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Modafinil as a cognitive enhancer

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Modafinil is a drug originally used to treat narcolepsy and sleep disorders, that has become more and more popular for off-label use as a cognitive enhancer. Modafinil is of particular interest, because its mechanism of action is largely unknown, yet it is overall considered to be a relatively safe drug with very low abuse potential. The advent of a "risk-free" "smart" drug raises many interesting social and ethical questions, striking right at the heart of Science, Technology, and Society. Modafinil use has increased dramatically in the past few years, and it's not because of a spike in narcoleptics. In 2004, Cephalon, the only company producing modafinil in the U.S. at the time, reported that 90% of prescriptions for modafinil were for "off-label" uses, such as fatigue, sleepiness, and attention deficit disorder (O'Connor, 2004). A 2013 study used data from the National Ambulatory Medical Care Survey and looked at modafinil use in patients rom January 1, 2002, through December 31, 2009. They found:

> The number of patients receiving modafinil increased almost 10-fold during the study period, from 57,768 in 2002 to 555 691 in 2009. On-label use increased by less than 3-fold, whereas off-label use increased more than 15-fold (Figure). Across all years, 89% of patients prescribed modafinil did not have an on-label diagnosis.
>
> The results strongly suggest that off-label indications are responsible for a large share of prescriptions given that patients receiving modafinil without an on-label diagnosis increased by 15-fold while those with an on-label diagnosis increased by only 3-fold. (Penaloza et al. 2013)

While they were looking at just a subset of the population, just ambulatory patients, this is still a very significant number – enough that the researchers deemed it "a nationally representative sample." It's clear that the dramatic growth in modafinil use and production cannot be attributed to more narcoleptic people alone. But modafinil isn't the only prescription drug seeing an

increase ins usage for off-label cognitive enhancement. A 2016 study found that from 2005 to 2011, in adults use of Adderall without a prescription rose 67%, and Adderall-related emergency visits rose 156%, and that of all Adderall nonmedical use, 60% was among 18 to 25-year-olds (Chen et al. 2016). This is a broader rising societal trend, with particular relevance for college students, academics, and white-collar professionals. We live in an increasingly global, connected, competitive, information-based society. With that, brings new challenges and situations that our parents and grandparents never had to face. In this context, a drug like modafinil could raise numerous important ethical and social issues to consider.

This thesis aims to first provide an overview of modafinil from a scientific perspective as well the social circumstances surroundings its off-label use for cognitive enhancement, and then address some of the major ethical questions surrounding modafinil, as well as cognitive enhancement in general. Modafinil has yet to reach the same mainstream awareness as drugs like Adderall and Prozac, so it is especially important to establish a baseline level of understanding possible before assessing the ethical issues. The first chapter will provide the scientific context, relying mostly on scientific publications and showing science's current understandings, as well as the progression for how research around modafinil has evolved since its discovery. The second chapter will introduce people's experiences, using modafinil specifically as a cognitive enhancer. These accounts will be from non-narcoleptic, otherwise healthy individuals, who used modafinil specifically to perform better in school or at their job. With the first two chapters providing a foundation, the third and final chapter will dive into some of the major tensions of a "smart" drug. Questions include, "What is the individual cost/benefit analysis of using modafinil? Is "enhancement" ethical? Where is the line between treatment and enhancement? What does it mean for a drug or technology to be "natural" or "unnatural?" And what makes

modafinil different, or potentially less ethical, than any other form of socially accepted technologies for enhancement, whether it's a drug like caffeine, or something like electricity or education?

My main argument is that because modafinil has a positive benefit-risk ratio with limited potential societal harm, that cognitive enhancement itself is not unethical, and that we should have more research into modafinil's usage as a cognitive enhancer in otherwise healthy people especially in the long term, as well as think about allowing the use of modafinil as a cognitive enhancer.

Chapter 1: Overview of the Scientific Research on Modafinil

This chapter will provide an introductory scientific background for understanding modafinil. I will address what modafinil does, how it works, and any safety concerns and abuse potential. First, an important disclaimer on the purpose of this chapter. The purpose is to introduce modafinil, from a scientific perspective, to someone completely new to it. It is not to create the ultimate scientific review article. Existing review articles have already done so far better than I could, and the science behind modafinil is just one part of my overall thesis. This chapter uses a mix of primary studies as well as review articles and secondary research referencing those studies.

History of modafinil

Modafinil is a drug used to treat narcolepsy and shift-work sleep disorder, and has become increasingly popular for off-label usage as a cognitive enhancer. It was first discovered in the late 1970's by French scientist Michel Jouvet (Guglietta, 2015). It was approved by the Food and Drug Administration (FDA) for treating narcolepsy in 1998 and for shift work sleep disorder in 2003 (Ballon et al. 2006). It was marketed by Cephalon under the brand name Provigil (Dubljevic, 2016). Narcolepsy is characterized by uncontrollable "sleep attacks" and an inability to control one's sleep-wake cycles (Narcolepsy Fact Sheet). Shift-work sleep disorder is "excessive sleepiness caused during night shifts and insomnia when trying to sleep during the daytime (Neubauer 2006). In the U.S., modafinil is a Schedule IV drug (Myrick et al. 2004), which means that it is only legally available by prescription. The U.S. Schedule of Controlled Substances describes Schedule IV drugs as:

A. The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule III.

B. The drug or other substance has a currently accepted medical use in treatment in the United States.
C. Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III.

For context, the other most commonly known schedule IV drug is Xanax, and schedule III drugs include anabolic steroids and the anesthetic ketamine (U.S. Code).

What are its effects?

The Physicians' Desk Reference, as well as the 2015 drug insert for Provigil from Teva Pharmaceuticals, reference the same clinical trials to establish modafinil as an effective treatment for narcolepsy, obstructive sleep apnea, and shift work sleep disorder. For narcolepsy, there were two 9-week parallel randomized, placebo-controlled, multi-center, double-blind clinical trials, for a total of 558 patients who met the criteria for narcolepsy. Both studies used two tests, the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test, as their main assessments, and reached similar conclusions: "The data indicate that modafinil has an excellent safety profile and is very well tolerated. Modafinil is an effective treatment for excessive daytime sleepiness in narcolepsy and shows continued efficacy with up to 9 weeks of daily use" (Randomized 2000), and

> Modafinil significantly reduced all measures of sleepiness and was associated with significant improvements in level of illness. Medication-related adverse experiences were few, dose-dependent, and mostly rated mild to moderate. Modafinil taken once daily was a very well tolerated and effective wake-promoting agent in the treatment of excessive daytime somnolence associated with narcolepsy. Modafinil demonstrated an excellent safety profile for up to 40 weeks of open-label treatment and efficacy was maintained,

> suggesting that tolerance will not develop with long-term use. Modafinil is a pharmacologically and clinically promising compound for the treatment of pathological daytime somnolence. (Randomized 1998)

Modafinil also showed significant improvement for obstructive sleep apnea (OSA) through two clinical trials, a 12-week multicenter randomized placebo-controlled study with 327 patients (Schwartz et al. 2003), and a 4-week multicenter randomized placebo-controlled with 157 patients (Pack et al. 2001). All the patients met the International Classification of Sleep Disorders (ICSD) for OSA. For shift-work sleep disorder (SWSD), a 12-week randomized placebo-controlled clinical trial showed significant improvements in 209 patients with chronic shift-work sleep disorder (Erman et al. 2007). All patients met the ICSD for SWSD, were required to work a minimum of 5 night shifts a month, and were tested with the MSLT test for sleep latency.

