



The Nightmare (1781) by Henry Fuseli: such hallucinations can plague people with narcolepsy.

NEUROSCIENCE

The wild frontiers of slumber

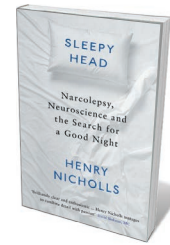
Emmanuel Mignot praises a searing account of a science writer's lifelong struggle with a sleep disorder.

A seven-year-old begins to fall asleep abruptly in class, gain weight and behave aggressively. A 50-year-old man sleeps poorly and dreams vividly; suddenly, he realizes that he has had an unrecognized sleep disorder for decades. These are just some of the ways that narcolepsy can manifest. The condition involves sleepiness and abnormal rapid eye movement (REM) sleep, and affects 4 million people globally. It can remain undiagnosed and untreated for years.

Henry Nicholls, a seasoned science writer (often for these pages), has narcolepsy. Thus, his book *Sleepyhead* offers a welcome

departure from most studies on the neuroscience of sleep and sleep disorders: his lived experience proves a valuable way in. His quest for the grail of perfect sleep — and the origins of his puzzling symptoms — turns into a broader journey into the complex, mysterious landscape of sleep. He meets scientists and physicians specializing in sleep disorders, and draws on historical accounts to eloquently describe conditions such as sleep paralysis, lucid dreaming, sleep apnoea and insomnia. As he shows, solutions to these harrowing problems are finally becoming available.

Sleep science is a young field. Its official birth is generally considered to be 1953, when



Sleepyhead:
Narcolepsy,
Neuroscience and
the Search for a
Good Night
HENRY NICHOLLS
Profile: 2018.

REM sleep — in which the brain is active and dreaming, the body is paralysed and the eyes move rapidly — was first described by Eugene Aserinsky and Nathaniel Kleitman. Just ten years later, sleep apnoea was officially described.

Exploring concepts, diseases or symptoms chapter by chapter, Nicholls reveals that, for centuries, society and scientists dismissed sleep as a loss of time, and thus a waste of effort to study. Research into circadian rhythms has uncovered the fundamental basis of time-keeping: a gene-protein feedback loop that is present in all cells, essential to survival and reproduction. But, by contrast, as Nicholls shows, basic research has yet to reveal the molecular mechanisms that explain why we feel increasingly overwhelmed by sleepiness when we don't sleep enough (sleep debt) — although theories abound. Meanwhile, clinical approaches have exploded, leading to an oversized clinical field with relatively little basic science.

Yet the biology that does exist has immediate applications. As Nicholls shows, behaviours such as midday napping and midnight insomnia are easily explained by the interplay between circadian control of sleep and sleep-debt accumulation and release. This understanding has emerged in practical approaches such as the use of light, melatonin and sleep restriction for the treatment of insomnia.

Nicholls does much to dispel misconceptions of narcolepsy. Aside from overwhelming sleep attacks, the disease is characterized by disturbed sleep with dream-like hallucinations and sleep paralysis. Cataplexy — sudden episodes of muscle weakness typically triggered by emotions such as mirth — is another symptom that, with hypnagogic hallucinations (on falling asleep), is thought to be behind the strange experience of sleep-stage dissociation: in this, a person is conscious and awake, but in REM sleep. Nicholls poignantly describes the devastating effects of narcolepsy on personal relationships, education and work, putting into context the huge cost of misdiagnoses. Too often, the hallmarks of the condition are mistreated as depression, epilepsy or simply 'conversion disorder' — physical symptoms thought to express repressed anxiety.

His stories reminded me of my early days in sleep research, in the 1990s. Well-designed studies had shown that narcolepsy was half as prevalent as multiple sclerosis — affecting 1 in 2,000 people. Yet at neurology conferences, I constantly heard: "It is impossible, I have never seen a case." Almost three decades

on, I have seen thousands of patients, many of whom have ‘slept their life away’ undiagnosed. Given that half of all people with the condition develop it before the age of 18, this is especially tragic for children, for whom every year is critical for development.

Yet narcolepsy’s cause is remarkably simple. It was discovered in 1999 by my team and that of Mashashi Yanagisawa through genetic studies in dogs and mice. In humans, research pinned it down to the loss of around 20,000 neurons in the brain’s hypothalamus containing hypocretin, a wakefulness-promoting protein. The next question is how they are lost. With data suggesting an autoimmune process following an influenza infection (in which the immune system confuses parts of the flu virus with hypocretin neurons), a full understanding of the condition might teach us much about autoimmunity in the brain. A more effective treatment will be available once hypocretin-stimulating compounds are developed that can penetrate the brain, which could happen in the next decade. These compounds help narcoleptics and many other people with unexplained sleepiness.

