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Sleep and Long-Term Health

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Overview

Sleep interacts with many biological processes in the body, affecting physical and mental health. Long-term sleep problems, such as short sleep duration and poor sleep quality, have been associated with a range of poor health outcomes, including impaired cognitive functioning and increased risk for mental health conditions, neurodegenerative diseases, obesity, type 2 diabetes, cardiovascular diseases, cancer, impaired immune functioning and chronic pain conditions.

For many long-term health outcomes, evidence for whether sleep causally contributes to health outcomes is not clear or firmly established. Some of this research is limited by the lack of high-quality and large-scale data on sleep duration, quality and timing. There is also a need for large, well-controlled intervention studies which test whether improving sleep leads to better long-term health outcomes. The mechanisms through which sleep affects health are also not well understood, but may include sleep's role in neural processing, inflammation, metabolism, gene regulation, clearance of toxins and hormonal regulation.

Future research is focused on developing and testing ways to prevent, diagnose and treat sleep problems. Other research is investigating sleep health in specific parts of the population (such as different age or minority ethnic groups) and whether treating sleep problems can improve long-term health outcomes.

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Background

Sleep is as important for survival as food and water.[1–3] It interacts with many other biological processes in the body, affecting performance and physical and mental health.[1,2] Long-term sleep problems may be common in up to a third of the UK population.[4] Night-time work can also disrupt sleep, with 12% of the UK workforce regularly working at night (see also POSTnote 585).[5–7] Sleep problems can also arise from sleep disorders (Box 1), other physical and mental health conditions, and social factors such as school schedules.[8] Productivity losses relating to sleep problems are estimated to cost the UK economy £30 billion annually.[9]

The biology of sleep

The duration, quality and timing are important dimensions of sleep which are regulated by two interacting biological processes:[10–12]

- **Circadian timing** – a process that generates 24-hour bodily rhythms in adaptation to Earth's light-dark cycle.[2] These determine periods of sleepiness and wakefulness and schedule other behavioural, physiological and metabolic processes.[2] Circadian clocks are present in almost every cell in the body, synchronising with each other through neural and hormonal signals.[2] They synchronise with the external environment primarily through light, which acts on the central clock in the brain.[2] Circadian timing is also affected by the timing of meals, physical activity and social cues (such as work schedules).[2]
- **Sleep-wake homeostasis** – a process which increases (or decreases) the pressure to sleep with the time spent awake (or asleep).[10,11] Its mechanism is not well understood.[10-12]

Common sleep and circadian disruptions (SCDs) include:

- **short sleep duration** (less than 6 hours in adults)[13–15]
- **poor sleep quality** (such as difficulties in initiating or maintaining sleep*)[13,16]
- **inappropriate timing in the 24-hour day** (tied to the disruption of circadian timing, occurring when the internal rhythm is misaligned with the external environment)[2,13]

Research suggests that long-term SCDs may be linked with a range of negative long-term health outcomes.[1,17] Although most research focuses on the above disruptions, long sleep duration (more than 9 hours in adults*) is also associated with negative health outcomes and napping is associated with both positive and negative outcomes.[1,18,19] However, these topics are less well understood (see later sections, Long sleep duration and Napping).[1,18,19] This POSTbrief provides an overview of the research evidence for each of the most widely studied areas of health, including cognitive function, mental health, neurodegenerative diseases, obesity, type 2 diabetes, cardiovascular diseases, cancer, immune function, and pain.

* This definition varies across studies

Box 1. Sleep-wake disorders[20]

Insomnia is a subjective disturbance in the initiation or maintenance of sleep, occurring at least three times per week and lasting for at least three months (chronic insomnia) or less than three months (acute insomnia), and which results in daytime impairment and cannot be better explained by another sleep disorder.[20,21] Acute insomnia is often caused by a stressor and may not require treatment.[21] The UK prevalence of a chronic insomnia diagnosis is around 6%, while around 40% of the population may have some insomnia symptoms.[22] Prevalence is higher with increasing age and in women.[23] The recommended first-line treatment is cognitive behavioural therapy for insomnia (CBT-I).[21,24] Sleeping tablets are only recommended if CBT-I is ineffective and then only for short-term use, as they carry a risk of tolerance, dependency and adverse effects (see also POSTnote 585).[21,24]

