Naval Health Research Center

HEALTH EFFECTS OF SLEEP DEPRIVATION

P. Naitoh

T. L. Kelly

C. Englund

Report No. 89-46

NAVAL HEALTH RESEARCH CENTER
P.O. BOX 85122
SAN DIEGO, CALIFORNIA 92186-5122

NAVAL MEDICAL RESEARCH AND DEVELOPMENT COMMAND
BETHESDA, MARYLAND

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATE COVERED

4. TITLE AND SUBTITLE
Health Effects of Sleep Deprivation

5. FUNDING NUMBERS
Program Element: 6370nN
Work Unit Number: M0096.002-5301

6. AUTHOR(S)
Paul Naitoh, Tamsin L. Kelly & Carl Englund

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Naval Health Research Center
P. O. Box 85122
San Diego, CA 92186-5122

8. PERFORMING ORGANIZATION
Report No. 89-46

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Naval Medical Research and Development Command
National Naval Medical Center
Building 1, Tower 12
Bethesda, MD 20889-5044

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11 SUPPLEMENTARY NOTES
Published in Occupational Medicine: State of the Art Reviews, 1990, 5(2),209-237.

12a DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

12b. DISTRIBUTION CODE

13 ABSTRACT *(Maximum 200 words)*

Biomedical and health consequences of total, selective, and partial sleep loss were documented in this paper by examining adrenimedullary activity, adrenocortical activity, metabolism, hematological and immunological changes, autonomic nervous system activity, epileptiform discharges, physical work capacity, antidepressant effects, and mental health.

14 SUBJECT TERMS
Mood
Performance
Sleep Loss

15. NUMBER OF PAGES
30

16. PRICE CODE

17 SECURITY CLASSIFICATION OF REPORT	18 SECURITY CLASSIFICATION OF THIS PAGE	19 SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

HEALTH EFFECTS OF SLEEP DEPRIVATION

PAUL NAITOH, PHD
TAMSIN L. KELLY, MD
CARL ENGLUND, PHD

Reprinted from **OCCUPATIONAL MEDICINE: State of the Art Reviews**
Published by HANLEY & BELFUS, INC. © 1990
210 S. 13th St., Philadelphia, PA 19107 (215) 546-7293

PAUL NAITOH, PhD
TAMSIN L. KELLY, MD
CARL ENGLUND, PhD

HEALTH EFFECTS OF SLEEP DEPRIVATION

From the Naval Health Research Center
San Diego, California

Reprint requests to:
Paul Naitoh, PhD
Naval Health Research Center
P.O. Box 85122
San Diego, CA 92138-9174

Report No. 89-46, supported by the Naval Medical Research and Development Command under Work Unit M0096.002-5301. The views presented in this paper are those of the authors and do not reflect the official policy or position of the Department of the Navy, the Department of Defense, or the U.S. Government.

Early to bed and early to rise, makes a man healthy, wealthy and wise.
Poor Richard's Almanac

Effects of sleep loss on job performance are well documented in many review papers and a recently published monograph.[118] In contrast, health consequences of acute and chronic sleep loss have been poorly documented except in a few social and epidemiological surveys on shift- and nightwork. The purpose of this chapter is to survey and critically review the results of laboratory and field studies on health consequences of sleep loss. Three kinds of sleep loss are identified: total, selective, and partial sleep loss. The most critical information for practitioners of occupational medicine is the health consequences of loss of several hours of sleep repeatedly every day over many days or months—that is, chronic partial sleep deprivation. Unfortunately, this survey found that very few chronic partial sleep loss studies were conducted owing to the prohibitive cost of running them and, more importantly, to the apparently minimal health effects of sleep loss. This paper describes and evaluates the currently available data base to determine the effects of different kinds of sleep loss on the functional integrity of the human organism. The factors discussed include: adrenomedullary activity, adrenocortical activity, metabolism, hematological and immunological changes, autonomic nervous system activity, epilepsy, physical working capacity, antidepressant effects, and mental health.

BACKGROUND

It is commonly believed that we need approximately 7–8 hours of sleep every night and that sleep serves a restorative function. Some people think that missing this period of restoration of mind and body may present an immediate threat to health, or that chronic sleep deprivation may shorten life span or increase morbidity. When we stay awake all night, our body misses the surge of putatively restorative human growth hormone (hGH) that occurs during nocturnal sleep and, at the same time, gets an overabundance of "stressor substance," such as norepinephrine and corticosteroids.

However, everybody has experienced going without sleep at one time or another, either totally for one or two nights, or for a few hours nightly over several days. Many ordinary life events, such as working to meet deadlines, earning a living as a night- or shiftworker, or managing family and business emergencies, can lead to temporary total or partial sleep deprivation. Can such a common life experience be dangerous or fatal?

A series of reports on sleep deprivation studies in rats by Rechtschaffen and his group[25,26,33–35,91,152,153,239,240] suggests that it might. Rats subjected to total sleep deprivation or to selective rapid eye movement (REM) sleep deprivation died in approximately three or five weeks, respectively. Rechtschaffen and others[240] speculated on the basis of energy requirements that humans would "survive sleep loss about 3.7 times longer than rats, or about 77 days of total sleep deprivation versus 21 days of rats, and 135 days of partial sleep deprivation versus 37 days of rats" (p. 80). Horne[118] raises serious doubts about generalizing the findings in rats to humans. The rat's small body requires much more constant effort, or larger energy expenditures, to maintain core body temperature than the much larger human body with its more adequate thermoregulatory mechanisms. Death in severely sleep-deprived rats might be due more to thermoregulatory failure, which would not be expected to occur in humans, than to sleep loss itself.

During World War II, greater London over a six-year period experienced frequent air raids with nightly disruptions of sleep, but Pai[218] reported no ill effects of sleep loss among a large number of people. Progressively increasing sleepiness serves as a built-in safety valve that works to prevent accumulation of an inordinate sleep loss (as hunger and thirst prevent us from going too long without food and water). Because of this, it takes great personal effort or vigorous social support to remain awake for more than 48 hours.

Our impression is that direct detrimental health consequences of sleep loss are probably minimal.[107,128,141–143] The reports of healthy insomniacs who need little or no sleep[128,180,181] seem to support this view. Nonetheless, it is possible that sleep loss interacts with stressful environments or biological weaknesses to the detriment of health. This might explain the cases of "sleep loss psychosis" reported in early literature.[43,319] In what follows we will summarize research findings on the health consequences of sleep loss and attempt to separate fact from myth in this somewhat controversial area.

The purpose of this report is to provide medical professionals who are responsible for maintaining the health of men and women in shift and irregular work environments with background information on the medical consequences of sleep loss. There is an increasing need for such knowledge because more and more military and civilian personnel are involved in shiftwork and round-the-clock sustained/continuous operation (SUSOP/CONOP). The increase in SUSOP/CONOP in the military is documented in a technical report by U.S.

Army Combined Arms Combat Development Activity on "Continuous Operations Study (CONOPS) Final Report," published in 1987 and available to U.S. Government Agencies (AD-B111424L). We will not here discuss the effects of partial and total sleep deprivation on psychomotor and cognitive tasks, because many readily available reviews[118,170,188,192,198,200,204,325,327] have been produced since the publication of the *Handbook of Human Engineering Data* in 1952 by Tufts College.

Before we discuss biomedical effects of sleep loss, we need to define what we mean by sleep deprivation. Researchers have, so far, recognized three kinds of sleep deprivation:

(1) Total sleep deprivation
(2) Partial sleep deprivation
(3) Selective sleep deprivation.

Total sleep deprivation means getting no sleep during at least one 24-hour cycle. For example, if a person who usually sleeps from 2300 to 0700 awakens one morning at 0700 and stays awake until 2300 of the following day, that person has gone 40 hours without sleep. During this 40-hour period, one 8-hour sleep period has been missed. Strictly speaking, 8 hours of total sleep deprivation have occurred. However, in general practice, we use the hours of continuous wakefulness—40 hours in this example—as the amount of total sleep deprivation.[197,200]

We frequently experience **partial sleep deprivation**. Partial sleep deprivation means sleeping less than usual.[198,274,316,325,326] In research, partial sleep deprivation has been created in two ways: (1) a gradual reduction in sleep duration; for example, a reduction by 30 minutes every two weeks, providing sleepers with an ample opportunity to adjust to longer waking hours each day,[100,125] or (2) a sudden reduction in sleep duration, for example, from a customary 8 hours to 5. The short sleep regimen is tried out for a few days[57,108,111,120,209,273] or continued for a long period of time so that sleepers can adapt to the new life-style.[100,315,325]

Unlike total and partial sleep deprivation, clear-cut **selective sleep deprivation** does not occur in real world situations. It is created only as a result of manipulation of sleep in a laboratory, where changes in sleep stages can be observed as they take place. When sleep is observed electrophysiologically, it is classified into seven states: wake; sleep stages 1, 2, 3, 4; REM sleep; and movement time. Often, sleep stages 3 and 4 are combined and designated as slow wave sleep (SWS), which is contrasted to the amount of REM sleep. Sleep stage 1 is thought to be a transition stage, when we are neither asleep nor awake.[131] Sleep stage 2 has a unique brain wave signature, "sleep spindles," indicating that at this stage we are fully asleep. Although the functions of sleep and the various sleep stages are not fully understood,[40,116-118] it has been suggested that SWS is needed for "body repair," whereas REM sleep is needed for "mind repair."[77-80,88,217,302] In nocturnal sleep of adults with no sleep disorders, these sleep stages follow each other in a fairly fixed pattern, creating a fairly predictable sleep profile. (For a more complete discussion of the sleep stages, see Rechtschaffen and Kales.[241])

Selective sleep deprivation consists of preventing the occurrence of a particular sleep stage. In REM sleep (or SWS) stage deprivation, sleepers are prevented from getting REM sleep (or SWS) by being awakened whenever they begin to enter that sleep stage.[5,13,77,305]

The sleep deprivation we experience in daily life is likely to be a mixture of these three types. For example, we may simultaneously experience both partial and REM sleep deprivation when we curtail our sleep by waking up a couple of

hours earlier in the morning, thus missing the early morning sleep that is rich in REM sleep. Taking antidepresssants or hypnotics has also been shown to reduce REM or SWS.[12,132,217] In this report, we are mostly concerned with health effects of total sleep deprivation, because that is what the majority of the research has dealt with.

SLEEP LOSS AND ADRENOMEDULLARY ACTIVITY

The adrenomedullary system produces two separate catecholamines, epinephrine (EP) and, in small quantities, norepinephrine (NE). These hormonal secretions are rapidly increased by stressors such as cold, pain, anoxia, shock, hypoglycemia, hypotension, physical exercise, psychological stimuli, and drugs in common use, such as caffeine, nicotine, and alcohol. Both EP and NE act on all organs of the body, causing "sympathetic activation," a collection of effects generally serving to improve physical effectiveness for "fight or flight" emergency situations.[116,118] These effects include increased heart rate, strengthened cardiac contraction, constriction of arterioles in the skin, and both vasodilation and constriction of voluntary muscle arterioles. NE is generally more powerful in raising blood pressure, while EP is generally more powerful in the mobilization of glucose and fat and the relaxation of smooth muscles. Urinary EP shows a strong circadian rhythm, but urinary NE shows no significant circadian rhythm.[9,102,103,110,116] Thus any changes in EP during sleep deprivation must be analyzed to partition out the circadian component.

Fiorica et al. observed no significant changes in total urinary catecholamines during 85 hours of total sleep deprivation.[95] Levi[158,159] also found no consistent changes in EP or NE up to 75 hours of total sleep deprivation, when he did not take experimental subjects' age into account. No significant increase in 24-hour urinary EP was seen in his older subjects (49–64 years, average age 56). However, 24-hour urinary EP increased in the young group (20–44 years, average age of 29). Levi attributed the results to differences observed in self-pacing between the young and old. Early in the experiment, the young subjects mobilized more physical and mental resources to achieve superior performance, but subsequently they slackened their work pace owing to exhaustion. The old subjects seemed more in control of and less reactive to the study environment and kept a more even pace throughout the experiment. Froberg found that "morning-type" people did not differ from "evening-type" people in circadian rhythms of urinary EP secretion during 72 hours of total sleep deprivation. Sleep loss neither disrupted circadian rhythm nor increased urinary EP excretion. Excretion of vanillylmandelic acid, a major metabolite of NE, did not change during a total of 205 hours of sleep deprivation.[102]

From these studies we could conclude, as previous review papers have,[110,116,199] that no consistent significant increase in the adrenomedullary activity occurs during total sleep deprivation. In other words, total sleep deprivation in itself does not cause "stress" in the usual sense.

Some studies, however, have suggested an adrenomedullary activation during total sleep deprivation. Steinberg and others[279] studied the effects of total sleep deprivation, sleep, and immobility on the levels of EP, NE, metanephrine, normetanephrine, and vanillylmandelic acid under a strictly controlled diet. They found higher urinary catechalomine excretion during nights of sleep deprivation when subjects lay on a bed (but remained awake) than during nights of normal sleep. Other urinary substances showed no change. They concluded that wakefulness caused significant elevation in EP and NE. Kuhn and his group performed a

series of studies[148] examining the effects of 5 days of total sleep deprivation on 24-hour urine levels of metanephrine, normetanephrine, and vanillylmandelic acid. They observed a significant increase of normetanephrine during sleep deprivation days (except day 2), a significant increase in metanephrine on day 3, and a significant increase in vanillylmandelic acid on the last day of the study. These responses were interpreted as reflecting stress caused by enforced sleep loss of 5 days. However, Kuhn et al. imposed greater psychological and physical demands and other situational factors on their subjects than the previously discussed studies. These stressors, rather than the sleep loss itself, may have caused the adrenomedullary activation.

