

## SLEEP PROBLEMS IN PATIENTS WITH MEDICAL ILLNESS

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### Factors that may indicate a disruption of sleep architecture in medically ill patients

- Movement arousals (number)
- Frequent changes in sleep stage (per hour of sleep)
- Awakenings in first six hours of sleep (number)
- Sleep efficiency (%)
- Apnoea index
- Leg kicks (total number)
- Abnormal REM latency
- Reduced slow wave sleep corrected for age (% below normal)
- Total sleep time
- Long awakenings (10 min)
- $\alpha$  Patterns on electroencephalogram

Sleep complaints are ubiquitous in patients with medical illness. A recent survey of outpatients attending hospital clinics indicated that the vast majority of patients reported sleep disruption concomitant with their condition. The proportion with complaints (> 70%) was more than twice that among control subjects. Doctors rarely ask about sleep problems in the context of medical illness despite the fact that the patient's first complaint may be that a particular symptom caused sleep disruption.

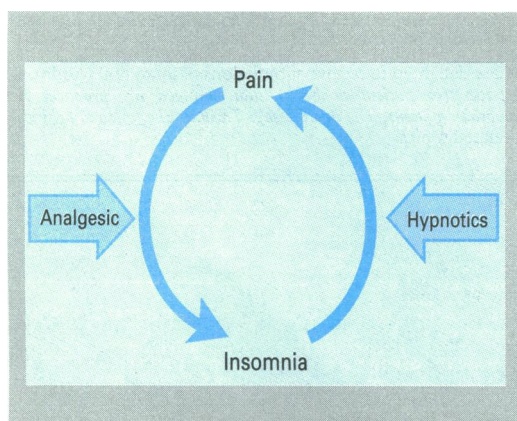
There are specific reasons for sleep disruptions in patients with medical illness—for example, people are often deprived of sleep before an operation. Polysomnography has shown that there is a preoperative reduction in slow wave sleep and that this is related to the anticipated importance of surgery. The increase in deep sleep that occurs after an operation is thought to facilitate the healing process.

A variety of sleep variables may be influenced by specific disorders and particular treatments and each of these effects is likely to differ. A decrease in deep (slow wave) sleep, for example, may lead to a sensation of having low energy, whereas repeated interruption of sleep may lead to daytime sleepiness.

Drugs may also disrupt sleep architecture by suppressing rapid eye movement (REM) sleep or by causing a withdrawal effect during the night. In both cases the drug clearly alters sleep, but the impact on health and recovery may differ.

Fatigue is common in several medical conditions. Clinicians, researchers, and patients themselves claim that the fatigue experienced in certain medical conditions differs qualitatively from the experience of tiredness or sleepiness. However, there have been few attempts to separate these states. In this article we provide an overview of the impact of medical disorders on sleep.

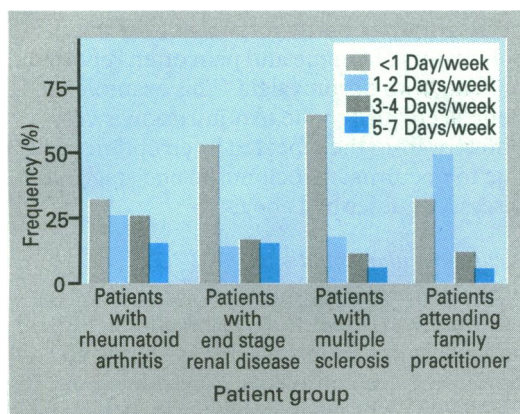
### Sleep problems in specific conditions



Although sleep related problems among medically ill patients have only recently begun to be investigated, there is a rapidly growing body of evidence that sleep can be profoundly affected by ill health.

#### End stage renal disease

Several studies have examined sleep disturbances among patients with end stage renal disease, in which sleep is significantly altered. Patients receiving renal replacement therapy by maintenance haemodialysis or peritoneal dialysis have considerably more severe sleep disorders compared with healthy controls. Patients receiving dialysis commonly complain of insomnia and daytime fatigue. However, the factors responsible for these problems remain to be elucidated. We could speculate that night time sleep problems might be attributable to the immobilisation imposed by maintenance haemodialysis and the propensity of patients to nap during treatment as a result, but no differences have been observed between the night time sleep characteristics of patients treated by haemodialysis as



Frequency of restless sleep across four patient groups.

compared with peritoneal dialysis. In one study caffeine intake and worry were the only factors associated with reported sleep disturbance in renal disease; Kt/V values did not predict reported sleep problems.

