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ABSTRACT

This paper deals with new pharmacological and technological developments in the manipulation and curtailment of our sleep needs. While humans have used various methods throughout history to lengthen diurnal wakefulness, recent advances have been achieved in manipulating the architecture of the brain states involved in sleep. The progress suggests that we will gradually become able to drastically manipulate our natural sleep-wake cycle. Our goal here is to promote discussion on the desirability and acceptability of enhancing our control over biological sleep, by illustrating various potential attendant ethical problems. We draw attention to the risks involved, possible conflicts of interests underlying the development of wake enhancement, and the potential impact on accountability for fatigue related errors.

THE WAR ON SLEEP

This paper aims to explore ethical issues related to emerging forms of "wake enhancement". We use this term to indicate those methods that enhance diurnal wakefulness by rendering more control over when and how much (or rather, how little) we sleep. This includes a broad range of means applied by humans, ranging from meditation to artificial lighting, the consumption of cocaine and amphetamines, caffeine, alcohol, nicotine and increasingly accurate pharmacological alterations of the sleep-regulating areas in the brain.

One stimulant that has attracted particular interest in recent years is modafinil. Studies suggest that this drug can help achieve up to 48 hours of continued wakefulness, significantly increased vigilance, alertness and perceptual/cognitive performance.[1] No clinically significant side effects have been observed, and drug intake does not seem to preclude the ability to reinitiate sleep. Ampakine CX717, originally developed as a cognitive stimulant for Alzheimer patients, has been shown to remove the effects of severe sleep deprivation on the cognitive performance of well-trained monkeys.[2] Drugs that significantly enhance slow-wave sleep are also being explored in the hope to achieve shorter but deeper sleep. Phase I clinical trials of APD125 have demonstrated significantly improved sleep maintenance in healthy volunteers.[3] Further advances within the near future are conceivable. A team funded by the US Defense Advanced Research Projects Agency discovered a strain of fruit flies that sleeps one third of the "wild type" amount of sleep without any impairments due to sleep deprivation.[4] It is believed that such flies carry a point mutation in the Shaker gene. This would suggest that genetic manipulations of the gene or drugs which directly target the potassium channels involved could be a realistic approach to curtail one's sleep need. Technological interventions such as the use of vagus nerve stimulation,[5–7] biofeedback[8] and transcranial magnetic stimulation[9] are also being applied to change biological regulation of sleep. These recent advances suggest that we are well on our way to drastically manipulating the architecture of the brain states involved in wake and sleep. Indeed, a (technologically) optimistic scenario is that we may one day be able to diminish our need for shuteye to a few hours a night, or to delay it for several days, while the lengthened vigilance is still equivalent to the effect of normal sleep.

Judging by the common use of stimulants such as caffeine, nicotine and existent sleep pharmaceuticals, it is conceivable that the use of wake enhancers—as they become more effective, safe and affordable—will become widespread. Indeed, melatonin supplements are already widely employed to help regulate the circadian cycle in case of jetlag. And although modafinil was originally marketed as a treatment for narcolepsy, drug makers Cephalon estimates that about 90% of its prescriptions are for off-label uses.[10] In the following, we wish to question how far we should go in embracing such a development by outlining some potential attendant ethical problems.

ETHICAL ISSUES RELATED TO WAKE ENHANCEMENT

Risks

Most discussions of wake enhancement focus on the potential health hazards of drastic sleep curtailment. It would indeed be false to claim that we fully grasp and understand why and how our regulation of sleep and wakefulness works. While the underlying processes remain largely obscure, sleep inadequacies have been related to significant physical and mental health hazards and it is known that persistent sleep deprivation can be fatal. Importantly, also, many wakefulness stimulants have either directly and/or indirectly produced health risks: either through their adverse side effects and/or through their inability to maintain all required sleep functions.

