Does getting up late cause cancer fatigue?

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Abstract

Introduction

- Fatigue is the most common cancer symptom
- Fatigue is often the most distressing symptom
- Closely linked:
  - fatigue and insomnia
  - fatigue and depression
- Goal of study: examine connections between sleep patterns, fatigue, and depression

Method

- Convenience sample of cancer outpatients
- Self-response questionnaire about:
  - sleep habits; insomnia; attitudes about sleep; fatigue; depression; cancer type; current treatment; psychotropic medication

Results

- 125 useable questionnaires returned
- higher fatigue in patients getting cancer treatment
- high fatigue group vs low fatigue group:
  - younger
  - more depressed
  - more insomnia
  - used sleeping pills more
  - spent more time in bed after 6 am
  - endorsed more: "Sometimes it's necessary to miss work or school because of lack of sleep or really poor sleep"

Discussion

- Hypothesis: fatigue and other depressive symptoms are adaptive mechanisms to promote healing after injury
- Putative mechanism:
  - Injury causes inflammation
  - Inflammatory cytokines promote sleep
  - More REM sleep causes fatigue and other depressive symptoms
  - Excessive REM sleep can cause fatigue even in the absence of injury and inflammation
- Getting up later increases REM sleep much more than simply sleeping longer
- Cancer patients may sleep longer because of increased opportunity, as a defence against psychological pain, or as a result of inflammation caused by cancer or by cancer treatment

Introduction

Fatigue occurs in up to 99% of cancer patients[1], and is frequently the most distressing symptom[2]. Fatigue is also found in many chronic medical conditions[3], and is responsible for significant impairment[4] even without an underlying medical illness.

The words fatigue and tiredness have multiple meanings[5]. For example, fatigue is frequently used instead of sleepiness to describe accident risk in long distance truck drivers[6].

To clarify usage, the following terms have been proposed:

Sleepiness (somnolence, drowsiness): difficulty staying awake, an overpowering desire to sleep;

Acute fatigue: after a sustained physical or mental effort; relieved by rest or sleep;

Chronic fatigue[7]: apathy, lack of energy and motivation, lethargy; found in depression, cancer and other illnesses, and in chronic fatigue syndrome; not relieved by rest or sleep.

Chronic fatigue and insomnia are closely linked in cancer[8] and in other conditions[3]. The most common sleep disturbance, psychophysiological insomnia, may be caused by attempting to exceed one's sleep needs[9]. If this effort to obtain more sleep results in excessive Rapid Eye Movement (REM) sleep, a clinical depression might result, according to Wiegand's "Depressiogenic theory of sleep"[10], at least in those predisposed to depression. In other people, it is hypothesized that too much REM sleep may cause fatigue.

How might one obtain excessive REM sleep? By sleeping too much, or by sleeping during the part of the diurnal cycle when REM sleep propensity is high. Since REM propensity increases through the night[11], peaking at around 8:30 am[12], sleeping late may be more important than sleep duration in determining the amount of REM sleep, and therefore on the degree of chronic fatigue and depression.

Method

A convenience sample of outpatients being followed by the Medical Oncology and Radiation Oncology clinics at the SMBD-Jewish General Hospital in Montreal, Canada, were asked to fill in a self-response questionnaire containing the following sections:

Sleep and Insomnia Questionnaire: based on a questionnaire designed by C. Fichten, E. Libman, and colleagues in the Sleep Research Unit at the SMBD-Jewish General Hospital;

Sleep Attitudes Scale: Visual Analogue Scales (VAS) rating six attitudes about sleep or its lack:

- If I don't sleep well, I know the next day will be difficult
- There is no such thing as too much sleep
- When I feel tired or fatigued, it means I need more sleep
- When I've had enough sleep, I'll wake up alert and refreshed
- If I don't get enough sleep during the night, I should make up for it by sleeping late or by taking a long nap
- Sometimes it's necessary to miss work or school because of lack of sleep or really poor sleep

Fatigue Scale: VAS rating the degree of each of sleepiness, acute fatigue, and chronic fatigue; both at the time of filling in the questionnaire, and also for the previous week. For chronic fatigue, the degree of distress and its impact on daily life were also rated;

Beck Depression Inventory (BDI): A widely used self-report scale, comprising 21 groups of 4 statements each. For this questionnaire, the two items dealing with sleep were omitted;

Mood Scale: Twelve VAS items rating both manic and depressive symptoms;

Single-item Screen for Depression: One question, "Are you depressed?" rated with a VAS;

Demographics: Age, gender, type of cancer, whether receiving chemotherapy or radiotherapy, and whether taking medication for anxiety, depression, or insomnia.

Results

Useable questionnaires were returned by 125 respondents, 87 (69.6%) women and 32 (25.6%) men. Mean age was 55.6 years, with a range of 23 to 84. Average sleep time was reported as 7.1 hours; however, respondents spent an average of 8.4 hours in bed. Women napped 0.8, and men 1.1 hours, on average. Average score on the Beck Depression Inventory was 8.7; only 11 out of 125 (8.8%) scored in the clinically depressed range (>20 out of a possible 63 points).