Patients with end stage renal disease can have some of the most intractable sleep difficulties, which do not easily respond to treatment. Profound sleep disturbances are commonly the result of sleep related periodic involuntary limb movements that occur at 20-40 second intervals, leading to a disruption of the continuity of sleep. These disruptions compromise sleep quality, which is different from the sleep problems in other conditions (see below).

Psychosocial factors also seem to be related to sleep disturbances in patients with end stage renal disease. It has been shown, for example, that patients receiving dialysis who report increased tiredness and sleep disturbance also report increased negative affect. These observations must be qualified, however, by the finding that the patients who experience sleep disturbances seem to lack insight into the problem. One study concluded that use of denial as a coping defence may decrease awareness of sleep dysfunction in end stage renal disease.

Increased insomnia coupled with increased self-administration of hypnotic drugs is often the forerunner of a worsening clinical state in patients receiving maintenance dialysis. Recent research on sleep problems and myocardial infarction showed a parallel finding: an increase in insomnia predicted increased risk of myocardial infarction two weeks later.

### Comparison of features in chronic fatigue syndrome and fibromyalgia

| Features                                                                          | Chronic fatigue syndrome            | Fibromyalgia                        |
|-----------------------------------------------------------------------------------|-------------------------------------|-------------------------------------|
| <b>Symptoms and signs:</b>                                                        |                                     |                                     |
| Fatigue                                                                           | +++ (97%)                           | ++ (90%)                            |
| Pain                                                                              | +                                   | ++                                  |
| Sleep disturbance                                                                 | +                                   | +                                   |
| α Pattern on electroencephalogram                                                 | + ve                                | + ve                                |
| Decreased slow wave sleep                                                         | ?                                   | +                                   |
| Depression                                                                        | ✓                                   | ✓                                   |
| Tender points*                                                                    | +                                   | ++                                  |
| Other physical symptoms (such as paresthesias)                                    | +/-                                 | +/-                                 |
| <b>Epidemiology</b>                                                               |                                     |                                     |
| Preponderance among women                                                         | 79%                                 | 87%                                 |
| Age at presentation                                                               | 25-40 years                         | 30-45 years                         |
| Weather effects                                                                   | ?                                   | ✓                                   |
| Comorbid diagnosis (for example, irritable bowel syndrome, premenstrual syndrome) | Common                              | Common                              |
| <b>Evolution</b>                                                                  |                                     |                                     |
| <b>Sociocultural</b>                                                              |                                     |                                     |
| "Workaholism"                                                                     | ✓                                   | ✓                                   |
| Masked depression                                                                 | ✓                                   | ✓                                   |
| Western disease                                                                   | ✓                                   | ✓                                   |
| Participation in self help groups                                                 | ++                                  | ?                                   |
| Relapse triggered or precipitated by stress                                       | ✓                                   | ✓                                   |
| No definitive investigations                                                      | True                                | True                                |
| Pathology delineated                                                              | No                                  | No                                  |
| <b>Treatment response</b>                                                         |                                     |                                     |
| Cognitive therapy                                                                 | Yes                                 | Yes                                 |
| Low dose antidepressants                                                          | Improve sleep and muscular symptoms | Improve sleep and muscular symptoms |
| High dose antidepressants                                                         | Improve comorbid mood               | Improve comorbid mood               |
| Improved sleep (for example, with cyclopyrrolone)                                 | Yes (anecdotal)                     | Yes                                 |
| Exercise treatment                                                                | +/-                                 | +/-                                 |
| Light therapy                                                                     | ?                                   | ?                                   |

\*Mean (SD) tenderpoint scores are as follows: 3.5 (2.6) in normal people; 16.9 (14.1) in those with chronic fatigue syndrome; 33.0 (11.8) in those with fibromyalgia.  
+/- = May be present; ✓ = Present but no degrees; ? = Uncertain.

#### Rheumatoid arthritis

Middle insomnia (that is, fragmented sleep) is associated with exacerbations of illness in patients with rheumatoid arthritis. Patients with fragmented sleep experienced increased fatigue and joint pain. This is consistent with findings in animals and humans that sleep deprivation reduces the pain threshold. Indeed, in one study, 70% of arthritic patients took benzodiazepines to overcome night pain. These findings suggest that it is profitable to treat pain and insomnia concurrently owing to their reciprocal effects. In another study, however, pain predicted subsequent increases in sleep problems in rheumatoid arthritis but the reverse predictive relation was not also observed, endorsing the traditional view to treat the primary cause.