Nicholls drives home, too, how in denial we are about our need for sleep, and the prevalence of disorders preventing it. Sleep apnoea, which involves snoring and pauses in breathing, affects 10–20% of the population, most often men. Until the 1980s, it was largely unknown to physicians, although attested in fiction: a famous sufferer is Joe in Charles Dickens’ 1837 *The Pickwick Papers*. It took decades for mainstream medicine to recognize it as a frequent cause of high

blood pressure. Apnoea affects people with a narrow upper airway, often due to obesity; when they breathe in, the back of their throat collapses, disturbing sleep and reducing the oxygen they take in. The standard treatment is simple — supporting the airway during sleep with pressurized air — but many find it hard to tolerate. Nothing better is available.

Some harbour fears linked to sleep. As Nicholls notes, many people with insomnia (which affects 10% of people, most often women) are terrified by their lack of sleep, and try to force themselves into it. They might spend too long in bed, making their sleep worse by reducing their sleep debt too much. This causes a vicious circle. Their anxiety might be exacerbated by the barrage of media stories on the need to sleep for eight uninterrupted hours a night, or even by accounts of fatal familial insomnia. In that extremely rare condition, slumber is impossible because of lesions in the thalamus, the brain region that filters out sensory perceptions as we fall asleep. The most effective treatment for insomnia is a better understanding of sleep physiology, notably restricting sleep to increase sleep pressure and break the vicious circle.

Parasomnias occupy a chunk of the book — ‘almost normal’ disorders such as sleep walking, night terrors and sleep paralysis. These mixed states have definitive physiological explanations. Sleepwalking and night

“We are in denial about our need for sleep, and the prevalence of disorders preventing it.”

terrors, in which people, typically children, arise screaming while still asleep, come from non-REM sleep, when one part of the brain attempts to wake the person while the cortex is still asleep. Sleepwalkers can experience fatal falls, or even have unconscious sex, which can have medical and legal consequences. In REM sleep behaviour disorder — in which REM sleep paralysis does not work and patients enact their dream — people might attack their bed partner. Most go on to develop Parkinson’s disease. Research has only recently started to outline the neural underpinnings of these pathologies.

For all its strengths, Nicholls’s fascinating book leaves us wanting more. As *Sleepyhead* shows, sleep sciences are still in their infancy, and current research is mostly descriptive. Luckily — although Nicholls doesn’t cover this — the field is now poised to benefit from two scientific transformations. The first is genomics, which has cracked open the molecular basis of some objectively measurable traits or behaviours. The second is tools such as activity trackers, electroencephalography electrodes, devices to track movement caused by the heartbeat, and snoring recorders, which are making the objective tracking of our waking and sleeping lives vastly easier. ■

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FILM

Bollywood takes on menstrual stigma

Subhra Priyadarshini lauds a biopic of an inspired Indian sanitary-pad innovator.

Frugal innovation is a new norm in India, emerging sporadically in pockets of brilliance — from rural hamlets to technology labs. It has even spawned a word in Hindi: *jugaad*.

Thanks to *jugaad*, bioengineer Manu Prakash is flooding rural schools in India with his US\$1 ‘foldscope’, an origami-inspired microscope teaching science to tens of thousands of children. It is also in this spirit that, in 2000, school dropout Arunachalam Muruganantham created a do-it-yourself unit in Coimbatore, Tamil Nadu, to manufacture the world’s cheapest sanitary pads. Now, Muruganantham’s story hits the big screen in *Pad Man*, billed as the first feature-length film on menstrual hygiene.

‘Period poverty’ is a health issue affecting women in countries across the globe. In Britain, 1 in 10 girls and women aged 14–21 cannot afford sanitary products, according to London-based charity Plan International UK. In India, according to a 2015–16 government health survey, just 58% of women aged 15–24 can afford to use a hygienic method of menstrual protection: 78% in urban areas and 48% in rural ones. And the average varies wildly between states — from 91% in Tamil Nadu to just 31% in Bihar. The rest resort to rags, leaves and even ash. This can result in serious health risks, such as toxic shock syndrome, and lead to absence from school or work.

Pad Man
DIRECTOR:
R. BALKI
Columbia/Hope:
2018.

Pad Man attempts to

open up this taboo topic for much-needed discussion through narrative sparked by melodrama and music. Like Shree Narayan Singh’s 2017 film *Toilet: Ek Prem Katha*, centred around the problem of open defecation, it has captured the imagination of a nation grappling with a massive burden of women’s health issues.

Directed by R. Balki, *Pad Man* has a starry cast. Muruganantham (renamed Lakshmikantham) is played by renowned Bollywood action-hero-turned-character-actor Akshay Kumar; the powerful theatre actor Radhika Apte plays his wife, Shanthi (called Gayatri). There is even a jingoistic cameo from superstar Amitabh Bachchan, who, playing himself, declaims: “India should not be seen as a country of one billion people. ▶