Treatment of Insomnia, Fatigue, and Other Depressive Symptoms by Reduction of Sleep

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Introduction

The object of the proposed research program is to explore the hypotheses that insomnia is a symptom of excessive sleep; that fatigue and other depressive symptoms are caused by excessive REM sleep, and that an effective treatment is sleep reduction. It is important to emphasize that the type of insomnia being addressed in this proposal is primary insomnia, not difficulty sleeping as a result of excessive stimulant intake (whether caffeine or medications), medical conditions such as sleep apnea, severe pain, or extreme anxiety.

Significance of insomnia, fatigue, and depressive symptoms

Insomnia: an epidemic

Insomnia is endemic, if not epidemic, in North America, with 15-20% of the population complaining of a serious insomnia (Spielman 1986). In rural elderly, half voiced an insomnia complaint (Ganguli et al 1996), while 40% of community-dwelling Alzheimer patients had disrupted sleep (Carpenter et al 1995). In cancer patients, insomnia is very common (Beszterczey & Lipowski 1977[1]; Nail et al 1991[2]) and can be severe (Cannici et al 1983[3]). Insomniacs suffer: they have more chronic psychological distress (Johns et al 1971b[4]); 56% in a general practice setting were significantly dissatisfied with life, and 40% described themselves as anxious, oversensitive, emotionally labile and having many problems (Schramm et al 1995[5]). Objectively, they are also poorly adjusted: compared to normals, they deviate significantly on 13 out of 18 MMPI (Minnesota Multiphasic Personality Inventory) scales (Schneider-Helmert 1987[6]). Depression and anxiety are frequent (Bazargan 1996[7]).

Costs of insomnia treatment

Treatment for insomnia is costly. Insomniacs utilize health care resorces more (Morin et al 1994[8]); 14% of the general public reported taking a hypnotic nightly; this number increased to 24% for hospital clinic outpatients (Shapiro & Bachmayer 1988[9]); for Dutch elderly, 16.5% use sedative-hypnotics regularly (Middelkoop et al 1996[10]). One-third of over-75's filled prescriptions for hypnotics, sedatives, or anxiolytics (Gustafsson et al 1996[11]).

Safety and occupational concerns

Insomnia and its treatments are associated with safety risks. Long-term insomniacs have 2.5 times more automobile accidents than good sleepers (Becker et al 1993[12]). Over half of sleep clinic clientele have had accidents at work, and almost half were involved in motor accidents (Martikainen et al 1992). Sedative/hypnotic users have more motor vehicle accidents (Skegg et al 1979), and visit emergency rooms more frequently (Oster et al 1987). In the elderly, long-acting benzodiazepines significantly increase the risk of hip fracture (Grad 1995).

It is believed that more than 2% of the US population in some regions may have used melatonin to improve sleep (Young 1996). Long-term effects of chronic melatonin usage are unknown.

In terms of occupational performance, flurazepam 30 mg (a widely prescribed hypnotic) taken at bedtime induces next day sleepiness and a tendency to poorer performance and more negative mood (Johnson et al 1990[13]). Substance use disorder is common among insomniacs (Schramm et al 1995[14]). Insomniacs take more sick leave (Morin et al 1994[15]

Fatigue and other symptoms

Fatigue in medical illness

Fatigue is reported to be the most distressing symptom by cancer patients (McCorkle & Quint-Benoliel 1983; Degner & Sloan 1995; Donnelly & Walsh 1995[16]; Irvine et al 1991; Taphoorn et al 1994; Sarna 1993b[17]; Smets et al 1993[18]; Graydon 1994), perhaps particularly so for those receiving treatment (Knobf 1986; Jamar 1989; Greenberg et al 1992, 1993; Richardson 1995), in whom tiredness and weakness interfered the most with self-care activities (Rhodes et al 1988).

Fatigue affects nearly 80% of patients with rheumatoid arthritis (Mahowald et al 1989) and in patients on hemodialysis for end stage renal disease, is related to inactivity and sleep disturbance (Brunier & Graydon 1993).

In chronic fatigue syndrome, 28% of patients described their fatigue as being so severe that they became bedridden, able to do virtually nothing (Buchwald et al 1987). Complaints of tiredness and fatigue were universal during the initial weeks of Epstein-Barr viral infection (Guilleminault & Mondini 1986).

Fatigue and occupational issues

20% of unemployed patients with ARC or AIDS reported that fatigue was largely responsible for the need to stop working (Darko et al 1992). Most patients with chronic fatigue syndrome are unable to continue with full-time work, and many receive some form of disability payments for an extended period (Abbey & Garfinkel 1991).

Common perceptions about insomnia and fatigue

cultural myths

"Insomnia means insufficient sleep"

Both insomniacs and insomnia researchers believe that insufficient sleep is the problem. For example, insomniacs use the strategies of getting into bed early, staying in bed late, and napping (Spielman, Saskin & Thorpy 1987[19]). Becker et al (1993) define severe insomnia as "a nearly nightly complaint of an insufficient amount of sleep", and Lamb (1982) as "... lack of sufficient sleep to maintain physical and mental health".

In reality, insomniacs have been found to sleep as much as normals (Carskadon et al 1976[20]; Waters et al 1993; Pace-Schott et al 1994), and also to sleep more during the day (Johns et al 1971a[21])

"You cannot sleep too much"

Many individuals voluntarily extend their sleep time when the opportunity presents itself, eg on weekends or vacations, when ill, or upon retirement, even though they are aware that they function adequately with the amount of sleep they obtain on work or school days. When feeling fatigued, the usual tendency is to sleep more (Skalla & Lacasse 1992). Knowledge that for anything else that the body needs; for example, food, water, vitamins, minerals, exercise, or sun, an excess is usually detrimental, does not automatically apply to sleep.

Various meanings for tiredness, fatigue, sleepiness

Although the dictionary definitions for tiredness and fatigue are similar, and bear no relationship to drowsiness or sleepiness, these terms are frequently used interchangeably, both by lay people (Carskadon et al 1982) and by researchers (Moldofsky 1992[22]; Nofzinger et al 1991). For example, Martikainen et al (1992) state, "Tiredness may take the form of sleepiness"; according to Glaus (1993) one aspect of fatigue is the "dull, sleepy" factor; the Piper Fatigue Self-Report Scale includes "sleepy" and "drowsy" as fatigue sensations (Piper et al 1989a). The idea that fatigue may be caused by insufficient sleep (Jamar 1989) may spring from this confusion in terminology.

Although tiredness or fatigue is difficult to assess reliably, daytime sleepiness, which increases with reduced nocturnal sleep, can be objectively measured with the Multiple Sleep Latency Test (MSLT) (Carskadon et al 1982[23]; Rosenthal et al 1993).

The hypotheses

Insomnia is a symptom of excessive sleep

Rather than considering insomnia as "lack of sleep", an alternative is to view a difficulty in falling asleep or staying asleep as an indication that the person is sleeping excessively in relation to their actual sleep need (Chambers & Keller 1993[24]). This point of view is supported by studies showing that insomnia patients tend to spend more time in bed than normals (Frankel et al 1976[25]; Schneider-Helmert 1987; Middelkoop et al 1996[26]), underestimate the amount they actually sleep (Frankel et al 1976[27]) in some cases to extreme lengths (McCall & Edinger 1992), and have worse sleep efficiency with longer times in bed (Levine et al 1988[28]). The amount of daytime sleep is directly related to sleeping problems (Johns et al 1971b[29]; Rosa 1993[30]; Bazargan 1996[31]). Furthermore, voluntarily extending sleep causes insomnia (Aserinsky 1969[32]. Insomniacs have less daytime sleepiness (Middelkoop et al 1996[33]) and better reaction times at night (Bonnet & Rosa 1987[34])

Excessive sleep leading to insomnia (Spielman et al 1987[35] could occur in the following situations:

- An individual with a below-average physiological sleep requirement believes he or she needs the oft-cited 7 or 8 hours of sleep and therefore spends at least that many hours in bed;
- Although elderly people require less sleep (Kales et al 1967[36]; Brendel et al 1980[37]; Prinz et al 1990[38]; Wauquier et al 1992; Bliwise 1993; Reyner & Horne 1995[39]) many increase their time in bed (Prinz et al 1990; Middelkoop et al 1996[40]). For example, nursing home residents in one study (Webb & Swinburne 1971[41]) spend an average of 12 hrs out of every 24 in bed, but may sleep only 6.2 hours (Alessi et al 1995[42]). That this can disrupt circadian rhythms (Carskadon et al 1982) and leads to insomnia symptoms (Reyner & Horne 1995[43]; Riedel et al 1995[44]) is evident from data by Foltz-Gray (1996[45]) who found that the average nursing home resident sleeps no more than 40 minutes per hour at night, and 50% wake three to four times per hour. Activities of daily living become increasingly impaired as total sleep hours increase (Meguro et al 1990[46]).
- When people become ill, they frequently sleep more (Acheson 1959[47]; Guilleminault & Mondini 1986[48]). In the case of viral or bacterial infections, it is known that various sleep-promoting agents are produced, including interleukin-1 and -2, interferon, and muramyl dipeptide (from bacterial cell walls) (Moldofsky 1993[49]). Hospitalized patients have more opportunities to nap and sleep (Globus 1969[50]), as do individuals who take time off work or school. Cancer patients receiving treatment sleep more (Dodd 1984[51]; Jamar 1989[52]; Greenberg et al 1992, 1993), and their physical fatigue correlates with the number of hours of rest during the day (Kobashi-Schoot et al 1985[53]). Too much rest may promote fatigue (Winningham 1991; Graydon et al 1995) while excessive sleep may be partly responsible for the exhaustion reported by some hospitalized medical or surgical patients (Globus 1969). The fatigue, misinterpreted as due to lack of sleep by both patients and clinicians, may cause patients to attempt to sleep even more (Dodd 1984[54]), promoting the insomnia symptoms which frequently coexist with fatigue in cancer patients (McCorkle & Quint-Benoliel 1983[55]; Knobf 1986[56]; Sarna 1993a[57]; Graydon 1994[58]; Irvine et al 1994[59]; Degner & Sloan 1995[60]), in chronic fatigue syndrome (Buchwald et al 1987[61]; Krupp et al 1993[62]).
- People without regular employment or school commitments, including retirees, have more opportunities for daytime sleep as well as earlier bedtimes and later rising times. Too much time in bed perpetuates insomnia (Spielman, Saskin & Thorpy 1987[63]) as do irregular retiring and arising times and napping (Spielman 1986[64])

Although insomniacs may believe that their performance and alertness suffer due to lack of sleep, objective testing indicates that daytime performance is no different from controls (Schneider-Helmert 1987[65]) and daytime alertness is higher (Regestein et al 1993[66]; Bonnet & Arand 1995[67]) again suggesting that sleep loss is not a factor.