Hasselman et al.[112] reported higher urinary EP and NE during bicycle ergonometric work after one night of sleep loss than after a normal night's sleep. It appears that sleep-deprived subjects may be able to perform the same amount of physical work as usual, but in doing so, they must increase adrenomedullary activity for greater mobilization of energy resources. They also found that ambient temperature is an important situational factor affecting adrenomedullary output. They observed a dramatic increase of urinary catecholamines when the sleep-deprived subjects worked with a bicycle ergonometer under high ambient temperature. Thus, sleep deprivation appears to interact with other stressors rather than directly affecting adrenomedullary activation.

In summary, total sleep loss of 3 days or less causes neither significant increases in adrenomedullary activity nor circadian disruption of EP rhythm if sleep deprivation is conducted under physically and mentally nondemanding, experimental environments. When total sleep deprivation takes place in high physical and mental workloads under uncomfortable ambient temperature, or the subjects are particularly energetic in their efforts to maintain top performance by adopting a high work pace, a significant activation of the adrenomedullary system may be reflected in increased urinary catecholamines.

SLEEP LOSS AND ADRENOCORTICAL ACTIVITY

The pituitary-adrenocortical system produces glucocorticoids, mineralocorticoids, and androgenic steroids. The main glucocorticoid is cortisol. Production of cortisol increases in response to many stressors—for example, surgery or illness. Cortisol increases hepatic glycogenesis, suppresses protein synthesis, and has anti-insulin action in peripheral tissues, thus providing energy needed for coping with prolonged, stressful circumstances. The cortisol level sensitively reflects psychological states, increasing with arousal and anticipation of stress.

Because of difficulties in assaying serum cortisol, early studies used the quantity of eosinophils, lymphocytes, and urinary 17-ketosteroids and electrolytes (factors affected by adrenal steroids) to indirectly monitor activation of the pituitary-adrenocortical system. Attempts to determine whether total sleep deprivation would activate the pituitary-adrenocortical system were further complicated by the presence of a strong circadian rhythm in these hormones.

Urinary 17-ketosteroids have been found to show no change after 72 hours of total sleep deprivation[43] and were even reported to decrease on the second, third, and fourth days of total sleep deprivation.[190,293,324] Urinary 17-hydroxycorticosteroids were also observed to show no change after 72 or 120 hours of total sleep deprivation,[43,143] and one night of total sleep deprivation did not change the time of the circadian peak of plasma 17-hydroxycorticoid.[98] Rubin et al.[252] found that plasma and urinary 17-hydroxycorticosteroid decreased from the baseline

value to a low point after 170 hours of total sleep deprivation. These differences in results probably reflect more the varied psychological and physical demands imposed on the subjects than the effects of sleep loss itself.[191,198] Opstad and Aakvaag[209] observed levels of serum cortisol during 5-day-long training field exercises. These training courses required heavy and continuous physical activities with less than a total of 2 hours of sleep per 24 hours. Serum cortisol decreased from a relatively high level on day 1 to a low level on day 5. Similarly, a reduced cortisol level was observed at the end of 48 hours of sleep deprivation among subjects who did not experience heavy physical work. Kant et al. observed slight decreases in urinary cortisol levels during sleep loss of 72 hours.[132]

In contrast, Kuhn et al.[148] reported an increase of urinary 17-hydroxycorticosteroid for the first two days of total sleep deprivation.

Briefly, total sleep deprivation of up to 72 hours has little effect on glucocorticoids, especially compared with the large increases in 17-hydroxycorticoid sometimes observed during baseline periods when subjects are experiencing pre-experiment excitement and anxiety. Total sleep loss does not cause the classical nonspecific emergency reaction.

SLEEP LOSS AND METABOLISM

People expend more metabolic energy during a sleepless day than during a normal 24-hour cycle. The metabolism slows down during sleep, and this energy conservation does not occur during sleep deprivation.

Biological energy is based on the adenosine triphosphate (ATP) system. Thus, total sleep loss might be anticipated to affect ATP. Luby et al. reported that after 4 days of sleep deprivation energy production (as measured by specific activity of ATP after whole blood was incubated with radioactive phosphorus) increased, while the ATP level dropped.[166] After 7 days of total sleep deprivation (TSD), energy production had dropped almost to baseline, whereas the level of ATP had risen but was still below baseline. Unfortunately, this study involved only one subject and has never been replicated.

When the ATP reserve is depleted, phosphocreatine is used as a high energy source. Under these conditions the level of urinary creatinine may indirectly signal the degree of energy expenditure. However, a number of studies have found that total sleep deprivation of up to 120 hours does not change the urinary creatinine level.[95,143,270] Resting metabolism as assessed by oxygen consumption also remain unchanged during total sleep deprivation of up to 120 hours.[95]

If total sleep deprivation is a catabolic state, it might cause an acceleration of protein turnover, which should be reflected by an increase in the urinary total nitrogen. However, total sleep deprivation of up to 126 hours did not affect the 24-hour urinary total nitrogen level.[148] Scrimshaw et al.[270] observed a decrease of urinary nitrogen on the first day of total sleep deprivation and an estimated 12% increase in protein requirement over the basal need during the second day. Kant et al.[132] found an increased urea excretion within 24–48 hours of sleep deprivation, and it stayed high during the remainder of a 72-hour sleep deprivation. This finding was interpreted to reflect the increased protein catabolism to supply energy needs. Adam and Oswald, studying rats' brains, found less protein synthesis during 13 hours of total sleep loss but increased protein synthesis during the subsequent recovery sleep.

Under some circumstances, where sustained physical activities are required, the body may convert from carbohydrates to lipids as the primary fuel for

biological energy. It appears that total sleep deprivation in environments requiring constant mental alertness and physical activity falls in this category.[249,250] The research findings of Kuhn et al.[110,148] indicate that lipids are a preferred energy source during total sleep deprivation. They found that plasma-free fatty acids increased by 130% and 182% after 48 hours and 72 hours of total sleep deprivation respectively. They detected a much slower fall in the blood glucose level after glucose ingestion after sleep loss than before; after 3–4 days of total sleep loss, a "glucose tolerance curve" resembled the curve for borderline diabetics. Vondra et al. found that hyperglycemia in response to an oral glucose tolerance test was prolonged after 120 hours of sleep deprivation.[311] This result was accompanied by a decreased input of pyruvate into the Krebs cycle. Van Helder et al.[297] believe that this change in glucose metabolism is a prediabetic type of metabolic state. They found that subjects who were deprived of sleep for 60 hours and physically exercised developed insulin resistance. Their proposal that sleep loss results in decreased insulin sensitivity at peripheral insulin receptor sites, eventually leading to "insulin exhaustion at pancreatic sites," needs confirmation because the receptive role played by physical exercise was not clearly separated from the role of sleep loss in itself. Unlike Kuhn et al.[148] and Vondra et al.,[311] they observed no protracted glycemia, possibly because of the relatively short (60 hours) sleep deprivation against that of 120 hours. Fiorica et al.[95] showed that the respiratory quotient also reflected a shift from carbohydrate- to lipid-dominated metabolism on the second and third days of total sleep deprivation.

Total cholesterol in plasma and in the vastus lateralis muscle and plasma triglycerides decreased during a 120-hour sleep deprivation.[311] The changes resembled alterations in cholesterol metabolism observed in cardiovascular diseases or the conditions preceding them.

Sleep deprivation was reported to increase plasma levels of thyroid (T_3, T_4, and rT_3) hormone,[214,220] increasing metabolic rate. Opstad and Aakvaag[211] found that the combined effect of sleep deprivation, prolonged heavy physical work, and caloric deficiency caused thyroxine to increase on day 1 but to decrease from day 2 to day 5, the end of the training course. Triiodothyronine showed a similar trend to T_4. Palmblad et al.[220] found very small increases of about 10% for T_3 and T_4 plasma levels after 48 hours of sleep deprivation.

Sleep loss reduces androgens.[68] Serum testosterone decreased during a 5-day training course involving sleep loss, hard physical work, and caloric deficiency.[1,210,211] Testosterone decreased to below 25% of precourse levels after 48 hours of sleep loss. This decrease reflected reduced production of testosterone, not increased metabolism.

Briefly, these findings suggest that, as total sleep loss continues, skeletal muscles and other tissues begin to derive more energy from the use of free fatty acids. Total sleep loss of two nights or more may result in switching the main energy substrate from carbohydrates to lipids to meet energy demands, resulting in increased plasma-free fatty acids, increased plasma glucose, and sluggish plasma glucose use.

SLEEP LOSS AND HEMATOLOGICAL AND IMMUNOLOGICAL CHANGES

Total sleep deprivation changed neither the erythrocyte count[98,138] nor the hematocrit level.[95,143] However, a drop in plasma iron was reported in

humans[147,161,300] and in rats.[83,84] Kuhn et al.[148] reported that plasma iron dropped to one-half its normal level during 120 hours of total sleep loss. Their report showed that the plasma iron decline was sharp during the first 48 hours of sleep loss and subsequently much more gradual. Return to the normal value was slow, taking roughly one week. Intestinal absorption and excretion rates of iron, as measured by radioactive iron uptake, showed no changes during total sleep loss. There was no evidence of impaired erythropoiesis. Thus the reduction in plasma iron was attributed to a failure of the reclamation process of removal of iron from plasma into the splenic-hepatic reticuloendothelial system and the erythropoietic tissue in the bone marrow.[110] Lindemann et al. used a 4- to 5-day training course involving continuous physical activities, limited caloric intake, and partial sleep deprivation (1 to 3 hours of sleep loss per night) and observed changes in hemoglobin, hematocrit, serum iron, bilirubin, and other values. Both hemoglobin and hematocrit decreased during the course. The serum iron increased until day 4 but decreased sharply to 50–60% below initial values on day 5. The bilirubin levels increased markedly, but they came down to the precourse value immediately after the training course. The elevated iron and bilirubin levels were attributed to damage to erythrocytes from the mechanical stress of heavy, continuous physical activities, and not to sleep loss itself. Similar results are reported during Japanese ranger training lasting 93 hours.[333]

The level of serum ferritin, which returns iron to the erythropoietic tissues in the bone marrow, was elevated during a 4- to 5-day training course.[300] The increase of ferritin was correlated with decreased hemoglobin values and increased total bilirubin. Iron released from disintegrated erythrocytes increased ferritin synthesis in the reticuloendothelial system and subsequently increased release of ferritin in blood. The effects of sleep deprivation itself on erythrocytes remain unclear. Levi[159] reported that total sleep deprivation of 24 hours resulted in serum iron decreases of 26% in older subjects (average age, 56), while iron decreased by 52% in younger subjects (average age, 29). Erythrocyte sedimentation rate (a measure that can be affected by many things, including anemia and inflammation) of the older subjects increased by 38% and that of the younger subjects by 168%.

Drucker-Colin[83] and Drucker-Colin et al.[84] found that normocytic anemia can be induced in rats by administration of phenylindanedione (PID, an indirect anticoagulant) during total sleep loss. Administration of parachlorphenylalanine (PCPA, a serotonin synthesis inhibitor) along with PID during sleep loss aggravated the anemic process; anemia without evidence of PID-induced internal bleeding was detectable after 3 days of treatment. These drugs do not produce anemia when administered without accompanying sleep loss, and, as Drucker-Colin emphasized, even an 8-day-long period of sleep deprivation without the drugs does not produce anemia, indicating that sleep loss interacts with the drugs rather than acting directly to produce anemia. Earlier animal studies reported decreases in erythrocyte count, down to as low as 60% of normal.[138] The studies of Drucker-Colin et al.[84] suggest vulnerability of the hemopoietic system to combined sleep loss and drug administration.

It is common belief that the "stress" of losing sleep causes us to catch cold. Immunodeficiency may follow stressful life changes.[118,219]

Palmblad[221] observed an increased production of interferon and decreased phagocytosis during 77 hours of total sleep deprivation. These changes were too small to be of clinical significance. In a subsequent study,[222] the immunological

measure of the rate of proliferation of white blood cells in response to an antigen was used. The proliferation of polymorphonuclear leukocytes and monocytes after antigen exposure was reduced after total sleep deprivation of 48 hours, but it remained within normal range; the drop appears to be of no clinical significance.

Briefly, no serious immunological changes follow sleep deprivation. Reduced lymphocyte stimulability and neutrophil phagocytosis and gradually increasing interferon production are expected after 48–72 hours of sleep deprivation,[219] but these changes in cell-mediated immunity would be too small to be of clinical significance. The body's iron equilibrium may be altered during sleep deprivation, and the addition of certain drugs or other stressors may lead to anemia.

SLEEP LOSS AND AUTONOMIC ACTIVITY

Mean core body temperature gets lower during total sleep deprivation. The circadian variation remains but its amplitude is reduced. Homeostatic ability to maintain core body temperature when exposed to cold is not impaired by 84–86 hours of total sleep deprivation,[95] but Sawka et al. suggest some degraded thermoregulation during exercise after total sleep deprivation.[260]

Resting systolic and diastolic blood pressures do not change during total sleep deprivation.[54,199] Resting heart rate has generally been found to show little systematic change during sleep loss,[67,116,198,203,324] except Bjerner reported general systematic slowdown of resting heart rate.[42] Fenz and Craig[94] reported that heart rate increased on day 2 of total sleep deprivation, but the increase was found only in one of the two daily measures. On the third day, heart rate dropped. Total sleep deprivation caused a progressive increase in heart rate variability, much of it related to an increase in the normal tendency of the heart rate to vary with respiration—"respiratory sinus arrhythmia."[116]

Endogenously depressive patients have a lower amplitude circadian heart rate curve than normal subjects. Twenty-four hours of total sleep deprivation caused further flattening of the circadian heart rate curve in this patient group. The circadian heart rate rhythms of neurotic depressives are more normal than those of the endogenously depressive at baseline and were unaffected by a 24-hour sleep loss.[253]

Levi[158] observed that one quarter of his subjects showed S-T segment depression during 75 hours of total sleep deprivation. In some cases, depression was pronounced and resembled a cardiac infarction in the apical area. The depression gradually disappeared after several days of sleep and rest.