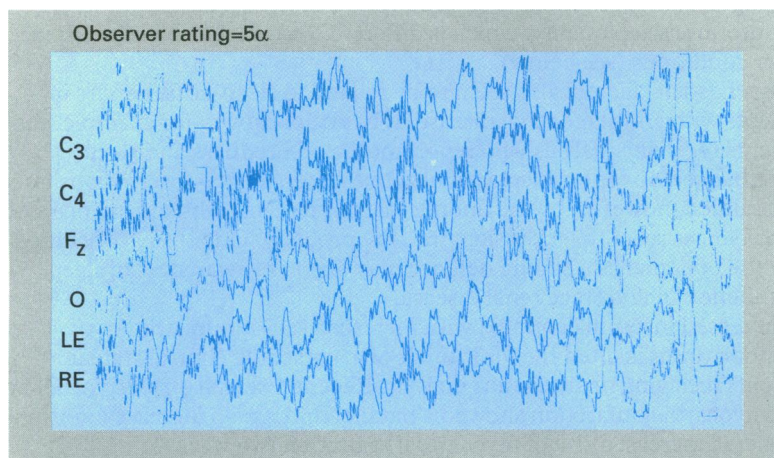
#### Fibromyalgia and the chronic fatigue syndrome

Fibromyalgia is characterised by multiple tender points and complaints of fatigue. In a recent overview the features of fibromyalgia and the chronic fatigue syndrome were found to be very similar. There is a high incidence of sleep abnormalities (67% in a recent polysomnographic study of patients with the chronic fatigue syndrome). A commonly reported feature in the sleep of these patients is an α electroencephalographic pattern. This implies that α waves, which are usually associated with relaxed wakefulness (with eyes closed), intrude into the sleep electroencephalogram. When it is explained to patients that this is an indication of poor quality sleep they often respond that they feel as if they "just skim below the surface of sleep."

These patients commonly describe feeling as if they are awake during sleep and completely misjudge the duration before sleep onset and the total duration of sleep. This qualitative change in sleep may be partly responsible for the complaints of fatigue and pain often reported by patients with fibromyalgia. This example of poor sleep quality due to  $\alpha$  intrusion is very different from the repeated interruption of sleep due to nocturnal myoclonus in end stage renal disease, as described above.

#### Neuromuscular conditions

Neuromuscular conditions can affect sleep profoundly. In one study, for example, 88% of patients with Parkinson's disease reported significant sleep problems. Bradykinesia during the night is especially problematic. Patients with advanced Parkinson's disease may experience sleep/wake dysfunction due to cumulative effects of motor abnormalities, neurochemical changes, depression, drugs, and dementia. Episodic muscle contractions, irregular fragmentary twitches, and jerks of the extremities may occur during light sleep. About 33% of patients with Parkinson's disease experience periodic leg movements. Vocalisations and prolonged activation of muscle tone may occur during REM sleep and may, in some cases, evolve into REM sleep behaviour disorders. Occasionally, visual hallucinations may be described and may be the consequence of sleep deprivation.



$\alpha$  Pattern on electroencephalogram in a patient with the chronic fatigue syndrome.

## Sleep disruptions that inhibit healing

### Aetiologic factors in the intensive care unit syndrome

- Patient's age
- Patient's psychological history
- Use of cardiopulmonary bypass pump
- Metabolic and drug factors
- Severity of illness
- Sleep deprivation

Given an adequate amount of sleep, patients in intensive care units will experience less physical and psychological stress and fewer mental status alterations and, thus, will have a more rapid and less traumatic recovery

There are many situations in which sleep may be disrupted, and this may prolong or worsen a disease process. An intensive care unit environment, with its attendant continuous lighting, noise throughout day and night, and the disruption of sleep for the purpose of investigations, is a typical example. The so called "intensive care unit syndrome" has been held responsible for inhibiting patient recovery. One associated aetiological factor is sleep deprivation. An alteration in mental state, including delusions and paranoia, has been noted with sleep deprivation, which is common in the intensive care unit setting. Recovery sleep in the experimental situation or transfer out of the intensive care unit often leads to a resolution of these symptoms.

