

Letter to the editor

Why is sleep deprivation an orphan drug?

Thirty years ago this past June, Burkhard Pflug in Tübingen carried out the first experimental sleep deprivation in a depressed patient. Changes in mood related to sleep loss had certainly been observed over the centuries, and even noted as a paradox (e.g. Heinroth in 1818¹). However, the series of studies initiated by W. Schulte and R. Tölle, head of Pflug's department, aimed to document whether the improvement after sleep loss reported by a patient (a teacher who went biking all night when depressed) was a chance event or could be generalized. Pflug's doctoral thesis (Pflug, 1973), much of which was never published, received a prize from the Anna Monika Foundation in 1971, a prescient recognition of the remarkable phenomenon described. Papousek's (Papousek, 1975) milestone article grounded these clinical observations in a theoretical background and was followed by a number of explanatory models (cf. Borbély and Wirz-Justice, 1982; van den Hoofdakker, 1997).

In the course of the 1970s, research into sleep deprivation spread from Europe to other countries. Any psychiatrist who had once observed the switch out of depression in the course of a night awake — even in, and particularly in, the most severe major depressives — became convinced that here was a marvellous tool for psychobiologi-

cal research. What other treatment could induce a change from a depressed to a euthymic (or more) state within a matter of hours, without drugs, not apparently dependent on psychosocial factors, biking, or even light, but rather, intimately and crucially linked to sleep? Sleep emerged as a depressogenic factor, as the depression usually returned after rebound sleep the following night. Or after even only a tiny nap. However, not only sleep was involved; the circadian phase at which sleep occurred, or did not occur, appeared to determine clinical state.

This is not a review, however, nor a review of reviews (see, e.g. Pflug, 1976; Leibenluft and Wehr, 1992; van den Hoofdakker, 1997). I am just surprised that 30 years have passed since the first scientific report, that we have had lots of clever ideas and experiments that tune the hypotheses (partial sleep deprivation in different parts of the night, phase advance of the sleep-wake cycle, combination with light or with classic antidepressants, or ever-more-selective 5HT-this-or-that-receptor drugs), but that I still have no idea how therapeutic sleep deprivation works. The acute and transient improvement after sleep deprivation is not comparable to the effects of antidepressant drugs. Although there are a few passionate adherents to the study of sleep deprivation, particularly in Europe, there is no cohort of the curious who have conspired together to wrestle comprehension out of carefully designed, cunning experiments. Sleep deprivation remains a strange attractor for a few biological psychiatrists instead of being at the center of attention, the paradigm par excellence for understanding affective disorder.

¹die Schlafentziehung.....ein Mittel, welches grausam scheint, aber doch wohltätig wirkt: die Kranken werden von Zeit zu Zeit, wenn sie sich dem Schlaf überlassen wollen, geweckt' (preventing sleep may seem cruel but it ameliorates their suffering: patients are awakened each time they appear to fall asleep).

Okay, so we do not understand how it works. Still, it should be used. We do not really understand the mechanism of action of antidepressants, but that does not prevent their application. This is the other fact that surprises — no, worries — me. Here is an amazingly rapid antidepressant modality that does not need FDA approval, does not need managed care, costs nothing, and has only one major side effect (inducing mania in the susceptible). Does the lack of attention reflect the fact that sleep deprivation cannot be patented? Obviously, the pharmaceutical industry is not interested. Is it the psychological barrier — how can we take sleep away from the already insomniac? Or has the uncontested efficacy of sleep deprivation (60% response within 1 day is not so bad) been dismissed just because the therapeutic effects are transitory? Sleep deprivation works, but usually not for long. So that inspires my question: Why, in all these decades, have there been so few controlled trials to follow up the initial hints of all sorts of putatively helpful clinical applications? To name but a few promising findings: diurnal mood variability predicts sleep deprivation response; sleep deprivation response may predict antidepressant response; repeated (partial) sleep deprivation may accelerate antidepressant treatment response; and relapse after recovery sleep can be prevented by combination with antidepressants or bright light, or with phase advance of the sleep–wake cycle. Does sleep deprivation not sound like something terribly practical for the everyday clinician, a simple behavioural manipulation that helps, and helps fast? Where is the multicentre network to carry out those large controlled trials? Would it help to have

another name, like the once-suggested positivistic-sounding ‘wake therapy’?

Or should I cite the poet (Kopland, 1991), alias sleep deprivation researcher (van den Hoofdakker, 1997):

‘... Give me
a question, no reply’.

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