Johnson et al.[127] reported that resting-finger pulse volume became very small due to peripheral circulatory constriction during a prolonged total sleep deprivation. Finger pulse volume showed a marked vasodilation, tripling in volume, during recovery sleep. Mirsky and Cardon[183] observed increased finger pulse volume near the end of their total sleep deprivation study during a complex vigilance task. Such transient increases may be attributable to periods of microsleep.

Generally, total sleep deprivation does not change respiratory rate,[95] although variability of rate was reported to increase over 60 hours of sleep loss.[116]

Skin conductance probably reflects sympathetic nervous activity. Different studies have reported equivocal and conflicting results as to sleep deprivation effects on skin conductance.[116] We conclude that total sleep loss has no consistent effect on skin conductance.[203] Strausbaugh and Roessler[280] reported that tonic

skin conductance was higher—that is, subjects were more alert and activated—in the sleep-deprived subjects who had high "ego strength" than in those whose ego strength was low.

Briefly, no major autonomic changes are expected in resting subjects during total sleep loss of 2 days or less, although amplitudes of circadian curves may be blunted and general variability may be increased.

SLEEP LOSS AND EPILEPTIFORM DISCHARGES

Total sleep deprivation initially increases cerebral irritability, which may result in epileptiform discharges in predisposed individuals.[3,16,22,27-29,36-38,41,71-76,87,104,177,184,201,236,248,267-269,318] Because of this, sleep deprivation has been used to provoke abnormal paroxysmal electroencephalographic discharges in individuals with suspected epilepsy.[87] One night of total sleep loss is combined with other techniques of activation in clinical practice.[201] However, increased irritability appears to be limited to the first 2 days of total sleep deprivation; after that, extreme sleepiness reduces cerebral electrical excitability.

Because total sleep deprivation of 2 days or less under clinical laboratory conditions does not induce epileptiform discharges in normal healthy individuals, false positives rarely occur.[28,29,202,318] Only one child (8%) of a group of 12 normal children showed an abnormal electroencephalogram after a short period of total sleep deprivation.[104]

However, prolonged total sleep deprivation combined with other stressors may induce abnormal cerebral discharges in healthy individuals.[3,111] On continuous recordings of brain waves over 90 hours, a third of healthy subjects exhibited paroxysmal activity lasting for only a few seconds at a time. One subject showed, however, a total of 2.5 hours of spike-and-wave activity in one day. None of the subjects experienced grand mal seizures, but some exhibited "absence" or psychomotor seizures. Especially for the individuals with a pre-existing susceptibility, sleep deprivation sets the stage for epileptic seizures resembling short periods of inattention and battle shock.[111]

Briefly, all of us could develop psychomotor-type epileptiform discharges under the combined influence of sleep loss and other stressors. Some individuals are more susceptible than others.

SLEEP LOSS AND PHYSICAL WORKING CAPACITY

Maximal oxygen consumption is a measure of cardiovascular fitness or overall aerobic work capacity. Oxygen consumption increases with increasing physical workload. As physical workload continues to increase, we eventually reach a point where the pulmonary/cardiovascular system becomes incapable of supplying additional oxygen to the working skeleton and muscles, and oxygen consumption plateaus despite increasing physical workload. This plateau represents the maximal rate of oxygen consumption—that is, maximal aerobic capacity, VO_2 max.[334] A psychological factor of willingness to endure acute discomfort enters into a VO_2 max testing because the test is terminated by subjects. Aerobic working capacity can also be measured indirectly by the increase in heart rate and the speed of return to resting heart rate following standardized physical work regimens, such as the Harvard Step Test.[52,66]

In 1970, Vogel and Glaser studied three male subjects who underwent maximal and submaximal working capacity tests on a bicycle ergonometer before and after sleep deprivation. Reviewing their data, Harris and O'Hanlon

reported that after 72 hours of total sleep deprivation, the VO_2 max values of the three subjects were reduced by 3.2%, 6.0%, and 3.8% against the baseline.[110] Plyley et al. observed a 6.9% decrease of VO_2 max during 64 hours of sleep deprivation.[233] Martin and Chen[175] reported a decline in physical performance after 50 hours of sleep derivation. The endurance-run time to exhaustion was reduced by 20% among the sleep-deprived. Takeuchi et al.[284] found that vertical jump performance decreased after 64 hours of sleep deprivation. Yeager et al., however, observed that 45 hours of sleep deprivation did not change maximal aerobic capacity.[334] Martin showed no change in VO_2 max after 30 hours of sleep deprivation.[173] Symons et al. found that sleep loss of up to 60 hours did not impair the capability for physical work.[283]

Pickett and Morris[231] found that cardiovascular endurance was not affected by total sleep deprivation of 30 hours, but it was affected by food and water deprivation of the same duration. Brodan and Kuhn,[52] using the Harvard Step Test, found that young men showed about a 5% drop in cardiovascular fitness during the first 48 hours of total sleep deprivation. Their cardiovascular fitness began to recover, however, and even increased, after continued sleep deprivation; after 5 days of total sleep loss, the mean score exceeded the baseline mean by 5%. The most surprising finding was a sharp drop of nearly 15% in cardiovascular fitness on the first day after the recovery sleep. In much younger subjects (ninth-graders), Copes and Rosentsweig[66] found a decline of cardiovascular fitness as measured by the Harvard Step Test during total sleep loss.

Orlee et al. reported that men lost their top physical conditioning quickly after one night of total sleep deprivation.[216] For physically conditioned men, however, the loss was limited to fitness gained by hard training. The degradation brought the fitness level down to the pretraining baseline but not below.

Total sleep deprivation of 24–30 hours slowed reaction time as well as speed of movement.[56,231] Resting electromyographic activity was reported to be reduced during total sleep deprivation.[116] Summarizing the results of past studies, Wilkinson commented, however, that electromyographic changes are unrelated to hours of sleep loss.[324]

It has been well established that continuous muscular activity, such as walking, can help sleep-deprived subjects remain awake.[138] Naitoh et al. observed that all subjects kept themselves physically active to stay awake; for example, a subject was willing to keep moving on his feet, walking 8.3 times more during the 165–191 hours of total sleep deprivation, compared with the 26-hour period at the start of the study.

Briefly, physical work capacity appears not to show major deterioration as a result of total sleep deprivation of 3 days or less. Movement speed, however, is slowed down. Willingness and ability to remain physically active (e.g., by walking) are severely tested by the increasing desire to rest.

ANTIDEPRESSIVE EFFECTS OF SLEEP LOSS

Health effects of sleep deprivation are not always negative. The antidepressant effects of total sleep deprivation have been well established. This is an area that is still actively researched. The bibliography of this chapter cites more than 30 references on it. Total sleep deprivation provides temporary relief from depression in one-third to one-half of endogenously depressed patients, but it is less effective in patients with involutional depression. With respect to the other major category of depression, reactively depressed patients benefit from sleep loss more if they

have more somatic complaints (such as disturbed sleep and poor appetite) and large diurnal fluctuation in moods, as compared with few somatic complaints and poor circadian rhythm. Typically, a single night of total sleep deprivation is repeated over several weeks until the desired amelioration of depression is achieved. The patients must remain awake between 0400 and 0600 to get full antidepressant benefit from sleep deprivation. Cole and Muller[63] reported that when elderly depressives (57–79 years old, average age 69) were given repeated (once or twice a week) 36-hour periods of total sleep deprivation therapy, 9 (60%) of 15 patients responded to the therapy and 6 (40%) had a good outcome. However, total sleep deprivation therapy may trigger a manic phase.[316,317]

Post et al.[235] sampled lumbar cerebrospinal fluid from depressive patients to study central amine metabolism as reflected by levels of 5-hydroxyindoleacetic acid (5-HIAA), homovanillic acid, and 3-methoxy-4-hydroxyphenylglycol. Total sleep deprivation changed the central amine metabolism of the depressed patients, causing a decrease in 3-methoxy-4-hydroxyphenylglycol. The other parameters increased. In a study by Livrea et al.,[163] lumbar cerebrospinal fluid was examined for homovanillic acid and 5-HIAA before and after total or REM sleep deprivation. Cerebrospinal fluid levels of homovanillic acid and 5-HIAA were not affected by 30 hours of total sleep deprivation, but 5-HIAA increased after 2 nights of REM sleep deprivation.

Two hypotheses attempting to explain the antidepressant effects of total sleep deprivation are:

(1) total sleep deprivation assists in resynchronization of disordered circadian rhythms and re-entrainment to the 24-hour societal rhythm

(2) total sleep deprivation lowers an abnormally high arousal level in depressives.

REM sleep deprivation also has antidepressant effects.[304,305] The REM sleep deprivation procedure consists of awakening subjects every time they go into REM sleep. This is continued for six nights or until 30 awakenings per night are reached (REM frequency increases as deprivation accumulates), whichever comes first. Subsequently patients are permitted a single night of uninterrupted sleep. The REM sleep deprivation procedure is repeated until the desired amelioration of depressive symptoms is obtained.

In brief, total or REM sleep deprivation helps to temporarily reduce depression in some depressive patients. Mood effects of total or REM sleep deprivation in normal individuals are discussed in the following section.

SLEEP LOSS AND QUALITY OF LIFE

The most serious health cost in its broadest sense is a lowered quality of life during sleep deprivation. Sleep loss results in chronic excessive fatigue and sleepiness, sagging motivation for work, and poor job performance leading to frustrations and conflicts with other workers. The quality of life will be discussed in terms of (1) mood and motivation to work, (2) excessive daytime sleepiness and fatigue, and (3) mental health.

Mood and Motivation to Work

In the *Handbook on Human Engineering Data* (second edition) published by Tufts College for the Office of Naval Research in 1952, 17 papers on sleep deprivation are reviewed. The editors were surprised to see that "there are no significant physiological changes with up to 200 hours of sleeplessness" and that

"subjective attitude (appearance, mood and behavior) is the only factor severely affected by sleep reduction." This conclusion is still valid.[116,118,119]

One night of total sleep deprivation was found to influence six factors: sleep/wakefulness, stress, euphoria, energy, irritation, and concentration, in a complex, but highly predictable, manner. For example, one night of total sleep deprivation lowered wakefulness and energy ratings, but did not significantly change stress and euphoria.[44] Simple negative mood changes, such as feeling tired, are consistently reported after total sleep deprivation and can be used to gauge the extent of accumulated sleep debt. Subjects felt progressively more negative and less positive during total sleep deprivation, and these mood changes showed strong circadian rhythm.[199,200] Thus, unlike depressives, normal subjects do not experience large positive mood changes or feelings of well-being after sleep deprivation.[44,69]

In the first scientific study of partial sleep deprivation, Mary Smith studied herself. She shortened the usual period of sleep over three consecutive nights by 1.5, 3.5, and 5.5 hours.[273] She experienced a double feeling tone—unpleasant muscular weariness that became pain at times, and pleasant sensations of exhaltation and power. For the most part, the pleasant aspect was dominant. Johnson and MacLeod[125] reduced the sleep of two subjects by 30 minutes, every two weeks, form their customary 7.5 hours to a minimum of 4 hours per 24 hours. Using the Profile of Mood States, they found that the subjects were less "happy," less "friendly," more "fatigued," and increasingly irritable. The subjects experienced difficulties maintaining concentration when the sleep period was reduced to 5.5 hours or less.

In another gradual sleep reduction study,[100] two young couples reduced their sleep by 30 minutes every two weeks until total sleep time reached 6.5 hours. They continued to reduce sleep at a rate of 30 minutes every three weeks. When total sleep time was down to 5 hours, the rate of sleep reduction became 30 minutes every four weeks to give the subjects more opportunity to adapt to the shorter sleep and longer day. Eventually, the subjects felt that they found the minimum sleep they needed, the point where their sleep was maximally reduced without jeopardizing their jobs and schoolwork. Over a 7-month period, one couple reduced their sleep time from 8 hours to 5 hours. The other couple reduced their sleep from 8 hours to 4.5 hours over an 8-month period. Both couples slept for a month at these low levels. Subsequently, the sleep period was lengthened by 30 minutes for a 2-week period, after which they were allowed ad lib sleep regimens.

The couples reported that they decided to stop reducing their sleep because they were overwhelmingly tired, they were falling asleep in class, playing cards, or visiting friends, and they had difficulty remaining alert while driving. However, objective school and job performances did not suffer during the partial sleep deprivation.

Webb and Agnew[315] examined 15 subjects who reduced sleep to 5.5 hours and maintained that amount for 60 days. The moods of these subjects showed initial dips but generally returned to baseline as partial sleep deprivation continued. During the study period, the subjects showed performance degradation that appeared to be due to boredom and lowered motivation.

In brief, mood deteriorates and motivation to work hard is lowered during total and partial sleep deprivation. Although controlled studies of regular gradual reduction in nightly sleep have demonstrated that we have a potential to

adjust to partial sleep deprivation, these results are not directly applicable to the shiftworker. In shiftwork, partial sleep deprivation occurs acutely when nightshift work begins and, unlike strictly controlled studies, the amount of sleep loss may vary from day to day. Greater experience on a shiftwork schedule has not been shown to be associated with reduced complaints about sleep loss.