In a German study of patients in intensive care units with neurological disorders who underwent polysomnographic monitoring, there was a pronounced reduction in REM sleep; occasionally no REM sleep was recorded. Changes in this group were related to specific neurological lesions. Patients with demyelinating diseases, such as multiple sclerosis, did not show many sleep pattern abnormalities.

In another study careful documentation of 62 subjects over their first three days in the intensive care unit showed that most (56%) were sleep deprived during the first day. This declined over time, but 20% were still judged to be sleep deprived in their third day in the unit. More severely ill patients were more sleep deprived. Patients who were sleep deprived to a comparatively greater extent were also significantly more likely to display the intensive care unit syndrome.

Several other factors which lead to a deterioration in sleep architecture in relation to the process of healing include pain, age related sleep deterioration, and the psychosocial stress associated with ill health. Drugs used in various illnesses have an impact on sleep and daytime alertness which, in some cases, may be unexpected—for example, sleep disruption attributable to hypertension may be compounded by drug effects, leading to the paradox where disruption is significantly greater in treated patients.

## Treating sleep problems in the context of medical illness

### Steps in tackling fatigue in a medical condition

- (1) Investigate standard medical possibilities—for example, thyroid disease—and make a diagnosis if possible. Contemplate multiple diagnoses. Query depression
- (2) Treat the medical illness to the extent this is possible. Give palliative treatment. Use stimulating antidepressants or electroconvulsive therapy if needed
- (3) Consider whether drugs contribute to the fatigue—for example, antiepileptic drugs. Can the specific drug or the dosing schedule be altered?
- (4) Review sleep hygiene of the patient. Even small changes in activity make a difference. Ensure that the patient does not take daytime naps or have any unnecessary nocturnal interruptions of sleep—that is, consolidate sleep and restrict bedtime to improve sleep efficiency
- (5) Paradoxically, a hypnotic which improves sleep may lessen daytime fatigue
- (6) Consider the possibility of a primary sleep disorder and investigate accordingly

There is a current trend against the use of hypnotic drugs. Particularly in the medically ill, this must be tempered insofar as improved sleep may facilitate recovery and poor sleep may lead to increasing anxiety and distress. Moreover, poor sleep may eliminate the opportunity of relief from physical symptoms.

Practical considerations must also be taken into account—for example, in chronic disabling conditions, such as Parkinson's disease, sleep disruption can be minimised by arranging for a portable commode to be placed at the bedside. Adjustments to the type, dose, or scheduling of drugs should be considered to minimise potential iatrogenic causes of insomnia. Respite admissions for the patient or advising a couple to use separate bedrooms may improve sleep quality for the spouse.

The interaction of many drugs with hypnotic drugs needs to be carefully balanced in medically ill patients.

Compliance with treatment may also be influenced by the sleep effects of non-hypnotic drugs. Impact on sleep may be the key determinant of quality of life differences across alternative treatments. In a study of patients with joint pain, for example, two treatment groups were compared in terms of quality of life. Patients treated with a combination of dextropropoxyphene and paracetamol reported a significant excess of tiredness and sleep disturbance compared with those treated with diclofenac sodium slow release but no other quality of life difference was detected.

## Quality of life

There is a reciprocal interaction between the influence of medical illnesses on sleep. Careful attention to the sleep complaints of medically ill patients will facilitate improved healing, wellbeing, and a greater ability to cope with disease. Improved compliance with treatments used in medical illnesses is promoted if sleep related issues are taken into consideration

Not surprisingly, sleep difficulties can compromise quality of life in patients with medical illness. Depression and negative effect occur, at least in part, because of the disruptions in lifestyle, activities, and interests ("illness intrusiveness") that occur as a result of illness induced reductions in energy, stamina, and cognitive arousal. Illness intrusiveness into important life domains (for example, work, family relationships, leisure, friendships) occurs with greater intensity among patients with chronic illness who experience relatively frequent episodes of restless sleep. A recent comparison of sleep problems across three chronic conditions indicated that restless sleep occurred most commonly among patients with rheumatoid arthritis, moderately commonly in those with end stage renal disease, and least commonly among people with multiple sclerosis. Moreover, the relation between restless sleep and emotional distress was mediated by illness intrusiveness—that is, restless sleep seemed to exert its impact on emotional distress through its disruption of lifestyle, activities, and interests. These relations were observed in both depressed and non-depressed patients, indicating that the phenomenon could not be attributed to a depressive response.

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The ABC of Sleep Disorders has been edited by Professor Shapiro.