Excessive sleep results in excessive REM sleep

If one remains in bed longer than usual, total sleep duration will be increased by an average of about 2 hrs (Phoebus et al 1970[68]; Harrison & Horne 1996[69]) even without prior sleep deprivation (Webb & Agnew 1975[70]). However, enforced bed rest for 24 hrs results in 12.3 hours of sleep, increasing to 16.9 hours of sleep out of 24 after a night of sleep deprivation (Rosenthal et al 1993[71]). Longer sleep leads to an increase in REM sleep (Phoebus et al 1970; Taub 1980, 1983[72]; Gagnon & de Koninck 1984[73]). REM sleep increases also when sleep duration is extended with long-acting hypnotics (Seidel et al 1986[74]). Conversely, shorter sleep leads to less REM sleep, for example in healthy elderly (Kales et al 1967[75]; Brendel et al 1990[76]).

timing of sleep is important

However, because REM sleep as a percentage of total sleep varies in a cyclical fashion according to a circadian rhythm (diurnal variation) (Åkerstedt et al 1993[77]) with a progressive increase throughout the normal sleep period (eg 11 pm to 7 am) (Kales et al 1967[78]; Webb & Agnew 1977[79]; Lange 1982[80]; Carskadon & Dement 1985[81]), to a peak at 8:30 am (Taub et al 1983[82]) and a progressive decrease during daytime (eg 9 am to 4 pm) (Webb & Agnew 1968[83]), it is possible to increase or decrease the amount of REM sleep accumulated by shifting the sleep period in time, ie earlier sleep leads to less REM, and later sleep induces more REM sleep (Taub & Berger 1973[84]; Knowles et al 1982[85]), a difference seen also in early vs. late partial sleep deprivation (Sack et al 1988[86]. Thus, both duration and timing of sleep affect the amount of REM sleep obtained.

Excess REM sleep causes fatigue and depressive symptoms

Although the present hypothesis has to do with excessive REM sleep, it is clear that some REM sleep is essential. REM sleep is believed to be necessary for learning (Smith et al 1991; De Koninck & Prévost 1991[87]) and in particular for the consolidation of memory (Herscovitch et al 1980[88]; Mandai et al 1989[89]; Kami et al 1992[90]). Many studies show that the REM sleep % is remarkably constant throughout the lifespan in healthy adults (Kahn & Fisher 1969[91]), and in the elderly the amount of REM sleep is strongly correlated with waking mental ability (Feinberg & Carlson 1968; Prinz 1977).

The connection between increased REM sleep and depression has been frequently noted (Montplaisir 1984; Thase et al 1994; Nofzinger et al 1995), although Wiegand et al (1987[92]) may have been the first to propose the hypothesis that too much REM sleep causes depression. Evidence for this hypothesis fits into several categories:

- effects of increasing REM sleep
- phenomena associated with increased REM sleep
- effects of increasing total sleep (which also increases REM sleep(Phoebus et al 1970[93]; Taub 1980, 1983[94]; Gagnon & de Koninck 1984[95]; Seidel et al 1986[96]))
- phenomena associated with increased total sleep (ie excess REM sleep)
- effects of sleeping later (which increases REM sleep)
- phenomena associated with sleeping later
- and finally, phenomena associated with insomnia, which, as noted above, can be caused by excessive sleep. Since excessive sleep increases REM sleep, these phenomena are thus associated with increased REM sleep.

effects of increasing REM sleep

Reserpine, an antihypertensive medication which increases REM sleep (Faber & Havrdova 1981; Jus et al 1975), has the side effect of causing depression. Benzodiazepines, which can increase REM sleep (Montplaisir 1984[97]), belong to the group of sedative/hypnotics which have depression as a side effect (Edwards et al 1991, Lydiard et al 1987, both cited in Patten et al 1996; Patten et al 1996). Patients who respond to total sleep deprivation will have a recurrence of depression if they have a daytime nap which includes REM sleep (Wiegand et al 1987[98]).

phenomena associated with increased REM sleep

It is known that REM sleep is increased in affective disorders (Benca et al 1992), particularly in depression (Cartwright 1983[99]; Montplaisir 1984[100]; Thase et al 1994; Lauer et al 1995[101]; Nofzinger et al 1995), or in relapse of depression following successful treatment (Kupfer et al 1991[102]), and that REM sleep amount correlates with minor psychopathology such as depression, anxiety, or shyness (Müller 1984[103]). However, it is important to stress that at least some patients with major depression have REM sleep abnormalities besides increased REM sleep; for example, short REM latency is found (De La Fuente et al 1992[104]); a very short REM latency is associated with more severe depression and bipolar depression (Schulz & Tetzlaff 1982[105]) and with delusional depression (Grunhaus et al 1994[106]); short REM latency also is characteristic of patients successfully treated with TCA's or ECT, whereas treatment failure is associated with long REM latency (Svendsen & Christensen 1981[107]. Depressed patients also have more REM sleep in the first third of the night (Gresham et al 1995[108]), with the first REM period being twice as long as in normals (Lauer et al 1995[109]). Short REM latency is found in many patients with other illnesses such as narcolepsy, schizophrenia, obsessive-compulsive disorder, mania, chronic psychogenic pain syndromes, drug-withdrawal states, and so forth, in which depressive symptoms are common, and many of these patients respond to antidepressant medications (Gillin & Borbély 1985[110]; Benca et al 1992).

Post-traumatic stress disorder patients, whose symptoms of insomnia, decreased concentration, anhedonia, and social withdrawal overlap those of depression, have increased REM sleep (Ross et al 1994).

Previously depressed patients who relapsed while on maintenance treatment with antidepressants had increased REM sleep (Kupfer et al 1991[111]).

effects of increasing total sleep (which also increases REM sleep)

Wiegand et al (1987[112]) proposed the "depressiogenic sleep theory": sleep may induce depression and sleep deprivation relieves it.

Globus (1969[113]) employed the concept "worn out" syndrome, described by the terms "worn out, tired, lethargic, in an irritable mood, fuzzy thinking, difficulty getting started" which occurred in students after a night of sleep prolonged to 10 or more hours. Sleep prolongation impairs mood and performance (Deaconson et al 1988[114]; Bartle et al 1988). Long sleepers have poorer psychological adjustment compared to short sleepers (Montplaisir 1984[115]).

The performance deficits seen after extended sleep (Wilkinson 1963[116]; Taub et al 1971[117]; Taub 1980, 1983) have also been hypothesized to be due to augmentation of REM sleep (Taub 1980[118]).

Melatonin, which increases sleep duration, also increases self-reported fatigue (Dollins et al 1994)

phenomena associated with increased total sleep (ie excess REM sleep)

In affective disorder, hypersomnia is characteristic of patients with bipolar depression (Nofzinger et al 1991) as well as young depressives (Hawkins et al 1985), and is associated with complaints of anergia and psychomotor slowing (Detre et al 1972[119]). People with depressed mood underestimate the actual length of their sleep (Bliwise et al 1993), and frequently nap (Kerkhofs et al 1991[120]) or rest in bed during the day (Kerkhofs et al 1992[121]). Longer sleep latencies and lower sleep efficiencies in depressives (Feinberg et al 1982[122]) and in brief recurrent depression (De La Fuente et al 1992[123]) suggest excessive sleep. Hypersomnia is also a feature of seasonal affective disorder (Oren et al 1992[124]).

The sleep disorders narcolepsy-cataplexy and idiopathic hypersomnia, both characterized by daytime sleep, are often associated with clinical depression (Herscovitch et al 1980[125])

Fatigue and hypersomnia are related in medical illness: persons who suffer from cancer, depression, fibromyalgia/chronic fatigue syndrome and HIV infection sleep more and nap more compared to normals; this may cause their higher fatigue levels (Darko et al 1992[126,127]). Most chronic fatigue syndrome (CFS) patients, in whom hypersomnia is characteristic (Morriss et al 1993[128]), had depressed mood (Whelton et al 1992[129]). According to Moldofsky (1993[130]) the symptoms of fibromyalgia or CFS are linked to the sleep-wake disturbance. Women with systemic lupus erythematosus (SLE) report more fatigue and longer total sleep time than normals (McKinley et al 1995). In cancer patients receiving radiotherapy, fatigue correlated highest with number of hours of daytime rest (Kobashi-Schoot et al 1985[131]).

Nursing home patients show increasingly impaired skills in activities of daily living as their total sleep hours increased (Meguro et al 1990).

Hyperactive children have longer total sleep time compared to controls (Luisada 1969[132]; cited in Tirosh et al 1993)

Independently of its relationship with fatigue and depressive symptoms, excessive sleep is unhealthy: in a large-scale epidemiological study in a typical California urban community, long sleep (9 hr or more) was associated with poorer physical health (Belloc & Breslow 1972[133]) and higher mortality (Belloc 1973[134]; Kripke et al 1979[135]; Wingard & Berkman 1983).

effects of sleeping later (which increases REM sleep)

Late sleeping itself may aggravate or precipitate depression (Globus 1969; Wehr et al 1979; Surridge et al 1987, cited in Regestein & Monk 1995)

Medical students who went to bed and arose later had MMPI scores reflecting arousal-seeking behaviour and a need for excitement (Johns et al 1974[136]).

A six-hour delay of sleep led to significant increases in subjective feelings of depression and decreased alertness, happiness, and energy (David et al 1991[137])

phenomena associated with sleeping later

Emergency room physicians working night shift and sleeping during the day have poorer performance on simulated clinical tasks compared to those working day shift (Smith-Coggins et al 1994[138]).

45% of delayed sleep phase syndrome patients use antidepressants (Regestein & Monk 1995[139]).

phenomena associated with insomnia

If one accepts the interpretation described above, that symptoms of primary insomnia are caused by sleeping more than physiologically required, then it is likely that insomniacs have excessive REM sleep, particularly since many insomniac persons tend to obtain their extra sleep in the morning when REM % has its circadian peak. Thus an examination of the vast insomnia literature may suggest symptoms of excessive REM sleep.

Insomnia is a risk factor for depression. In a study involving almost 8000 community respondents, people who still had insomnia a year after the initial interview were 40 times more likely to develop a new major depression than those without insomnia (Ford & Kamerow 1989[140]). In another study (Schramm et al 1995[141]) insomniacs had 4 times the rate of affective disorder and double the rate of anxiety disorder compared to the general population. The rate of depression was highly correlated with insomnia in a study of caregivers of dementia patients (McCurry & Terri 1995[142]).

