MODAFINIL IN ICU

By

**Amr M. Luka**

**Senior Resident of Anesthesiology, Intensive care and Pain  
Management**



# OVERVIEW

- **What is Modafinil**
  - **Why Modafinil in ICU**
  - **Mechanism of action**
  - **Studies discussion**
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# WHAT IS MODAFINIL?

**Non-amphetamine (CNS) stimulant.**

**Has wakefulness-promoting properties.**

**Used in the treatment of excessive daytime sleepiness.**

Gilleen J, Michalopoulou PG, Reichenberg A, Drake R, Wykes T, Lewis SW, Kapur S. Modafinil combined with cognitive training is associated with improved learning in healthy volunteers--a randomised controlled trial. Eur Neuropsychopharmacol. 2014

Apr;24(4):529-39.



# FDA-APPROVED USES

## Treatment of

**Narcolepsy.**

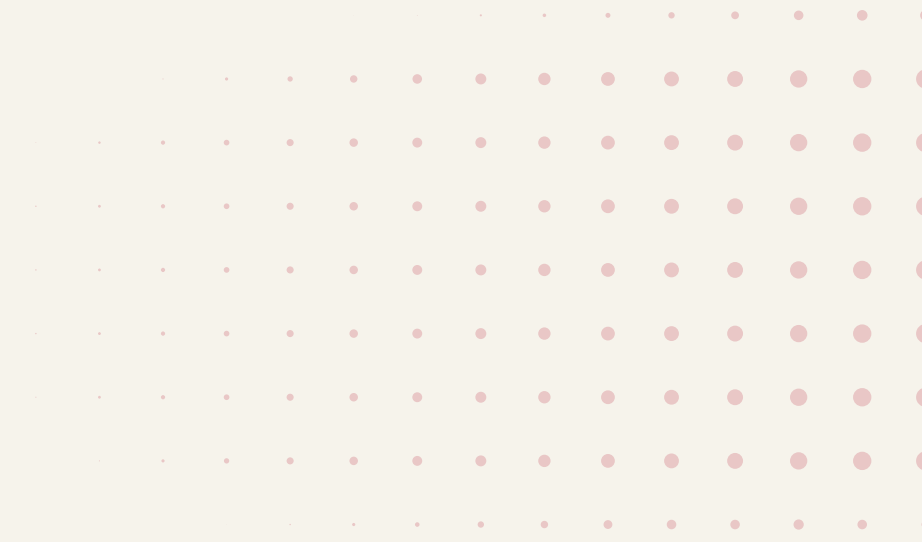


**Sleep work shift disorder.**

**Obstructive sleep apnea in adults.**





# OFF-LABELED USES

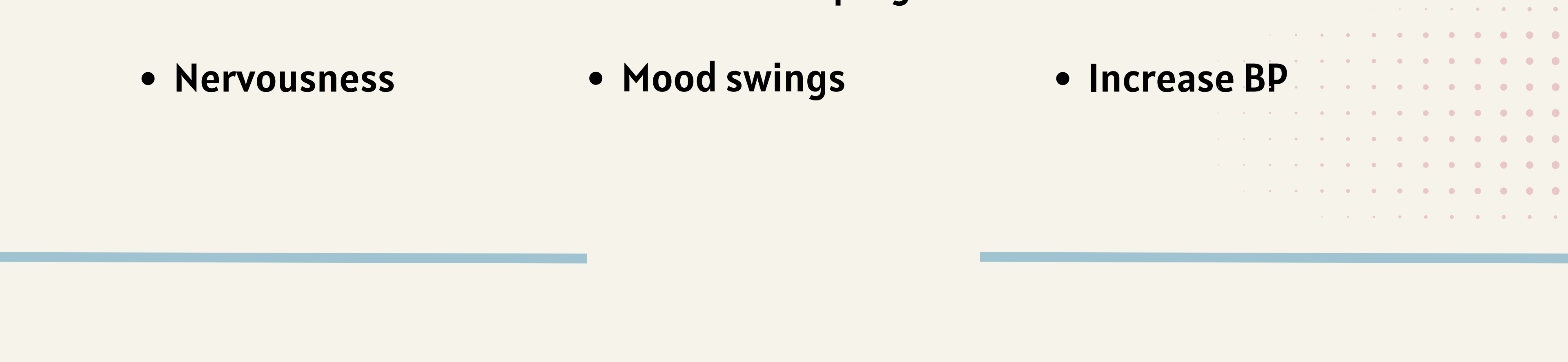
- **ADHD**
  - **Acute unipolar and bipolar depressive episodes**
  - **Cancer-related fatigue**
  - **Multiple sclerosis-related fatigues**
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# MECHANISM OF ACTION

- **Inhibitor of dopamine reuptake**, which is the primary clinically important property. It has little affinity for the (5HT) or (NE) transporters.
- Elevated concentrations of NE and 5HT in the prefrontal cortex and hypothalamus can be attributed to indirect effect of increased extracellular dopamine.