In numerous studies, modafinil has been shown to be a very effective and safe treatment for narcolepsy and sleep disorder, due to its powerful wakefulness-promoting effects (Ballon et al. 2006) (Czeisler et al. 2005), even over extended use (Moldofsky et al. 2000). Its effects have also been studied in non-narcoleptic, "healthy" patients. In a helicopter simulator, pilots kept awake for 40 hours performed significantly better when they were given three 200 mg doses of modafinil rather than a placebo (Caldwell et al. 2000). Sleep-deprived doctors who were given modafinil scored high on tests on working memory, planning, and attention (Sugden et al. 2012). Modafinil does not allow for indefinite, 100% optimal function without sleep, however, as one study concluded that "repeated doses of modafinil were unable to prevent deterioration of cognitive performance over a longer period of sleep deprivation though maintaining wakefulness and possibly even inducing overconfidence in a person's own cognitive performance" (Repantis,

2010). A clinical study in patients with multiple sclerosis (who were screened to exclude those that were taking medication affecting fatigue and had diagnoses for narcolepsy, sleep apnea, or similar diseases) showed significant improvements in fatigue (Rammohan et al. 2002). Due to its effectiveness in improving performance in sleep-deprived and/or fatigued subjects, modafinil sparked an interest in its potential as a cognitive enhancer. The question was whether modafinil had any cognitive benefits besides just keeping people awake. Researchers wanted to see if modafinil could improve performance in non-sleep deprived, "healthy" people.

The results have been mixed. The general consensus is that at best, modafinil slightly improves performance in certain areas of cognition, while having insignificant or slightly negative effects on others. The study "Cognitive enhancing effects of modafinil in healthy volunteers" found that modafinil "significantly enhanced performance on tests of digit span, visual pattern recognition memory, spatial planning and stop- signal reaction time," but that "These performance improvements were complemented by a slowing in latency on three tests: delayed matching to sample, a decision-making task and the spatial planning task" (Turner et al. 2003). In 2004, Muller et al. tested 16 healthy volunteers with tests on working memory, and found that the group given modafinil significantly outperformed the placebo group in some tests, but had no effect in other tests, as well as no significant differences in reaction times. They concluded that "In healthy volunteers without sleep deprivation modafinil has subtle stimulating effects on maintenance and manipulation processes in relatively difficult and monotonous working memory tasks, especially in lower performing subjects." Randall et al. 2005, in their study "Does Modafinil Enhance Cognitive Performance in Young Volunteers Who Are Not Sleep-Deprived?", tested 60 healthy volunteers in a double-blind study with either a placebo, 100 mg, or 200 mg of modafinil. Again, they found that modafinil improved some areas such as

pattern recognition while having no significant effect on others, concluding that "those from 100 mg are limited to the span of immediate verbal recall and short- term visual recognition memory, which is insufficient for it to be considered as a cognitive enhancer in non–sleep-deprived individuals" and that overall the 200 mg group did not perform significantly better than the 100 mg group. Similarly, another review observed a "relatively weak pooled effect of modafinil on some aspects of cognitive performance in normal, rested adults" (Kelley et al. 2012).

In 2015, in their review "Modafinil for cognitive neuroenhancement in healthy non-sleep-deprived subjects: A systematic review," Battleday et al. "reviewed all resultant primary studies in English from January 1990 until December 2014 investigating the cognitive actions of modafinil in healthy non-sleep-deprived humans," and came to the following conclusions:

> We found that whilst most studies employing basic testing paradigms show that modafinil intake enhances executive function, only half show improvements in attention and learning and memory, and a few even report impairments in divergent creative thinking. In contrast, when more complex assessments are used, modafinil appears to consistently engender enhancement of attention, executive functions, and learning.
>
> Importantly, we did not observe any preponderances for side effects or mood changes.

Yet even their finding that modafinil was beneficial in "more complex assessments" was soon tested. Shortly after the review, Fernandez et al. in 2015 conducted the largest study on modafinil to date, with 160 volunteers in a double-blind study. Based on a battery of cognitive tests, they concluded that:

> The study demonstrated that modafinil does not enhance the global cognitive performance of healthy non-sleep deprived students, except regarding non-demanding tasks. In particular, this drug does not seem to have positive effects on mental processes

that sustain studying tasks in the college population under normal conditions. We expect these findings to demystify the use of this drug and help decision making concerning pharmacological public policies.

While modafinil clearly works as a wakefulness-promoting agent, science still haven't arrived at a consensus as to how effective modafinil is in terms of cognitive enhancement. Most agree that modafinil does have an effect, but they disagree to what degree modafinil helps, and for which kinds of tasks. Even in sleep-deprived subjects, Wesenten et al. 2001 found that modafinil was no more effective than caffeine in maintaining performance and alertness. A general consensus might be that modafinil is far from an end-all-be-all smart drug, and at best, provides wakefulness and slightly increased performance for certain kinds of work.

How does it work in the brain?

Modafinil has a unique mechanism of action that is not yet completely understood. The Physicians' Desk Reference states, "Modafinil has wakefulness promoting actions similar to sympathomimetic agents like amphetamine and methylphenidate, although the pharmacologic profile is not identical to that of sympathomimetic amines. Modafinil has weak to negligible interactions with receptors for norepinephrine, serotonin, dopamine, GABA, adenosine, histamine-3, melatonin, and benzodiazepines." Researchers have found that while modafinil does affect several different compounds, the effects are unclear, tenuous, and not well understood (Minzenberg et al. 2008). Ballas et al. 2002 captured this frustration in the statement, "The precise mechanism of action of modafinil is unknown, and some preclinical information appears contradictory."

Much of the research on modafinil's mechanism of action has focused on its relationship with dopamine. Dopamine is the "feel-good" neurotransmitter. Our brains emit dopamine from

food, sex, and stimulants such as caffeine, ADHD medication, and cocaine, and drugs that affect dopamine levels have high potential for abuse and addiction (Psychology Today). Thus, it is critical to understand modafinil's effects on dopamine in order to assess its abuse potential. Similar pharmacological stimulants, such as Adderall and Ritalin, mainly act as dopamine reuptake inhibitors. This means that they increase the concentration of dopamine in the synapses by preventing the dopamine transporter, DAT, from shuttling dopamine out. Ballon et al. 2006 states that "the mechanisms underlying modafinil's clinical effects are complex and distinct from other known wakefulness agents," which "work as sympathomimetic drugs that increase levels of norepinephrine, serotonin, and dopamine by blocking reuptake and stimulating release at the presynaptic terminals."

The understanding of modafinil of how modafinil affects dopamine has changed over the years. In 1994, Mignot et al. published the first study linking modafinil to dopamine. They found that modafinil did bind to a dopamine reuptake site with "low affinity," but commented that "it is likely that dopamine uptake inhibition alone does not explain the potency of modafinil as a stimulant compound." A 2002 review stated that "the wakefulness promoting factor of modafinil is not blocked by dopamine blockers," and that "unlike the amphetamines or Ritalin, modafinil does not produce the rhythmic, purposeless movements that are very common in those with excess dopamine movements that are very common in those with excess dopamine states. Thus, while modafinil does have a weak interaction with the dopamine uptake site, it is unclear how this action influences its overall activity and pharmacology" (Ballas et al. 2002).

