

New York-Presbyterian Hospital  
Department of Public Affairs • 525 East 68<sup>th</sup> Street, Box 144  
New York, New York 10021 • Telephone: 212-821-0560

Weill Medical College of Cornell University

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Contact: Jonathan Weill 212-821-0566; [jweill@med.cornell.edu](mailto:jweill@med.cornell.edu)  
Or Camille Tibaldeo 212-246-6543; [cammillebuzz@yahoo.com](mailto:cammillebuzz@yahoo.com)

**New York-Presbyterian Hospital-Weill Medical College of Cornell University**  
**ENADAlert® (NADH), A NUTRITIONAL SUPPLEMENT,**  
**IMPROVED ASPECTS OF COGNITIVE PERFORMANCE**  
**FOLLOWING SLEEP DEPRIVATION**

White Plains, N.Y. Researchers in the Sleep-Wake Disorders Center, New York Weill Cornell Medical Center, tested the ability of oral stabilized NADH\* (ENADAlert) to improve alertness, mood, and performance on cognitive (thinking) tasks in 25 healthy middle-aged adults after one night of total sleep deprivation. In previously published clinical studies, NADH has been shown to increase energy and alertness in adults with Chronic Fatigue Syndrome<sup>1</sup> and to reduce the effects of jet lag on cognitive performance and sleepiness<sup>2</sup>.

Sleep deprivation is a common problem affecting most people during adulthood. It impacts otherwise healthy individuals who cross time zones, work during evening or nighttime hours, or have infant children, as well as patients with sleep disorders, certain psychiatric disorders, and medical conditions such as those that produce a chronic pain. Sleep deprivation can lead to declines in cognitive performance, impacting the quality of waking time and, if severe enough, can lead to vehicle collisions and occupational consequences.

In this double-blind crossover study, subjects performed significantly better on some measures of cognitive performance following one night of total sleep deprivation when they received the NADH supplement compared to placebo. In Particular, overall performance efficiency (number of correct answers per minute) measured one hour after consuming 20 mg of sublingual NADH was significantly higher than after placebo. In a second analysis, math throughout visual sequence comparison speed and throughput were themselves significantly better following NADH. Self-reported alertness, sleepiness (both self-reported and objectively quantified), and mood did not differ when the subjects consumed NADH or placebo. Although several subjects reported typical effects of total sleep deprivation, no adverse effects were attributed to NADH.

This study is among the first to rigorously evaluate a non-prescription substance other than stimulants, like caffeine, for alleviating the effects of sleep deprivation. Dr. Margaret Moline, the lead researcher and Director of the Sleep-Wake disorders Center at the Westchester Division of New York-Presbyterian Hospital in White Plains, states, "NADH is the first non-stimulant, non-herbal product to show signs of improved cognitive performance, despite normally reported increased sleepiness and fatigue following sleep deprivation. These results suggest that NADH may have an important role to play in mitigating some of the effects of unavoidable sleep deprivation."

**REFERENCES:** \*Coenzyme; *nicotinamide adenine dinucleotide hydrogen*

(1) Forsyth LM, Preuss HG, MacDowell AL, Chiazze L, Birkmayer GD, Bellanti JA. Therapeutic Effects of oral NADH on the symptoms of patients with chronic fatigue syndrome. Annals of Allergy Asthma & Immunology 1999, 82:185-191.

(2) Kay GG, Viirre E, Clark J. Stabilized NADH as a countermeasure for jet lag: Abstract presented and published in the proceedings of the 48<sup>th</sup> International Congress of Aviation and Space Medicine, September 2000.