# SIDE EFFECTS

- Anxiety
  - Headache
  - NVD
  - Nervousness
  - Trembling
  - Shaking
  - Trouble sleeping
  - Mood swings
  - Chest pain
  - Blurry vision
  - Increase HR
  - Increase BP
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# DRUG INTERACTIONS

- 1 Other brain stimulants:** Amphetamine or dextroamphetamine
- 2 CNS depressants:** Benzodiazepines, barbiturates, MAOIs
- 3 Others:** Antifungal as ketoconazole Propranolol, phenytoin, warfarin.



# WHY ICU ?

- **The focus of intensive care unit (ICU) has become rehabilitation.**
- **Fatigue, excessive daytime somnolence (EDS), and depression can delay their recovery and potentially worsen outcomes. Critically ill patients are at risk of neurological as well as musculoskeletal complications of critical care.**
- **Those who are somnolent, fatigued, and depressed may not be able or willing to participate and may have a delayed recovery.**

Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet. 2009; 373(9678):1874-1882.

Bailey P, Thomsen GE, Spuhler VJ, et al. Early activity is feasible and safe in respiratory failure patients. Crit Care Med. 2007; 35(1):139-145.



**Early mobilization** of these patients has  
become the standard of care





# STUDIES DISCUSSION

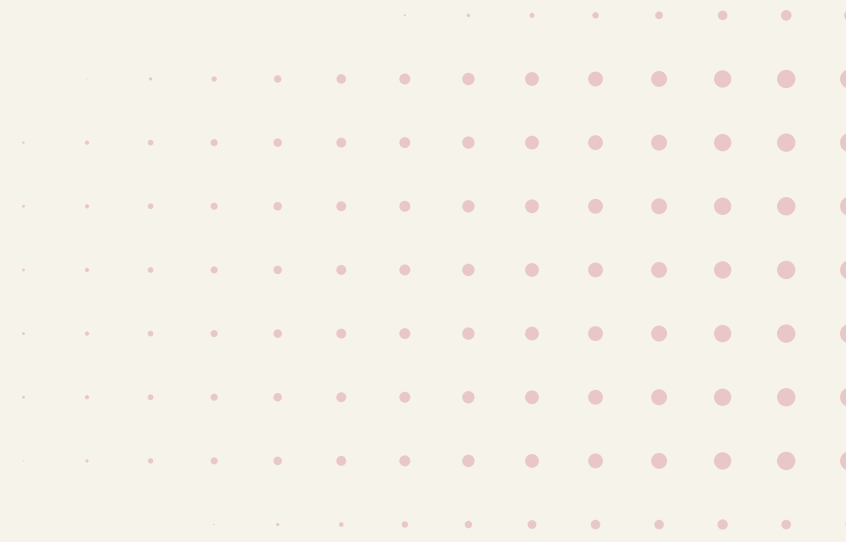


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# TRAUMATIC BRAIN INJURY

- **20 patients with TBI had fatigue, excessive daytime somnolence (EDS) or both.**
  - **Given a dose of 100 to 200 mg modafinil.**
  - **The ability to stay awake on the maintenance of wakefulness test improved in the modafinil group.**
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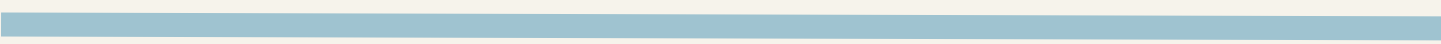
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P.R. Kaiser, P.O. Valko, E. Werth, J. Thomann, J. Meier, R. Stocker, C.L. Bassetti, C.R.