Fatigue and insomnia are closely linked in cancer (Nail et al 1991[143]; Sarna 1993a[144]; Graydon 1994[145]) and during cancer treatment (Knobf 1986[146]; Irvine et al 1994[147]); following myocardial infarct (McCorkle & Quint-Benoliel 1983[148]); in hemodialysis patients (Brunier & Graydon 1993[149]); in rheumatoid arthritis (Mahowald et al 1989[150]); and especially in chronic fatigue syndrome, in which most patients complain of difficulty sleeping (Buchwald et al 1987[151]; Whelton 1988[152]; Krupp et al 1993[153]).

Finally, insomnia patients have the same levels of fatigue as fibrositis syndrome patients (Saskin et al 1987[154]).

“It appears that insomnia is associated with reduced natural cytotoxicity even in subjects in whom other depressive symptoms are minimal” (Irwin et al 1992)

Reducing REM sleep improves fatigue and depressive symptoms

If the above hypothesis is true, then one would expect that fatigue and depressive symptoms caused by excessive REM sleep could be improved by reducing REM sleep. Evidence for this fits into several categories:

- effects of decreasing REM sleep
- phenomena associated with decreased REM sleep
- effects of reducing total sleep (which also reduces REM sleep (Carskadon & Dement 1981[155]))
- phenomena associated with decreased total sleep (ie decreased REM sleep)
- effects of sleeping earlier (which reduces REM sleep)

effects of decreasing REM sleep

Chronic deprivation of the REM sleep phase has been found to have an antidepressant effect comparable to that of imipramine (Vogel et al 1975; cited in Klysner et al 1985).

phenomena associated with decreased REM sleep

Suppression of REM sleep and prolongation of REM latency are characteristic of antidepressant treatments, including most antidepressant medications (Montplaisir 1984; Nofzinger et al 1995) such as paroxetine (Saletu et al 1991[156]), citalopram (von Bemmel et al 1993[157]), nortriptyline and amitriptyline (Kupfer et al 1982[158]); electroconvulsive therapy (Cohen & Dement 1966[159]); stimulants including methylphenidate (Chatoor et al 1983[160]) and d-amphetamine (Saletu et al 1989[161]); and exercise (Driver et al 1988[162]; Montgomery et al 1988; Trinder et al 1988). Cognitive behavioural therapy for depression led to decreased REM density (Thase et al 1994[163]).

The amount of REM sleep suppression after initial administration of tricyclic antidepressants predicts the amount of clinical improvement (Kupfer et al 1981[164]; Höchli et al 1986).

Amitriptyline, which potently suppresses REM sleep, causes clinically significant improvements in pain and patient well-being in fibrositis patients (Scudds et 1989[165]

effects of reducing total sleep (which also decreases REM sleep)

Total sleep deprivation, which clearly suppresses REM sleep entirely, leads to an immediate and substantial reduction of depressive symptoms in 60% of patients with major depression (Post et al 1976[166]; Beersma & van den Hoofdakker 1992[167]; Dressing et al 1992; Wu et al 1992; Gill et al 1993[168]). However, it also impairs divergent thinking (Horne 1988[169]). Leibenluft & Wehr (1992[170]) reviewed 60 studies and concluded that partial sleep deprivation late in the night also has a significant antidepressant effect. This antidepressant response correlates with shorter REM duration (Sack et al 1988[171]).

Sleep deprivation can precipitate mania in patients with bipolar affective disorder (Wehr et al 1987; Wehr 1989; Wehr 1991; Kasper & Wehr 1992) and possibly also in previously normal individuals (Wright 1993).

Unfortunately, the antidepressant effect of sleep deprivation is usually very short-lived.

Long naps (2 hrs average), but not short naps, cause a return of depressive symptoms (Wiegand et al 1987[172]). The presence of REM sleep during the nap was associated with recurrence of depression (Wiegand et al 1987[173])

Sleep deprivation was shown to reverse severe cognitive impairment in a treatment-resistant depression; it can therefore be helpful in differentiating pseudodementia from true dementia (Williams et al 1994[174]).

Sleep deprivation precipitates mania in patients with bipolar affective disorder (Wehr et al 1987; Wehr 1989; Wehr 1991; Kasper & Wehr 1992) and possibly also in previously normal individuals (Wright 1993).

Partial sleep deprivation improves performance on some tasks (Herscovitch et al 1980[175]; Herscovitch & Broughton 1981a[176]; Ford & Wentz 1984[177]; Rosenthal et al 1991[178]) and does not impair exercise performance (Helder & Radomski 1989[179]). Other studies show either no effect or impairment in task performance (Deaconson et al 1988[180]; Bartle et al 1988).

In demented elderly, preventing daytime napping with regular activities improves sleep-wake disturbances (Björkstén et al 1995[181]).

phenomena associated with decreased total sleep (ie decreased REM sleep)

Reduced sleep is associated with mania (Linkowski et al 1994).

Some antidepressants reduce sleep, eg clomipramine which increases sleep latency and early morning awakening (Höchli et al 1986)

Several studies confirm the eighteenth century proverb "Six hours sleep for a man, seven for a woman, and eight for a fool" (Aserinsky 1969) that short sleepers are better adjusted psychologically than long sleepers (Montplaisir 1984). For example, male college students who have short sleep durations have significantly more internalized locus of control than long sleepers (Kumar & Vaidya 1986). Individuals with an internal locus of control seem to be more resistant to the effects of sleep deprivation in causing mood disturbance, tension, anger, and subjective fatigue (Hill et al 1996). These people will be better able to use their additional wake time productively.

In premenstrual dysphoric disorder, partial sleep deprivation improves depressive symptoms (Parry et al 1995); in insomnia due to chronic pain, sleep restriction improves mood states (Morin et al 1989).

Methylphenidate, effective in treating Attention Deficit Hyperactivity Disorder (ADHD) in children, significantly reduces sleep duration (Tirosh et al 1993).

effects of sleeping earlier (which reduces REM sleep)

Depressed patients were successfully treated by advancing their sleep period by several hours without reducing their sleep time (phase-advance therapy) (Wehr et al 1979; Sack et al 1985). Late partial sleep deprivation has an antidepressant effect which increases with repeated nights of PSD (Sack et al 1988).

In premenstrual syndrome, late-night partial sleep deprivation had greater benefit than early PSD (Parry & Wehr 1987[182], cited in Parry et al 1995).

Perhaps, as Ben Franklin said, “Early to bed, early to rise, makes a man healthy, wealthy, and wise.”

Circadian rhythms and light

Bright light is the most powerful external stimulus which can entrain the circadian rhythm. This suggests the possibility that the REM sleep peak, found to occur in the morning (at 8:30 am, in one study, may in fact be synchronized to morning light. Thus, sleeping after dawn would entail a risk of experiencing excessive REM sleep, while arising at dawn would minimize this risk.

This would help to explain the observation that people in ages past slept more than they do today. In all likelihood, people slept when it became dark, and arose when it became light, because artificial lighting would be too costly for daily use, and the necessity to eat would ensure that people did not sleep past the time when natural light would permit searching for or preparation of food.

Urban societies base arising time on the clock, rather than on the timing of the dawn. In the fall, when the clock is shifted backward from Daylight Saving Time to standard time, dawn arrives earlier, and individuals who do not arise earlier but now sleep after dawn, may suddenly increase their REM sleep amount. Is this possibly a trigger for winter seasonal depression?

Clinical Implications

The elderly

Frequently, when people retire, they begin to sleep more, either out of boredom or time availability. If the extra sleep occurs in the morning, it may precipitate fatigue and other depressive symptoms. In addition, excessive sleep or excessive time in bed may result in insomnia. If the individual interprets the fatigue and insomnia as indicative of a lack of sleep, he or she will attempt to sleep even more, perhaps with the aid of hypnotic medications, thus worsening and perpetuating the fatigue and insomnia in a vicious cycle. Long daytime naps add to the problem.

Education to overcome attitudes which have been ingrained since infancy may be insufficient to help these individuals overcome long-standing habits.

Nursing home residents

Physically or mentally handicapped residents of nursing homes are often unable to set their own schedules for going to bed or getting up. Staff may have schedules for the residents which are more related to shift hours, workloads, availability of personnel, and unavailability of scheduled activities during evening hours, than to the sleep needs of the residents themselves. As a result, many residents are in bed considerably longer than their physiological sleep requirement. Insomnia and depressive symptoms ensue, which are treated with hypnotics and/or antidepressants. Daytime sleeping may increase with long-acting hypnotic medications; a reversal of sleep-wake rhythms can contribute to the delirium-producing effects of psychotropic medications and common nursing home ailments such as urinary tract infections, to produce the agitation of “sundowner sydrome” which is then treated with antipsychotic agents.

Changing this pattern would require higher levels of staffing particularly in the evenings, with more scheduled activities, so that residents will not spend excessive time in bed.

Medical illness

As noted above, medical illnesses such as bacterial or viral infections may cause increased levels of sleep-promoting substances in the circulation. This is also true for cancer treatments. When increased opportunities for sleep present themselves due to increased bedrest and/or a reduction in usual activities (eg time off from work or school), the medically ill individual is at risk of worsening fatigue and insomnia from excessive sleep. One might speculate that the symptoms of chronic fatigue syndrome which frequently begins as an acute viral infection, are due to such a mechanism.

If the present hypothesis is valid, then a significant attitudinal change towards the supposedly beneficial aspects of sleep in medical illness would be required of physicians, nurses, and other medical personnel, as well as the patient and his or her family.

Contradictory Findings

Many studies report findings which conflict with the hypotheses expressed above. Some of these apparently contradictory results may be due to failure to accurately assess total sleep duration, to ignore daytime sleep, or to impose a brief experimental regime which may be different from the usual sleep patterns of the subjects.

Sleep duration

The total duration of sleep is often not reported in studies (for example, see Lamb 1982; Cartwright 1983; Höchli et al 1986; Lund et al 1991; Vitiello et al 1991; Shaver et al 1991; Krupp et al 1993). In some cases, total sleep time is reported, but not time in bed (eg Waters et al 1993).

Daytime sleep

While daytime naps are proscribed in some studies (eg, Salin-Pascual et al 1992), many fail to control for napping (eg, Taub 1981; Lund et al 1991; Shaver et al 1991; Hudson et al 1992; Holsboer-Trachsler et al 1994; Bonnet & Arand 1995), while many sleep lab studies fail to report whether subjects doze or sleep during the day (eg Gresham et al 1965; Hawkins & Mendels 1966; Mendels & Hawkins 1967a; Johns et al 1971; Feinberg et al 1982; Cartwright 1983; Höchli et al 1986; Whelton et al 1992; Krupp et al 1993; Thase et al 1994; Lauer et al 1995).

Standardized conditions

Sleep lab studies may impose standard conditions for sleep length, bedtimes or arising times, without reference to the usual sleep habits of subjects at home. For example, Salin-Pascual et al (1992) required subjects to spend 8 hrs in bed. Bonnet & Arand (1995) imposed a standard wake time of 8 am in their study. A number of studies on extended sleep required subjects to retire at unusually early hours (eg, Taub et al 1971; Taub & Berger 1973; Taub & Berger 1976a).