Excessive Daytime Sleepiness and Fatigue

Naitoh[199] reported that the levels of fatigue and sleepiness increase and decrease in a circadian manner and that total sleep deprivation of 2 nights increased subjectively rated fatigue and sleepiness without destroying these circadian rhythms. Sleepiness, as measured by the Stanford Sleepiness Scale,[114] peaks around 0200–0600 of the first night of total sleep deprivation. Once subjects pass this critically sleepy period, they feel much less sleepy even though they remain awake. However, Carskadon and Dement[58] found that objective sleepiness, as measured by the Multiple Sleep Latency Test, lost its normal circadian rhythm during the first night of total sleep deprivation; sleepiness peaked around 0600 the next morning and remained at peak level throughout the 2 nights of total sleep deprivation.

As shown in the studies of Friedman et al.[100] and Johnson and MacLeod[125] discussed in the preceding section, subjective feelings of tiredness and sleepiness provide an early warning of excessive sleep debt. Impairment of job performance appears much later than daytime feelings of excessive tiredness and sleepiness. In real workplace situations, worker motivation is an important variable with respect to how closely performance decrements follow sleep loss.

In brief, increased feelings of tiredness and sleepiness reliably follow total or partial sleep deprivation, reducing quality of life. These feelings constitute an early warning that serious deterioration in job performance will follow unless more sleep is obtained.

Mental Health

As mentioned previously, the most obvious and consistent changes due to total and partial sleep deprivation are psychological. When investigators lived with sleep-deprived subjects, they often observed frequent, but transient, psychotic behavior.[32] These behavioral pathologies are easily missed because of their transience. Whether a subject shows transient psychopathology during total sleep deprivation depends on age, physical health, psychological stability, and the environment of the study.

Total sleep deprivation experiments represent a complicated social psychological arrangement.[191–193] An illustration of the impact of experimental environments is found in the differences between the results of Tyler's study[293–295] and those from the Walter Reed Army Medical Institute of Research.[192,327]

Tyler's study involved 350 volunteers under military discipline during the period of 1942–1946. Under the stringent, stressful military exercise environment, 112 hours of total sleep deprivation caused more than 70% of the subjects to complain of auditory and visual illusions. Seventy-six of these men dropped out before the conclusion of the study for a variety of psychosomatic complaints. Seven men had to be removed from the study because they developed hallucinations and bizarre "psychotic" behaviors. The high attrition occurred despite excellent morale at the start and a considerable incentive offered for completing the study.

The Walter Reed study was conducted in a laboratory environment. The staff maintained a friendly and egalitarian atmosphere in order to keep frustration and aggression at a minimum. Gentle methods such as walking, playing games, holding conversations, and encouragement from staff were used to help 74 soldiers stay awake for 72–98 hours. No subjects dropped out, and no "psychotic" breakdowns were observed although visual hallucinations were reported.

Thus, the sociology of total sleep deprivation or the psychological characteristics of the environment play a critical role in determining mental health during total sleep loss.

Prior mental stability is also a determinant of a subject's psychological responses to total sleep deprivation.[134,167,168] Pasnau et al. reported a study involving 205 hours of total sleep deprivation.[224] One of the volunteer subjects experienced a panic response and all subjects had psychological problems, but they found no evidence of psychosis. In 1968, an editorial in the *Journal of the American Medical Association*[272] stated, on the basis of data later published by Kollar et al.[142] and Pasnau et al.,[224] that sleep deprivation does not cause mentally healthy people to become psychotic. Dement[79] similarly pointed out that REM sleep deprivation does not lead to psychosis. REM sleep deprivation does not cause intensification of thought disturbances, perceptual and motor disorganization, or increased withdrawal.[301,305,306]

In brief, total sleep deprivation does not cause permanent psychosis. Bizarre visual illusions, hallucinations, paranoid mentations, and other behavioral pathologies may be seen, but they are limited to the period of sleep deprivation and disappear after recovery sleep. Hostile or stressful work environments are more prone to produce abnormal responses than friendly supportive environments.

DISCUSSION AND SUMMARY

On the whole, the health consequences of total, partial, or selective sleep deprivation appear to be much smaller than might have been anticipated from the overwhelming sense of sleepiness, tiredness, and sluggishness it can cause. We can conclude that the only substantial and potentially serious effect of sleep deprivation is a reduction in the quality of life as defined by a person's feeling of well-being, willingness to work hard, and feeling of being efficient, wide awake, fresh, and in control. This does not mean that sleep deprivation fails to cause small changes in human biochemistry and physiology.

The belief that sleep should be 7–8 hours long, should offer a refreshed feeling upon awakening, and is needed for physical and mental recuperation appears to have resulted in unwarranted anxiety about sleep loss. This anxiety can affect how a person interprets minor, but perceptible, changes during sleep loss, such as tiredness, sleepiness, lapses of attention, inability to concentrate, and an overall feeling of not being well. With anxiety, these minor psychological changes may be interpreted as representing serious mental harm. The emotional reaction following such an interpretation can cause a person to urgently seek sleep in hopes of avoiding further harm, even to resort to the use of ethanol, sedatives, tranquilizers, and hypnotics.

Schachter[261] and Schachter and Singer[262] have proposed that the nature of emotional response is determined by two components: some perceptible physiological changes and the individual's appraisal of these physiological changes. For example, an increase in heart rate and facial flushing after drinking alcoholic beverages may be implicitly interpreted as a warm satisfying alcohol effect by a

habitual drinker, but as a dangerous or uncomfortable effect by someone who rarely drinks.

Carskadon et al.[60] reported that a group of 109 chronic insomniacs actually differed very little, in terms of total sleep time and sleep latency, from a group of 87 normal sleepers. They did differ in the number of awakenings during sleep. The chronic insomniacs may have physiological or biochemical problems that cause their sleep to be fragmented. It could be argued that, since these insomniacs have normal total sleep time, they may only be suffering psychologically from the awakenings because they interpret them as life or health threatening. Their chronic fear of getting nothing but poor sleep may cause them to suffer much more than a normal sleeper would from a nocturnal awakening. Perhaps an overlay of fear can aggravate what is basically a physiological variation on the norm into a significant psychological problem.

How has the popular belief that poor sleep is dangerous to health come about? Anxiety about the effects of poor sleep or total lack of sleep may have an origin in experiments conducted near the turn of the century and reported by Pieron in 1913[232] and later by Kleitman.[138] They reported physical harm and even death among animals that had been subjected to total sleep deprivation. We have shown that, at least in humans, total sleep deprivation of up to 205 hours does not pose serious health problems.[130,141,142,202,203,224,252] Similarly, chronic reduction of sleep time does not produce any physical harm.[100,125,315]

In addition to supposedly producing physical harm, sleep deprivation is also believed to result in mental harm, i.e., psychosis or intensification of psychopathology.[319] The belief that psychosis of sleep deprivation occurs in normal individuals developed many years ago and is based on dramatic examples reported by Katz and Landis[133] and others. Katz and Landis described a 24-year-old man who was convinced that sleep was a habit and could be broken without any ill effects. He remained awake for 231 hours before developing delusions of persecution, at which time the study was terminated. In another study, a large number of young soldiers, marines, and civilians underwent paratrooper-like training that included a 35-mile night march; some subjects suffered a transient psychosis with paranoid mentation.[293,294]

Careful evaluation of these and other studies shows that psychosis was not caused by sleep deprivation itself, but by a combination of sleep loss with other stressors. The previously mentioned 1968 editorial in the *Journal of the American Medical Association* made a clear effort to correct the view that sleep deprivation causes mental harm. The editorial stated that sleep loss would not produce psychopathological reactions extending beyond the period of sleep deprivation and that "patients who suffer from periods of insomnia can be reassured as to the transiency and safety of a brief sleepless period"; it also said that no medication is necessary to protect patients against the psychosis of sleeplessness. The editorial cited the studies that found total sleep deprivation to be beneficial for temporarily relieving depression in some depressive patients.

In the 1960s and 1970s, REM sleep deprivation was also thought to cause mental harm.[61,79,88,119,160] However, it has since been shown to provide safe and effective, although temporary, relief from endogenous depression.

Thus, fear that total sleep and REM sleep deprivation directly cause physical and mental harm is groundless.

This report has attempted to provide information about health consequences of total sleep deprivation. We are surprised to learn from the surveyed literature

that sleep deprivation produces only very small biomedical effects. However, some caveats are necessary.

For workers needing maximum alertness and uninterrupted concentration, such as air traffic controllers, heavy equipment operators, power plant operators, and blood bank technicians, anxiety about the effects of chronic partial sleep deprivation is warranted, particularly insofar as it may cause lapses of attention and inability to concentrate. Many physiological changes have the potential to cause major catastrophes. These workers' appropriate anxiety about their sleep loss may increase the likelihood of errors and may also produce health complaints associated with chronic anxiety.

Almost all of the past and current research on sleep deprivation is based on highly controlled laboratory studies using short-term data collection. Such studies are not able to assess the complex patterns of sleep deprivation combined with various stressors seen in working environments. Thus, the surveyed literature may be biased by protocols designed more to be simple, clean, and easy to interpret than to answer questions about the biomedical consequences of sleep loss in real life circumstances. Hence, the surveyed literature may have underestimated the true biomedical impact of sleep loss.

For example, most research reports are based on responses to a single exposure to sleep deprivation. Since real life experience more often involves repeated exposures to sleep loss, the findings in the literature may not be directly applicable. Health problems in shiftworkers, who are more apt than other workers to endure chronic sleep deprivation, have been extensively investigated (see Chapter 7). Gastrointestinal disorders, cardiovascular disease, and numerous other medical conditions occur more frequently or are aggravated in this group. These effects may be due wholly to disruption of biological rhythms, but the possibility that chronic sleep deprivation contributes to them cannot be dismissed.

Another caveat is that the findings of these studies cannot be generalized to the middle-aged or older population, especially not to people with less than ideal physical and mental fitness. Most of the studies have been conducted on young, physically and mentally fit people, usually students at universities. Worst of all, only a few (e.g., a series of fascinating studies on 5-day military training courses by Opstad, Palmblad, and others at the Norwegian Defense Research Establishment[1,2,209-215,219-222,249-251]) measured the interaction of physical and psychological stressors with sleeplessness. Since sleeplessness in daily experience often occurs concurrently with job-related, and other, stressors, results of these single-factor studies cannot be generalized to determine health consequences of sleep deprivation in daily life. If combining sleep loss with various stressors is still found to lead to no lasting physical or mental harm, it must be kept in mind that even a transient psychotic episode can be detrimental to health if it happens during dangerous military or industrial activity.

It has been said in jest that all sleep deprivation does is make us sleepy. However, sleepiness is a mystery of life worth careful investigation. Understanding it would help us gain a full appreciation of the nature of sleep and the impact of sleep loss on our bodies.

REFERENCES

1. Aakvaag A, Bentdal O, Quistad K, et al: Testosterone and testosterone binding globulin (TeBG) in young men during prolonged stress. Int J Androl 1:22-31, 1978.
2. Aakvaag A, Sand T, Opstad PK, Fonnum F: Hormonal changes in young men during prolonged physical strain. Eur J Appl Physiol 46:9-19, 1981.

3. Abraham P, Docherty TB, Haslam DR: Ambulatory EEG recording for extended periods under adverse conditions. In Acott FD, Raferty EB, Sleight P, Goulding (eds): ISAMM 77. London, Academic Press, 1978, pp 85–91.
4. Adam K, Oswald I: Sleep is for tissue restoration. J R Coll Physicians Lond 11:376–388, 1977.
5. Agnew H Jr, Webb W, Williams R: The effects of stage four sleep deprivation. Electroencephalogr Clin Neurophysiol 17:68–70, 1964.
6. Agnew HW Jr, Webb WB, Williams RL: Comparison of stage four and 1-REM sleep deprivation. Percept Mot Skills 24:851–858, 1967.
7. Ahnve S, Theorell T, Akerstedt T, et al: Circadian variations in cardiovascular parameters during sleep deprivation: A noninvasive study of young healthy men. Eur J Appl Physiol 46:9–19, 1981.
8. Akerstedt T, Froberg JE: Psychophysiological circadian rhythms in women during 72 h of sleep deprivation. Waking and Sleeping 1:387–394, 1977.
9. Akerstedt T, Froberg J: Sleep and sleep deprivation in relation to circadian rhythms in catecholamine excretion. Biol Psychol 8:69–80, 1979.
10. Akerstedt T, Froberg JE, Friberg Y, Wettenberg L: Melatonin excretion, body temperature and subjective arousal during 64 hours of sleep deprivation. Psychoneuroendocrinology 4:219–225, 1979.
11. Akerstedt T, Palmblad J, de la Torre MR, Gillberg M: Adrenocortical and gonadal steroids during sleep deprivation. Sleep 3:23–40, 1980.
12. Akindele MO, Evans JI, Oswald I: Mono-oxidate inhibitors, sleep and mood. Electroencephalogr Clin Neurophysiol 29:47–56, 1970.
13. Anders TF, Roffwarg HP: The effects of selective sleep state deprivation in the human newborn. Psychophysiology 6:264–265, 1969.
14. Anders TF, Roffwarg HP: The effects of total sleep deprivation on the human newborn. Psychophysiology 6:265, 1969.
15. Amin MM, Khalid R, Khan P: Relationship between sleep deprivation and urinary MPGH levels. Int Pharmacopsychiatry 15:81–85.
16. Armington JC, Mitnick LL: Electroencephalogram and sleep deprivation. J Appl Physiol 14:247–250, 1959.
17. Aschoff J: Features of circadian rhythms relevant for the design of shift schedules. Ergonomics 21:739–754, 1978.
18. Aschoff J, Giedke H, Poppel E, Wever R: The influence of sleep-interruption and of sleep-deprivation on circadian rhythms in human performance. In Colquhoun WP (ed): Aspects of Human Efficiency. London, English Universities Press, 1959, pp 135–150.
19. Ax A, Luby ED: Autonomic responses to sleep deprivation. Arch Gen Psychiatry 4:55–59, 1976.
20. Azumi K, Jinnai S: The effects of REM deprivation on electrodermal-activity in human sleep. In Weitzman ED (ed): Adv Sleep Res 2:164–176, 1976.
21. Baust W, Moppeney H, Schlosser A: The influence of REM sleep deprivation on heart rate and respiration. Arztl Forsch 26:302–308, 1972.
22. Bechinger D, Kriebel J, Schlager M: The EEG following sleep deprivation: An important tool for diagnosis of epileptic seizures. Z Neurol 205:193–206, 1973.
23. Beck U, Wenzel D, Sauer M: Selective deprivation of sleep in narcoleptic children. Arch Psychiatr Nervenk 223:107–115, 1977.
24. Beersma DGM, van den Hoffdakker RH: Depressive mood and physiology during sleep deprivation. Sleep Res 12:321, 1983.
25. Benca RM, Everson C, Kushida C, et al: Effect of sleep deprivation on immune function in rats. Sleep Res 15:8, 1986.
26. Benca RM, Kushida CA, Everson CA, et al: Sleep deprivation in the rat: VII. Immune function. Sleep 12:47–52, 1989.
27. Bennett DR: Sleep deprivation and major motor convulsions. Neurology 13:953–958, 1963.
28. Bennett DR, Mattson RH, Ziter FA, et al: Sleep deprivation: Neurological and electroencephalographic effects. Aerospace Med 35:888–890, 1964.
29. Bennett DR, Ziter FA, Liske EA: Electroencephalographic study of sleep deprivation in flying personnel. Neurology 19:375–377, 1969.
30. Benoit O, Foret J, Merle B, Bouard G: Diurnal rhythm of axillary temperature in long and short sleepers: Effect of sleep deprivation and sleep displacement. Sleep 4:359–365, 1981.
31. Bergamasco B, Brignoli F, Doriguzzi T, et al: Longitudinal polygraphic study of sleep in 11 patients with delirium tremens: Physiopathological considerations of "sleep deprivation." Acta Neurol (Napoli) 23:289–299, 1968.