In 2009, in response to the general attitude that modafinil had minimal to no effects on dopamine and therefore had almost no abuse potential (Myrick et al. 2004), Volkow et al. published the first significant study to unequivocally link modafinil to dopamine. They were

specifically interested in researching modafinil, in the context of its use as a cognitive enhancer in otherwise healthy people. They found that "modafinil blocked dopamine transporters and increased dopamine in the human brain (including the nucleus accumbens), and stated that "Because drugs that increase dopamine in the nucleus accumbens have the potential for abuse, and considering the increasing use of modafinil, these results highlight the need for heightened awareness for potential abuse of and dependence on modafinil in vulnerable populations." More studies in 2009 (Zolkowska), 2013 (Federici) and 2014 (Okunola-Bakare) found evidence that modafinil interacted with DAT sites in the brain, but that it did so uniquely from stimulants such as cocaine and amphetamines (2014 Oluyomi). The general consensus is that "modafinil is an exceptionally weak, but apparently very selective, DA transporter inhibitor" (Wisor 2013). A 2016 review describes: "All in all, the mechanisms underlying modafinil's neuromodulatory effects are complex and somewhat different from older stimulant drugs such as methylphenidate and amphetamine, potentially incorporated extracellular and intracellular effects" (Dubljevic, 2016).

Side effects, safety, and abuse potential

Overall, modafinil is a relatively safe, well-tolerated drug with limited abuse potential (Minzenberg et al. 2008). Ballas et al. 2002 stated that regular doses of 200 mg to 600 mg are well tolerated, and that it was even safe in overdose, with patients taking 1200 mg/day for 21 days. In addition, they referenced a study where patients did not experience any dependence upon discontinuation after taking up to 400 mg/day for 9 weeks. Taking all this into account, as well as the fact that modafinil cannot be smoked or injected due to its chemical properties, they concluded that "modafinil is unlikely to have any significant abuse potential." Turner et al. 2003 found that health subjects showed no significant difference in test performance between shows

not dose-dependent when given either 100 or 200 mg of modafinil. A lack of dose-dependency is important, because there is less incentive for overdose and abuse. The Teva 2015 drug insert recommended a maximum dosage of 200 mg a day, and that 400 mg was well tolerated but that there was no consistent evidence for benefit beyond 200. Regarding dependence issues, they reference a placebo-controlled clinical trial, which showed no reported withdrawal symptoms in modafinil use in narcoleptic patients.

It is important to put modafinil's effects on dopamine into perspective. Volkow et al. 2009 had stated that the purpose of the study was simply to highlight that modafinil did in fact dopamine, and that therefore its abuse potential should not be disregarded. They even acknowledged that "modafinil is much less potent as a reinforcer than stimulant drugs, and reports of modafinil abuse are rare and much less frequent than those for stimulant drugs." Modafinil's effects do not lend themselves to recreational use for a "high." Just because modafinil may affect dopamine, does not mean that it is suddenly abusive, because it is important to consider the degree to which modafinil increases dopamine levels. Another reason modafinil has limited abuse potential is because its effects do not lend themselves to abuse. Myrick et al. 2004 reported that "In general, in over four years of surveillance, this group has not detected any generalized or persistent misuse or abuse of modafinil. In internet discussions about abuse/misuse, the drug was discussed as not worthwhile, boring, or a 'bust.'" Its effect on dopamine is much subtler compared to stimulants like ADHD medication, and it has little to no effects on mood (Battleday et al. 2015).

There are some safety concerns. Other than relatively minor potential side effects, such as headaches, nausea, anxiety, hypertension, and insomnia (DailyMed), there have been some rare cases of serious and life-threatening skin reactions, including Stevens-Johnson syndrome (SJS),

erythema multiforme EM), and toxic epidermal necrolysis (TEN). A 2007 product report by Cephalon, the manufacturer of modafinil at the time, stated that "No serious skin rashes have been reported in adult clinical trials (0 per 4,264) of modafinil." However, between December 1998 and January 30, 2007, the FDA received six cases of these skin reactions as a result of modafinil use, with no deaths (Postmarketing, 2007). Still, the cases are extremely rare, and while "The reporting rate of TEN and SJS associated with modafinil use, which is generally accepted to be an underestimate due to underreporting, exceeds the background incidence rate," "Estimates of the background incidence rate for these serious skin reactions in the general population range between 1 to 2 cases per million-person years" (Modavigil 2007)." Due to concerns over skin reactions, it not approved for use in children:

> Serious rash requiring hospitalization and discontinuation of treatment has been reported in adults and children in association with the use of modafinil. Modafinil is not approved for use in pediatric patients for any indication. In clinical trials of modafinil, the incidence of rash resulting in discontinuation was approximately 0.8% (13 per 1,585) in pediatric patients (age <17 years); these rashes included 1 case of possible Stevens-Johnson Syndrome (SJS) and 1 case of apparent multiorgan hypersensitivity reaction. Several of the cases were associated with fever and other abnormalities (e.g., vomiting, leukopenia). The median time to rash that resulted in discontinuation was 13 days. No such cases were observed among 380 pediatric patients who received placebo.

While these are very serious reactions, they still appear to be extremely rare. Finally, while there are some studies which have looked at modafinil's long-term effects in narcoleptic patients, and found that modafinil had very few safety issues and was well-tolerated (Bastuji et al. 1988) (Mitler et al. 2000), they are outdated and focused on narcoleptic patients. There is a lack of

recent research concerning the safety of long-term modafinil use in healthy patients. According to the Physician's Desk, "The effectiveness of modafinil in long-term use (greater than 9 weeks in Narcolepsy clinical trials) has not been systematically evaluated in placebo-controlled trials. The physician who elects to prescribe PROVIGIL for an extended time in patients with Narcolepsy, OSAHS, or SWSD should periodically reevaluate long-term usefulness for the individual patient" (974). The main open questions are long-term safety in healthy patients, its effects on brain plasticity, and further understanding its mechanisms of action.

Chapter 2: The experiences of everyday people with using modafinil for off-label cognitive enhancement

This chapter will examine first-hand experiences from people using modafinil as a cognitive enhancer, in order to better understand the sociology around its use. Understanding the social context, in tandem with the scientific understanding from the previous chapter, will provide the necessary groundwork for understanding modafinil, from an ethical perspective, in the next chapter.

First, I must address the sources used for these first-person accounts. One of the biggest challenges was the shortage of "reputable" sources for people taking modafinil for cognitive enhancement. While there was no shortage of forum posts, blogs, and sites set up to sell modafinil online (illegally), I tried to stick to websites that had at least some established name – first-person accounts from Vice Media make up the majority of what I used. Part of the difficulty in finding first-person accounts is that modafinil is not approved by the FDA for use as a cognitive enhancer, and is illegal to obtain without a prescription. Although modafinil can be prescribed for off-label use, many of those looking to use it as a cognitive enhancer choose to order it online illegally, in order to avoid a prescription. Ordering it online is significantly cheaper than through a pharmacy, and alarmingly easy to do for a controlled substance (Kolker, 2013; Renton, 2016). There is also the problem of selection bias in those who post these accounts. Not everyone who takes modafinil for cognitive enhancement posts online, and those who do, might not be a good representation of the overall population. Those who do post may be those who had particularly positive/negative experiences, which can create an unbalanced and skewed perspective.