Sleep-related breathing disorders are defined by abnormal breathing during sleep.[20,23] Obstructive sleep apnoea (OSA), a common sleep disorder, is caused by a recurrent blockage or narrowing of the upper airway during sleep, leading to interrupted breathing, sleep disturbance and therefore daytime sleepiness (see also POSTnote 585).[20,25] Estimates suggest that moderate-to-severe OSA occurs in around 13% of men and 6% of women aged 30-70 years, with prevalence increasing with age and in those who are overweight.[25,26] OSA symptoms can be treated effectively by keeping the airway open during sleep.[25] Depending on severity, this can be done by applying continuous positive airway pressure via a face mask, wearing a dental device or losing weight.[25]

Sleep-related movement disorders are defined by repetitive movements that disrupt night-time sleep.[20,23] An example is restless legs syndrome, a neurological condition involving an urge to move the legs, often accompanied by uncomfortable sensations, which leads to sleep disturbances and daytime sleepiness.[27] Depending on the definition, prevalence ranges from 2–15% in the population, with rates higher in women and with increased age.[27] Treatment of mild symptoms can include education and self-help measures.[27] More severe cases may require the use of drugs.[27]

Hypersomnolence disorders are characterised by extended sleep duration and/or excessive daytime sleepiness.[20,23] One example is narcolepsy, a rare chronic neurological disorder.[28] It involves sudden transitions from wakefulness to sleep, disturbed night-time sleep, muscle paralysis upon waking and hallucinations when going to sleep or waking up.[29] It is often accompanied by cataplexy, a sudden loss of muscle tone triggered by strong emotions.[29] It is managed with drug therapy.[29]

Circadian rhythm sleep-wake disorders involve a disruption in the circadian rhythm (such as an advance or delay relative to the external environment), leading to sleep disturbances including an inability to sleep at night or sleepiness during the day.[30] This can be due to an impairment in the body's circadian timing system or a misalignment of the internal rhythm with the external environment (for example, due to night-time work).[30] Treatments include drugs, light therapy, and behavioural therapy.[31]

Parasomnia disorders, such as sleepwalking or nightmares often occur during the transitions between sleep stages.[32] They are more common in children, and unless disruptive or physically dangerous, often do not require treatment beyond patient education and ensuring a safe sleeping environment.[32] One exception is rapid eye movement (REM) sleep behaviour disorder, named so because it occurs during the REM stage of sleep (see also POSTnote 585).[32] It is more common in men over 50 and is characterised by the absence of normal muscle paralysis leading to the enactment of often violent dreams.[33] It is often managed with sleeping tablets.[33] It is associated with an increased risk of developing neurodegenerative diseases such as Parkinson's disease (see Neurodegenerative diseases).[33]

Sleep research methods

The highest quality research on sleep is conducted in specialist laboratory settings under controlled conditions and with specialised equipment; this limits the size of studies that can be undertaken.[1,34] These conditions also limit the studies' generalisability to real populations, as the laboratory is an artificial setting.[1,34] Large-scale sleep research – such as across a representative sample of a national population – is limited by the difficulty of collecting high-quality and detailed data on sleep duration, quality and timing.[1,35] Many studies have relied on self-reports of sleep duration, which are criticised for being limited in quality and for overlooking the importance of sleep timing and quality.[1,35,36] Research in children often relies on parental reports of their children's sleep, which may be inaccurate.[37] The methods used to assess self-reported sleep also vary, as does the definition of healthy sleep duration and quality, making comparisons and estimation of prevalence difficult.[1]

Some experts have also questioned the impact of sleep on health relative to other important lifestyle factors such as stress, diet, and levels of physical activity.[1,38] Some researchers emphasise that although sleep may be a useful early marker of health problems, it may not itself causally contribute to poor health.[1,39] There is a consensus amongst researchers that large, well-controlled intervention studies are needed that investigate whether improving sleep leads to better long-term health outcomes.[1,40,41]

Sleep and long-term health

Cognitive function

Chronic short sleep has been linked with impaired cognitive functioning in children, adolescents, adults and older adults.[1,40,42–44] However, the magnitude of these effects and which aspects of cognition are most impaired are not clear.[1,40,42,43,45] Irregular sleep-wake patterns have also been associated with poorer academic performance in children and adolescents.[46]

The brain mechanisms underlying these associations are poorly understood.[1,40] In children and adolescents, sleep may play a role in normal brain development.[46] Sleep is also thought to allow the neural processing of learned information and therefore may support memory.[46] In older adults, impaired cognition may be a consequence of neurodegeneration (see Neurodegenerative diseases).[47]