Approaches to Treatment

Sleep restriction for insomnia

Sleeping less improves sleep efficiency (Roehrs et al 1983[183]) and together with a daytime nap may improve sleep quality and daytime wakefulness (Carskadon et al 1982[184]). Sleep restriction/compression treats insomnia (Spielman, Saskin & Thorpy 1987; Morin et al 1990; Friedman et al 1991; Lacks & Morin 1992; Bliwise et al 1995); including in the elderly (Brendel et al 1990; Bootzin & Perlis 1992[185]; Bliwise et al 1995; Riedel et al 1995); and for insomnia due to chronic pain (Morin et al 1989[186]). In psychiatric inpatients, insomnia improves when long daytime naps and late rising times are eliminated (Edinger et al 1989[187]).

Sleep deprivation for depressive symptoms

While total sleep deprivation, or late partial sleep deprivation, have only a short-lived effect on major depression, possibly because there is an underlying abnormality of REM sleep, it is hypothesized that strategies which reduce REM sleep will be effective in reducing the fatigue and other depressive symptoms that are associated with insomnia, with chronic medical illnesses, and possibly with disorders including PMS and ADHD.

Strategies for REM sleep reduction

In individuals without the underlying REM sleep abnormality associated with major depression and some other disorders, strategies for reducing REM sleep include:

- reducing time in bed;
- eliminating long daytime naps;
- arising early (at dawn is probably most effective);
- exercise and caffeine-containing beverages to reduce daytime sleep;
- stimulant medication (eg methylphenidate) for medical patients with daytime fatigue or sleepiness;
- reducing or eliminating medication which increases REM sleep;
- adding medication which suppresses REM sleep.

How does one know when the amount of sleep (and the amount of REM sleep) is adequate but not excessive? When total sleep is insufficient, one would expect drowsiness or sleepiness during the day, in addition to the usual early afternoon period of drowsiness. The response would be to increase sleep duration by an earlier bedtime. Daytime drowsiness can conveniently be dealt with by brief naps (Harrison & Horne 1996) of less than 20 minutes (Naitoh 1992) which reverse sleepiness without causing significant sleep inertia (Stampi et al 1990[188]) and are sufficient to maintain performance (Naitoh 1992[189]) after partial sleep deprivation (Gillberg et al 1994[190]).

If one experiences no daytime sleepiness, not even in the early afternoon, total sleep duration is possibly excessive. The presence of primary insomnia may be a cardinal symptom of too much sleep, and can be treated by sleep restriction or compression. If there is chronic fatigue or other depressive symptoms, REM sleep may be excessive. The response would be to curtail REM sleep, using the strategies above.

Is it possible to have excessive REM sleep even when total sleep is insufficient? Probably yes; for example, if sleep takes place during the time in the diurnal variation when REM sleep % is highest (usually early morning, but in individuals with disordered circadian rhythms, such as in major depression, the REM peak may occur at other times of the day or night). Another example might be the of taking medication which increases REM sleep, such as reserpine or benzodiazepines.

Implications of Successful Treatment

Productivity

For individuals suffering from fatigue, insomnia, or other depressive symptoms, strategies to reduce REM sleep will improve mood, reduce chronic fatigue, improve energy and performance. If the symptoms are caused by excessive sleep, then a reduction in sleep will make more hours available each day for work or leisure pursuits.

When individuals sleep less, daytime drowsiness may become more frequent. This increases the risk for motor vehicle and occupational accidents. Sleepiness can be effectively counteracted by short naps, and employers may find that providing time and facilities for naps “on the job” leads to improvements in employee morale and job satisfaction, job safety, and productivity. Motor vehicles and industrial equipment might be appropriately outfitted with devices to detect operator drowsiness.

On the other hand, a reduction in the use of hypnotic medication to treat insomnia might lead to fewer medication-related accidents.

Health Care Costs

Treatment of insomnia and mild depressive symptoms by reduction of REM sleep is cost-effective through a variety of mechanisms: as a relatively simple public health measure, its use can be promulgated via public information campaigns rather than through the medical establishment; besides the potential savings in doctors’ fees, clinic costs, and salaries for other health professionals, there can also be a reduction in medication costs.

In nursing homes, keeping residents awake until later in the evening will also reduce depression and insomnia and the resultant treatment costs. However, this will be offset by the increased staffing required in the evenings to provide activities, etc.

Programme of Research

Goals

We propose a programme of research to confirm or refute the present hypotheses; to further explore the relationship between REM sleep and fatigue and other depressive symptoms; to investigate in more detail the influence of sleep timing, light exposure, and daytime sleep on REM sleep; to establish parameters for effective treatment of insomnia, fatigue and depressive symptoms.

Phases

The proposed programme of research consists of four phases:

- Demographic study on the internet
- Questionnaire studies of clinical populations
- Ambulatory sleep monitor studies of clinical populations
- Intervention trials of sleep reduction treatment

Each of these phases is described below.

Demographic Study on the Internet

In this phase, a questionnaire will be set up as a World Wide Web site on the Internet, to collect responses regarding sleep habits including daytime sleep, insomnia, fatigue, affect, depression including seasonal variation, daytime sleepiness, exercise, level of functioning, activities, sleep attitudes, life satisfaction, physical health, medications, and demographics.

According to a 1995 Nielsen random sample survey[191], there are 23 million internet users in the United States and Canada, of which about 65% are male; 22% are ages 16-24, 30% 25-34, 26% 35-44, 17% 45-54, and 5% 55 and older. In terms of ethnic background (based on the 1995 FIND/SVP survey[192]) 83% are white, 5% black, and 3% each Hispanic, Asian, or other. About 50% of users have household incomes in the range $30,000 to 80,000 US, with 12% having lower incomes. A demographics questionnaire posted as a Web site[193] (ie conditions similar to our internet questionnaire) between April 10 and May 10 1996, obtained 11,700 responses. The average age was 33 years, 68.5% were males, and the average household income of respondents was $59,000 US. Percent of respondents who were married was 41%, with 41% being single, and 5% divorced. 30% were in educational occupations, and 28% in computer related jobs.

We expect to find that shorter durations of sleep will be associated with better daytime mood, more daytime drowsiness, and better sleep quality; with greater success in life as determined by higher educational achievement, higher satisfaction with income, and more time spent on hobbies, sports, and recreation; and with better perceived health. On the other hand, we expect that longer sleep durations will predict higher depression scores, higher chronic fatigue levels, and poorer physical and emotional health (more medications, more chronic illnesses, higher likelihood of living alone, and poorer perceived health).

Insomnia will be expected to have associations with longer time in bed, more daytime napping, higher levels of chronic fatigue, lower daytime drowsiness, higher depression scores, poorer perceived health, increased use of sedative/hypnotic medication, less time spent on exercise, hobbies, sports, or recreation, and a greater importance attached to “getting enough sleep”.

Chronic fatigue is expected to associate with longer time in bed, more daytime napping, poorer sleep quality, lower daytime drowsiness scores, higher depression scores, less time spent working, or on hobbies, sports, or recreation, and less exercise.

We expect that winter seasonal affective disorder (ie winter weight gain, depression, and hypersomnia) will correlate positively with latitude (ie occur more frequently in northern areas).

Questionnaire Studies of Clinical Populations

A modified and shortened version of the Internet questionnaire will be used with selected clinical populations and with matched control groups. Planned modifications consist of the inclusion of commonly used depression scales such as the Beck Depression Inventory (which could not be used on the Internet because of copyright difficulties). Sample sizes will be determined based on results from the Internet questionnaire.

In addition to the questionnaire, clinician ratings for depression, fatigue, and Global Assessment of Functioning will be obtained.

Geriatric Psychiatry outpatients

This sample will be drawn from outpatients attending the Psychogeriatrics Clinic at the SMBD - Jewish General Hospital. Patients will be screened for the presence of depressive symptoms and/or insomnia. Controls will be other patients without affective disorders or insomnia complaints.

We expect that the associations described above for the internet questionnaire study will be found also in this clinical population, and that in addition both objective ratings of depression and subjective ratings using well-validated instruments such as the Beck Depression Inventory, will correlate with longer sleep durations.

Oncology outpatients

The SMBD - Jewish General Hospital Oncology Clinic will be the source of outpatients receiving active treatment or followup for cancer. Only patients with chronic fatigue and insomnia will enter the study, while controls will be cancer patients with neither fatigue nor insomnia complaints.

It is expected that chronic fatigue will be associated with the same variables as in the internet questionnaire study above, and in addition in this population with higher pain scores (in terms of intensity, duration, and frequency).

Nursing Home residents

Residents of the Maimonides Hospital Geriatric Centre, Cote St-Luc, Québec, will be sampled. The control group will be drawn from spouses and other relatives, living at home, without affective disorder, fatigue or sleep problems.

Ambulatory sleep monitor studies of clinical populations

The same clinical populations described above will also participate in studies using ambulatory sleep monitoring instrumentation. The wrist actigraph was selected as the most appropriate technology. Other technologies considered included Behavioural Response systems (Kuderian et al 1991[194]; Bonato & Ogilvie 1989[195]), portable multi-channel EEG recorders (Broughton 1991[196]; Wauquier et al 1992[197]), and the Nightcap portable sleep monitor. The accuracy of the wrist actigraph is 93% (Levine et al 1986[198]) compared to 87% for the Nightcap monitor (Ajilore et al 1995199) and it is not dependent on user motivation to provide accurate results as are Behavioural Response systems (Bonato & Ogilvie 1989).

Discussions are currently underway with Thought Technology Ltd. of Montréal, Québec, regarding the feasibility of developing and producing a multichannel EEG-EMG digital recorder with computer interface packaged as a lightweight headband, which would permit accurate, convenient, and user-friendly monitoring not only of sleep but more specifically of REM sleep, including daytime REM sleep, in the ambulatory setting.

Using the wrist actigraph to measure time asleep, including daytime sleep, sleep logs to provide a measure of time in bed, and a modified questionnaire, it is expected that longer time in bed will be associated with higher insomnia scores, higher chronic fatigue scores, lower drowsiness scores, and higher sedative/hypnotic medication use. Higher sleep efficiency scores are expected to associate to lower depression scores and lower chronic fatigue scores.