Despite these shortcomings, these sources offer a unique value proposition. While their medium and tone may be less formal than those of an academic journal, they provide a chance to show the personal side, and for real people to talk about their experiences. Additionally, the cognitive "tests" used in the scientific studies have little resemblance to real-world work. While abstract pattern-recognition and memory tests may provide a benchmark for understanding cognitive performance, they are no substitute for examining modafinil's use in the context of day-to-day work outside of a lab, with all of its complexities and external factors. These especially important to consider, when trying to make a broader argument within the context of STS. For example, in his discussion on laboratories in *The Pasteurization of France*, Bruno Latour emphasizes a critical quote from Pasteur: "Outside their laboratories, the physicists and chemists are unarmed soldiers in the battlefield" (Latour, 73). The crucial element of laboratories is control, where man finally has the upper hand over nature, where science reigns supreme. But outside the laboratory and in the network, control is limited. While scientists can study modafinil in a controlled lab setting, outside, they cannot unanimously apply what they found in the lab to the complicated network of our society. Overall, user accounts on their experiences with modafinil are very consistent. Here are the main frequently mentioned effects:

It significantly, yet subtly, increases focus. A 2013 article in *The Tab,* a youth UK news site, provides the best summary for modafinil's effects: "It gives you a kind of tunnel vision. You can concentrate for hours on reading a book, taking meticulous notes, not looking up once. You don't eat, you don't really talk to people," also noting that it was "Quite subtle: this isn't an overwhelming experience" (Rivlin, 2014). Interviewed in New York Magazine, Peter Borden, working two jobs in quantitative analysis and high frequency trading for a Wall Street Startup, describes his experiences:

> "Not fuzzy-headed," he says, "but crisp. A crisp softness to it." Soon he was experiencing a level of concentration he'd never imagined. "My senses sort of shifted to the visual, and my auditory sense went down. Sounds didn't even register. It was like walking around on a winter day when it just snowed. It was very easy to stay visually focused." Next came a head rush. "I sensed it was blood actually moving to the optic nerve. Your eyes start to feel very sort of engorged, and your awareness comes to the front of your face, which is kind of a freaky sensation. I would describe it as being very much like Adderall, but without the speediness." (Kolker, 2013)

Peter's comparison, "like Adderall, but without the speediness," matches with the scientific studies about modafinil's mild effect on dopamine, especially compared to ADHD medication and caffeine. Just as Peter compared to modafinil to caffeine, but subtler and more focused, many of the accounts made similar comparisons to caffeine:

> The effects are similar to that of too much caffeine but with some subtle differences. You become very aware of your thoughts and how fast you are typing/your leg is twitching, nothing extreme but noticeable; similar to the initial stages of coming up on coke. These however, are just the effects of your body being sped up; the real effect is related to the subtlety I mentioned earlier. You develop a tunnel vision of sorts, becoming extremely focused on whatever you are doing with little regard for anything else. The best example I can give is that it is now late afternoon and I haven't eaten anything but a banana since 8am; this is the first time the thought of hunger has entered my mind- my brain was simply too focused to think about food. (Maxwell, 2014)

> He likens his experience with Modafinil to downing five coffees in the day, minus the heart palpitations. Rory recounts a day where he slept for four hours, woke up hungover,

took half a tablet, then powered through a 17-hour shift at his part time job, and still slept normally that night. When studying, he says he can hit the books for 12 hours straight on Modafinil without feeling fatigued. "It's not like Ritalin, which is like an amphetamine," he says. "You're not going to retain information when you're getting cooked. Modafinil just makes me really productive." (Do, 2015)

I felt the effects by midday: it was like having a really strong coffee without the edginess. I realized that I didn't want to do anything else that day other than write this piece. I was supposed to be calling my friend at lunch and I was annoyed that I had to do that. I could definitely see how this would be great if you had an essay to write and you had all the research there for you. Other effects: I'm usually ready to chew someone's arm off by 1PM, but I'd lost my appetite completely. My mouth was like a bag of sawdust, no matter how much water I drank. I didn't have any caffeine all day and didn't need it or even think about needing, which is unusual, as it's normally a pretty vital part of my routine. (Vice: Ewens, 2016)

Sonia, 30, is a newly qualified lecturer at a London university. She started using modafinil in 2013 when she was writing her thesis at the same time as teaching and marking. "My thesis involved a lot of data analysis. Before modafinil I could work for six hours, but I would be distracted – looking at my phone, making coffee, going to the toilet. Now I'm able to do 10 hour days and I am more efficient, instead of taking lots of breaks where I lose concentration and the quality of work goes down." (Daly, 2016)

This kind of focus is one of the biggest differentiators between modafinil, and drugs like caffeine and ADD medication, and it might come down to the differences in how they interact with

dopamine. Modafinil is much calmer, smoother, and seems to provide a more appropriate level of focus and attentiveness then the alternatives.

It seems to be especially effective for detail-heavy, "processing" type work that tends to be dull and require more focus. Almost none of the accounts mentioned benefits in terms of creativity or problem-solving. The main benefits seemed to be staying awake, and being able to focus on a pre-determined, often mechanical tasks – tasks which weren't so much cognitively demanding, as they were downright repetitive and "soul-crushing."

> Tasks that were usually soul-crushing now had his undivided attention. He spent hours fine-tuning ad campaigns for his new business, and his output wasn't just faster and longer—it was better. "I didn't take as many breaks; I didn't get as frustrated; the stuff came out with fewer errors," he says. "I never felt, *Oh, let's just get it done.* I polished things." As long as he kept taking the pill, his focus never wavered. "Time took on an entirely different sort of quality." (Kolker, 2013)
>
> My second task of the day was to transfer data mapping out the effects of robberies in Bogotá (by time and location) from a PDF file into an Excel worksheet. That's exactly the kind of mechanical task that usually sends me—an easily distracted person—straight to Facebook. But this time, it was different. Typing cold, flat figures became the highlight of my day, and I felt better and better as I inserted numbers into that worksheet. (Serrano, 2015)
>
> It seems bad to say, but marking essays is quite dull work. It's hard to keep focused and motivated when you've got to your 59th essay answering the same question. But with modafinil it's brilliant. My concentration is phenomenal and my brain never gets tired. My eyes can just skim over the page and I'll take it all in. I'm better at writing comments

– on modafinil I go into serious detail. I get it done twice as quick and I feel cheerful about doing it," says Rachel. (Daly, 2016)

"The pressure of marking is massive on anyone but for me it's worse because I'm dyslexic. No one likes marking, but it took me three times as long as anyone else. I love my job but this was actually the most horrible thing for me. I would read and re-read the same paragraph. I was having a cup of tea every half an hour. Marking sometimes made me want to explode with anger. I would rather do anything else in the world," Will tells me. After a PHD student suggested he use modafinil, Will started taking 100-200mg a day on mornings he was marking. "Suddenly marking became almost a pleasurable thing to do. I couldn't even recognize myself. I can't skim read, but I can read faster now. It helps me memorize what students have written, so my feedback is immensely better. I can write pages of comment, it's much better quality of marking." (Daly, 2016)