In light of this, it is worth questioning how much risk is acceptable against anticipations of lengthened vigilance and activity. For all medications, there is concern for adverse health effects, but the risks are usually weighed against the need of the treatment and the degree of benefit that is expected.[11] Such a balance would appear to be particularly adverse in case of enhancements. Nonetheless, although little is known about how

modafinil works, market sales have grown from US$25 million in 1999 to around US$575 million in 2005.[12] This suggests that, for many, the short term benefits prevail over potentially unknown long-term effects.[10] Indeed, the lack of reported side-effects related to this drug may feed hope that other drugs and technologies will gradually emerge that do not pose any significant harmful side effects or compromise the quality of the curtailed sleep. It is also conceivable that our understanding of sleep mechanisms will increase substantially within the near future, for instance through further advances in transcranial magnetic stimulation research. Furthermore, at least theoretically, methods to curtail sleep may prove to provide an overall health benefit. Over the past decades, data has accumulated relating sleep of more than 8 hours to significantly increased risks of mortality and morbidity conditions such as diabetes, coronary heart disease, and increase in depressive symptoms.[13] Although the causality has not been explained, one could hypothesise that mild sleep restriction can decrease mortality in long sleepers and that wake enhancement may be useful for that end. In any case, if there is some ground to claim that future wake enhancers will be safe, the question is whether we would still be cautious in embracing this progress? As others have noted, questions of this sort have not been considered.[14]

Social values

In many ways, the drive for wake enhancement is—like other forms of neuroenhancement—in line with fundamental social values. By advancing our wakefulness, we promote our capabilities for autonomy, self-improvement and actively taking part of and contributing to the world. By contrast, it may be argued that sleep—during which one is completely unconnected to reality, self and others—has no virtue aside of rather self-centred values of idleness.

Nonetheless, some features of "natural" sleep may actually convey important facets of our inter-individual world. It is, for instance, highly probable that, psychologically, we need moments of sleep as a suspension from a series of overwhelming and perhaps unpleasant stimuli and interactions. Sleep may also be a necessary tool to process these stimuli and to prepare us for further interactions. Indeed, it is possible that dreams play an important role in this regard. According to contemporary theories of memory consolidation, dreaming helps us organise the various memories, thoughts and images that have submerged throughout the day in a more or less coherent narrative.[15 16] It has been suggested that dreaming may therefore also be an essential medium for self-expression and creativity.[17] Importantly, even in stages where one is not dreaming, sleep may still be a significant expression of social interaction. Williams[18] has identified various ways in which individuals will try to resolve long-term emotional issues or concerns that have cropped up during encounters over the day when preparing for sleep. Sleep is also, Williams notes, an essential expression of our most intimate relationships. The vulnerability of sleeping children, for instance, implies that we extend our care for and intimacy with them throughout the night. Sleeping together is also a symbol of mutual trust and intimacy for modern couples. If individuals acquire means to drastically reduce or postpone sleep, they could adapt their sleep patterns to their specific, individual lifestyle. Theoretically, this could generate a society with non-stop forms of social activities. However, it could coincidently undermine the quality of the social bonds that are valued most.

Conflicting interests

Our society is becoming one of around the clock services and needs and it increasingly demands that we adapt our circadian rhythms to altered production schedules. In all urban economies, one fifth of the population works outside the standard 08:00–17:00 working day.[19] Currently, however, a substantial proportion of the population suffers from sleep deprivation and/or sleep inadequacies. The related health risks and effects on performance and productivity induce enormous financial and social costs.[20] Certainly, effective wake enhancements could be beneficial in terms of diminishing these costs. Nonetheless, one may question how far we should go in adapting our sleep and wake patterns to social utility, and whether future wake enhancers will not lead us to increasingly reorganise repose in favour of new practices of social control rather than our own individual interests.

This concern has been expressed by sociologists Kroll-Smith & Gunter[21]. Following Foucault's discourse analysis, they illustrate that a new truth about sleepiness is being created. Whereas fatigue was once generally described as "a benign, naturally occurring corporeal moment, a precursor to sleep", a new discourse is gradually being formed that depicts the state as "hazardous to self and others" in terms of pathological inadequacies in alertness, reaction time, memory and decision making. Various institutional practices and techniques increasingly portray sleepiness as a troubling, risk-prone state and a personal, moral failing.[21] Importantly, many of the sources which create this "new truth", the authors observe, are corporations, the military and state/federal governments. As such, the changing connotation of weariness is a novel exercise of social control and relates to a clear interest in extending hour operations.

In this regard, one may fear that by gradually emphasising the collective interests and concerns regarding fatigue and sleep, we are allowing an essential dismantlement of our private freedoms. While our wakefulness is now constrained by biological limits, the inevitable moments of rest are essentially beyond the grasp of collective aspirations, demands and burdens. It is difficult to believe that future wake enhancement will not have some impact on our work load. Will we still have the freedom to withhold using wake enhancers, or will the norms of success and maximum productivity be too powerful? If we do chose to maintain a naturally limited wakefulness, will we be able to compete with those who don't? What if large-scale use of wake enhancement will create a looping effect so that social integration will become increasingly difficult with natural sleep and wake cycles?