Intervention trials of sleep reduction treatment

Instruments and Scales

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[1] A questionnaire study of cancer patients referred for radiotherapy showed that insomnia was very common and correlated with anxiety and depression but not with pain (Beszterczey & Lipowski 1977)

[2] Fatigue was reported by 81% of cancer patients, and sleeping difficulty by 51% (Nail et al 1991)

[3] the secondary insomnia in cancer patients can be severe. A mean pretreatment sleep onset

latency of 125 min was reported on a sleep questionnaire (Cannici et al 1983)

[4] In students studied by questionnaire, disturbed sleep was associated with more daytime sleep (Johns et al 1971a) and also with more chronic psychological distress (Johns et al 1971b)

[5] People who sleep fewer hours will be less depressed and fatigued, and may thus be more successful in life (in terms of work, love, and play). In a group of insomniacs in a general practice setting, 56% were significantly dissatisfied with life, and 40% described themselves as anxious, oversensitive, emotionally labile and having many problems. The mean value on the GAF (Global Assessment of Functioning scale was 65, indicating some difficulty in social or occupational functioning (Schramm et al 1995)

[6] Insomniac patients had psychosomatic personality profiles on the MMPI. Compared to normal controls, they deviated significantly on 13 out of 18 MMPI scales (Schneider-Helmert 1987)

[7] In Black elderly, self-reported sleeping problems were directly related to depression/anxiety (Bazargan 1996)

[8] Individuals with chronic sleep disturbances utilize health care resources more often than good sleepers (Morin et al 1994)

[9] In a random sample of 400 members of the general public, 14% reported taking a hypnotic every night. The figure was 24% for 400 consecutive outpatient clinic attendees at a general hospital (Shapiro & Bachmayer 1988). In the combined sample, 17% had consulted their doctor specifically concerning a sleep problem.

[10] In a questionnaire study of 1485 noninstitutionalized Dutch elderly aged 50-93, 16.5% reported using sedative-hypnotic medication on a regular basis (Middelkoop et al 1996)

[11] A study of 421 noninstitutionalized elderly 75 and over using a linkage to a research register of prescription drug purchases, showed that 33% used hypnotics, sedatives, or anxiolytics (Gustafsson et al 1996). Those with insomnia had a higher use of these medications.

[12] Persons with long-term insomnia had 2.5 times more automobile accidents than did good sleepers (National Sleep Foundation 1991, cited in Becker et al 1993)

[13] Flurazepam 30 mg at bedtime induces next day sleepiness, and a tendency to poorer performance and a more negative mood (Johnson et al 1990)

[14] In a group of general practice patients with insomnia, substance use disorder was the second most frequent axis I diagnosis: 17% as a current diagnosis, 36% as a lifetime diagnosis. The great majority of these showed abuse of or dependence on hypnotics, primarily benzodiazepines (Schramm et al 1995)

[15] Individuals with chronic sleep disturbances experience more psychological distress, report greater impairments of daytime functioning, take more sick leave, and are more preoccupied with somatic problems (Morin et al 1994)

[16] The fatigue which is a prominent symptom of cancer (Donnelly & Walsh 1995; Irvine et al 1991; Taphoorn et al 1994) and is the most disturbing symptom reported during cancer treatment (Richardson 1995) may also be precipitated or perpetuated by excessive sleep. Resting and limiting activity can increase fatigue (Graydon et al 1995). In patients receiving radiation treatment for prostate cancer, both sleep and fatigue increased over the course of treatment (Greenberg et al 1993); similarly for breast cancer patients receiving radiation (Greenberg et al 1992)

[17] In 24 patients with non-small cell lung cancer, 79% experienced serious fatigue (Sarna 1993b).

[18] "Fatigue is without doubt the symptom most commonly experienced" by cancer patients (Smets et al 1993)

[19] Insomniacs use the strategies of getting into bed early, staying in bed late, and napping (Spielman, Saskin & Thorpy 1987)

[20] Approximately half of insomniacs cannot be distinguished from normals on the basis of total sleep time or sleep latency (Carskadon et al 1976). Fewer than one patient in five with a complaint of very short sleep or very long sleep latency will have the complaint confirmed in the sleep lab (Carskadon et al 1976)

[21] In students studied by questionnaire, disturbed sleep was associated with more daytime sleep (Johns et al 1971a) and also with more chronic psychological distress (Johns et al 1971b)

[22] Drowsiness or sleepiness, which is caused by insufficient sleep, is frequently confused with tiredness or fatigue (Moldofsky 1992; Nofzinger

et al 1991), which may be the result of too much sleep

[23] The Multiple Sleep Latency Test provides an objective measure of daytime sleepiness. Daytime sleepiness increases with reduced nocturnal sleep (Carskadon et al 1982; Rosenthal et al 1993).

[24] Symptoms of insomnia, when not related to pain, ingestion of stimulants such as caffeine, or extreme arousal, indicate that the person is sleeping excessively (in relation to their actual sleep need) (Chambers & Keller 1993)

[25] insomniac patients had a nonsignificant tendency to spend more time in bed (Frankel et al 1976; Schneider-Helmert 1987) compared to controls

[26] In a questionnaire study of 1485 Dutch noninstitutionalized elderly aged 50-93, women spent significantly longer time in bed than men, and also complained of poorer sleep quality, longer sleep latency, and number of night-time awakenings; however, fewer women had complaints of excessive daytime sleepiness, although more women used sedative-hypnotics (Middelkoop et al 1996)

[27] insomniacs typically underestimate the amount they actually sleep (Frankel et al 1976). An example of the extreme is a report (McCall & Edinger (1992) on two patients who believed they had almost total sleeplessness. Ambulatory polysomnographic sleep monitoring showed that actual sleep duration was 433 min in the patient who believed he slept less than 1 hr per night for 4.5 years, and 411 min in a woman who complained of 13 years of total sleeplessness.

[28] Sleep restriction improves sleep efficiency, while increasing time in bed worsens efficiency (Levine et al 1988)

[29] Medical students with mild to moderate sleep disturbance slept significantly more during the day than good sleepers (Johns et al 1971b)

[30] Shift workers who took naps (average nap lengths ranged from 1.62 hrs to 2.20 hrs) had longer total sleep times (0.31 hrs longer for 8-hr evening shift workers, 0.95 hrs longer for 8-hr night shift workers, 1.65 hrs longer for 12-hr night shift workers) on nap days compared to non-nap days. The quality and depth of the main sleep period was worse on nap days, and performance and subjective alertness were also worse on nap days (Rosa 1993). It is possible that the decrements in sleep quality, alertness and performance were due to excessive sleep on nap days.

[31] In Black elderly persons, number of daytime naps were directly related to sleeping problems (Bazargan 1996)

[32] Young people who were asked to sleep as much as possible during a 30-hour period, became increasingly wakeful and were unable to sleep more than about 20 hours on average (Aserinsky 1969)

[33] In a questionnaire study of 1485 Dutch noninstitutionalized elderly aged 50-93, women spent significantly longer time in bed than men, and also complained of poorer sleep quality, longer sleep latency, and number of night-time awakenings; however, fewer women had complaints of excessive daytime sleepiness, although more women used sedative-hypnotics (Middelkoop et al 1996)

[34] Elderly long-term insomniacs had significantly better reaction times during night-time performance testing than either elderly normals or young normals (Bonnet & Rosa 1987), indicating higher levels of alertness.

[35] "Excessive time spent in bed often perpetuates insomnia" and has potentially deleterious effects (Spielman et al 1987)

[36] Although healthy elderly sleep less than younger people, percentage of REM sleep is essentially unchanged, which results in less total REM sleep (Kales et al 1967)

[37] Brendel et al (1990) showed that 80-year-olds had significantly less REM sleep, REM %, and total sleep than 20-year-olds. Moreover, the elderly had less daytime sleep tendency, and experienced less performance and mood disturbance following a night of total sleep deprivation, all suggesting that elderly need less sleep.

[38] As people age, their need for sleep decreases (Prinz et al 1990; Bliwise 1993). For those over 88 years, females spend an average of 9 hours in bed and sleep about 7 hours, while men spend about 7.5 hours in bed and sleep 5.5 hours (Wauquier et al 1992). If individuals are unaware of this, they will not reduce their time in bed. Instead, many elderly increase their time in bed (Prinz et al 1990) upon retirement or in response to chronic illness such as arthritis. This will lead to insomnia (Lichstein 1988,cited in Riedel et al 1995) and possibly depression. When the insomnia is treated with hypnotics,

depression also may ensue. Alternatively, older people who perceive their sleep as getting worse may lengthen the amount of time in bed, to 12 hours a day in the extreme (Webb & Swinburne 1971), which may disrupt normal circadian rhythms (Carskadon et al 1982)

[39] Home-based sleep monitored by morning logs and wrist actimetry in 400 adults showed that men and women woke up earlier and had shorter sleep periods with increasing age. Women had poorer sleep but had markedly longer sleep period times (Reyner & Horne 1995)

[40] A questionnaire study of 1485 non-institutionalized people aged 50-93, time in bed as well as percentage of subjects reporting daytime napping increased significantly with age, as did the number of individuals reporting regular use of sedative-hypnotic medication (Middelkoop et al 1996)

[41] Elderly patients in a nursing home spent an average of 12 hrs out of every 24 in bed, with bedtimes ranging from 5 to 8 pm, and rising times from 5 to 8 am. Almost all took daytime naps, probably related to boredom (Webb & Swinburne 1971)

[42] Sixty-five residents in 7 nursing homes were assessed with night-time wrist activity monitors and daytime observation every 15 minutes; on average, total sleep time was 6.2 hours, with an average duration of 21.2 minutes per sleep episode. Residents were observed to be asleep for 14.5% of the daytime observations (Alessi et al 1995)

[43] Home-based sleep monitored by morning logs and wrist actimetry in 400 adults showed that men and women woke up earlier and had shorter sleep periods with increasing age. Women had poorer sleep but had markedly longer sleep period times (Reyner & Horne 1995)

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depression also may ensue. Alternatively, older people who perceive their sleep as getting worse may lengthen the amount of time in bed, to 12 hours a day in the extreme (Webb & Swinburne 1971), which may disrupt normal circadian rhythms (Carskadon et al 1982)

[45] The average nursing home resident sleeps no more than 40 minutes per hour at night, and 50% wake three to four times per hour (Foltz-Gray D 1996)

[46] Both demented and non-demented nursing home patients showed increases in impairment in activities of daily living as total sleep hours increased (Meguro et al 1990)

[47] A similar illness, variously labelled benign myalgic encephalomyelitis, Iceland disease, or epidemic neuromyasthenia, has hypersomnia as a symptom during the acute phase, and includes depression and difficulty in concentration as prominent features during the convalescent stage (Acheson 1959)

[48] During the initial weeks of their illness, 12 patients with Epstein-Barr viral infection complained of tiredness and fatigue, and began taking daytime naps. Over time, they began to complain of lack of alertness, daytime sleepiness, and were sleeping an average of 8.5 hrs at night and 1.5 hrs during the day (Guilleminault & Mondini 1986)

[49] Interleukin-1 promotes slow-wave sleep in animals; interleukin-2, interferon, muramyl dipeptide (a product of bacterial cell walls) may be key mediating agents in promoting sleep. Other substances associated with viral or bacterial infections also induce sleep. Some of these same substances (eg IL-1, IL-2, alpha-interferon, when injected in humans, produce symptoms of chronic fatigue syndrome/fibromyalgia (Moldofsky 1993)

[50] The exhaustion reported by some hospitalized medical or surgical patients may be partly due to the production of a syndrome related to excessive sleep, as the hospital increases opportunities to nap and sleep (Globus 1969)

[51] Fatigue was reported by 15 out of 30 cancer patients receiving radiotherapy; 12 patients responded with increasing their sleep through naps or decreasing activities (Dodd 1984)

[52] Twelve of 16 women receiving chemotherapy for ovarian cancer reported fatigue, and 11 reported a change in their sleep pattern, usually

more sleep at night or daytime naps (Jamar 1989)

[53] In cancer patients receiving outpatient radiotherapy, physical fatigue correlated highest with the number of hours of rest during the day (Kobashi-Schoot et al 1985), suggesting that rest (and possibly sleep, since many patients sleep while resting) may worsen fatigue.