Mental health

Understanding how sleep and mental health are linked is an active area of research.[48,49] SCDs of all types are core features of almost all mental, behavioural and neurodevelopmental disorders across the lifespan; including depression, anxiety, schizophrenia, bipolar disorder, autism and attention deficit hyperactivity disorder (ADHD).[48–51] Studies of the UK population show

that SCDs are the most common expression of mental health issues, regardless of gender, age, location or ethnicity.[52,53] Furthermore, SCDs are associated with worse clinical outcomes in many mental health conditions.[54]

Ongoing research is focused on understanding whether SCDs may be early markers, causal risk factors or maintenance factors of these disorders.[51] For example, people with insomnia are twice as likely to develop depression than those without.[55] Studies have also found that insomnia is associated with increased risk of developing anxiety, bipolar disorder, and suicidal thoughts and behaviour.[56–59] Some research suggests that SCDs may predict increased symptom severity in schizophrenia in both the short and long term.[60–62] In children, some evidence suggests that SCDs are associated with impaired emotional regulation and behavioural problems, effects which can sometimes lead to a misdiagnosis of ADHD.[40] In adolescents, long-term short sleep duration is associated with poor mental health, substance abuse and suicidal thinking.[40]

Researchers have suggested that the link between sleep and mental health may be partially determined by genetics, as some mental disorders are associated with genes that relate to circadian timing, and genes that are linked with psychiatric traits overlap with those linked with insomnia.[63,64] SCDs are also associated with increased inflammation and stress reactivity, and impaired cognitive function and emotional regulation, all of which are implicated in mental health.[48,51]

Researchers are investigating whether treating SCDs can prevent the development of mental health conditions and whether it can improve sleep, symptoms, and quality of life in those with existing conditions.[51,54] In several studies, treating depressed patients with cognitive behavioural therapy for insomnia (CBT-I) not only improved sleep but also symptoms of depression.[54,65] Such effects on depression may depend on the severity of the disorder, as some studies focusing on those with major depressive disorder did not find any effects.[54,65] CBT-I may also help treat symptoms of anxiety, psychosis, bipolar disorder, and suicidal thinking.[54,66–70] More research is needed in order to understand these effects and to optimise treatments, including the delivery of CBT-I face-to-face and digitally (for example, via smartphones or computers).[54,69–71]

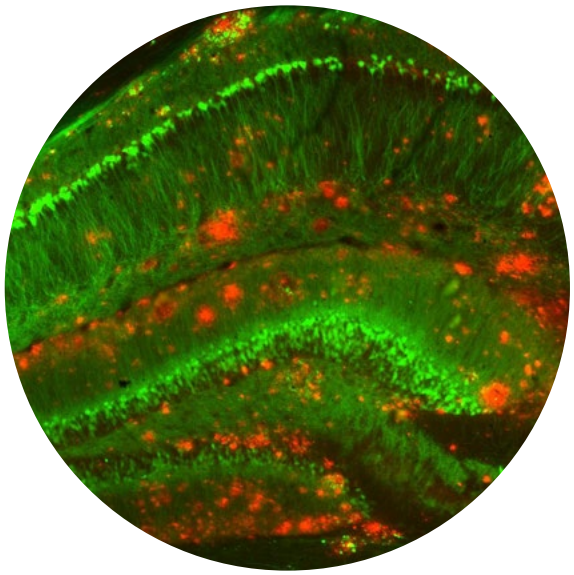
Neurodegenerative diseases

SCDs of all types are present in most neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's diseases, and in some cases may be one of the most frequent reasons that people move into care facilities.[47,49] In Alzheimer's and Parkinson's diseases, changes in brain tissue directly affect sleep and circadian timing physiology.[72] SCDs can occur much earlier than full disease onset and may act as early markers of neurodegeneration.[47] For example, REM-sleep behaviour disorder (Box 1), more common in older men, often precedes and predicts the onset of Parkinson's disease or other dementias in over 80% of cases, often by years.[73]