**This study was sponsored by Menuco Corporation.**

## Effectiveness of NADH in Alleviating Effects of Sleep Deprivation in Healthy Middle-Aged Adults\*

Moline ML, Rebeta JL, Flye BL, Zendell SM, Broch L, Ford T, Zak R, Kay GG (2)

(1) Sleep-Wake Disorders Center, Department of Psychiatry, New York Presbyterian Hospital-Weill Medical College of Cornell University

(2) Department of Neurology, Georgetown University School of Medicine

### STUDY ABSTRACT

**Aims:** Sleep deprivation affects cognitive performance and quality of life. It impacts otherwise healthy individuals who cross time zones, work shifts, or have certain sleep, psychiatric, or medical disorders. Despite manufacturers' claims, few over-the-counter substances have been shown in rigorously designed studies to improve daytime alertness following sleep deprivation.

We tested the ability of oral stabilized NADH (ENADAlert®, a nutritional supplement) to improve alertness, mood, and performance on cognitive tasks in middle-aged subjects after one night of total sleep deprivation. NADH has been shown to increase subjective measures of energy in Chronic Fatigue Syndrome<sup>1</sup>. NADH has also been shown to reduce the effects of jet lag on cognitive performance and sleepiness<sup>2</sup>.

**Methods:** A double blind placebo-controlled, randomized crossover study involving 25 healthy men and women ages 40-59 was conducted. Subjects were screened for medical, psychiatric, and sleep disorders and then underwent baseline cognitive assessment using a computerized battery (described below). On the baseline test day, subjects consumed sublingual placebo and had electrodes placed to stimulate experimental conditions. They returned for one night of enforced, polygraphically-monitored wakefulness followed by morning consumption of sublingual NADH (ENADAlert 20mg) or placebo determined randomly. During the day, cognitive testing, mood assessment (Profile of Mood States), and assessment of subjective (Stanford Test – 3 naps) were performed. The complete CogScreen-Aeoromedical Edition (CogScreen-AE) computerized cognitive battery assessed attention, memory, and throughput (correct responses/minute), accuracy, and speed (median reaction time to correct responses). All variables with sufficient data were combined in summary measures; two were discarded.

**Results:** Cognitive performance as assessed by overall throughput was significantly better ( $p=.018$ ) following NADH than after placebo, after readjusting for baseline performance. Analysis of individual cognitive tests revealed that math throughput and visual sequence comparison throughput were significantly better following NADH (math throughput,  $p=.023$ ; visual sequence comparison throughput,  $p=0.032$ ; see figures). Overall accuracy and speed were not different between conditions. Subjective measures of sleepiness and mood and polygraphically recorded sleep latency did not differ between conditions. Although several subjects reported typical effects of total sleep deprivation, no adverse effects were reported.

**Conclusions:** This study is among the first to rigorously evaluate a non-prescription substance, aside from stimulants, for sleep deprivation. NADH is the first non-stimulant to show enhancement of cognitive performance following acute sleep deprivation. On the other hand, NADH did not reduce daytime sleepiness or enhance mood. NADH may have an important role to play in mitigating the effects of unavoidable sleep deprivation.

**References:**

(1) Forsyth LM, Preuss HG, MacDowell AL, Chiazze L, Birkmayer GD, Bellanti JA: Therapeutic effects of oral NADH on the symptoms of patients with chronic fatigue syndrome. Annals of Allergy Asthma & Immunology 1999, 82:185-191.

(2) Kay GG, Viirre E, Clark J. Stabilized NADH as a countermeasure for jet lag. Abstract presented and published in the proceedings of The 48<sup>th</sup> International Congress of Aviation & Space Medicine, September 2000.

\*Moline ML, Rebeta JL, Flye BL, Zendell SM, Broch L, Ford T, Zak R, Kay GG. Effectiveness of NADH in Alleviating Effects of Sleep Deprivation in Healthy Middle Aged Adults. Abstract presented and published in the proceedings of The First International Conference on Mechanisms of Action of Nutraceuticals, October 2001.

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**Please send Correspondence to:**

Maragaret L. Moline, Ph. D., Director  
Sleep-Wake Disorder Center  
Department of Psychiatry  
New York Weill-Cornell Medical Center  
White Plains, NY 10605  
(914) 997-5863 [mmoline@med.cornell.edu](mailto:mmoline@med.cornell.edu)