The intense level of focus can be too much at times, and can lead to impatience and antisocial tendencies. Modafinil made people much less tolerant of distractions, particularly from others. "Makes you unsociable and even, as your mum might say, 'a bit snappy' when people talk to you (The Tab)." Another writer describes, "Later, my editor asked me to draft someone else's piece and I can't remember the last time I was so irritated. I realized I was growling at the screen" (Ewens, 2016). Skipping meals was another commonly mentioned side-effect. The work can almost become a compulsion:

I was so into my work that I wasn't even that interested in getting lunch when my colleague asked if I felt like pizza, which was quite unusual for me. The day after my initial experiment, I decided to take another pill. The effects were basically the same—pleasure and well-being in the library. Sweating outside. I even decided not to buy a

> water bottle at the cafeteria because I couldn't stand waiting in line. I had another mishap with my bike: This time I just left it and walked to the university. Usually, I love walking, but because of the drug, it suddenly seemed like a complete waste of time. Modafinil may be the least fun drug there is (at least of the ones I've tried), but in the rat race that is modern life, it's sort of the only one that makes sense. (Serrano, 2015)
>
> But Sonia says there are downsides to the unnatural levels of concentration modafinil provides. Sometimes she can sometimes become too focused, spending far too long marking individual essays or rooted like a statue to her chair. The first time she took a pill she was so focused on her screen that she got bad backache because her posture had not moved an inch in three hours. Sometimes the act of eating lunch just passes her by totally unnoticed. (Daly, 2016)

This level of focus, along with the previous bolded section about modafinil being optimal for "processing" type work, suggests that modafinil might not be a one-size-fits-all drug, and might be better suited for a computer programmer than a painter. It also might be detrimental in tasks that require large amounts of collaboration and communication.

The final consistent trend is that the main purpose seems to be for productivity and focus, either to handle a busier schedule or to deal with tedious work, and not as a recreational party drug. As one of the accounts so aptly stated, "Modafinil may be the least fun drug there is (at least of the ones I've tried), but in the rat race that is modern life, it's sort of the only one that makes sense." The reported uses for modafinil have overwhelmingly been for cognitive enhancing purposes, by individuals looking to get ahead with their work – which may suggest that modafinil lacks the dangerousness and abuse potential of drugs used for instrumental recreation or enjoyment. This is important in terms of ultimately weighing the costs and benefits

of considering increased availability and usage of modafinil in otherwise healthy adults, which will be discussed in the next chapter.

Chapter 3: The Ethical Issues Surrounding Modafinil's Use as a Cognitive Enhancer

Before I get into the ethical arguments, I want to clarify my own stance, and clearly set boundaries for what I am arguing for. The first disclaimer I would like to make is that I am not arguing for its deregulation. The previous chapters may have framed modafinil as a relatively safe and effective drug that lends itself to responsible use, and there are some truths to that. However**,** I believe modafinil is a very powerful compound, and that we should in fact not rush to deregulate it and make it more easily available.

First, using an STS perspective and considering the possible use of modafinil in real-world settings outside of the lab, I do not necessarily agree with the scientific community's consensus that modafinil has low abuse potential. My first counter-argument is that modafinil has high potential to be extremely dangerous in recreational settings. The scientific consensus is that modafinil has vey limited abuse potential, but they were only studying modafinil in isolation. Due to its extremely powerful wakefulness effect, modafinil's biggest dangers could be mixing it with other substances during recreational use. Specifically, the danger of combining a stimulant (modafinil, caffeine) with a depressant (alcohol, marijuana etc.). The dangers of combining the two are that the stimulant can mask the effects of the depressant (most commonly alcohol). This can lead to to a false sense of sobriety and alertness, which could lead to increased and dangerous levels of alcohol consumption, and/or a false sense of security and engaging in dangerous activities such as driving or operating heavy machinery.

For example, there has been considerable controversy surrounding alcoholic cocktails containing energy drinks – a 2016 study even found that mixing caffeine and alcohol in mice induced effects similar to cocaine (Robins et al. 2016). In the late 2000's, alcoholic drinks containing caffeine, such as Four Loko, were becoming increasingly popular among partiers,

especially on college campuses, and resulted in a number of blackouts and hospitalizations which resulted in a wave of negative publicity. Several states banned the sale of drinks containing alcohol and caffeine (Storms 2010), and in 2010, the FDA banned all such drinks, calling caffeine an "unsafe food additive" in the drinks and declaring them a "public health concern" (FDA, 2010). Modafinil is a prescription-strength substance, which along with dextroamphetamines has been shown to be effective for sleep-deprived military pilots (Estrada et al. 2012). It has a half-life of 15 hours (Teva, 2015) vs. 5 hours for caffeine (Kim, 2012). Given how powerful modafinil is, it could be exponentially more dangerous than caffeine in this situation. The drug insert from Teva Pharmaceuticals states to physicians, "Advise patients that the use of PROVIGIL in combination with alcohol has not been studied. Advise patients that it is prudent to avoid alcohol while taking PROVIGIL"; and to patients, "You should avoid drinking alcohol. It is not known how drinking alcohol will affect you when taking PROVIGIL."

While there haven't been any studies or concrete empirical evidence of modafinil's adverse reactions with alcohol, there are some anecdotal reports. The *New York Magazine* article referenced in the previous chapter, which covered one Peter Borden, the modafinil-taking New York professional juggling multiple jobs, states:

> For Borden, life on modafinil really did feel like a real-life (if somewhat toned-down) *Limitless.* Things get hairy for the character in the movie—there's addiction and withdrawal and tragedy before the tidy Hollywood ending. The first downside Borden noticed was in line with the film: He couldn't drink. "I went out for a drink, and then I had another drink. And because I was so energized and focused, I got drunk faster. It kind of freaked me out, because time would sort of fly by. I'd be here, and then I'd be here. Almost like mini-blackouts. I very quickly cut out alcohol." (Kolker 2013)

Borden's experiences reflect the expected dangers of mixing stimulants with alcohol – feeling "energized," not feeling alcohol's usual warning signs, and compensating by drinking more. While modafinil may not have as much adverse publicity for dangers and recreational use, as well as just in general, this might be because modafinil is still not widely know and has not permeated into mainstream usage, to the extent of other drugs like caffeine or ADD medication. However, the sheer power of modafinil's wakefulness effects compared to caffeine makes this an important potential societal harm to consider.

The second counter-argument to the scientific consensus, is that people might not become physically dependent, but instead, might become dependent on their new potentially increased productivity, and use modafinil at the expense of their sleep. The drug insert states, "PROVIGIL does not take the place of getting enough sleep" (Teva 2015), yet some might be tempted, at the risk of sleep deprivation and the harmful effects, such as stress responses and impaired immune function (Kim 2012). The lab tests in the scientific studies were assessing modafinil's potential for physical addiction. Drugs with high risk for physical addiction include heroin, cocaine, amphetamines, because they heavily impact dopamine levels. Modafinil may not be addictive physically, but it might be "addictive" in that it might make your work better.