[54] Fatigue was reported by 15 out of 30 cancer patients receiving radiotherapy; 12 patients responded with increasing their sleep through naps or decreasing activities (Dodd 1984)

[55] Fatigue was identified as the most distressing symptom by groups of newly diagnosed lung cancer patients and myocardial infarct patients. insomnia was rated as being almost as distressing by both groups (McCorkle & Quint-Benoliel 1983)

[56] Breast cancer patients receiving adjuvant chemotherapy identified fatigue as the most distressful physical symptom, while insomnia was nearly universal (Knobf 1986)

[57] Out of 69 women with lung cancer, 56% complained of profound fatigue; 31% of those with profound fatigue also complained of insomnia (Sarna 1993a)

[58] In women with breast cancer, fatigue and insomnia were the most frequent symptoms (Graydon 1994).

[59] The increased fatigue experienced by cancer patients experiencing radiation or chemotherapy was significantly correlated with mood disturbance and difficulty sleeping (Irvine et al 1994).

[60] In a consecutive sample of 434 newly diagnosed cancer patients, the most problematic symptoms were fatigue (40% of patients) and insomnia (30%) (Degner & Sloan 1995)

[61] In a sample of patients with Chronic Fatigue Syndrome, 28% described their fatigue as being so severe that they became bedridden, able to do virtually nothing; 78% complained of depression or unusual mood changes, and 73% of difficulty sleeping (Buchwald et al 1987)

[62] Sleep disturbance is a frequent complaint in CFS, with complaints of sleeping lightly, badly, with early morning awakening, and still feeling drowsy on awakening being most common (Krupp et al 1993)

[63] Factors that perpetuate insomnia include: too much time in bed (Spielman, Saskin & Thorpy 1987), irregular retiring and arising times, napping, sedative-hypnotics or alcohol, and conditioning (Spielman 1986)

[64] Factors that perpetuate insomnia include: too much time in bed (Spielman, Saskin & Thorpy 1987), irregular retiring and arising times, napping, sedative-hypnotics or alcohol, and conditioning (Spielman 1986)

[65] Daytime performance of insomniac patients did not differ from controls (Schneider-Helmert 1987)

[66] During the day, primary insomniacs are more alert both subjectively and using electrophysiological measures, compared to normals (Regestein et al 1993) suggesting that they are sleep-sated and not sleep-deprived.

[67] Insomniacs reported increased confusion, tension, and depression and decreased vigor compared to normals; their memory ability was also worse. These impairments were not due to sleepiness because daytime sleep latencies were increased on the MSLT (Bonnet & Arand 1995)

[68] Normal male college students who habitually slept 7 or 8 hr, when permitted to sleep up to 11 hrs, increased their sleep from an average 7.1 to 9.1 hrs. SWS sleep did not increase, but REM sleep increased from 99 to 142 min, which represents an increase in REM% from 23% to 26% (Phoebus et al 1970)

[69] Normal, healthy young people can voluntarily extend their sleep from a baseline of 7.5 hours average to 9.4 hours on the first extended night, steadily declining to 8.6 hours over 14 days, by going to bed 1.5 hours earlier and arising .5 hours later. There were no improvements in self-rated mood or sleepiness, and MSLT scores showed small (about 1 min) reductions. These results suggest that the average 7.5 hour sleeper does not have chronic sleep deprivation; the extended sleep is "optional" and is associated with a deterioration in sleep latency and wakefulness (Harrison and Horne 1996)

[70] Permitting subjects to sleep ad libitum under conditions which have not increased sleep need by prior deprivation or increased eneergy expenditure will consistently result in increased sleep length (Webb & Agnew 1975). Thus, if sleep is seen as pleasurable, or if it is used as a way to escape painful reality, or if the person overestimates their sleep need, it will be quite easy to sleep in excess of the amount required. there does not seem to be a signal which indicates sufficient sleep has been obtained.

[71] When 24 hrs of enforced time in bed was imposed immediately after a night of sleep deprivation, subjects slept on average 16.9 hrs out of 24. When subjects had a normal 8 hrs of sleep immediately prior to the 24 hrs enforced bed rest, they still accumulated 12.3 hrs of sleep out of 24 (Rosenthal et al 1993) suggesting that extended sleep can occur even without prior sleep deprivation.

[72] In healthy young males allowed to extend sleep ad libitum, REM sleep and REM cycle length increased (Taub 1980; Taub 1983)

[73] in young adults who voluntarily extended their sleep to 15 hours, the percent REM remained constant, but the total REM sleep more than doubled (Gagnon & de Koninck 1984)

[74] In an artificially induced insomnia condition, flurazepam 30 mg and triazolam 0.5 mg increased REM sleep compared to placebo, essentially by increasing sleep duration compared to placebo (Seidel et al 1986)

[75] Although healthy elderly sleep less than younger people, percentage of REM sleep is essentially unchanged, which results in less total REM sleep (Kales et al 1967)

[76] Brendel et al (1990) showed that 80-year-olds had significantly less REM sleep, REM %, and total sleep than 20-year-olds. Moreover, the elderly had less daytime sleep tendency, and experienced less performance and mood disturbance following a night of total sleep deprivation, all suggesting that elderly need less sleep.

[77] A study of young females sleeping in an isolation unit according to an irregular schedule resulted in large variations in sleep efficiency; short prior time awake and bedtime in late afternoon were the factors which most disrupted sleep length. REM sleep was influenced mostly by circadian phase, and not by prior time awake (Åkerstedt et al 1993)

[78] In healthy elderly, intervals between successive REM periods decrease during the night, while durations of REM periods do not increase, in contrast to young adults, in whom intervals decrease and REM period durations increase through the night. Thus, in the elderly, total REM in the second half of the night is 50% greater than in the first half, while for young adults the increase is 300% (Kales et al 1967)

[79] This is confirmed by a study which found that REM sleep is highest between midnight and early morning, and lowest between noon and midnight. The amount of REM sleep is essentially independent of prior wakefulness (ie how long the person has been awake) (Webb & Agnew 1977)

[80] The REM period decreases in normals in the second part of the night (Lange 1982)

[81] REM sleep increases in amount later in the sleep period (Webb & Agnew 1968; Carskadon & Dement 1985), due to decreased intervals between REM periods in elderly males (71-95 yrs) (Kahn & Fisher 1969), thus sleep reduction decreases the percentage of sleep time spent in REM sleep. However, in the old elderly (>88 years), REM sleep was found to be highest at the beginning of the night and decreased during the course of the night (Wauquier et al 1992)

[82] In a study of ad libitum extended sleep in young males, REM cycle duration peaked at 55 min at 8:30 am and declined by 33 min on average at 10 am (Taub et al 1983)

[83] The percentage of REM sleep during a two-hour sleep at different times during the day decreases progressively from 9 am to 4 pm (Webb & Agnew 1968)

[84] In a group of young healthy males, acutely shifting the normal 12-8 am sleep pattern to 3-11 am did not produce changes in total REM sleep, nor did a longer duration of sleep when the extra sleep was added at the beginning (9 pm-8 am). In contrast, advance shifting sleep to 9 pm-5 am produced a reduction in total REM sleep similar to that from partial sleep deprivation (3-8 am) (Taub & Berger 1973). This suggests that the 9-12 pm time period produces relatively little REM sleep, while 5-8 am produces significant amounts.

[85] In a group of 9 healthy young adult males, advancing or retarding normal bedtime by 3 hrs did not affect REM sleep percentage per hour for the first three hours of sleep, but during the last five hours of sleep REM sleep percentage each hour was higher for later hours of sleep (Knowles et al 1982)

[86] Late partial sleep deprivation (ie sleep limited to 5 hours max between 8 pm & 2 am) reduced REM sleep, while early PSD (5 hours max sleep between 2 am & 8 am) increased REM sleep (Sack et al 1988)

[87] In an experiment in which subjects wore glasses which completely inverted their visual fields, there was a significant increase in REM

sleep on the nights following the visual field inversion compared to baseline, which supports the hypothesis that REM sleep contributes to information processing (De Koninck & Prévost 1991)

[88] following active learning there are increases in REM sleep (summarized by Herscovitch et al 1980) suggesting that REM sleep is important in learning and memory

[89] learning Morse code led to increases of REM sleep time and number of REM episodes (Mandai et al 1989)

[90] Selective REM sleep deprivation, but not NREM deprivation, disrupted the consolidation of memory after a visual discrimination task. Neither type of deprivation affected performance on an already learned task (Karni et al 1992)

[91] Many studies show that the REM sleep % of normal adults is remarkably constant from post-pubescence to age 90, after which it drops off (Kahn & Fisher 1969)

[92] "The depressiogenic effect of sleep may be specifically due to rapid eye movement (REM) sleep" (Wiegand et al 1987)

[93] Normal male college students who habitually slept 7 or 8 hr, when permitted to sleep up to 11 hrs, increased their sleep from an average 7.1 to 9.1 hrs. SWS sleep did not increase, but REM sleep increased from 99 to 142 min, which represents an increase in REM% from 23% to 26% (Phoebus et al 1970)

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[97] Sedative/hypnotic medications (eg benzodiazepines) have depression as a side effect (Edwards et al 1991, Lydiard et al 1987, both cited in Patten et al 1996; Patten et al 1996); the mechanism of action may be through an increase in sleep time caused by the medication. More specifically, it is known that benzodiazepines can increase REM sleep (Montplaisir 1984); possibly this is the mechanism for inducing depression.

