

Modafinil as an adjunctive treatment to sleep deprivation in depression

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Sleep deprivation (SD) is a rapid-acting treatment for depression, but its clinical efficacy is hampered by high relapse rates after recovery sleep, and its effectiveness is reduced by the demanding effort needed for the patient to stay awake. To our knowledge, this is the first reported case of a successful treatment of depression with the combination of SD and the wakefulness-promoting agent modafinil. We suggest that modafinil may reinforce the action of SD, possibly by preventing daytime naps and microsleep, and may sustain the antidepressant effect of SD, possibly by stabilizing the resynchronization between the circadian clock and the sleep-wake cycle.

La privation de sommeil est un traitement à effet rapide contre la dépression, mais les taux élevés de rechute après un sommeil réparateur en réduisent l'efficacité clinique et l'effort exigeant que le patient doit faire pour rester éveillé en réduit l'efficacité. Sauf erreur, il s'agit du premier cas signalé de traitement fructueux de la dépression qui combine la privation de sommeil et le modafinil, promoteur de la vigilance. Nous sommes d'avis que le modafinil peut renforcer l'effet de la privation de sommeil, peut-être en prévenant les siestes et le microsommeil le jour, et peut maintenir l'effet antidépresseur de la privation de sommeil, peut-être en stabilisant la resynchronisation entre le rythme circadien et le cycle sommeil-éveil.

Introduction

Sleep deprivation (SD) is a rapid-acting treatment for depression,¹ but its clinical efficacy is hampered by high relapse rates after recovery sleep, and its effectiveness is reduced by the demanding effort needed for the patient to stay awake. The use of the wakefulness-promoting agent modafinil appeared to be a reasonable means to help patients carry out SD. Besides, modafinil has shown efficacy in depression as an augmenting treatment^{2,3} or in monotherapy.⁴ To our knowledge, this is the first reported case of a successful treatment of depression with the combination of SD and modafinil.

Case report

A 70-year-old retired engineer with bipolar disorder was admitted to our mood disorders ward for a recurrence of depression of severe intensity according to *International Statistical Classification of Diseases and Related Health Problems*, 10th rev. (ICD-10), criteria (F31.4). He had been a regular patient in our department and had been treated with lithium for 11 years. His lithium plasma level at admission was 0.70 mmol/L, and the findings of routine laboratory tests were not remarkable.

Previously, antidepressants had induced manic switches

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several times even while the patient was taking mood stabilizers. Four years before, a depressive recurrence had been successfully treated with partial SD (PSD). At that time, despite treatment with lithium, which has been reported to sustain the antidepressant effect of SD,⁵ he had had to continue SD twice a week for a few months. At admission, he told us "it is a pity that I am unable and too exhausted to carry out SD because it is the best treatment for me." We proposed that he undergo PSD while in hospital, with the help of the wakefulness-promoting agent modafinil. He underwent 4 PSDs (awakening at 2 am) on a twice-a-week basis. On the day after each PSD, he was prescribed modafinil, 100 mg, at awakening (2 am) and at midday. Observer ratings of mood were performed with the 17-item version of the Hamilton Rating Scale for Depression (HAM-D). The self-rating scales used were a 100-mm Visual Analog Scale (VAS) to rate mood at 9 am and 6:30 pm the day before and the day after each PSD and the Epworth Sleepiness Scale (ESS)⁶ at 6:30 pm on these same days. At admission, the 17-item HAM-D score was 27. After the PSDs, the VAS for mood improved on average 52.3 (standard deviation [SD] 29.1) mm in the morning and 20.8 (SD 31.8) mm at 6:30 pm. The mean ESS score slightly decreased (-0.75) at 6:30 pm after PSD.

The patient was discharged 2 days after the last PSD (17-item HAM-D score = 3), and modafinil was then continued at 200 mg/d, administered at 8:30 am and midday. He displayed no sign or symptom of hypomania and was still euthymic 1, 2, 4, 8 and 12 weeks after discharge as shown by a HAM-D score below 7.

Discussion

Current evidence suggests that modafinil has no addictive potential in animals⁷ and has limited potential for large-scale abuse in humans,⁸ but a thorough characterization of the abuse potential of this compound may be needed as its use increases. However, this case suggests that modafinil may increase the willingness of depressed patients to accept SD therapy; alleviate the difficulty of carrying out SD; reinforce the action of SD, possibly by preventing daytime naps and microsleep; and sustain the antidepressant effect of SD,

possibly by stabilizing the resynchronization between the circadian clock and the sleep-wake cycle. Further research should assess, in a larger sample, whether the combination of modafinil and SD represents the much needed rapid-acting and enduring treatment for depression.

Competing interests: None declared.

Contributors: Drs. Even and Bourgin conceived and designed the study; Drs. Thuile and Santos acquired the data; and Dr. Even analyzed the data. Drs. Even, Thuile and Bourgin wrote the article; and Dr. Santos critically revised it. All authors gave final approval for the article to be published.

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