This is an aspect that lab tests, with their abstract cognitive tests, cannot capture. People might not be excited or "addicted" to getting positive results on a memory test – but outside of the lab, they might, for example, experience better focus when grading papers or updating spreadsheets. They then might start getting addicted (or just used to) their new level of productivity and performance, and become reliant on modafinil. Maybe "addictive" is too strong – instead, it might be "habit-forming," and that habit of foregoing sleep could create long-term health problems. Peter Borden ran into problems with dependence:

> Then he ran into an even bigger problem: Skip a dose, and there would be hell to pay. "I really would feel it. It was sort of like being thrust into dirty, messy reality, as opposed to a clean, neatly organized place. It was like crashing, and I actually found what would happen is the anxiety that got dialed down on the way in, when you were coming off it, all of a sudden you went through the reverse. So I got incredibly anxious. Eventually that concerned me." He stopped after three weeks. (Kolker 2013)

His description seems to describe both physical (anxiety) and emotional dependence on modafinil. Modafinil allowed him to focus on his work, and made his mind clear and orderly. Getting used to that, and then being thrust back into the distractions and chaos of the world, would understandably influence someone to keep taking modafinil indefinitely. At the extreme end of this, is someone who takes this repeatedly to stay up multiple days in a row, to work, to study, to party, or perhaps for some college students, all three. This could have significant health dangers. Modafinil might be potentially relatively safe by itself, but to use an STS framework, nothing exists in a vacuum. While I will later argue that becoming "dependent" on standpoint from a results standpoint is not necessarily bad or unethical, the potential for severe sleep-deprivation is still an important health risk to consider in weighing the cost-benefit of loosening restrictions on modafinil usage.

Modafinil's potential for creating social inequity is not as powerful as that of a blanket "smart" drug. However, it is still powerful and does have cognitive enhancing effects in healthy people, which raises ethical issues, especially in our modern 24/7 society. Many of the philosophical and moral/ethical the arguments against "smart drugs" state that they might cause inequities. They warn of a dystopian future where smart drugs are so powerful that people will be forced to take it whether they want to or not, just to survive in such a competitive world. They

entertain thought experiments about smart drugs creating societal rifts and increasing social inequity. Modafinil is far from this universal "smart" drug, but there are still ethical issues to examine.

Modafinil provides a level of focus that might not be ideal for all kinds of work. In *The New Yorker*, Talbot explains: "Cognitive psychologists have found that there is a trade-off between attentional focus and creativity. And there is some evidence that suggests that individuals who are better able to focus on one thing and filter out distractions tend to be less creative." This might be the case with modafinil. While the results in scientific studies are mixed, all the first-person accounts in Chapter 2 talked about the amount of focus they got, and how it was best for certain kinds of work. Specifically, work that was mechanical, usually tedious, left-brain "processing" type work. While this type of work is important, the greatest innovation and progress comes from applying this mechanical mindset and focus, to the ideas spawned from creativity and right-brain thinking. In that sense, modafinil is not a well-rounded or complete "smart" drug ideal for all situations. There are many different kinds of work, beyond dull processing type work, that one must perfect in order to truly excel in their career, and while being good at this type of work is definitely helpful, it will not be the contributing factor to one's success. Furthermore, Chapter 2 mentioned the anti-social effects of this kind of focus. Teamwork and collaboration are incredibly important skills contributing to one's success. In addition, politics and making friendships can play an equally important role in determining one's success in moving up the ladder. Finally, many modern work environments require workers to be on their feet and adaptable, to be able to switch between focusing on a spreadsheet, to going to meetings, to thinking up big picture strategies. Modafinil might not be optimal for this constant shifting back and forth with environments and tasks.

However, this isn't to say modafinil isn't without its legitimate enhancements and ethical concerns. Perhaps the most potentially ethically controversial feature of modafinil is its powerful wakefulness promoting effects, and how it significantly enhances cognitive performance in sleep-deprived people. While there are some debates over the details of its cognitive enhancing effects, the research is in agreement that modafinil allows individuals to forego sleep, at least in the short-term. And the scientific studies showed that it improved performance in sleep-deprived people, compared to those who hadn't taken it. This is already an advantage, but in our 24/7, hyper competitive society, foregoing sleep could be even more of an advantage. Sleep deprivation is an epidemic. The CDC (Center for Disease Control) found that over a third of Americans are not getting the minimum recommended 7 hours of sleep (2016), and identifies insufficient sleep as a public health problem (2015). Someone enhanced with modafinil would not only be solving their own sleep-deprivation, they would also be in a better position that the increasing number of sleep-deprived "competition." In addition, modafinil could create more hours in the day for someone to work and allow them to sleep less, which could give them a decided advantage in their career, or allow them to fit in more activities such as hobbies, exercise, and spending time with family.

In these examples, modafinil use is an "enhancement," rather than a "treatment." In general, "enhancement" incites many more ethical debates. That is the reason why some maybe question the ethics of modafinil use for enhancement. They argue that drugs should only be used for treatment, not enhancement. However, I argue that modafinil use for enhancement is not unethical, because we already have enhancement in our medical practices and drugs, and while the line between enhancement and treatment for modafinil use may be easy to define, it is not as

easy for other drugs – therefore, to call modafinil use for enhancement unethical is myopic because it ignores all the other enhancement and fuzzy distinctions.

Western medicine has starkly different attitudes towards drug use for "treatment" vs. "enhancement." However, in 1972, in response to the advent of antidepressants at the time, psychiatrist Gerald Klerman first described the U.S.' attitude towards drugs as "pharmacological Calvinism," defined as

> a general distrust of drugs used for nontherapeutic purposes and a conviction that if a drug "makes you feel good, it must be morally bad." The dominant American value system condones and sanctions drug use only for therapeutic purposes and then only under professional supervision by physicians and pharmacists. In this view, abstinence is the highest ideal, the purest route to pharmacological salvation. (Klerman 1972)

He goes on to state that

> The conviction is often held that the use of psychotropic drugs in psychiatric treatment is morally wrong, independent of its efficacy, because it promotes gradual dependency. Drug therapy is thus a secondary road to salvation; the highest road to salvation is through insight and self-determination. This view, although held only by a minority of psychiatrists is also embodied in the popular media's current attempts at drug abuse education.

In his discussion of pharmacological Calvinism, John Kramer echoes Klerman's of the United States in his book *Listening to Prozac:*

> Study after study has shown that, when it comes to prescribed drugs, Americans are conservative. Doctors tend to underprescribe (relative to the recommendations of academic psychiatrists) for mental conditions, and patients tend to take less medicine

> than doctors prescribe…Relative to the practice in other industrialized countries, prescribing in the United States is moderate. (274)

Kramer also states that “One aspect of pharmacological Calvinism is the belief that pain is a privileged state, a view inherent in the arguments concerning affect tolerance and the adaptive value of sadness” (275). In the case of modafinil, pharmacological Calvinists would consider sleepiness and fatigue as part of the human experience, and would view cognitive enhancers as dehumanizing, as productivity in pill form. The United States’ pharmacological Calvinism is the main reason behind the lack of support for research on “enhancement.” There are regulatory issues, if there’s not a clear therapeutic target. The authors of the influential modafinil review, Battleday and Brem, state: "It appears that funding for drug-based studies on healthy individuals fails to attract typically medical-oriented grants and awards” (Loria, 2016). Dr. Sahakian of the University of Cambridge states that "The big issue is that there are no long-term safety studies in healthy people with drugs such as modafinil" (Oberhaus, 2016). In a June 2016 release, The American Medical Association clearly laid out its opinion on using prescription drugs for cognitive enhancement in healthy individuals:

> Prescription drugs that are FDA-approved to treat attention-deficit hyperactivity disorder or narcolepsy are commonly associated with the off-label use by students and others seeking to boost memory, learning or other aspects of cognition. Such use is associated with a variety of adverse mental health conditions and patterns of substance misuse. As temptation grows to use prescription drugs for a competitive advantage at work and school, the nonmedical use of these drugs should be discouraged given potential for substance misuse and other adverse consequences," said AMA Member Maya A. Babu,

> M.D., M.B.A. "The AMA believes physicians can support this goal by not prescribing any drug for the purpose of cognitive enhancement in otherwise healthy individuals." While prescription stimulants carry real risks, they do not make people smarter.
>
> The available evidence suggests the cognitive effects of prescription stimulants appear to be highly variable among individuals, are dose-dependent, and limited or modest at best in healthy individuals.