32. Berger RJ, Oswald I: Effects of sleep deprivation on behaviour, subsequent sleep and dreaming. J Ment Sci 108:457–465, 1962.
33. Bergmann BM, Everson CA, Kushida CA, et al: Sleep deprivation in the rat: V. Energy use and mediation. Sleep 12:31–41, 1989.
34. Bergmann B, Fang VS, Kushida C, Everson C: Hypothalamic-adrenal variables in paradoxical and total sleep deprivation of rats. Sleep Res 15:212, 1986.
35. Bergmann B, Kushida C, Hennessy C, Winter J, Rechtschaffen A: Paradoxical sleep deprivation in the rat: II. Energy consumption. Sleep Res 13:185, 1984.
36. Berti-Ceroni G: Clinical and EEG effects of sleep deprivation in epileptics. Electroencephalogr Clin Neurophysiol 23:188, 1967.
37. Berti-Ceroni G, Pazzaglia P, Mantovani M, Sabatinni L: Effects of total deprivation of sleep in the narcoleptics. Rev Neurol (Paris) 123:263–265, 1970.
38. Berti-Ceroni G, Sabatinni L, Gambi D, Lugaresi E: Effects of sleep deprivation in epileptics. Riv Neurol 37:305–320, 1967.
39. Bhanji S, Roy GA: The treatment of depression by sleep deprivation: A replication study. Br J Psychiatry 127:222–226, 1975.
40. Billiard M: Competition between the two types of sleep and the recuperative function of REM sleep versus NREM sleep in narcoleptics. In Guilleminault C, et al (eds): Adv Sleep Res 3:77–96, 1976.
41. Billiard M, Echenne B, Besset A, et al: Comparative activating effects of sleep, sleep deprivation and sleep after sleep deprivation in children with suspected epileptic seizures. Sleep Res 12:302, 1983.
42. Bjerner B: Alpha depression and lowered pulse rate during delayed actions in a serial reaction test: A study of sleep deprivation. Acta Physiol Scand 19(suppl):65, 1949.
43. Bliss EL, Clark LD, West CD: Studies of sleep deprivation: Relationship to schizophrenia. Arch Neurol Psychiatry 81:348–359, 1959.
44. Bohlin G, Kjellberg A: Self-reported arousal during sleep deprivation and its relation to performance and physiological variables. Scand J Psychol 14:78–86, 1973.
45. Bol'shakova TD, Meshcheryakova SA, Tyabenkova VF, et al: Effect of 24-hour sleep deprivation on biogenic amine turnover. Hum Physiol 11:291–295, 1985.
46. Bond V, Balkisoon B, Franks BD, et al: Effects of sleep deprivation on performance during submaximal and maximal exercise. J Sports Med Phys Fitness 26:169–174, 1986.
47. Borbely AA, Wirz-Justice A: Sleep, sleep deprivation and depression. A hypothesis derived from a model of sleep regulation. Hum Neurol 1:205–210, 1982.
48. Brezinova V, Hort V, Vojtechofsky M: Sleep deprivation with respect to age: An EEG study. Act Nerv Super (Praha) 11:182–187, 1969.
49. Brezinova V, Hort V, Vojtechovsky M: The effect of centrophenoxine on EEG vigilance in the course of sleep deprivation and on the EEG pattern of all-night sleep. Act Nerv Super (Praha) 12:54–56, 1970.
50. Brezinova V, Oswald I, Loudon J: Two types of insomnia: Too much waking or not enough sleep. Br J Psychiatry 126:439–445, 1975.
51. Broadbent DE: Variations in performance arising from continuous work. Conference on Individual Efficiency in Industry. Cambridge, England, Medical Research Council, 1955, pp 1–5.
52. Brodan V, Kuhn E: Physical performance in man during sleep deprivation. J Sports Med Phys Fitness 7:28–30, 1967.
53. Brodan V, Vojtechovsky M, Kuhn E, Cepelak J: Changes of mental and physical performance in sleep deprived healthy volunteers. Act Nerv Super (Praha) 11:175–181, 1969.
54. Bruce LC: Some observations upon the general blood pressures in sleeplessness and sleep. Scott Med Surg J 7:109–117, 1900.
55. Buchsbaum MS, Gerner R, Post RM: The effect of sleep deprivation on average evoked response in depressed patients and in normals. Biol Psychiatry 16:351–363, 1981.
56. Buck L: Sleep loss effects on movement time. Ergonomics 18:415–425, 1975.
57. Bugge JF, Opstad PK, Magnus PM: Changes in circadian rhythm of performance and mood in healthy young men exposed to prolonged heavy physical work, sleep deprivation and caloric deficit. Aviat Space Environ Med 50:663–668, 1979.
58. Carskadon MA, Dement WC: Effects of total sleep loss on sleep tendency. Percept Mot Skills 48:495–506, 1979.
59. Carskadon MA, Dement WC: Sleep deprivation in insomniacs: Effects on daytime alertness and recovery sleep. Sleep Res 14:148, 1985.
60. Carskadon MA, Dement WC, Mitler MM, et al: Self-rated versus sleep laboratory findings in 122 drug-free subjects with complaints of chronic insomnia. Am J Psychiatry 133:1382–1388, 1976.

61. Cartwright RD, Ratzel RW: Effects of dream loss on waking behaviors. Arch Gen Psychiatry 27:277–280, 1972.
62. Clark RE, Warren N: The effect of loss of sleep on visual tests. Am J Opthalmol 16:80–95, 1939.
63. Cole MG, Miller HF: Sleep deprivation in the treatment of elderly depressed patients. J Am Geriatr Soc 243:308–313, 1976.
64. Collins WE: Some effects of sleep loss on vestibular responses. Aviat Space Environ Med 59:523–529, 1988.
65. Cooperman NR, Mullin FJ, Kleitman N: Studies on the physiology of sleep. XI. Further observations on the effects of prolonged sleeplessness. Am J Physiol 107:589–593, 1934.
66. Copes K, Rosentswieg J: The effects of sleep deprivation upon motor performance of ninth-grade students. J Sports Med Phys Fitness 12:47–53, 1972.
67. Corcoran DWJ: Changes in heart rate and performance as a result of loss of sleep. Br J Psychol 55:307–315, 1964.
68. Cortes-Gallegos V, Castaneda G, Alonso R, et al: Sleep deprivation reduces circulating androgens in healthy men. Arch Androl 10:33–37, 1983.
69. Cutler NR, Cohen HB: The effect of one night's sleep loss on mood and memory in normal subjects. Compr Psychiatry 20:61–66, 1979.
70. Davies B, Shapiro CM, Daggett A, et al: Physiological changes and sleep responses during and following a world record continuous walking record. Br J Sports Med 18:173–180, 1984.
71. Declerck AC, Martens WL, Wauquier A: Evaluation of the effects of antiepileptic drugs on sleep-wakefulness patterns following 1 night total sleep deprivation in epileptic patients. Neuropsychobiology 13:201–205, 1985.
72. Degen R: The diagnostic significance of sleep after sleep deprivation under antiepileptic-therapy. Nervenarzt 48:314–320, 1977.
73. Degen R, Degen HE: A comparative study of the diagnostic value of drug-induced sleep EEGs and sleep EEGs following sleep deprivation in patients with complex partial seizure. J Neurol 225:85–93, 1981.
74. Degen R, Degen HE: The diagnostic value of sleep. EEG with and without sleep deprivation in patients with atypicalabsende. Epilepsia 24:557–566, 1983.
75. Degen R, Degen HE, Reker M: Sleep EEG with or without sleep deprivation? Does sleep deprivation activate more epileptic activity in patients suffering from different type of epilepsy? Eur Neurol 26:51–59, 1987.
76. Degen R, Niedermeyer R (eds): Epilepsy, Sleep, and Sleep Deprivation. Amsterdam, Elsevier, 1984.
77. Dement W: The effect of dream deprivation. Science 131:1705–1707, 1960.
78. Dement WC: Sleep deprivation and the organization of the behavioral states. In Clemente CD, et al (eds): Sleep and the Maturing Nervous System. New York, Academic Press, 1972, pp 319–355.
79. Dement WC: Commentary to "The biological role of REM sleep (circa 1968"). In Webb WB (ed): Sleep: An Active Process. Glenview, IL, Scott, Foresman, 1973, pp 48–58.
80. Dement WC: The relevance of sleep pathologies to the function of sleep. In Drucker-Colin R, et al (eds): The Functions of Sleep. New York: Academic Press, 1979, pp 273–293.
81. Dessauer M, Goetze U, Tolle R: Periodic sleep deprivation in drug-refractory depression. Neuropsychology 13:111–116, 1985.
82. Dowd PJ: Sleep deprivation effects on the vestibular habituation process. J Apply Psychol 59:748–752, 1974.
83. Drucker-Colin RR: Sleep deprivation: Effects on the EEG and on the blood of anticoagulant treated rats. Unpublished Doctoral Dissertation, University of Saskatchewan, 1971.
84. Drucker-Colin RR, Jaques LB, Winocur G: Anemia in sleep-deprived rats receiving anticoagulant. Science 174:505–507, 1971.
85. Duncan WC Jr, Gillin JC, Post RM, et al: Relationship between EEG sleep patterns and clinical improvement in depressed patients treated with sleep deprivation. Biol Psychiatry 15:879–889, 1980.
86. Edwards AS: Effects of the loss of one hundred hours of sleep. Am J Psychol 54:80–91, 1941.
87. Ellingson RJ, Wilken K, Bennett DR: Efficacy of sleep deprivation as an activation procedure in epilepsy patients. J Clin Neurophysiol 1:83–101, 1984.
88. Ellman SJ, Spielman AJ, Luck D, et al: REM deprivation: A review. In Arkin AM, et al (eds): The Mind in Sleep: Psychology and Psychophysiology. Hillsdale, NJ, Lawrence Erlbaum, 1978, pp 419–457.
89. Elsenga S, van den Hoofdakker RH: Clinical effects of several sleep/wake manipulations on endogenous depression. Sleep Res 12:326, 1983.