Cancer Type	# of Respondents	Per Cent
Breast	61	53.0
Colon, rectal, colorectal	21	18.3
Malignant melanoma	6	5.2
Lung	5	4.3
Ovarian	4	3.5
Testicular	3	2.6
Other	15	13.0

Men and women did not differ significantly in amount of time spent in bed, nap time, responses to 5 out of 6 of the sleep attitude questions, frequency of use of hypnotic medication, scores on the BDI, or scores on the fatigue scales.

Women experienced insomnia significantly more often than men (8.8 times per month, women; 3.1, men; P=0.0017). Women were significantly more distressed by their insomnia, expressed significantly more difficulty returning to sleep after waking earlier than desired, and agreed significantly more with the statement "If I don't get enough sleep during the night, I should make up for it by sleeping late or by taking a long nap".

Chronic fatigue scores by treatment modality:

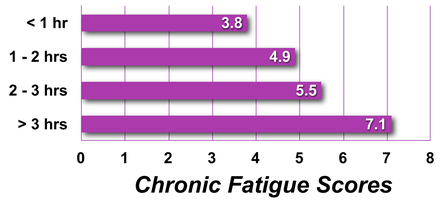
	# of Respondents	Per Cent	Chronic Fatigue Score†
No treatment	70	56.0	4.2 ± 4.4*
Chemotherapy	46	36.8	6.2 ± 5.1*
Radiotherapy	6	4.8	7.7 ± 5.7
Both chemo and radio	3	2.4	10.3 ± 4.4
Totals	125	100	5.2 ± 4.9

† Maximum 16.0; Mean ± S.D. *P=0.0338

Low chronic fatigue vs high chronic fatigue respondents (only significant differences shown):

	Low Fatigue N = 74	High Fatigue N = 49	P value
Chronic fatigue score	1.7	10.5	<0.0001
Age (years)	58.3	51.7	0.0039
BDI score	4.7	14.4	<0.0001
Insomnia score	3.8	7.9	<0.0001
Hypnotic meds (times / week)	0.8	2.3	0.0071
Arising time	7.3	7.8	0.0324
Time in bed after 6 am (hrs)	1.5	2.3	0.0102
Total time in bed (hrs)	8.6	9.2	0.0223
Attitude re missing work	1.2	2.3	0.0016

Chronic fatigue scores vs time in bed after 6 am (including nap time). The fatigue score for < 1 hr is significantly different from that for > 3 hrs (P = 0.0094):



Discussion

This questionnaire study supports the hypothesis that late rising is associated with higher levels of fatigue and depression. It also replicates findings of other studies demonstrating an association between cancer fatigue, insomnia, and depression[8, 13].

Why would sleeping more than usual or sleeping late be associated with fatigue? I hypothesize that fatigue and other depressive symptoms are adaptive mechanisms which support healing after injury, and that these symptoms are mediated through sleep.

Suppose a bear receives a long, deep slash in a fight. Its best chance for survival is to move as little as possible until the wound is sufficiently healed so it will not reopen and become infected. Movement is minimized when the animal has a loss of appetite, loss of sex drive, no interest in otherwise pleasurable activities, fatigue and lack of energy, and fibromyalgia-type pain, all in the context of hypersomnia.

It is known that some inflammatory cytokines produced after an injury, such as IL-1b and TNF-a[14], promote sleep. I suggest that the additional sleep caused by these cytokines, specifically additional REM sleep, causes the depressive symptoms such as loss of appetite and fatigue, which in the context of an injury improve an animal's chances for healing.

Cancer patients, particularly those undergoing treatment, may have increased somnolence not only from inflammation and associated cytokines, but also from cell wall breakdown products[15].However, attempts to sleep excessively can occur even in the absence of injury or inflammation. For example, cancer patients who have stopped working may have more opportunity for sleep, and may attempt to use sleep as a way of escaping psychological distress or boredom. Attempts to increase sleep in the absence of sleep-inducing cytokines are likely to result in insomnia; insomniac patients usually believe that they are not getting enough sleep[16], and may attempt to sleep even more. Similarly, a belief that one's fatigue is caused by poor sleep may stimulate spending more time in bed.

Spending more time trying to sleep will increase the amount of sleep obtained. How much of this additional sleep is REM sleep depends on the timing of the sleep in relation to the individual's circadian rhythm. Morning sleep typically has the most REM sleep[3]. Thus, sleeping late may have the greatest impact on fatigue

Limitations of this study

- Depressed or highly fatigued patients would be less likely to consent to fill in the questionnaire. This would skew the sample towards those with little fatigue.
- The word "fatigue" has several meanings.
- The sleep habits questionnaire does not account for differences in sleep patterns between weekdays and weekends.

Treatment implications

If the hypothesis that late rising causes excessive REM sleep which in turn results in fatigue and possibly depression is valid, treatment strategies might involve reducing total sleep time (eg sleep restriction as used to treat insomnia[17]); reducing REM sleep by rising earlier[18]; suppressing REM sleep (most antidepressants[19]; exercise[20]); or psychostimulants such as methylphenidate[21] given early in the morning (methylphenidate reduces sleep and also decreases REM sleep[22]).

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