Pharmacological Neuroenhancement with Modafinil

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Background: Modafinil — an FDA-approved substance for the treatment of narcolepsy — is known to promote wakefulness and attention, and improve memory. These features make it a prime choice for pharmacological neuroenhancement in healthy subjects. But what are the risks and side effects that can be expected? And what are the ethical implications of such a practice, both for the user and the prescriber? The current work addresses these questions. **Materials and methods:** A systematic review of the current literature, illustrated with a clinical vignette.

NEUROENHANCEMENT

The term neuroenhancement refers to the targeted enhancement of cognitive and affective functions resorting to neuroscience-based methods that act directly in the human nervous system. Even though most methods are yet to have robust scientific evidence backing them up, pharmacological manipulation with the compound modafinil stands above as a strategy that has been studied extensively, with favorable outcomes. Psychometric assessment of neuroenhancement requires: 1) simple tasks, which involve basic cognitive exercises targeting discrete sub-components of cognitive functions; and, 2) more complex tasks, which incorporate multiple difficulty levels and test more integrated features of cognition.

PHARMACODYNAMICS AND INVOLVED CIRCUITS

Modafinil is a wakefulness-promoting substance that acts by directly inhibiting central dopamine and norepinephrine reuptake transporters; the ensuing elevation of catecholamine levels subsequently raises extracellular levels of histamine, orexin neuropeptides, glutamate and serotonin, and decreases concentrations of γ -aminobutyric acid. These neurochemical changes constitute the postulated biological underpinnings of heightened arousal and wakefulness; implicated areas of the brain that are modulated include the striatum, amygdala, hippocampus, hypothalamus and frontal cortex.

The effect modafinil exerts in the dopamine transporter as an uptake inhibitor is analogous to that of other stimulants like methylphenidate and cocaine, albeit significantly weaker; this particularity gives it a safer side effect profile, with little to no potential for abuse.

CLINICAL VIGNETTE

ID: Y is a 28 year old male patient. He is single and works in a tech startup company as a data scientist.

CLINICAL HISTORY: Y finished his degree in engineering while never experiencing any major academic setback, always performing according to his expectations and being an above average student. He started working as a big data scientist in a startup company and greatly enjoyed his functions.

At the moment of the consultation he was under extra stress because of important projects he was involved in, and he felt like if he somehow improved his executive functions and attention he would feel more in control.

He was in very good physical shape and worked out most days of the week before going to work. He had a regular sleep/wake cycle, sleeping about 7h30 hours per day.

PREVIOUS MEDICAL/SURGICAL/PSYCHIATRIC HISTORY: No relevant issues.

CURRENT MEDICATION: None.

PROPOSED STRATEGY: 50mg of modafinil ($1/2$ tablet) taken once in the morning for one week; gauge the effect and consider scaling up to 200mg (2 tablets) in the morning over the course of four weeks.

RE-EVALUATION: Five weeks after the initial evaluation, Y was taking 150mg (1 $1/2$ tablets) of modafinil in the morning. He felt significant improvements in his numeric manipulation/working memory skills and cognitive flexibility, which were briefly assessed via simple tests like the Trail-making task A and Digit ordering test. The medication had not interfered with his circadian rhythms and he didn't experience any symptom like nausea, headache or dry mouth.

After the bulk of the work for the projects he was involved in was finished, he stopped taking the medication and experienced no withdrawal effects.

NEUROETHICS: Large scale surveys have shown that many people are in favor of the technology to improve the abilities of healthy people, while being concerned with the safety of non-medical interventions, risks associated with inequity and authenticity; proponents of the proactionary principle accept that neuroenhancement will promote competition between people and will be important to cope with the ever-increasing demands in life, while those who have a protective view fear this practice will hamper social cohesion. Further societal engagement with these questions will be needed in the near future in order to settle the ongoing debate.

RESULTS AND CONCLUSIONS: Maintained wakefulness and executive functions and improved attention and memory are shown in both well-rested and sleep-deprived subjects who take modafinil. When taken correctly, it doesn't disturb the sleep/wake cycle, though subjects may experience nausea, dizziness and even bruxism. Special attention should be given towards the tolerance phenomenon. The current debate on the ethical implications of pharmacological neuroenhancement is yet to be settled.

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