90. Elsenga S, Zulley J: Rectal temperature and depression during total sleep deprivation. Sleep Res 15:520, 1987.
91. Everson CA, Kushida CA, Bergmann BM, et al: Recovery from chronic sleep deprivation in the rat. Sleep Res 16:521, 1986.
92. Fahndrich E: Effects of sleep deprivation on depressed patients of different nosological groups. Psychiatry Res 5:277–285, 1981.
93. Fahndrich E: Effect of sleep deprivation as a predictor of treatment response to antidepressant medication. Acta Psychiatr Scand 68:341–344, 1983.
94. Fenz WD, Craig JG: Autonomic arousal and performance during sixty hours of sleep deprivation. Percept Mot Skills 34:543–553, 1972.
95. Fiorica V, Higgins EA, Iampietro PF, et al: Physiological responses of men during sleep deprivation. J Appl Physiol 24:167–176, 1968.
96. Fort A, Mills JM: Influence of sleep, lack of sleep, and circadian rhythms on short psychometric test. In Colquhoun WP (ed): Aspects of Human Efficiency. London, English Universities Press, 1972, pp 115–127.
97. Fortune RF: Sleep and muscular work. Aust J Psychol 4:36–40, 1926.
98. Frank G, Halberg F, Harner R, et al: Circadian periodicity, adrenal corticosteroids, and the EEG of normal man. J Psychiatr Res 4:73–86, 1966.
99. Friedman RC, Kornfeld DS, Bigger TJ: Psychological problems associated with sleep deprivation in interns. J Med Ed 48:436–441, 1973.
100. Friedmann J, Globus GG, Huntley A, et al: Performance and mood during and after gradual sleep reduction. Psychophysiology 14:245–250, 1977.
101. Froberg JE: Psychophysiological circadian rhythms: A literature review. WHO Tech Rep Ser 9:6, 1975.
102. Froberg JE: Twenty-four-hour patterns in human performance, subjective and physiological variables and differences between morning and evening active subjects. Biol Psychol 5:119–134, 1977.
103. Froberg J, Karlsson C-G, Levi L, Lidberg L: Circadian variations in performance, psychological ratings, catecholamine excretion, and diuresis during prolonged sleep deprivation. Int J Psychobiol 2:23–36, 1972.
104. Geller MR, Gourdji N, Christoff N, Fox E: The effects of sleep deprivation on the EEGs of epileptic children. Dev Med Child Neurol 11:771–776, 1969.
105. Gerner RH, Post RM, Gillin C, Bunney W Jr: Biological and behavioral effects of one night's sleep deprivation in depressed patients and normals. J Psychiatr Res 15:21–40, 1979.
106. Gillberg M, Akerstedt T: Sleep deprivation in normals: Some psychological and biochemical data from three studies. In Koella WP (ed): Sleep. Basel, Karger, 1980, pp 16–22.
107. Glaubman H, Orbach I: How healthy is "healthy insomnia"? Waking and Sleeping 1:395–399, 1977.
108. Hamilton P, Wilkinson RT, Edwards RS: A study of four days partial sleep deprivation. In Colquhoun WP (ed): Aspects of Human Efficiency. London, English Universities Press, 1972, pp 101–113.
109. Handbook of Human Engineering Data. Medford, MA, Tufts College, 1952.
110. Harris W, O'Hanlon JF: A study of recovery function in man. Technical Memorandum No. 10-72. U.S. Army Human Engineering Laboratories, MD, Aberdeen Proving Ground, April, 1972.
111. Haslam DR, Abraham P: Sleep loss and military performance. In Belenky G (ed): Contemporary Studies in Combat Psychiatry. Contributions in Military Studies Number 62, Westport, CT, Greenwood Press, 1987.
112. Hasselman M, Schaff G, Metz B: Respective influences of work, ambient temperature and sleep deprivation on urinary excretion of catecholamines of normal man. C R Soc Biol (Paris) 154:197–201, 1960.
113. Hendrick C, Lilly RS: The structure of mood: A comparison between sleep deprivation and normal wakefulness conditions. J Pers 38:453–465, 1970.
114. Hoddes E, Zarcone V, Smythe H, et al: Quantification of sleepiness: A new approach. Psychophysiology 10:431–436, 1973.
115. Holmboe J, Bell H, Norman N: Urinary excretion of catecholamines and steroids in military cadets exposed to prolonged stress. Swed J Def Med 11:183–191, 1975.
116. Horne JA: A review of the biological effects of total sleep deprivation in man. Biol Psychol 7:55–102, 1979.
117. Horne JA: Restitution and human sleep: A critical review. Physiol Psychol 7:115–125, 1979.
118. Horne JA: Why we sleep: The functions of sleep in humans and other mammals. Oxford, Oxford University Press, 1988.

119. Hoyt MF, Singer JL: Psychological effects of REM ("Dream") deprivation upon waking mentation. In Arkin AM, et al (eds): The Mind in Sleep: Psychology and Psychophysiology. Hillsdale, NJ, Lawrence Erlbaum, 1978, pp 487–510.
120. Husband RW: The comparative value of continuous versus interrupted sleep. J Exp Psychol 18:792–796, 1935.
121. Jimerson DC, Lynch HJ, Post RM, et al: Urinary melationin rhythms during sleep deprivation in depressed patients and normals. Life Sci 20:1501–1508, 1977.
122. Joffe R, Brown P: Clinical and biological correlates of sleep deprivation in depression. Can J Psychiatry 29:530–536, 1984.
123. Joffe R, Brown P, Bienenstock A, Mitton J: Neuroendocrine predictors of the antidepressant effect of partial sleep deprivation. Biol Psychiatry 19:347–352, 1984.
124. John MW: Factor analysis of subjectively reported sleep habit, and the nature of insomnia. Psychol Med 5:83–88, 1975.
125. Johnson LC, MacLeod WL: Sleep and awake behavior during gradual sleep reduction. Percept Mot Skills 36:87–97, 1973.
126. Johnson LC, Naitoh P, Lubin A, Moses J: Sleep stages and performance. In Colquhoun WP (ed): Aspects of Human Efficiency. London, English Universities Press, 1972, pp 81–100.
127. Johnson LC, Slye ES, Dement W: Electroencephalographic and atuonomic activity after prolonged sleep deprivation. Psychosom Med 27:415–423, 1965.
128. Jones HS, Oswald I: Two cases of healthy insomnia. Electroencephalogr Clin Neurophysiol 24:378–380, 1968.
129. Jovanovic UJ, Liebaldt GP, Muhl M, et al: Sleep deprivation and its symptoms. Arch Psychiatr Nervenkr 214:183–202, 1971.
130. Kales A, Tan T-L, Kollar EJ, et al: Sleep patterns following 205 hours of sleep deprivation. Psychosom Med 32:189–200, 1970.
131. Kamiya J: Behavioral, subjective and physiological aspects of drowsiness and sleep. In Fiske DW, Maddi SP (eds): Functions of Varied Experience. Homewood, IL, Dorsey, 1961, pp 145–174.
132. Kant GJ, Genser SG, Throne DR, et al: Effects of 72 hour sleep deprivation on urinary cortisol and indices of metabolism. Sleep 7:142–146, 1984.
133. Katz SE, Landis C: Psychological and physiologic phenomena during a prolonged vigil. Arch Neurol Psychiatry 34:307–316, 1935.
134. King D: Pathological and therapeutic consequences of sleep loss: A review. Dis Nerv Sys 38:873–879, 1977.
135. King D: Sleep deprivation therapy in depression syndromes. Psychosomatics 21:404–407, 1980.
136. King D, Dowdy S, Jack R, et al: The dexamethasone suppression test as a predictor of sleep deprivation antidepressant effect. Psychiatr Res 7:93–99, 1982.
137. Klein KE, Wegmann HM, Bruner H: Circadian rhythm in indices of human performance, physical fitness and stress reistance. Aerospace Med 39:512–518, 1968.
138. Kleitman N: Sleep and Wakefulness, 2nd ed. Chicago, University of Chicago Press, 1963.
139. Knowles J, Southmayd S, Delva N, et al: Sleep deprivation: Outcome of controlled single case studies of depressed patients. Can J Psychiatry 26:330–333, 1981.
140. Kolka MA, Stephenson LA: Exercise thermoregulation after prolonged wakefulness. J Appl Physiol 64:1575–1579, 1988.
141. Kollar EJ, Namerow N, Pasnau RO, Naitoh P: Neurological findings during prolonged sleep deprivation. Neurology 18:836–840, 1968.
142. Kollar EJ, Pasnau RO, Rubin RT, et al: Psychological, psychophysiological and biochemical correlates of prolonged sleep deprivation. Am J Psychiatry 126:488–497, 1969.
143. Kollar EJ, Slater GR, Palmer JO, et al: Stress in subjects undergoing sleep deprivation. Psychosom Med 28:101–113, 1966.
144. Koranyi EK, Lehmann HE: Experimental sleep deprivation in schizophrenic patients. Arch Gen Psychiatry 2:534–544, 1960.
145. Kripke DF, Simons RN, Garfinkel L, Hammond EC: Short and long sleep and sleeping pills. Is increased mortality associated? Arch Gen Psychiatry 36:103–116, 1979.
146. Kuhn E, Brodan V: Changes in the circadian rhythm of serum iron induced by a 5-day sleep deprivation. Eur J Appl Physiol 49:215–222, 1982.
147. Kuhn E, Brodan V, Brodanova M, Friedman B: Influence of sleep deprivation on iron metabolism. Science 213:1041–1042, 1967.
148. Kuhn E, Brodan V, Brodanova M, Rysanek K: Metabolic reflection on sleep deprivation. Act Nerv Super (Praha) 11:165–174, 1969.
149. Kuhn E, Brodan V, Valek J: Changes in the white blood cell count due to deprivation of sleep. Cas Lek Cesk 106:513–514, 1967.

150. Kuhn E, Rysanek K, Brodan V, Spankova H: Changes in blood tryptophan level during sleep deprivation. Experientia 32:1117, 1976.
151. Kuhn E, Rysanek K, Spankova H, et al: Changes in cyclic AMP and dopamine-beta-hydroxylase during sleep deprivation. Act Nerv Super (Praha) 17:257-259, 1975.
152. Kushida C, Bergmann B, Everson C, et al: Paradoxical sleep deprivation in the rat. I. Physiological effects. Sleep Res 13:191, 1984.
153. Kushida C, Bergmann B, Fang VS, et al: Physiological and biochemical effects of paradoxical sleep deprivation in the rat. Sleep Res 15:219, 1986.
154. Larsen JK, Lindberg ML, Skovaard B: Sleep deprivation as treatment for endogenous depression. Acta Psychiatr Scand 54:167-173, 1976.
155. Lebedun A, Bootzin RR: Differential effects of sleep deprivation on the recovery sleep of insomniacs and good sleepers. Sleep Res 15:142, 1986.
156. Legg SJ, Haslam DR: Effect of sleep deprivation on self-selected workload. Ergonomics 27:389-396, 1984.
157. Legg SJ, Patton JF: Effects of sustained manual work and partial sleep deprivation on muscular strength and endurance. Eur J Appl Physiol 56:64-68, 1987.
158. Levi L: Emotional stress and biochemical reactions as modified by psychotrophic drugs with particular reference to cardiovascular pathology. Proceedings of an International Symposium on Psychotropic Drugs in Internal Medicine. Excerpta Medica International Congress Series, No. 182, pp 206-220, 1968.
159. Levi L: Psychological and physiological reaction to and psychomotor performance during prolonged and complex stressor exposure. In Levi L (ed): Stress and Distress in Response to Psychosocial Stimuli. Oxford, Pergamon, 1972, pp 119-139.
160. Lewin I, Glaubman H: The effect of REM deprivation: Is it detrimental, beneficial, or neutral? Psychophysiology 12:349-353, 1975.
161. Lindemann R, Ekanger R, Opstad PK, et al: Hematological changes in normal men during prolonged severe exercise. Am Correct Ther J 37:107-111, 1978.
162. Lisper H-O, Kjellberg A: Effects of 24-hour sleep deprivation in rate of decrement in a 10-minute auditory reaction time task. J Exp Psychol 96:287-290, 1972.
163. Livrea P, di Reda L, Puca FM, et al: Homovanillic acid and 5-hydroxyindoleacetic acids in lumbar cerebrospinal fluid after total and REM sleep deprivation in humans. Eur Neurol 16:280-285, 1977.
164. Loveland NT, Williams HL: Adding, sleep loss, and body temperature. Percept Mot Skills 16:923-929, 1963.
165. Lovett-Doust JW, Christie H: Repeated sleep deprivation as a therapeutic zeitgeber for circular type manic depressive disturbance. Chronobiologia 7:505-511, 1980.
166. Luby ED, Frohman CE, Grisell JL, et al: Sleep deprivation: Effects on behavior, thinking, motor performance, and biological energy transfer systems. Psychosom Med 22:182-192, 1960.
167. Luby ED, Gottlieb JS: Sleep deprivation. In Arieti S (ed): American Handbook of Psychiatry, Vol. 3. New York, Basic Books, 1966, pp 406-419.
168. Luby ED, Grisell JL, Frohman CE, et al: Biochemical, psychological, and behavioral responses to sleep deprivation. Ann NY Acad Sci 96:71-79, 1962.
169. Lund PM: Marathon volleyball: Changes after 61 hours play. Br J Sports Med 19:228-229, 1985.
170. Malmo RB, Surwillo WW: Sleep deprivation changes in performances and physiological indicants of activation. Psychol Monogr 74(15), Whole No. 502, 1960.
171. Mangold R, Sokoloff L, Conner E, et al: The effects of sleep and lack of sleep on the cerebral circulation and metabolism of normal young men. J Clin Invest 34:1092-1100, 1955.
172. Martin BJ: Effect of sleep deprivation on tolerance of prolonged exercise. Eur J Appl Physiol 47:345-354, 1981.
173. Martin BJ: Sleep deprivation and exercise. Exerc Sport Sci Rev 14:213-229, 1986.
174. Martin BJ, Bender PR, Chen H: Stress hormonal response to exercise after sleep loss. Eur J Appl Physiol 55:210-214, 1986.
175. Martin BJ, Chen HI: Sleep loss and the sympathoadrenal response to exercise. Med Sci Sports Exerc 16:56-59, 1984.
176. Martin BJ, Haney R: Self-selected exercise intensity is unchanged by sleep loss. Eur J Appl Physiol 49:79-86, 1982.
177. Mattson RH, Pratt KL, Calverley JR: Electroencephalograms of epileptics following sleep deprivation. Arch Neurol 13:310-315, 1965.
178. Matussek N, Ackenheil M, Athen D, et al: Catecholamine metabolism under sleep deprivation therapy of improved and not improved depressed patients. Pharmakopsychiatrie 7:108-114, 1974.