The question over enhancement vs. treatment debates is an ethical issue at the root of research in long-term responsible use in healthy people. Why is "treatment" OK, but not "enhancement?" The problem is that there is no clear demarcation between the two. One effect of the enhancement vs. treatment dichotomy is broader medicalization, and recognizing more states as medical conditions. In the article "Brain Gain" published in the *New Yorker*, Talbot describes: "New psychiatric drugs can create markets for themselves. Disorders often become widely diagnosed after drugs come along that can alter a set of suboptimal behaviors. In this way, Ritalin and Adderall helped make A.D.H.D. a household name, and advertisements for antidepressants have helped define shyness as a malady." Modafinil went through a similar process – what Talbot calls "mission creep," where the "official" use of the drug becomes looser, with the suspected intention being increased sales:

> In 1998, Cephalon, the pharmaceutical company that manufactures it, received government approval to market the drug, but only for "excessive daytime sleepiness" due to narcolepsy; by 2004, Cephalon had obtained permission to expand the labelling, so that it included sleep apnea and "shift-work sleep disorder." Net sales of Provigil climbed from a hundred and ninety-six million dollars in 2002 to nine hundred and eighty-eight million in 2008. Cephalon executives have repeatedly said that they do not condone off-

> label use of Provigil, but in 2002 the company was reprimanded by the F.D.A. for distributing marketing materials that presented the drug as a remedy for tiredness, "decreased activity," and other supposed ailments. And in 2008 Cephalon paid four hundred and twenty-five million dollars and pleaded guilty to a federal criminal charge relating to its promotion of off-label uses for Provigil and two other drugs. (2009)

For modafinil, the line between enhancement and treatment might not be so blurry, as one can just look at the FDA's lawsuit Cephalon to find this line. Treatment is for narcolepsy and shiftwork sleep disorder, but "decreased activity," "tiredness," and other terms Cephalon used in their marketing materials fall under enhancement.

However, I'm not arguing that the line for modafinil is blurry. What I hope to dispel is the specific objection that enhancement with modafinil is radically different from the enhancement that we already have. That calling enhancement through modafinil unethical, simply on the grounds of it being "enhancement" rather than "treatment," is myopic, because we already allow enhancement with many other substances.

One example prominent example of the blurry line between treatment and enhancement is the use of Prozac for treating depression. *Listening to Prozac* describes a woman named Tess who, after taking Prozac, not only fixed her depression, became a fundamentally different person. She became much more outgoing, charismatic, and satisfied with her social life. Prozac made her "better than well." In this case, Prozac not only acted as a treatment for her depression, but it also enhanced who she was as a person, making it difficult to determine whether Prozac is more one than the other. In another example, who didn't meet the criteria for any of the depressive disorders, wanted Prozac for the two days a week she felt apathetic or unmotivated (252). Prozac made her feel better than normal, to the point that her normal state felt

unsatisfactory. This is a much clearer case of enhancement and cosmetic pharmacology, where likely the only medical "case" she might have had was a case of the "Mondays." In both cases, Prozac fundamentally changed their personalities, and arguably enhanced who they were.

Another example of the blurriness is ADD medication such as Adderall. Both modafinil and Adderall are used for off-label cognitive enhancement, and by largely the same student/white-collar demographic. Adderall is still much more commonly used than modafinil for these purposes. It's been around for much longer, and modafinil still has not reached mainstream awareness, in part because the conditions it's supposed to treat are much less common than ADD. This also makes it more difficult for a patient to fake the symptoms and receive a prescription.

The social situation around ADD drugs is very complex, especially around its use for sedating hyperactive school children. Of course some children might very well have real conditions that lead to classroom disruption. But is it a medical condition that young boys can't sit still inside on a sunny spring day, studying addition and subtraction for hours on end? It can be hard to differentiate between a real condition, and simply being a child. What if, similar to the examples above where Prozac went above and beyond, a child with true ADD started taking Adderall and outperforming their peers? Adderall would then be both a treatment and an enhancement.

Other examples of the blurry line, include Viagra for erectile dysfunction, drugs for baldness, and Botox for wrinkles, which could all be considered enhancements given that none of these conditions are considered diseases that directly threaten one's health. While one could argue that these substances are different from modafinil in that they "restore" one's "natural" functions and thus don't qualify as "enhancement," maybe it's only natural for elderly men to be

balding and have erectile dysfunction. One could argue that for a fatigued professor grading papers late in the afternoon, taking modafinil would "restore" the "natural" intense focus he had the beginning of the day – or maybe, the focus he had when he was a college student. Why does the medical establishment decide that certain enhancements are allowed, but others are not? Why isn't "tiredness" yet a medical condition to be treated like baldness?

To reference Thomas Kuhn seminal work, *The Structure of Scientific Revolutions*, we need a new paradigm shift in how the medical establishment's treatment vs. enhancement dichotomy. To say "enhancement" is unethical, is itself a complex statement, instead of a dichotomy, there is a spectrum between enhancement and treatment that must be properly examined. Below are some common arguments that I foresee against modafinil's use as a cognitive enhancer, and some counter-arguments.

Enhancement is unethical. It's not ethical to take "smart" drugs to get ahead, gives some people an unfair advantage, and creates unfair pressure on their peers to take the drug, and artificially increases the standard of work.

As previously argued, defining something as "enhancement" is inherently problematic. One example, is if Botox, Viagra, and Rogaine can be considered restorative, can't modaifnil also be restorative for older people? What if a patient complains, "Doctor, I can't focus like back when I was a kid. I'm not as sharp, my memory is weaker. I need a drug to restore my ability to focus." In this case, would modafinil still be called enhancement, or would it also be treatment for slowed brain activity and inability to focus? Another major reason why enhancement is not necessarily unethical, is that outside of sports and competition, there are no rules to break, and life is not always zero sum. One person's success does not necessarily prevent others from

achieving that success. While there are social stigmas and pressures, there are no set rules (outside of legal ones) that people must follow.

What about claims of unfair pressure and coercion, and creating an artificial standard? First, modafinil use does not always have to lend itself to competition. Those taking modafinil may choose to do so, not so much because they want to beat out their coworkers for the promotion, but to balance their career and give them more energy for their activities outside of work, such as spending time with their family. In response to the sleep arguments, it is undeniable that modafinil could let someone function better with less sleep. But first, one still has to do the work, and secondly, not everyone, is willing to take prescription grade drugs just to work harder. Just because can choose to take modafinil to sleep less and hopefully get ahead in the workplace and earn that promotion, doesn't mean they will necessarily choose to. It could let someone sleep less and work more – but I would argue that most people have different lifestyle goals and would not choose to do that, at least not regularly.