Researchers are investigating whether SCDs may also be potential contributory factors to neurodegeneration.[47,49] Across multiple studies, SCDs, such as short sleep duration and poor sleep quality, are associated with increased risk of developing Alzheimer's disease.[74] Potential explanations for this link include increased inflammation or metabolic stress, or disruption of the clearance of toxins in the brain.[47] For example, the toxic plaques (harmful proteins) that build up in the brain and that are a central feature of Alzheimer's disease (Figure 1) follow a circadian rhythm, accumulating during wakefulness and clearing during sleep.[47] In mice, chronic sleep deprivation increased the number of plaques, while sleep promotion decreased it.[75] Improving sleep is therefore a potential way to help prevent or slow the development of some neurodegenerative diseases.[47,49] In those who already have Alzheimer's disease or similar conditions, some studies show that using light to help regulate the circadian rhythm may improve sleep, mood and other functions.[76]

Figure 1. Mouse model of Alzheimer's disease:

In a mouse model of Alzheimer's disease, amyloid beta plaques (red) build up among neurons (green) in a memory-related area of the brain. Image credit: National Center for Advancing Translational Sciences, Strittmatter Laboratory, Yale University Photo/Adam Kaufman,



Obesity

In children and adolescents, long-term short sleep duration has been consistently associated with increased risk of obesity.[77,78] The few studies performed on sleep quality show similar effects.[79] In adults and older adults, evidence for this relationship is less clear, perhaps because other obesity risk factors emerge with age, masking any effects of sleep.[78,80–84]

Current understanding is that SCDs may lead to an imbalance between food intake and energy expenditure, leading to weight gain.[85] In lab studies, acute sleep deprivation for several nights leads to increased food intake and preference for high-caloric foods.[85] This may be related to changes in appetite-regulating hormone levels and in the brain's response to food.[86,87] The relationship between short sleep and energy expenditure is less clear, with evidence showing that acute sleep deprivation leads to no or only

slightly increased energy expenditure[85,86]. Although some studies have found moderate increases in body weight following acute sleep deprivation, others, conducted over several weeks, have not.[86] Two small-scale studies have found that improving sleep decreases weight gain in children.[88] More research is needed to determine the effectiveness and longevity of such interventions.[86]

Type 2 diabetes and cardiovascular diseases

In adults, chronic short sleep and poor sleep quality is associated with increased risk of type 2 diabetes, hypertension (high blood pressure), and cardiovascular diseases, including coronary heart disease and stroke.[41,83,89–94] In children and adolescents, some evidence suggests that short sleep also contributes to risk of type 2 diabetes, although obesity may be a mediating factor.[95] Evidence for effects on hypertension (high blood pressure) is less clear.[96]

Acute sleep deprivation in humans induces insulin resistance and glucose intolerance, activates the stress response, and increases cortisol and growth hormone levels and inflammation, among other changes.[80,85] Other experimental studies show that circadian disruption amplifies the effects of sleep deprivation on glucose metabolism.[97,98] These alterations could explain the links between poor sleep and type 2 diabetes, hypertension and cardiovascular diseases.[80] An indirect contribution could also arise through sleep-related changes in food intake and obesity (see Obesity).[85] Research is needed to establish whether improving sleep can decrease disease risk.[85]

Cancer

Poor sleep has also been linked with an increased risk of breast, ovarian, lung, prostate, and colorectal cancer, although this is controversial.[99] Much of the research has focused on shift workers who often experience both sleep and circadian rhythm disruption (see POSTnote 586).[100,101] Evidence of an association is mixed, with a lack of clarity about the role of other shift work-related factors such as diet and levels of physical activity.[100] Meta-analyses (which combine data from smaller studies for a more powerful analysis) of research in the general population have not found consistent associations between chronic short sleep and increased cancer risk.[99,102] Short sleep or circadian disruption may potentially increase cancer risk by exposing workers to light at night, which suppresses the normal release of the hormone melatonin, a known anti-carcinogen.[99,103] In mice and humans, sleep deprivation also disrupts the expression of circadian clock genes which have been linked to the cell cycle and to tumour development.[104] Obesity, a risk factor for breast cancer, may also mediate the link between sleep and cancer.[105]