179. McMurray RG, Brown CF: The effect of sleep loss on high intensity exercise and recovery. Aviat Space Environ Med 55:1031-1035, 1984.
180. Meddis R: The Sleep Instinct. London, Routledge and Kegan Paul, 1977.
181. Meddis R, Pearson AJS, Langford G: An extreme case of healthy insomnia. Electroencephalogr Clin Neurophysiol 35:213-214, 1973.
182. Miles WR, Laslett HR: Eye movement and visual fixation during profound sleepiness. Psychol Rev 38:1-13, 1931.
183. Mirsky AF, Cardon P: A comparison of the behavioral and physiological changes accompanying sleep deprivation and chlorpromazine administration in man. Electroencephalogr Clin Neurophysiol 14:1-10, 1962.
184. Molaie M, Cruz A: The effect of sleep deprivation on the rate of focal interictal epileptiform discharges. Electroencephalogr Clin Neurophysiol 70:288-292, 1988.
185. Moldofsky H, Davidson JR, Lue FA: Sleep-related patterns of plasma growth hormone and cortisol following 40 hours of wakefulness. Sleep Res 17:69, 1988.
186. Moldofsky H, Lue FA, Davidson JR, Gorczynski R: The effect of 40 hours of wakefulness on immune functions in humans. II. Interleukins-1 & -2-like activities. Sleep Res 17:34, 1988.
187. Moldofsky H, Lue FA, Saskin P, et al: The effect of sleep deprivation on immune functions in humans. I. Mitogen and natural killer cell activities. Sleep Res 16:531, 1987.
188. Morgan BB Jr: Effects of continuous work and sleep loss in the reduction and recovery of work efficiency. Am Ind Hyg Assoc J 35:13-20, 1974.
189. Morris GO, Williams HL, Lubin A: Misperception and disorientation during sleep deprivation. Arch Gen Psychiatry 2:247-254, 1960.
190. Murawski BJ, Grabbe J: Effect of sleep deprivation on plasma 17-hydroxycortocoids. J Appl Physiol 15:280-282, 1960.
191. Murray EJ: Conflict and repression during sleep deprivation. J Abnorm Soc Psychol 59:95-101, 1959.
192. Murray EJ: Sleep, Dreams, and Arousal. New York, Appleton-Century-Crofts, 1965.
193. Murray EJ: Sleep deprivation and personality adjustment. In Abt LE, Riess BF (eds): Progress in Clinical Psychology, Vol. 8. New York, Grune and Stratton, 1968, pp 44-[illegible]
194. Murray EJ, Schein EH, Erikson KJ, et al: The effects of sleep on social behavior. J Soc Psychol 49:229-236, 1959.
195. Murray EJ, Williams HL, Lubin A: Body temperature and psychological ratings during sleep deprivation. J Exp Psychol 56:271-273, 1958.
196. Myles WS: Sleep deprivation, physical fatigue and the perception of exercise intensity. Med Sci Sports Exerc 17:580-584, 1985.
197. Naitoh P: Sleep deprivation in humans. In Venables PE, Christie MJ (eds): Research Psychophysiology. New York, John Wiley, 1975, pp 153-180.
198. Naitoh P: Sleep deprivation in human subjects: A reappraisal. Waking and Sleeping 1:53-60, 1976.
199. Naitoh P: Circadian cycles and restorative powers of naps. In Johnson LC, Tepas DI, Colquhoun WP, Colligan MJ (eds): Biological Rhythms, Sleep and Shiftwork. Advances in Sleep Research, Vol. 7. New York, Spectrum, 1981, pp 553-580.
200. Naitoh P: Chronopsychological approach for optimizing human performance. In Brown FM, Graeber RC (eds): Rhythmic Aspects of Behavior. Hillsdale, NJ, Lawrence Erlbaum, 1982.
201. Naitoh P, Dement WC: Sleep deprivation in humans. In Remond A (ed-in-chief): Handbook of Electroencephalography and Clinical Neurophysiology, Vol. 7. Amsterdam, Elsevier, 1975, pp 7A46-7A51.
202. Naitoh P, Kales A, Kollar EJ, et al: Electroencephalographic changes after prolonged sleep loss. Electroencephalogr Clin Neurophysiol 27:2-11, 1969.
203. Naitoh P, Pasnau RO, Kollar EJ: Psychophysiological changes after prolonged deprivation of sleep. Biol Psychiatry 3:309-320, 1971.
204. Naitoh P, Townsend RE: The role of sleep deprivation research in human factors. Hum Factors 12:575-585, 1970.
205. Nakazawa Y, Kotorii M, Ohshima M, Haruzawa H: Changes in sleep pattern after sleep deprivation. Folia Psychiatr Neurol Jpn 32:85-93, 1978.
206. Nowlis V: Research with the mood adjective checklist. In Tomkins SS, Izard CE (eds): Affect, Cognition and Personality. New York, Springer, 1965, pp 352-389.
207. Oektedalen O, Flaten O, Opstad PK, Myren J: hPP and gastrin response to a liquid meal and oral glucose during prolonged severe exercise, caloric deficit, and sleep deprivation. Scand J Gastroenterol 17:619-624, 1982.

208. Oektedalen O, Opstad PK, Fahrenkrug J, Fonnum F: Plasma concentration of vasoactive intestinal polypeptide during prolonged physical exercise, calorie supply deficiency, and sleep deprivation. Scand J Gastroenterol 18:1957-1062, 1983.
209. Opstad PK, Aakvaag A: The effect of a high calorie diet on hormonal changes in young men during prolonged physical strain and sleep deprivation. Eur J Appl Physiol 46:31-39, 1981.
210. Opstad PK, Aakvaag A: Decreased serum levels of oestradiol, testosterone and prolactin during prolonged physical strain and sleep deprivation and the influence of high calorie diet. Eur J Appl Physiol 49:343-348, 1982.
211. Opstad PK, Aakvaag A: The effect of sleep deprivation on the plasma levels of hormones during prolonged physical strain and calorie deficiency. Eur J Appl Physiol 51:97-107, 1983.
212. Opstad PK, Aakvaag A, Rognum TO: Altered hormonal response to short-term bicycle exercise in young men after prolonged physical strain, caloric deficit, and sleep deprivation. Eur J Appl Physiol 45:51-62, 1980.
213. Opstad PK, Ekanger R, Nummestad M, Raabe N: Performance, mood and clinical symptoms in men exposed to prolonged, severe physical work and sleep deprivation. Aviat Space Environ Med 49:1065-1073, 1978.
214. Opstad PK, Falch D, Oektedalen O, et al: The thyroid function in young men during prolonged exercise and the effect of energy and sleep deprivation. Clin Endocrinol 20:657-669, 1984.
215. Opstad PK, Oektedalen O, Aakvaag A, et al: Plasma renin activity and serum aldosterone during prolonged physical strain: The significance of sleep and energy deprivation. Eur J Appl Physiol 54:1-6, 1985.
216. Orlee HD, Corbin B, Dugger G, Smith C: An evaluation of the effects of bed rest, sleep deprivation and discontinuing of training on the physical fitness of highly trained young men. NASA-CR-134044.N73-32008. Washington, D.C., NASA, 1973.
217. Oswald I: Human brain protein, drugs and dreams. Nature 223:893-897, 1969.
218. Pai MN: Searchlight on sleep disorders. London, Literary Services and Production, 1969.
219. Palmblad JEW: Stress-related modulation of immunity: A review of human studies. Cancer Detect Prev 1(suppl):57-64, 1987.
220. Palmblad J, Akerstedt T, Froberg J, et al: Thyroid and adrenomedullary reaction during sleep deprivation. Acta Endocrinol (Copenh) 90:233-239, 1979.
221. Palmblad J, Cantell K, Strander H, et al: Stressor exposure and immunological response in man: Interferon producing capacity and phagocytosis. J Psychosom Res 20:193-199, 1976.
222. Palmblad J, Petrini B, Wasserman J, Akerstedt T: Lymphocyte and granulocyte reactions during sleep deprivation. Psychosom Med 41:273-278, 1979.
223. Parker DC, Rossman LG, Pekary AE, Hershman JM: Effect of 64-hour sleep deprivation on the circadian waveform of thyrotropin (TSH): Further evidence of sleep-related inhibition of TSH release. J Clin Endocrinol Metab 64:157-161, 1987.
224. Pasnau RO, Naitoh P, Stier S, Kollar EJ: The psychological effects of 205 hours of sleep deprivation. Arch Gen Psychiatry 18:496-505, 1968.
225. Patrick GTW, Gilbert JA: on the effects of loss of sleep. Psychol Rev 3:469-483, 1986.
226. Paul A: Effects of sleep deprivation on visual function. Aerospace Med 36:617-620, 1965.
227. Pearson RG, Byars GE: The development of validation of a checklist for measuring subjective fatigue. Report No. 56-115. San Antonio, U.S. Air Force School of Aerospace Medicine, 1956.
228. Pflug B: Therapeutic aspects of sleep deprivation. In Koella WP, Levin P (eds): Sleep. Basel, Karger, 1973, pp 185-191.
229. Pflug B, Tolle R: Disturbance of the 24-hour rhythm in endogenous depression and the treatment of endogenous depression by sleep deprivation. Int Pharmacopsychiatry 6:187-196, 1971.
230. Phillips B, Cooper KR, Newsome HH, Dewey WL: Effect of sleep loss on beta-endorphin activity, epinephrine levels, and ventilatory responsiveness. South Med J 80:16-20, 1987.
231. Pickett G, Morris A: Effects of acute sleep and food deprivation on total body response time and cardiovascular performance. J Sports Med Phys Fitness 15:49-56, 1975.
232. Pieron G: The Physiological Problem of Sleep. Paris, Masson, 1913.
233. Plyley MJ, Shephard RJ, Davis GM, Goode RC: Sleep deprivation and cardiorespiratory function: Influence of intermittent submaximal exercise. Eur J Appl Physiol 56:338-344, 1987.
234. Poley GE, Shively CA, Vesell ES: Diurnal rhythms of aminopyrine metabolism: Failure of sleep deprivation to affect them. Clin Pharmacol Ther 24:726-732, 1978.
235. Post RM, Kotin J, Goodwin FK: Effects of sleep deprivation on mood and central amine metabolism in depressed patients. Arch Gen Psychiatry 33:627-632, 1976.

236. Pratt KL, Mattson RH, Weikers NJ, Williams R: EEG activation of epileptics following sleep deprivation: A prospective study of 114 cases. Electroencephalogr Clin Neurophysiol 24:11-15, 1967.
237. Rakestraw NW, Whittier FO: The effect of loss of sleep on the composition of the blood and urine. Proc Soc Exp Biol Med 21:5-6, 1923.
238. Rechtschaffen A: The control of sleep. In Hunt WA (ed): Human Behavior and Its Control. Cambridge, MA, Schenkman, 1971, pp 75-92.
239. Rechtschaffen A, Bergmann BM, Everson CA, et al: Sleep deprivation in the rat. X. Integration and discussion of the findings. Sleep 12:68-87, 1989.
240. Rechtshaffen A, Gilliland MA, Bergmann BM, Winter JB: Physiological correlates of prolonged sleep deprivation in rats. Science 221:182-184, 1983.
241. Rechtschaffen A, Kales A: A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Public Health Service, National Institutes of Health publication no. 204, 1968.
242. Remes K, Kuoppasalmi K, Adlercreutz H: Effect of physical exercise and sleep deprivation on plasma androgen levels: Modifying effect of physical fitness. Int J Sports Med 6:131-135, 1985.
243. Reynolds CF III, Kupfer DJ, Hoch CC, et al: Sleep deprivation effects in older endogenous depressed patients. Psychiatr Res 21:95-109, 1987.
244. Richardson GS, Carskadon MA, Flagg W, et al: Excessive daytime sleepiness in man: Multiple sleep latency measurement in narcoleptic and control subjects. Electroencephalogr Clin Neurophysiol 45:621-627, 1978.
245. Ringer C: Psychological and physiological parameters of circadian periodicity in sleep deprivation. Medical dissertation, Ludwig Maximillians-Universitat zu Munchen, 1972.
246. Robinson ES, Herman SO: Effects of loss of sleep. I. J Exp Psychol 5:19-32, 1922.
247. Robinson ES, Richardson-Robinson F: Effects of loss of sleep. II. J Exp Psychol 5:93-100, 1922.
248. Rodin EA, Luby ED, Gottlieb JS: The electroencephalogram during prolonged experimental sleep deprivation. Electroencephalogr Clin Neurophysiol 14:544-551, 1962.
249. Rognum TO, Rodahl K, Opstad PK: Regional differences in the lipolytic response of the subcutaneous fat deposits to prolonged exercise and severe energy deficiency. Eur J Appl Physiol 4:401-408, 1982.
250. Rognum TO, Vaage O, Hostmark A, Opstad PK: Metabolic responses to bicycle exercise after several days of physical work and energy deficiency. Scand J Lab Invest 41:565-571, 1981.
251. Rognum TO, Vartdal F, Rodahl K, et al: Physical and mental performance of soldiers on high- and low-energy diets during prolonged heavy exercise combined with sleep deprivation. Ergonomics 29:859-867, 1986.
252. Rubin RT, Kollar E, Slater GG, Clark BR: Excretion of 17-hydroxycorticosteroids an vanillylmandelic acid during 205 hours of sleep deprivation in man. Psychosom Med 31:68-79, 1969.
253. Rudolf GA, Tolle R: Circadian rhythm of circulatory function in depressives and on sleep deprivation. Int Pharmacopsychiatry 12:174-183, 1977.
254. Rudolf GA, Tolle R: Sleep deprivation and circadian rhythm in depression. Psychiatr Clin (Basel) 11:198-212, 1978.
255. Rutenfranz J, Aschoff J, Mann H: The effects of a cumulative sleep deficit, duration of preceding sleep period and body-temperature on multiple choice reaction time task. In Colquhoun WP (ed): Aspects of Human Efficiency. London, English Universities Press, 1972, pp 217-229.
256. Safer DJ: The effect of LSD on sleep-deprived men. Psychopharmacology (Berlin) 17:414-424, 1970.
257. Safer DJ: the concomitant effects of mild sleep loss and an anticholinergic drug. Psychopharmacology (Berlin) 17:425-433, 1970.
258. Saito Y: Specification of variation patterns of physiological and performance measurements in sleep loss. J Hum Ergol (Tokyo) 1:207-216, 1972.
259. Salin-Pascual RJ, Ortega-Soto H, Huerto-Delgadillo L, et al: The effect of total sleep deprivation on plasma melatonin and cortisol in healthy human volunteers. Sleep 11:362-369, 1988.
260. Sawka MN, Gonzales RR, Pandolf KB: Effects of sleep deprivation on thermoregulation during exercise. Am J Physiol 246:R72-R77, 1984.
261. Schachter S: The interaction of cognitive and physiological determinants of emotional state. In Berkowitz L (ed): Advances in Experimental Social Psychology. New York, Academic Press, 1964, pp 49-80.