Even if they do choose to use modafinil for that purpose, modafinil probably isn't the only piece of technology they are going to use. They might use caffeine, might change their diet, adopt new time-management strategies, do a light workout in the morning to increase blood-flow, maybe use sleep aids like melatonin to help them sleep better when they need to. Modafinil may make the work easier to do than otherwise, but the internet makes our research easier, caffeine makes it easier to stay awake, and heating and air conditioning make our working conditions bearable. People who want to accomplish more will always find new ways to get ahead. The tools are available for those who want them.

"Enhancement" shouldn't be a bad word. Our species has always tried to improve itself. If it's not zero-sum, which in most cases its not, there's nothing wrong with it, and in most

situations, it's additive and could contribute to society. A productive worker, on the surface, should be a net benefit, such as an entrepreneur who could build a product that could help millions of people and creates thousands of jobs. A rising tide raises all ships. In fact, arguments could even be made that in some cases, it would be wrong *not* to enhance performance. Sleepy physicians who have to be attentive. Researchers on the brink of discovering cures for debilitating diseases, but who need more alertness and focus. A parent having the energy and mental sharpness to devote to their children after a long day of work, to help them with their homework, that bully in school, or coming of age issues. If it's the choice between falling asleep, or taking a pill and being there for your children, why should we not provide our children with the "best" version of ourselves?

Modafinil is an "unnatural" piece of technology. It's not equally accessible, which could lead to increased inequality.

With all our existing technologies, our entire lives are already unnatural and enhanced. Coffee, reading, computers, the internet, exercise, better tutors, and prep courses, are common examples of brain-altering, cognitive enhancing technologies that are both unnatural and unequally distributed or leveraged in our society. There is no "natural." Everything from the food we eat, to the cars we drive, to the clothes we wear, houses we live in, to the medical care we receive, are profoundly unnatural. Yet we choose to use them, even though others may not have the same access, even it that's "unfair," because these technologies enhance our lives. There may be barriers to accessing modafinil, but no piece of technology is equally available to everyone. There is no such thing as "equal access" or "equality."

In the context of all the other incredibly powerful forms of technology, and in a world that is, always has been, and always will be, "unfair," modafinil is unlikely to cause major

changes in equality at all. We have so many existing cognitive-enhancing technologies. Why would we draw the line at modafinil? Greely et al, argue that so-called drugs aren't necessarily any different from other "brain-altering" technologies such as exercise, nutrition, sleep, instructions and reading, and "should be viewed in the same general category as education, good health habits, and information technology — ways that our uniquely innovative species tries to improve itself" (702). A counter argument could be that instead of increasing inequality, it could lead to greater equality, as another tool for for people to get ahead.

While modafinil may not be physically addictive, isn't it bad that people could choose to take modafinil indefinitely and become reliant on it for everyday use? And we still don't know much about it's potential dangers for long-term effects in healthy people – so why should we allow modafinil's use as a cognitive enhancer when it doesn't necessarily save lives, but could be dangerous (skewed risk/benefit analysis)?

I agree, we don't know long term effects. I understand we still need more studies. And as mentioned previous with adverse reactions with caffeine and alcohol, there are still potential dangers for how modafinil will work outside of the lab, in different contexts. With that said, first 1. Modafinil seems safe, and 2. We should do more research on the long term effects, especially given number 1, because modafinil could have real benefits to society, and I would argue has a higher potential benefit than risk, based on the overall positive accounts for focus on healthy people referenced in Chapter 2, and over a decade of scientific research demonstrating its relative safety and very low abuse potential, In their landmark review article, Battleday et al. note that while the ethics remain complex, "However, it is noteworthy that with more protracted and complex testing, more benefits are being associated with modafinil use rather than less,

which suggests that modafinil may well deserve the title of the first well-validated pharmaceutical 'nootropic' agent" (2015).

With more research, we can promote more responsible use, better assess the risks and prevent the downsides of potential abuse. There is value in create a dialogue of looking at potential new ways of leveraging pharmacological technology, towards enhancing our lives, just as people have been using technology to enhance their lives for all of human history.

In their seminal Nature 2008 article "Towards responsible use of cognitive-enhancing drugs by the healthy," Greely et al. mention some guidelines for more research and policy for cognitive-enhancing drug use in the healthy. They argue that the importance of understanding the patterns of use, benefits, risks for dependence when used for cognitive enhancement, and importantly, understanding just how big the effects of the drug are, and how they actually work in the real world, compared to simple laboratory tasks (704). In addition, they call for information to be broadly disseminated concerning the risks, benefits and alternatives to pharmaceutical cognitive enhancement" in a manner "similar to the way that information about nutrition, recreational drugs and other public-health information is now disseminated" (705). This would facilitate a dialogue and clarify the risks benefits and alternatives, promote safer and responsible use, and better awareness of what these drugs actually do, how to use them, and if they are necessary at all.

Is there anything necessarily wrong with being "reliant" on modafinil for every day use? If there were an "ideal" drug, that had positive benefits with little negative side effects and was overall relatively safe, would it be wrong to take that drug indefinitely? As mentioned before, we are already "reliant" on, and perhaps even "addicted" to, many technologies to live our lives.

For example, what makes modafinil different from caffeine? Many people rely on caffeine daily for cognitive-enhancement. Caffeine has its own downsides, and health risks, such as nausea, heart palpitations, insomnia and nervousness, but there is relatively little social stigma or controversy around its use. Modafinil has stronger wakefulness effects, and may have some reported negative side effects, but because it's much newer compared to caffeine, and comes only in pill form, we tend to judge it by a different set of standards, becoming more critical and discerning of any potential safety risks.

Consider a student or white-collar worker tasked with a seemingly insurmountable work that must be completed in the morning. In other words, an all-nighter is inevitable. The drug of choice in this case is usually caffeine. Our hero could choose to consume multiple cups of coffee, perhaps with cream and sugar, or a few sugary energy drinks loaded with sugar and artificial sweeteners. The caffeine and the dopamine might keep them awake, it could also make them jittery and anxious. Or instead, they could take one modafinil pill, or maybe a half tablet or none at all if they had already taken one earlier, given modafinil's much longer, 15-hour half life. In this case, modafinil would likely provide them with a much more efficient level of focus and wakefulness, and allow them to sidestep all the inconveniences and potential health risks of unhealthy caffeinated beverages. What's the difference between taking one modafinil pill, instead of downing endless cups of coffee, as many already do?

Just like any other form of technology, modafinil has its benefits and its risks, that we should be able to weigh and consider. What are we willing to accept? We can live with some things. It's a relatively safe, not addictive, and potent yet specific and limited performance enhancement. It seems perfectly reasonable to take it. Perhaps, in our post-industrial, knowledge economy, broader accepted use might be inevitable. Just like we "need" electricity and clothes in

our modern society, drugs like modafinil might become just another reasonable way of dealing with the requirements of life in our always-connected, always-on world. In conclusion, modafinil shows promise as a relatively safe and effective cognitive enhancer for certain tasks when used responsibly, and there should be further research into modafinil's long term effects as a cognitive enhancer for healthy individuals.

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