

## **Sleep, modafinal, and questions about our capacity to change human behavior**

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Must humans sleep? Can we do without it? These questions become relevant as an increasing number of prescriptions are written for modafinal, a drug that allows people to delay sleep and decrease nighttime sleep with seemingly no side effects. But, cautions one sleep expert, the long-term effects of modafinal have not been studied. It may be wisest to proceed cautiously when tinkering with something that the human body appears to desperately need.

Helene A. Emsellem, M.D., described the properties of sleep and of the drug modafinal at a September 12th lecture sponsored by the Dialogue on Science, Ethics, and Religion (DOSER), a program of the American Association for the Advancement of Science (AAAS). Emsellem is medical director of the Center for Sleep & Wake Disorders in Chevy Chase, Maryland.

The sleep doctor listed the problems that occur from lack of sleep including inattentiveness, irritability, edginess, delays in auditory, visual, and motor reaction time, impaired memory function, tremors, and loss of motor stability. Another little-understood response from lack of sleep is the increasing sensation of sleepiness. A sleep-deprived person will experience sudden, fraction-of-a-second bursts of sleep.

It is believed that most people require seven to nine hours of sleep in a regular pattern. To be restorative, sleep must occur in several stages. From a relaxed “alpha” wake state, a sleeping person moves through four stages in which brain waves steadily slow down. People who are disturbed during slow-wave sleep are likely to wake up in the morning aching and feeling tired.

Another key part of sleep is the rapid eye movement stage, or REM. Dreaming, the formation and storage of memories, and learning all occur during REM sleep.

Very little research has been done with humans to learn the effects of going for long periods without sleep. From studies with rats forcibly kept awake, it appears that sustained sleep deprivation disrupts the proper functioning of various complex and multi-synaptic pathways. Rats kept awake for several days begin to overeat yet lose weight. They become debilitated and then die of massive infection.

Modafinal is unrelated to other chemicals that induce wakefulness such as amphetamines, dexadrine derivatives, methylphenidates (such as Ritalin), methylxanthine (the substance found in caffeine and chocolate), and antihistamines.

The largest study on modafinal involved 358 subjects with narcolepsy. For these patients, modafinal improves alertness without disrupting regular nighttime sleep. Studies indicate that the drug also improves alertness for persons suffering from other

fatigue-inducing health problems such as multiple sclerosis, obstructive sleep apnea, Parkinson's disease, and shift work sleep disorder.

Many clinical studies on subjects without narcolepsy support the conclusion that modafinil improves wakefulness for up to 64 hours and perhaps longer. Subjects treated with modafinil perform better on subjective measures of mood compared to subjects receiving the placebo, and they performed better on simple tasks.

The biggest side effects appear to be headache and nausea. Other infrequent side effects include infection, diarrhea, jitteriness, and suppression of appetite. Side-effects from long-term use are simply unknown. Emsellem pointed out that most studies conducted to date have included very few subjects — in the neighborhood of a dozen or less — and they have followed subjects for a short period, from around 30 to 80 hours, following a single dose. “There is no data on multiple use over periods of time,” she emphasized.

Audrey Chapman, director of the Science and Human Rights program at AAAS, and previous director of the DOSER program, provided a response to Emsellem's presentation. Chapman suggested that a neuropharmacological revolution has begun and modafinil is simply one drug among many leading us to question our assumptions about human behavior and our ability to manipulate it.

Chapman noted that a fundamental principle in medical ethics is to do no harm, yet “the ability to develop substances that alter human functioning has proceeded faster than our ability to understand how those substances work.” She suggested that what may be needed is a new approach to drug testing: testing not only for a drug's therapeutic purposes but also for “off-label” uses.

She cited two drugs — Prozac and Ritalin — as evidence for the need for this kind of testing. Both were introduced for therapeutic reasons (to treat depression and attention deficit disorder, respectively) and both are now being used for non-therapeutic reasons (to make normal people feel better about themselves and to boost focus and energy).

A similar profile may emerge for modafinil, she asserted. Only 125,000 to 200,000 people in the U.S. suffer from narcolepsy. Manufacturers of this drug may be tempted to market to a broader population, she said.

Chapman concluded by posing a list of questions rising from the non-therapeutic use of drugs, including:

“Who is likely to use these agents, under what circumstances, and with what implications?

“What will it mean to society and to individuals to increasingly medicalize behavior?

“Will such a trend reduce a sense of responsibility?

“Will modafinil be employed for social control or engineering purposes?

“Will it change our sense of what constitutes normality in human beings?

“Will the availability of modafinil become an issue of justice and equality of opportunity?

“Finally — am I, like other ethicists, over-reacting?”