262. Schachter S, Singer JE: Cognitive, social and physiological determinants of emotional state. Psychol Rev 69:379–399, 1962.
263. Schiffman PL, Trontell MC, Mazar MF, Endelman NH: Sleep deprivation decreases ventilatory response to CO_2 but not load compensation. Chest 84:695–698, 1983.
264. Schilgen B, Tolle R: Partial sleep deprivation as therapy for depression. Arch Gen Psychiatry 37:267–271, 1980.
265. Schmocker M, Baumann P, Reyero F, Heinemann H: Sleep deprivation: A clinical, psychophysiological and biochemical study. Arch Psychiatr Nervenkr 221:111–122, 1975.
266. Scholander I: The effects of moderate sleep deprivation on the habituation of autonomic response elements. Acta Physiol Scand 51:325–342, 1961.
267. Schwarz JR, Zangemeister WH: The diagnostic value of the short sleep and other provocative methods following sleep deprivation. J Neurol 218:179–186, 1978.
268. Scollo-Lavizzari G, Pralle W, de la Cruz N: Activation effects of sleep deprivation and sleep in seizure patients. Eur Neurol 13:1–5, 1975.
269. Scollo-Lavizzari G, Scollo-Lavizzsari GR: Sleep, sleep deprivation, photosensitivity and epilepsy. Eur Neurol 11:1–21, 1974.
270. Scrimshaw NS, Habicht JP, Pellet P, et al: Effects of sleep deprivation and reversal of diurnal activity on protein metabolism of young men. Am J Clin Nutr 19:313–319, 1966.
271. Shapiro CM, Trinder J: Hormone release after sleep deprivation. J Physiol (Lond) 325:54P–55P, 1982.
272. Sleep deprivation and mental health. Editorial. JAMA 204:166, 1968.
273. Smith M: A contribution to the study of fatigue. Br J Psychol 8:327–350, 1916.
274. Soule RG, Goldman RF: Pacing of intermittent work during 31 hours. Med Sci Sports 5:128–131, 1973.
275. Southmayd SE, Cairns J, Brunet DG: Antidepressant response to sleep deprivation in relation to psychophysiologically defined wakefulness. Sleep Res 16:538, 1987.
276. Southmayd SE, Cairns J, Brunet D, Delva N: Spectral analysis of baseline sleep in depressed patients: Relation to outcome of sleep deprivation and the "S-deficiency hypothesis." Sleep Res 16:537, 1987.
277. Spadetta V: Deprivation of sleep in the electroencephalographic diagnosis of epilepsy. Acta Neurol (Napoli) 26:7–13, 1971.
278. Stack JA, Reynolds CF, Hoch CC, et al: Effects of sleep deprivation in the treatment of elderly endogenous depressives. Sleep Res 15:221, 1986.
279. Steinberg H, Guggenheim F, Baer L, Snyder F: Catecholamines and their metabolites in various states of "arousal." J Psychosom Res 13:103–108, 1969.
280. Strausbaugh LJ, Roessler R: Ego strength, skin conductance, sleep deprivation, and performance. Percept Mot Skills 31:671–677, 1970.
281. Stuss D, Broughton R: Extreme short sleep: Personality profiles and a case study of sleep requirement. Waking and Sleeping 2:101–105, 1978.
282. Svendsen K: Sleep deprivation therapy in depression. Acta Psychiatr Scand 54:184–192, 1976.
283. Symons JD, Vanhelder T, Myles WS: Physical performance and physiological responses following 60 hours of sleep deprivation. Med Sci Sports Exerc 20:374–380, 1988.
284. Takeuchi L, Davis GM, Plyley M, et al: Sleep deprivation, chronic exercise and muscular performance. Ergonomics 28:591–601, 1985.
285. Taub JM: Effects of habitual variations in napping on psychomotor performance, memory and subjective states. Int J Neurosci 9:97–112, 1979.
286. Taub JM, Berger RJ: Performance and mood following variations in the length and timing of sleep. Psychophysiology 10:559–570, 1973.
287. Teichner WH: Interaction of behavioral and physiological stress reactions. Psychol Rev 75:271–291, 1968.
288. Thayer RE: Measurement of activation through self-report. Psychol Rep 20:663–678, 1967.
289. Todor JI: Changes in depth perception during a non-stop walk of 302¼ miles. Percept Mot Skills 40:762, 1975.
290. Torsvall L, Akerstedt T: Extreme sleepiness: Quantification of EOG and spectral EEG parameters. Int J Neurosci 38:435–441, 1988.
291. Toru M, Shibuya H, Shimazono Y: Monoamine metabolism in rat brain after total sleep deprivation. In Weitzman ED (ed): Advances in Sleep Research, Vol. 2. New York, Spectrum, 1976, pp 116–130.
292. Tyler DB: The effect of amphetamine sulphate and some barbiturates on the fatigue produced by prolonged wakefulness. Am J Physiol 149:253–262, 1947.

293. Tyler DB: Psychological changes during experimental sleep deprivation. Dis Nerv Sys 16:293–299, 1955.
294. Tyler DB, Goodman J, Rothman T: The effect of experimental insomnia on the rate of potential changes in the brain. Am J Physiol 149:185–193, 1947.
295. Tyler DB, Marx W, Goodman T: Effect of prolonged wakefulness on the rate of urinary excretion of 17-ketosteroids. Proc Soc Exp Biol Med 62:38–40, 1946.
296. Van den Burg W, van den Hoofdakker RH: Total sleep deprivation on endogenous depression. Arch Gen Psychiatry 32:1121–1125, 1975.
297. Van Helder T, Symons JD, Radomski MW: Effects of sleep deprivation and exercise on glucose tolerance and insulin sensitivity. Submitted for publication.
298. Vein AM, Dallakyan IG, Levin YAI, Shakun KE: Physiological and psychological consequences of single sleep deprivation. Hum Physiol 8:392–396, 1983.
299. Vestergaard P, Bojer B, Kleist N: Prolactin response to sleep deprivation. In Schou M, Stromgren E (eds): Origin, Prevention and Treatment of Affective Disorders. London, Academic Press, 1979, pp 179–183.
300. Vidnes A, Opstad PK: Serum ferritin in young men during prolonged heavy physical exercise. Scand J Haematol 27:165–170, 1981.
301. Vogel GW: A review of REM sleep deprivation. Arch Gen Psychiatry 32:749–761, 1975.
302. Vogel GW: A motivational function of REM sleep. In Drucker-Colin R, et al (eds): The Functions of Sleep. New York, Academic Press, 1979, pp 233–250.
303. Vogel GW: Evidence for REM sleep deprivation as the mechanism of action of antidepressant drugs. Prog Neuro-Psychopharmacol Biol Psychiatry 7:343–349, 1983.
304. Vogel GW: REM sleep deprivation and depression. In Chase M, Weitzman ED (eds): Sleep Disorders: Basic and Clinical Research. New York: Spectrum, 1983, pp 393–400.
305. Vogel GW, Thompson F Jr, Thurmond A, Rivers B: The effect of REM deprivation on depression. Psychosomatics 14:104–107, 1973.
306. Vogel GW, Thurmond A, Gibbons P, et al: REM sleep reduction effects on depression syndromes. Arch Gen Psychiatry 32:765–777, 1975.
307. Vogel GW, Vogel F, McAbee RS, Thurmond AJ: Improvement of depression by REM sleep deprivation: New findings and a theory. Arch Gen Psychiatry 37:247–253, 1980.
308. Vojtechovsky M, Hort, V, Krus D, Simane Z, Brezinova V: The effect of centrophenoxine in sleep deprived subjects. Med Psicosom 13:1–12, 1968.
309. Vojtechovsky M, Hort V, Krus D, Skala J: Sleep deprivation in alcoholics. In Bertini M (ed): Psicofisiologia del sonno e del sogno. Milan, Editrice Vita e Pensiero, 1970, pp 232–240.
310. Vojtechovsky M, Hort V, Simane Z, et al: The influence of centrophenoxine (Lucidril) on the course of sleep deprivation in alcoholics. Act Nerv Super (Praha) 11:193–201, 1969.
311. Vondra K, Brodan V, Bass A, et al: Effects of sleep deprivation on the activity of selected metabolic enzymes in skeletal muscle. Eur J Appl Physiol 47:41–46, 1981.
312. Warren N, Clark B: Blocking in mental and motor tasks during a 65-hour vigil. J Exp Psychol 21:97–105, 1937.
313. Webb WB: Theories of sleep functions and some clinical implications. In Drucker-Colin R, et al (eds): The Functions of Sleep. New York, Academic Press, 1979, pp 19–35.
314. Webb WB, Agnew HW Jr: Sleep deprivation, age, and exhaustion time in the rat. Science 136:1122, 1962.
315. Webb WB, Agnew HW Jr: The effects of chronic limitation of sleep length. Psychophysiology 11:265–274, 1974.
316. Wehr TA, Rosenthal NE, Sack DA, Gillin JC: Antidepressant effects of sleep deprivation in bright and dim light. Acta Psychiatr Scand 72:161–165, 1985.
317. Wehr TA, Sack DA, Rosenthal NE: Antidepressant effects of sleep deprivation and phototherapy. Acta Psychiatr Belg 85:593–602, 1985.
318. Welch LK, Stevens JB: Clinical value of the electroencephalogram following sleep deprivation. Aerospace Med 61:349–351, 1971.
319. West LJ, Janszen HH, Lester BK, Cornelison FS: The psychosis of sleep deprivation. Ann NY Acad Sci 96:66–70, 1962.
320. White DP, Douglas NJ, Pickett CK, et al: Sleep deprivation and the control of ventilation. Am Rev Respir Dis 128:984–986, 1983.
321. White RM: The lengths of sleep. Abstr. JSAS Catalog of Selected Documents in Psychology, MS No. 1001, 5:274, 1975.
322. Wilkinson RT: Interaction of lack of sleep with knowledge of results, repeated testing, and individual differences. J Exp Psychol 62:263–271, 1961.

323. Wilkinson RT: Effect of up to 60 hours of sleep deprivation on different types of work. Ergonomics 7:175–186, 1964.
324. Wilkinson RT: Sleep deprivation. In Edholm OG, Bachrach AL (eds): The Physiology of Human Survival. New York, Academic Press, 1965, pp 399–430.
325. Wilkinson RT: Sleep deprivation: Performance tests for partial and selective sleep deprivation. In Abt LA, Riess BF (eds): Progress in Clinical Psychology. New York, Grune and Stratton, 1968, pp 28–43.
326. Wilkinson RT, Edwards RS, Haines E: Performance following a night of reduced sleep. Psychosom Sci 5:471–472, 1966.
327. Williams HL, Lubin A, Goodnow JJ: Impaired performance with acute sleep loss. Psychol Monogr 73(#14):1–26 (Whole No. 484), 1959.
328. Wolfe JW, Brown JH: Effects of sleep deprivation on the vestibulo-ocular reflex. Aerospace Med 39:947–949, 1968.
329. Wu JC, Buchsbaum MS, Gillin JC: Positron emission tomography study of sleep deprivation. Sleep Res 16:543, 1987.
330. Wu JC, Gillin C, Buchsbaum MS, et al: Regional cortical metabolism after sleep deprivation. Sleep Res 17:32, 1988.
331. Wyatt RJ, Fram DH, Kupfer DJ, Snyder F: Total prolonged drug-induced REM sleep suppression in anxious-depressed patients. Arch Gen Psychiatry 24:145–155, 1971.
332. Yamaguchi N, Maeda K, Kuromaru S: The effects of sleep deprivation on the circadian rhythm of plasma cortisol levels in depressive patients. Folia Psychiatr Neurol Jpn 32:479–487, 1978.
333. Yamasaki S: The effects of prolonged severe physical activities with food and water restriction and sleep deprivation on the total body water and psychological-physiological performance. Jpn J Aerospace Environ Med 24:47–57, 1987.
334. Yeager JE, Crisman RP, Sucec AA: The effect of sleep deprivation and moderate intermittent exercise on maximal aerobic capacity. Naval Health Research Center Report No. 86-36. San Diego, Naval Health Research Center, 1986.
335. Young DR, Pelligra R, Shapira J, et al: Glucose oxidation and replacement during prolonged exercise in man. J Am Physiol 23:734–741, 1967.
336. Zander KJ, Lorenz A, Wahllander B, et al: Biogenesis of the antidepressive effect of sleep deprivation. In Koella WP (ed): Sleep 1980. Basel, Karger, 1981, pp 9–15.