[98] In a study of recurrence of depressive symptoms after daytime napping in patients who had responded to total sleep deprivation, The presence of REM sleep during the nap was associated with recurrence of depression (Wiegand et al 1987)

[99] Following a decision to divorce, depressed women had significantly decreased REM latency and increased REM density compared to non-depressed women. There was a trend for REM % to increase with increasing depression (Cartwright 1983)

[100] Depression is associated with increase in REM sleep and decrease in REM latency (Montplaisir 1984; Thase et al 1994; Nofzinger et al 1995)

[101] Depressed patients had more REM sleep than controls and high-risk probands (people with close relatives with depression) (Lauer et al 1995).

[102] In a study of 32 patients with recurrent unipolar depression, a comparison of EEG sleep between a state of clinical wellness following successful treatment, and a subsequent relapse while receiving maintenance treatment, showed that at relapse patients were sleeping significantly longer, and had increased REM sleep (due primarily to increased sleep, increased number of REM periods and shortened REM latency) (Kupfer et al 1991)

[103] "Healthy persons with habitually short sleep (less than 6 hours per night), medium sleep, and long sleep (more than 9 hours) have similar amounts ot SWS and differ much in REM sleep amount. The REM sleep amount was found correlated with minor psychopathology such as depression, anxiety, or shyness; in contrast, the short sleepers were typically non-worriers..." (Müller, 1984)

[104] Patients with Brief Recurrent Depression and major depressives had significantly shortened REM latencies compared to controls (De La Fuente et al 1992)

[105] Very short REM latency was associated with more severe depression and with bipolar depression (Schulz & Tetzlaff 1982)

[106] Very short REM latency, including sleep onset REM, is associated with delusional depression (Grunhaus et al 1994)

[107] Endogenously depressed patients had short REM latencies after successful treatment with TCA's or ECT, whereas normals and depressed patients in whom antidepressant treatment failed had long REM latencies (Svendsen & Christensen 1981)

[108] Depressed patients obtained about 25% of their REM sleep in the first third of the night, compared to 13% for controls (Gresham et al 1965).

[109] Depressed patients had twice as long REM periods during the first sleep cycle compared to normal controls and to high-risk probands (Lauer et al 1995).

[110] Short REM latencies are present in a significant number of patients with illnesses such as narcolepsy, schizophrenia, obsessive-compulsive disorder, mania, chronic psychogenic pain syndromes, drug-withdrawal states, and so forth, in which depressive symptoms are common, and many of these patients respond to antidepressant medications (Gillin & Borbély 1985 ; Benca et al 1992)

[111] In a study of 32 patients with recurrent unipolar depression, a comparison of EEG sleep between a state of clinical wellness following successful treatment, and a subsequent relapse while receiving maintenance treatment, showed that at relapse patients were sleeping significantly longer, and had increased REM sleep (due primarily to increased sleep, increased number of REM periods and shortened REM latency) (Kupfer et al 1991)

[112] "The depressiogenic sleep theory declares that sleep may induce depression and that sleep deprivation relieves it" (Wiegand et al 1987)

[113] In a questionnaire study, students reported feeling either a syndrome characterized by the descriptors "just great, rested, refreshed, in a good mood, clear mind, ready to start the day" or a "worn out" syndrome, described by the terms "worn out, tired, lethargic, in an irritable mood, fuzzy thinking, difficulty getting started". After a night of sleep prolonged to 10 or more hours, the worn out syndrome was reported more frequently, whereas the just great syndrome was more frequent following extended sleep of under 10 hours if this was makeup for lost sleep (Globus 1969)

Globus (1969) observed that late sleepers sometimes complain of feeling washed out and blah; in spite of extra sleep, they feel tired or even exhausted, have difficulty getting going, complain of a foggy mind and difficulty concentrating, feel irritable and depressed, and possibly have mild headaches.

[114] Sleep deprivation and prolongation both impair mood and performance in some studies, but other studies show no effect on cognitive or motor performance from lack of sleep (Deaconson et al 1988 [not in EndNote]; Bartle et al 1988 [not in EndNote]), while performance on certain tasks may even improve with less sleep (Ford & Wentz 1984)

[115] Several studies have shown that short sleepers are better adjusted psychologically than long sleepers (Montplaisir 1984)

[116] After a night of restorative sleep (typically 9 hr) following 34 hr of sleep deprivation, performance was significantly worsened compared to baseline (Wilkinson 1963)

[117] Extended sleep impairs performance on vigilance tasks (Taub et al 1971); on auditory memory and vigilance and on visual reaction tests (Taub 1980) and impairs alertness (Taub 1983). However, extended recovery sleep following several nights of partial deprivation returns performance to baseline levels (Herscovitch & Broughton 1981a).

[118] Taub (1980) hypothesized that the performance decrements after ad lib extended sleep could be due to augmentation of REM sleep.

[119] Complaints of anergia and psychomotor slowing are associated with hypersomnia (Detre et al 1972; cited in Reynolds & Kupfer 1987)

[120] In a study of 12 hospitalized depressed non-hypersomnic patients, 50% took daytime naps; naps were taken at various times of the day, in contrast to controls who napped in the early afternoon (Kerkhofs et al 1991)

[121] daytime bedrest is more prevalent in depression than usually assumed (Kerkhofs et al 1992)

[122] Depressed patients had longer sleep latencies and lower sleep efficiencies than normals (Feinberg et al 1982), suggesting that they are sleep-sated, possibly from sleeping more than they need

[123] Patients with Brief Recurrent Depressions had similar total sleep times to controls, but had longer sleep onset latencies (De La Fuente et al 1992), indicating more time spent in bed.

[124] Hypersomnia in seasonal affective disorder predicts response to phototherapy (Oren et al 1992)

[125] Narcolepsy-cataplexy, which is often characterized by daytime sleep pressure, and idiopathic hypersomnia which is characterized by chronic daytime sleepiness and diurnal sleep periods, are both often associated with clinical depression (Herscovitch et al 1980)

[126] Compared to normals, HIV-infected patients feel fatigued through more hours of the day, sleep more, and nap more; there is a possibility that the sleep disturbance could be cause rather than effect (Darko et al 1992).

[127] Daytime naps are frequent in persons who suffer from cancer, depression, fibromyalgia/chronic fatigue syndrome, HIV infection (Darko et al 1992)

[128] Hypersomnia is characteristic of fibromyalgia/chronic fatigue syndrome (Morriss et al 1993) [[not in EndNote]

[129] In 14 patients with chronic fatigue syndrome, 13 out of 14 had a depressed mood, and 12 expressed an increased need for sleep. Compared to controls, the CFS patients had a non-significant trend to a longer time in bed, and were not hypersomnolent on MSLT, indicating that they were not sleep-deprived. Daytime sleep was not controlled for or reported (Whelton et al 1992)

[130] Moldofsky (1993) holds that a dysfunction of the sleeping-waking system of the brain is associated with the symptoms and altered neuroimmune functions that affect patients with the diagnosis of fibromyalgia or chronic fatigue syndromes.

[131] In cancer patients receiving outpatient radiotherapy, physical fatigue correlated highest with the number of hours of rest during the day (Kobashi-Schoot et al 1985), suggesting that rest (and possibly sleep, since many patients sleep while resting) may worsen fatigue.

[132] Children with hyperactivity have increased total sleep time compared with normal controls (Luisada 1969; cited in Tirosh et al 1993)

[133] In the almost 7000 individuals studied using the Human Population Laboratory questionnaire, the physical health index was highest for those reporting 8 or 7 hours of sleep, lowest for those with 6 or less hours, and intermediate for 9 or more hours of sleep (Belloc & Breslow 1972)

[134] In a large (almost 7000) sample of the general adult population in a typical California urban community (Belloc 1973), men who reported sleeping 8 hours had lower mortality rates than those who slept more or less. For women the optimum rate was for 7 hours of reported sleep, although the mortality rate for those reporting less than 6 hours of sleep was essentially the same. Analysis with a longer mortality followup (Wingard & Berkman 1983) showed that men sleeping 6 h or less or 9 h or more had 1.7 times the total age-adjusted death rate of men sleeping 7 or 8 h per night, while for women the relative risk was 1.6. Simultaneous adjustment for age, sex, race, socioeconomic status, physical health status, smoking history, physical inactivity, alcohol consumption, weight status, use of health services, social networks, and life satisfaction reduced the relative mortality risk to 1.3.

[135] In epidemiological studies, both short and long sleep is associated with increased mortality (Kripke et al 1979).

[136] In a group of medical students, those who slept less at night, had more frequent night awakenings, and slept more during the day, had higher scores on the MMPI scale for hysteria; later times for going to bed and for arising were related to high scores on scale 4 (psychopathic deviate) and scale 9 (hypomania), ie to arousal-seeking behaviour and a need for excitement (Johns et al 1974)

[137] A six-hour delay of sleep produced non-significant REM changes resembling the depressive pattern, and significant increases in subjective feelings of depression and decreased alertness, happiness, and energy, whereas a six-hour advance produced a decrease in REM % (David et al 1991)

[138] In emergency room physicians working shifts, night shift work with day sleep resulted in significantly less REM sleep (72.9 min average) using ambulatory EEG monitoring, compared to day work with night sleep (138.3 min REM). Night work physicians had significantly poorer performance in simulated clinical tasks such as intubating a mannequin or a simulated triage test (Smith-Coggins et al 1994)

[139] In a group of 33 delayed sleep phase syndrome patients, 45% were using antidepressants when first evaluated, and an additional 30% had been on antidepressants previously (Regestein & Monk 1995)

[140] The risk of developing a major depression is much higher for insomniacs. In a longitudinal epidemiological study involving almost 8000 community respondents, Ford & Kamerow (1989) found that 10.2% were insomniac, and 3.2% hypersomnic (ie they said they were sleeping too much for a two week period). People who had insomnia at two interviews a year apart were almost 40 times more likely to develop a new major depression than those without insomnia. The risk of developing depression for those with hypersomnia at both interviews was 46.9 compared to those with no sleep complaints. These insomniacs may simply be individuals who try to sleep more than they need. By so doing, they may precipitate depression .

[141] Insomniacs in a sample of general practice patients had four times the rate of a current affective disorder compared to the general population sample (24% vs 6%) and twice the rate of current anxiety disorders (15% vs 7%) (Schramm et al 1995)

[142] Depression in caregivers of dementia patients was more highly correlated with insomnia than any other variable, accounting for 27% of the variance in sleep scores (McCurry & Teri 1995)

[143] Fatigue was reported by 81% of cancer patients, and sleeping difficulty by 51% (Nail et al 1991)

[144] Out of 69 women with lung cancer, 56% complained of profound fatigue; 31% of those with profound fatigue also complained of insomnia (Sarna 1993a)

[145] In women with breast cancer, fatigue and insomnia were the most frequent symptoms (Graydon 1994).