Baumann November 15, 2010, DOI: WNL.0b013e3181fd62a2



# WHAT IS THE MAINTENANCE OF WAKEFULNESS TEST (MWT)

- **How alert you are during the day.**
  - **Whether you can stay awake for a defined period of time.**
  - **Creates an environment which favors sleep conditions and see how the person can perform activities without the temptations of sleep.**
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# AMYOTROPHIC LATERAL SCLEROSIS

- **15 patients were treated for 2 weeks with either 200 or 400 mg of modafinil.**
- **The study showed significant improvement in the Fatigue Severity Scale (FSS).**

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Modafinil treatment of fatigue in patients with ALS: a placebo-controlled study

Judith G Rabkin <sup>1</sup>, Paul H Gordon, Martin McElhiney, Richard Rabkin, Sheena Chew, Hiroshi Mitsumoto

PMID: 19208404 DOI: [10.1002/mus.21245](https://doi.org/10.1002/mus.21245)

# **HYPOACTIVE DELIRIUM**

- **Two case studies showed improved daytime alertness and nighttime sleep.**
- **Case 1: An 85-year-old man with three-vessel coronary artery disease, who showed somnolence after TAVR**
- **Case 2: An 86-year-old woman who developed hypoactive dementia after SDH evacuation.**

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Manuel A. Eskildsen, MD, MPH Use of Modafinil in Two Patients with Hypoactive Delirium

Proceedings of UCLA Health -VOLUME 23 (2019)-



# POSTOPERATIVE COGNITIVE DYSFUNCTION IN THE ELDERLY

- 76 subjects completed the trial 3 months post-surgery.
- Subjects who received modafinil pre and post operatively showed better scores in Trail Making Test (TMT) and Rey Auditory Verbal Learning Test (RAVLT) preoperatively as well as in the immediate postoperative period.

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Ronak Desai • Kinjal Patel • Sandeep Krishnan • Ludmil V. Mitrev • Keyur Trivedi • Marc Torjman • Michael

Goldberg Postoperative Cognitive Dysfunction in the Elderly: A Role for Modafinil PMID: 35891830

PMCID: [PMC9306402](#) DOI: [10.7759/cureus.26204](#)



# META-ANALYSIS FOR MODAFINIL IN OSA

- Modafinil was used to treat residual sleepiness despite continuous positive airway pressure in obstructive sleep apnea (res-OSA).
- 1466 patients were included in the study.
- Modafinil improved the Epworth Sleepiness Scale score by 2.2 and the Maintenance of Wakefulness Test over placebo by 3 min.
- Modafinil and armodafinil improve subjective and objective daytime sleepiness in res-OSA.

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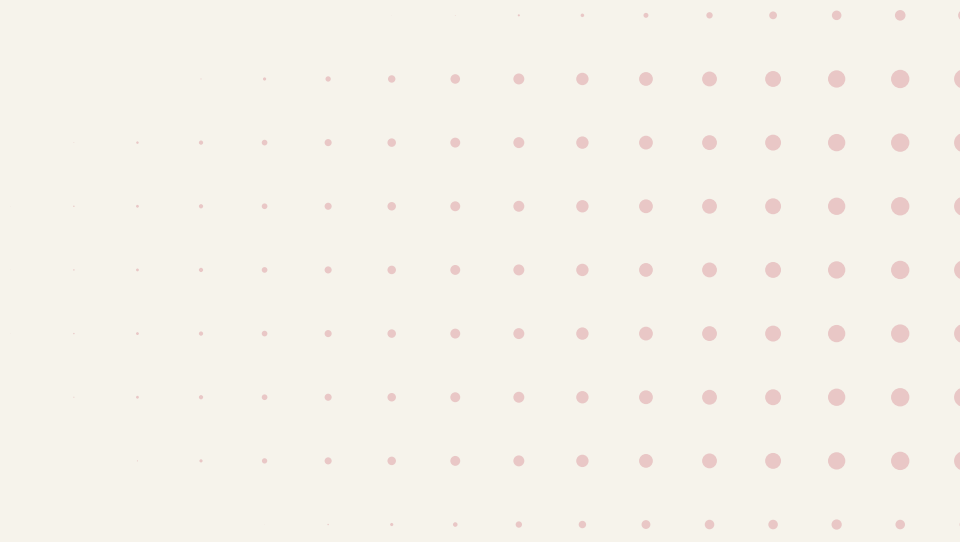

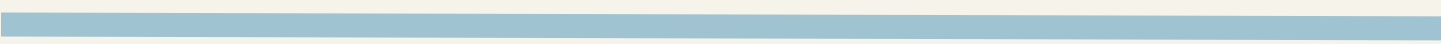
Julia L. Chapman, Andrew Vakulin, Jan Hedner, Brendon J. Yee, Nathaniel S. Marshall

European Respiratory Journal 2016 47: 1420-1428; DOI: 10.1183/13993003.01509-2015



# **SHEDDING THE LIGHT**

**It is possible that modafinil has potential benefits when administered to certain critically ill patients categories:**

- **Hypoactive**
  - **Lethargic**
  - **Depressed**
  - **Conservative treatment has failed**
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# MORE RESEARCH

**Further evidence** from prospective  
randomized trials is still needed.



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**THANK YOU**