

# Cancer Fatigue and Sleep: A Possible Role for Rising Time?



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## Abstract

### Background

Fatigue is the symptom most frequently reported by cancer patients, and is often the most distressing. Given that fatigue and insomnia are closely linked not only in cancer but also in other illnesses, and that fatigue is frequently associated with depression, the connection between sleep patterns, fatigue, and depression was explored.

### Method

A convenience sample of outpatients being followed by the Medical Oncology and Radiation Oncology clinics at the SMBD-Jewish General Hospital were asked to fill in a self-response questionnaire about their sleep habits, insomnia complaints, attitudes about sleep, fatigue, depression, cancer type and current treatment, and use of psychotropic medication.

### Results

One hundred and twenty-five usable questionnaires were returned. Those receiving cancer treatment had a significantly higher average level of fatigue compared to those not undergoing treatment.

When respondents were divided into a low fatigue group (N=74) and a high fatigue group (N=49) using as a cutoff the mean fatigue score for the entire sample, the high fatigue group was significantly younger, more depressed, more insomniac, used sleeping pills more, and spent more time in bed after 6 am than the low fatigue group. They were also significantly more likely to believe that "Sometimes it's necessary to miss work or school because of lack of sleep or really poor sleep."

### Discussion

The intriguing finding that sleeping late is associated with higher levels of fatigue, can be explained by a variation of Michael Wiegand et al's "Depressogenic sleep theory" that excessive REM sleep may induce depression. It is hypothesized here that cancer patients are more likely to attempt to sleep more than usual, either to escape painful feelings, or because of somnogenic effects ascribable to their illness or its treatment, or because of increased opportunity. Sleeping late results in large increases in REM sleep. If physiologic needs for REM sleep are exceeded, clinical depression may result in individuals who are genetically predisposed. Others may develop a subclinical form of depression, such as chronic fatigue.

This hypothesis also suggests that treatment approaches such as earlier rising times or psychostimulants taken early in the morning may be helpful in cancer 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, peaking at around 8:30 am, sleeping late may be more important than sleep duration in determining the amount of REM sleep obtained, 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 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 were analyzed using Data Desk (version 6.1.1; Data Description, Inc.) on a Macintosh computer.

## Results

Useable questionnaires were returned by 125 respondents, 87 (69.6%) women and 32 (25.6%) men; 6 did not specify gender. 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 was reported by 115 patients (table 1).

Table 1

Cancer Type	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

Responses of the male and female groups were not significantly different in terms of 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".

Table 2 breaks down the sample by treatment modality. For each group, chronic fatigue scores (out of a possible 16) are shown.

Table 2

	Respondents		Chronic Fatigue Mean Score
	N	%	
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	3	2.4	10.3 ± 4.4
Totals	125	100%	5.2 ± 4.9

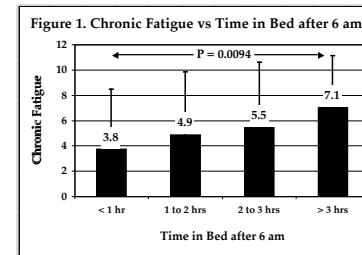
\*P=0.0338

The entire sample was divided into two groups, those with low scores for chronic fatigue (<5.2), the sample mean) and those with high chronic fatigue scores. Characteristics which differed significantly between the high and low chronic fatigue groups are shown in table 3.

Table 3

	Low Fatigue	High Fatigue	P value
N	74	49	
Chronic fatigue score	1.7	10.5	<.0001
Age (years)	58.3	51.7	.0039
BDI score	4.7	14.4	<.0001
Insomnia score	3.8	7.9	<.0001
Hypnotic meds (per wk)	0.8	2.3	.0071
Arising hour	7.3	7.8	.0324
Time in bed after 6 am (hrs)	1.5	2.3	.0102
Total time in bed (hrs)	8.6	9.2	.0223
Attitude re missing work	1.2	2.3	.0016

The sample was split into four groups based on the amount of time spent in bed after 6 am, including nap time. Chronic fatigue scores varied as shown in figure 1.

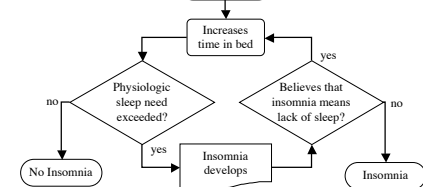


Besides the excessive REM sleep hypothesis, what other possible explanations are there for an association between late rising and fatigue? First, patients may ascribe their fatigue to lack of sleep, especially if they believe that their insomnia means insufficient sleep, and they may simply remain in bed later in the morning in an attempt to get more sleep. Second, both fatigue and a tendency to somnolence in the morning may be caused by a common factor, for example, cytokinins secreted in response to the cancer or to its treatment. A third possibility is that fatigue itself causes late rising, perhaps through some effect on the normal arousal and waking mechanisms. Fourth, it may be that extending one's sleep by getting up later may cause fatigue, but through a mechanism involving circadian rhythms or sleep factors other than REM sleep, such as delta sleep.

Assuming that excessive REM sleep due to late rising is the cause of fatigue, it is reasonable to ask why cancer patients would be affected, or why these individuals would be attempting to sleep more by getting up later than when they were well. There are three possibilities:

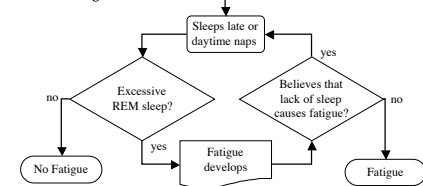
- Sleep represents an escape from anxiety and other painful feelings;
  - More time to sleep & boredom when on sick leave from work or school;
  - During treatment, cell wall breakdown products<sup>8</sup> & cytokines<sup>10</sup> cause somnolence.
- Sleeping longer than needed contributes to insomnia (figure 2):

Figure 2. Vicious circle of insomnia



If the extra sleep results in excessive REM sleep (figure 3):

Figure 3. Vicious circle of fatigue



### Limitations of the present 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, treatment strategies might involve reducing total sleep time (eg sleep restriction as used to treat insomnia<sup>11</sup>); reducing REM sleep by rising earlier; suppressing REM sleep (most antidepressants<sup>12</sup>; exercise<sup>13</sup>); or psychostimulants given early in the morning (eg methylphenidate reduces sleep and also decreases REM sleep<sup>14</sup>).

## 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.