On the other hand, it must be noted that our society's sleep and wakefulness patterns have always been regulated in accordance with its cultural-specific norms of efficiency and productivity. For instance, while siestas have not been implemented by western corporations, less-time consuming "power naps" are increasingly being promoted for their performance enhancing effect. Historically, most western societies have long preferred compressed stages of sleep over multiple cycles spread through the day and night. Also, short sleepers and early risers have typically been favoured. Prior to artificial illumination, of course, these sleep patterns enabled the most efficient means of productivity. Against the dominant western separation of sleep-wake states, there is increasing evidence of both individual and cross-cultural diversity in sleep regulations. For one, individuals have changing sleep patterns throughout the years, from the frequent altering between waking and sleeping typical for young infants, to later sleep

onset and offset in adolescent years, and the opposite pattern in elderly years. There also appear to be significant genetic variations in circadian rhythms due to variations of *period* genes.[22] Moreover, research has initiated to examine how repose is managed both cross-culturally and from an evolutionary perspective. Worthman & Melby's[23] investigation of traditional societies reveals systematic variation in distribution, length and variability in sleep. Attempts have also been made to reverse-engineer the sleeping patterns of prehistoric humans through experimental environments without artificial lighting. Studies have found that test subjects who were used to compressed sleep showed spontaneous sleep interruptions of one or two hours.[24] A (natural) diversity in sleep episodes had an important survival advantage over compressed and short sleep: having individuals relatively alert at variable points throughout the night enabled them to warn others of a threat or emergency. Ironically, therefore, if future drug use creates an inter-individual continuum of wakefulness to accommodate the increase in shift work and work hours, this will be more in balance with our evolved "nature" of rest than our commonly preferred sleep models.

It is also clear that, while wake enhancement could indirectly turn out to be exploitative measures, it may just as well be liberating through its potential to create more opportunities. There may therefore be compelling ethical reasons to support application. Obviously, increased wakefulness will enable us to extend our leisure time and enjoy the goods and services that are produced throughout the day and night. Importantly, also, future wake enhancers may bring about a more equitable access to various employment opportunities. In terms of professional productivity, one could feel that fatigue and sleep are the ultimate "equalisers": everyone is alike in the need to stop daily activities for rest and sleep. However, inter-individual biological variations in the body clock gene undermine this intuition. Comparative research suggests that two variants of the *period3* gene, encoding either long or short versions of the corresponding protein, determine individual sensitivity to the effects of sleep deprivation.[25] It has been shown that, during sustained wakefulness for two days, carriers of the longer variant performed much worse on tests for attention and working memory. If so, and if enhancers could be applied to manipulate the effects of the longer gene variant, they could alleviate genetically determined restraints on night and shift work. In lack of such "corrective measures", by contrast, employers may—in light of safety and efficiency concerns—discriminate against carriers of the longer variant. Furthermore, it is known that particularly shift work has major adverse health effects.[26 27] One could suggest that wake enhancements should be made available (and perhaps even distributed by employers) to those who suffer from the health effects of sleep irregularities, in order to promote a more equitable distribution of employment-related health risks and regained access to employment.[21]

New responsibilities

The perception that fatigue is hazardous is supported by suggestions that a number of major disasters over the past decades, including Three Mile Island, the Chernobyl nuclear power-plant melt down, Bhopal, Exxon-Valdez and the sinking of the Estonia ferry are, at least partly, attributable to tiredness.[28] Within the medical profession, a link is increasingly drawn between night work/long work hours and impaired alertness, memory, cognition and performance.[29–31] These effects are in turn coupled to an increased rate of medical errors and accidents.[32 33] Sleep cycle disturbances are also said to contribute significantly to an increased risk of accidents on the road. For instance, a French study demonstrated that 10% of almost 68 000 serious road crashes involving one motor vehicle were related to fatigue.[34] In areas where there is a high risk of severe harm to self and others, such evidence may have important implications for our concept of responsibility. It is conceivable that the availability of safe and effective wake enhancers will create or fortify a responsibility to ensure that fatigue no longer affects performance, particularly within professional contexts.