[146] Breast cancer patients receiving adjuvant chemotherapy identified fatigue as the most distressful physical symptom, while insomnia was nearly universal (Knobf 1986)

[147] The increased fatigue experienced by cancer patients experiencing radiation or chemotherapy was significantly correlated with mood disturbance and difficulty sleeping (Irvine et al 1994).

[148] Fatigue was identified as the most distressing symptom by groups of newly diagnosed lung cancer patients and myocardial infarct patients. insomnia was rated as being almost as distressing by both groups (McCorkle & Quint-Benoliel 1983)

[149] In 43 patients with end stage renal disease on chronic hemodialysis, high levels of fatigue were significantly related to inactivity and to sleep disturbance, but not to anemia (Brunier & Graydon 1993)

[150] Fatigue affects nearly 80% of patients with rheumatoid arthritis (Mahowald et al 1989). In a study of 16 RA patients, all patients had some type of marked sleep disturbance, and 7 were found by MSLT to be hypersomnolent (Mahowald et al 1989). This suggests that at least some RA patients probably nap during the day.

[151] In a sample of patients with Chronic Fatigue Syndrome, 28% described their fatigue as being so severe that they became bedridden, able to do virtually nothing; 78% complained of depression or unusual mood changes, and 73% of difficulty sleeping (Buchwald et al 1987)

[152] Fourteen patients with Chronic Fatigue Syndrome had higher ratings than normals on depression, and showed poor sleep with a delayed onset to sleep and reduced sleep efficiency; however, they were not hypersomnolent on the MSLT (Whelton 1988, cited in Moldofsky 1989)

[153] Sleep disturbance is a frequent complaint in CFS, with complaints of sleeping lightly, badly, with early morning awakening, and still feeling drowsy on awakening being most common (Krupp et al 1993)

[154] A comparison of 30 fibrositis syndrome patients and 30 insomniacs showed that the insomniacs had similar moderate fatigue ratings before and after sleep (Saskin et al 1987, cited in Moldofsky 1989)

[155] Sleep restriction to five hours over several nights resulted in a significant decrease in REM sleep, although REM % increased with greated accumulated sleep deprivation (Carskadon & Dement 1981)

[156] Paroxetine given as a single dose to young normals significantly decreased REM sleep time and percent over two nights. In addition, total sleep time and sleep efficiency were also reduced for one night (Saletu et al 1991)

[157] Citalopram decreased both REM minutes and REM percentage, and increased REM latency, in a group of 16 depressed outpatients, both initially upon starting citalopram and after 5 weeks of treatment (van Bemmel et al 1993)

[158] Nortriptyline and amitriptyline even at low doses (25 mg and 50 mg respectively) suppress REM sleep by increasing REM latency, decreasing the number of REM periods, and REM intensity (Kupfer et al 1982)

[159] Electroconvulsive therapy also decreases REM sleep (Cohen & Dement 1966). In cats, this decrease is due to a decrease in the number of REM periods, an effect which is sustained for several days after treatment (Kaelbling et al 1968).

[160] Methylphenidate when administered to children with hyperactivity decreased total REM sleep by increasing REM latency and decreasing the number and duration of REM periods (Chatoor et al 1983)

[161] Paroxetine given as a single dose to young normals significantly decreased REM sleep time and percent over two nights. In addition, total sleep time and sleep efficiency were also reduced for one night (Saletu et al 1991)

[162] submaximal exercise decreased REM sleep during the first 6 hours of sleep (Driver et al 1988). Exercise reduced SWS in females, and REM sleep in males (Montgomery et al 1988). A review of the literature (Trinder et al 1988) concluded that exercise has little effect on sleep duration or sleep onset latency, but significantly reduces REM sleep and increases REM sleep latency.

[163] EEG sleep profiles of 45 depressed males treated with Cognitive Behavioral Therapy showed a decrease in REM density after treatment (Thase et al 1994)

[164] The amount of REM sleep suppression with initial administration of a tricyclic antidepressant correlated positively with clinical response (Kupfer et al 1981). Reduction in REM sleep by nortriptyline predicts its effectiveness against depression (Höchli et al 1986). The higher the REM sleep reduction during the first night of treatment, the better the clinical improvement.

[165] Thirty-six fibrositis patients received low-dose amitriptyline or placebo in a randomized double-blind crossover study. Amitriptyline resulted in clinically significant improvements for pain and patient well-being (Scudds et al 1989). Although the effect on sleep or fatigue was not reported on, amitriptyline potently suppresses REM sleep and this may be important.

[166] Ten out of 19 hospitalized depressed patients had a transient (one-day) response to one night of total sleep deprivation. Responders were initially more depressed and tendedto be older (Post et al 1976)

[167] total sleep deprivation, which leads to an immediate and substantial reduction of depressive symptomatology in 60% of patients with a major depressive disorder (Beersma & van den Hoofdakker 1992), also decreases REM sleep. “The beneficial effects of total sleep deprivation are antagonized by naps containing REM sleep, but not by naps consisting of non-REM sleep alone” (Wiegand et al 1987, cited in Sack et al 1988)

[168] In rapidly cycling bipolar depressed patients, sleep deprivation later in the time course of the depressive episode produced better antidepressant response (Gill et al 1993)

[169] Total sleep deprivation significantly impairs performance in tasks requiring “divergent” thinking (Horne 1988)

[170] In about 60 studies involving more than 1700 depressed patients reviewed by Leibenluft & Wehr (1992), a single night of total or partial (second half of the night) sleep deprivation resulted in response in almost 60% of patients on average.

[171] Partial sleep deprivation late in the night had a significant antidepressant effect which correlated with shorter REM duration (Sack et al 1988)

[172] Long naps (120 min avg) after an antidepressant response to sleep deprivation were associated with a return of depressive symptoms, whereas short naps (62 min avg) had no effect on mood (Wiegand et al 1987)

[173] In a study of recurrence of depressive symptoms after daytime napping in patients who had responded to total sleep deprivation, The presence of REM sleep during the nap was associated with recurrence of depression (Wiegand et al 1987)

[174] Sleep deprivation reversed the severe cognitive impairment in a 59 year old man with treatment-resistant depression, thus helping to differentiate pseudodementia from true dementia (Williams et al 1994)

[175] Performance on an anagrams test showed continuous improvement even over five days of partial sleep deprivation, while non-perseverative errors on the Wisconsin Card

Sorting Test decreased with partial sleep deprivation and increased in extended recovery sleep (Herscovitch et al 1980

[176] After one night of partial sleep deprivation, morning performance in a vigilance task was superior to baseline, while morning performance after a night of recovery oversleep was worse than baseline (Herscovitch & Broughton 1981a)

[177]Sleep deprivation and prolongation both impair mood and performance in some studies, but other studies show no effect on cognitive or motor performance from lack of sleep (Deaconson et al 1988 [not in EndNote]; Bartle et al 1988 [not in EndNote]), while performance on certain tasks may even improve with less sleep (Ford & Wentz 1984 [not in EndNote])

[178] In a study of 36 healthy men aged 19 to 35, sleep restriction from 8 hours to 5 hours time in bed resulted in a non-significant decrease in vigilance reaction time. However, even small amounts of caffeine (75 mg) improved reaction time to levels significantly below placebo, whether sleep restricted or not (Rosenthal et al 1991)

[179] Exercise performance is unaffected by sleep deprivation (Van Helder & Radomski 1989 [not in EndNote])

[180] Sleep deprivation and prolongation both impair mood and performance in some studies, but other studies show no effect on cognitive or motor performance from lack of sleep (Deaconson et al 1988[180]; Bartle et al 1988), while performance on certain tasks may even improve with less sleep (Ford & Wentz 1984)

[181] Demented elderly show sleep fragmentation during the night and daytime napping (Björkstén et al 1995); treatment by regular daytine activities improved disrupted sleep-wake disturbance (Okawa et al 1991 [not in EndNote], cited in Björkstén et al 1995)

[182] Late-night partial sleep deprivation (sleep from 8 pm to 2 am) had greater benefit than early PSD (sleep from 2 am to 8 am) in premenstrual syndrome (Parry & Wehr 1987, cited in Parry et al 1995)

[183] People who habitually sleep a self-reported average of 6.4 hours on weekdays, had high sleep efficiency in the sleep lab (Roehrs et al 1983)

[184] Carskadon et al (1982) hypothesized that limiting nocturnal sleep and introducing a midday nap might improve both sleep and daytime wakefulness.

[185] Sleep restriction is an effective treatment for insomnia in elderly patients (Bootzin & Perlis 1992; Bliwise et al 1995; Riedel et al 1995)

[186] in insomnia due to chronic pain, sleep restriction improves mood states (Morin et al 1989)

[187] Insomnia in psychiatric inpatients improves when ward routines are changed to eliminate long (2 hr) daytime nap periods and late rising times on weekends (Edinger et al 1989)

[188] 20-minute naps are effective in reversing sleepiness without causing significant sleep inertia (Stampi et al 1990 [not in EndNote])

[189] naps of between 4 and 20 minutes' duration can be sufficient to maintain performance (Naitoh 1992)

[190] After partial sleep deprivation characterised by 4 hrs sleep between midnight and 4 am, a 30 minute nap at 11 am counteracted both the subjective sleepiness and the decreased performance caused by the PSD (Gillberg et al 1994)

[191] Interactive Market Access Systems, Inc. IMAS Charts on Internet Demographics. Tampa FL, 1995. http://www.imas.com/demographics/index.html

[192]Interactive Market Access Systems, Inc. IMAS Charts on Internet Demographics. Tampa FL, 1995. http://www.imas.com/demographics/ethnic.html

[193] Graphic, Visualization, & Usability Center, Georgia Institute of Technology. GVU's 5th WWW User Survey. Atlanta GA, 1996. http://www.cc.gatech.edu/gvu/user_surveys/survey-04-1996/

[194] a behavioural response system is able to distinguish good sleepers from insomniacs by measuring the insomniac's greater sleep onset latencies, lower sleep efficiencies, and greater number of arousals (Kuderian et al 1991)

[195] this type of system had difficulty differentiating good from "fair" sleepers; moreover, there was an increase in the percent sleep measured over three nights (Bonato & Ogilvie 1989 [not in EndNote]) which may

reflect a decreased motivation to respond to the cuing tones.

[196] with these systems, a first-night effect is minimal and often absent; they can show phenomena which do not occur in the sleep laboratory, such as light sleep occurring in late evening before the overnight sleep period begins; they have been successfully used in a variety of settings, including operating a train, mountain climbing, and flying (Broughton 1991).

[197] Daytime napping can be quantified, and the effects of environmental factors on sleep can also be measured (Wauquier et al 1992)

[198] The actigraph has been shown to predict polysomnographically determined sleep or wake with 93% accuracy (Levine et al 1986)

[199] Agreement between Nightcap sleep values and those derived from sleep laboratory polysomnography was 87% in healthy young adults (Ajilore et al 1995)