Immune function

Sleep has been linked with immune function.[106] Individual studies have shown that experimental sleep deprivation in humans increases susceptibility to the common cold and is associated with a weaker immune response to the seasonal influenza vaccine.[107,108] One study has found that chronic short sleep

duration is associated with increased risk of pneumonia.[109] Many studies have investigated the link between sleep and levels of inflammatory markers (reflecting the immune system's inflammatory response), finding mixed evidence.[110–113] A review of this work has found evidence for the link between poor sleep quality and increased inflammatory markers, but no or only weak evidence for a link to short sleep duration.[114] Associations may depend on the type of inflammatory marker investigated, as well as gender and age.[115] The mechanisms underlying sleep's effects on the immune system are not well-understood but may be mediated by the body's stress system, with acute sleep deprivation in humans resulting in elevated levels of the hormone cortisol, a known immunosuppressant.[110] One experimental study has found that circadian disruption in humans also alters immune signalling.[116]

Pain

Although chronic pain disrupts sleep, emerging evidence suggests that poor sleep is itself associated with an increased risk of developing or maintaining a pain condition.[117,118] Studies show that day-to-day changes in sleep predict pain symptoms more strongly than vice versa.[117] A recent review found that decreases in sleep quality are associated with long-term development of pain-related conditions.[118] The link between sleep and pain may be explained by impaired immune function, including increases in inflammation, although this is not well understood.[118] According to a recent review, treating sleep problems with interventions such as CBT-I improves self-reported sleep quality, reduces fatigue in patients with pain and may also reduce pain symptoms.[119] More large and high-quality intervention studies are needed to understand if and how interventions work.[119]

Long sleep duration on health

Long sleep duration (often defined as more than nine hours in adults) has also been associated with increased risk of cognitive impairment, type 2 diabetes, and cardiovascular diseases, including coronary heart disease and stroke.[91,92,120,121] Possible explanations include underlying poor sleep quality, reductions in daylight exposure and depression.[122,123] Evidence for these explanations is limited, preventing conclusions about the causal role of long sleep duration in poor health.[1,80,122,123] Many interpret the associations as reflecting an underlying disease state causing both long sleep and negative health outcomes.[1,80] One study has found that the prevalence of long sleep duration has increased over time in the UK, raising this as a potentially important area for further research.[1,124]

Napping

Although naps can counteract some of the short-term cognitive effects of sleep deprivation, studies of the effects of chronic napping on health report conflicting results.[19] Some studies find that chronic napping may have a protective effect on obesity and cardiovascular health, while others find napping to be associated with an increased risk of type 2 diabetes, cardiovascular disease, respiratory disease, and all-cause mortality.[80,125–128] Age

may be a factor, with older adults showing a stronger link between napping and poor health outcomes in some studies.[18,126] The timing and duration of naps may also be important.[18,19] Some studies show that short naps are not associated with increased risk of type 2 diabetes and cardiovascular disease or may have a protective effect.[126,129,130] Cultural and environmental factors may also play a role.[80]

The mechanisms underlying the link between napping and poor health are poorly understood.[80] Explanations include increased inflammation during sleep and increased activation of the stress response upon awaking, each of which have been associated with adverse outcomes, such as type 2 diabetes and cardiovascular diseases.[18,19,131] Napping may also be a marker of underlying ill health or may reflect an attempt by those with chronic sleep insufficiency to catch up on sleep.[18,19] However, there is no evidence of a causal link between napping and health, and therefore further research is needed.[18]

Future research

Sleep is a cross-disciplinary and rapidly expanding area of research. One focus is the development and testing of early interventions to prevent sleep problems.[132] For example, researchers are studying sleep as part of a 24-hour day, including its link to meal times and daily physical activity.[133–135]

Another focus is on interventions to improve sleep, including the development of easy screening and diagnostic tools for OSA, insomnia and overall sleep health.[136–138] Initiatives are also exploring the expansion and facilitation of OSA treatment and digital CBT-I as a way to improve sleep at the population level.[139–141] Furthermore, researchers are testing the effectiveness of digital CBT-I for improving other aspects of health via an impact on sleep, both in the general population and in those with other physical and mental health conditions.[142–144] Research is also underway to understand whether light-based interventions (such as improving day-time light or minimising night-time light exposure) can improve circadian rhythm, sleep and health.[76,145]

Other efforts are focused on understanding sleep health in different segments of the population (for example, defined by age, gender, ethnicity or socioeconomic status).[132] 'Big Data' approaches are sometimes used in this research.[132] One large-scale US study is collecting detailed subjective and objective sleep data from 30,000 people, with an aim to provide an understanding of how different sleep measures relate to each other and to aspects of health.[146] Data from wearable consumer sleep trackers, despite their limitations, may also be a potentially useful and vast resource for studying sleep.[147,148]

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