Indeed, various professions already call for increased control over sleepiness related risks. Although human errors are to some extent inherent to the medical profession, there are ongoing efforts to ensure that house staff work schedules are implemented and respected. In the US, resident work has been formally limited to 80 hours per week and no more than 24 hours at a time.[35] This raises questions of accountability for errors that occur outside of accepted work schedules. In the transport industry, where such regulations are very strict, there have already been various claims of employer and employee liability for accidents related to violations of work hours. In 2007, for instance, a lorry driver was sentenced to five years of jail for falling asleep at the wheel and causing the death of four people.[36] It was argued that the man had "deliberately" decided to ignore regulations on minimum periods of rest.

Currently, it may be inevitable that some workers will regularly find their wakefulness impaired to some extent. Some positions simply must provide around the clock services, and therefore necessarily require shift work. Long work hours may even have certain advantages that countervail risks of fatigue: for medical trainees, for instance, they are regarded as valuable in terms of educational experience.[37] Interestingly, this does not necessarily imply that the responsibility for fatigue-related accidents is thereby alleviated. Indeed, the medical profession is increasingly voicing the need to become aware of one's state of wakefulness and to actively take appropriate precautionary measures. For instance, in a discussion on the effects of sleep deprivation on physician performance, Steven Howard[37] pleads for cultural acknowledgement that physicians should *abstain* from work if their alertness and performance are *in any* way impaired. This rationale equates the obligation to abstain from work when feeling drowsy and the accepted obligation to abstain from certain acts when mental impairment is caused by other factors, most notably intoxication.

The analogy between fatigue and intoxication has been very powerful within the transport industry and has given rise to explicit notions of moral culpability for driving when sleepy. Studies have shown that both acute sleep deprivation (~24 hour) and short-term chronic sleep deprivation (<6 hours sleep per night for a week) are equal to moderate alcohol consumption in terms of performance in simulated driving tests.[38] Acute sleep deprivation of 27 hours causes greater cognitive impairment than a blood alcohol concentration of 0.085%.[39] In response to these findings, advocacy groups are calling for restrictive measures and New Jersey has even enforced legislation to allow a sleep-deprived driver to be convicted of vehicular homicide.[37]

In terms of liability, actions that are done while sleeping are regarded as involuntary and beyond the control of the individual.[19] However, it appears that *sleepiness* itself is not held to be completely beyond one's control and there is a tendency to

promote taking reasonable precautions if one can foresee the potential dangers of one's exhaustion. This raises the question whether use of wake enhancement could one day be recommended as part of "reasonable" precautions, or even demanded from certain employees. Note that the US Uniform Code of Military Justice requires soldiers to accept medical interventions that make them fit for duty,[14] suggesting that there is at least one domain where wake enhancement may be explicitly required. Moreover, if there is an increasing duty to control fatigue, could it not also apply to professions which bear other than safety-related risks of harm to self and others? For instance, recent research suggests an effect of sleep disturbance on judgement concerning moral and emotionally charged events. Killgore *et al*[40] tested 26 healthy active-duty military employees on judgment performance in various hypothetical dilemmas, both after having rested well, and after sleep deprivation of 53 hours. The study showed that, after sleep deprivation, the participants needed two seconds longer on average to solve complex moral dilemma's compared to problems with a neutral content. If moral reasoning is impaired or, in this case, decelerated through lack of sleep, does the duty to ensure wakefulness also apply to professionals who are responsible for making on the spot yet important decisions? For instance, it can be questioned whether police officers, who work much overtime, may be sufficiently able to deal with difficult and emotionally charged situations and people.[41] Indeed, why attribute this responsibility only within the professional context? To what extent will we start to feel that all citizens should maximise wakefulness and alertness so to advance safety, performance, or even moral judgements?

CONCLUSION

Even if it is doubtable that large-scale use will be made of wake enhancers any time soon, it is important to start discussions on whether, and to what extent, such a development would be desirable. The above review implies that there is no simple truth about the value of wake enhancement, but that we will have to attune it to societal and individual concepts of the good life. Much will depend on the long-term health risks of the enhancement and on the weight of its expected benefits. Clearly, wake enhancement could allow us to better adapt our sleep-wake cycle to altered production/consumption schedules and to broaden our individual lifestyle options. However, it is highly questionable whether this is the appropriate response to such demands. Crucial in this regard is the extent to which wake enhancement may suppress individual autonomy rather than advance it, for instance, by gradually creating standards of safety and performance that become unattainable with natural sleep rhythms. Ultimately, furthermore, some collective motivations to employ wake enhancement may conflict with individual interests. Most illustrative in this respect is that, even though one could regard wake enhancement as a laudable instrument of promoting fair access to professions with non-standard work schedules, it remains dubious to choose to facilitate a 24 hour production process in the first place.

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