Why conventional insomnia advice fails in ME

For many patients with severe ME, the question is not whether long-term hypnotic therapy is ideal. It is whether allowing a patient with documented neurological disease to remain chronically sleep deprived is a safer alternative. That decision should be based on the pathophysiology of ME - not on the mistaken belief that it has a psychological basis.

- Sleep hygiene does not correct brainstem dysfunction.
- No treatment has been shown to reverse the underlying neurological pathology of ME.
- Treating sleep can reduce autonomic stress, and overall symptoms, while failure to treat results in disease exacerbation.
- Preserving restorative sleep reduces post-exertional deterioration.
- Withdrawal may precipitate severe rebound insomnia, prolonged autonomic instability and significant deterioration in some patients. Relapses, that can be triggered by medication changes, can become life-threatening in ME.
- Specialist ME physicians also raise the issue of potential autonomic chaos resulting in fatal arrhythmias if long-term sleep medication is withdrawn. A number of cases are known, including recent ones of young people.

This has important implications for treatment. Severe insomnia arises because the neurological mechanisms responsible for generating sleep have become dysfunctional. Simply advising patients to improve their sleep hygiene or withdrawing medication that provides even a few hours of sleep is unlikely to address the underlying problem. Until treatments exist that restore normal brainstem and autonomic function, symptomatic treatment of severe insomnia may remain an essential component of compassionate care. **Severe insomnia in ME is a symptom of neurological disease.**

Sleep is Treatment: it is essential for:

- autonomic stability
- immune regulation
- memory consolidation
- endocrine regulation
- cerebral waste clearance
- cardiovascular function

Conversely, prolonged sleep deprivation may worsen:

- post-exertional malaise
- dysautonomia
- orthostatic intolerance
- cognitive impairment
- pain
- cardiovascular instability

Sleep in severe ME is not simply rest, but a critical component of neurological homeostasis. Preserving sleep represents an essential part of protecting autonomic, cardiovascular and cognitive function from further dysfunction until disease-modifying treatments become available.

Why this matters clinically

- Severe insomnia in ME should be regarded as a neurological manifestation of the disease rather than as primary insomnia.
- Withdrawal of established sleep medication may precipitate significant clinical deterioration.
- Conventional sleep-hygiene advice alone is unlikely to address the underlying pathology.
- Management should focus on preserving restorative sleep while avoiding treatments that increase post-exertional symptom exacerbation.

References - **Myalgic encephalomyelitis /chronic fatigue syndrome: diagnosis and management**

- NICE guideline
- Reference number:NG206
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The Neurology of Severe Insomnia in ME/CFS

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Myalgic Encephalomyelitis is documented as a serious multisystem neuroimmune-endocrine-cardiovascular disease with autoimmune features. The Q-of-L scores are lower than those of all the major chronic diseases with which it has been compared, including MS, heart failure and certain cancers (Hvidberg, 2015). The WHO classifies it as a neurological disease.

The impact on the functional status of the patient with severe ME is immense. Severe complications and preventable deaths have been documented, particularly where appropriate medical care has been withheld, or the illness has been seriously mismanaged. Twenty-five per cent are bedbound, lying in dark, silent rooms, intolerant of light, sound, smells, and unable to move, eat or drink. Even the mildest are 50% disabled. Few, if any, other diseases inflict so much long-term suffering.

ME researcher Dr Alan Cochetto encapsulated the extent of devastation experienced by ME/CFS when he said, *"Every time you look at this disease, you see immense suffering. There appears to be no limit to the toll of human suffering that this disease is capable of inflicting on patients.'*

Sleep is not a luxury. It is a biological necessity.

For many people with ME, sleep is no longer a restorative process, and chronic insomnia is severe and intransigent. Patients may remain awake for days, sleep only a few fragmented hours, or awaken feeling exhausted. This is not ordinary insomnia, but is recognised as another manifestation of the neurological, autonomic and vascular abnormalities that characterise ME.

Converging evidence from research and the known pathophysiology suggests that the severe insomnia, typical of ME, is the result of the convergence of cerebral hypoperfusion, neuroinflammation, vascular abnormalities, autonomic dysfunction, and abnormalities involving the brainstem, hypothalamus and thalamus. The neural network responsible for generating normal sleep has, in this disease, become functionally impaired. The consequence is profound, chronic insomnia despite overwhelming physiological exhaustion.

Causes of insomnia in ME

Cerebral Hypoperfusion

One of the earliest discoveries in ME was that of hypovolaemia in these patients, and blood volume or cerebral perfusion can be as little as 50% of normal (Bell, 2015, Vink, 2025)

Reduced blood volume in ME appears to result from several interacting mechanisms, including impaired RAAS signalling, abnormalities of vasopressin regulation, endothelial dysfunction and increased vascular permeability. This results in cerebral hypoperfusion, which can be severe, affecting not only cognition, the so-called 'brain fog', but also the normal neurological mechanisms required for sleep.

The Ascending Reticular Activating System (ARAS): a Major Contributor to Insomnia in ME.

Recent neurological research points towards a key structure deep within the brainstem known as the **Ascending Reticular Activating System (ARAS)**. This network acts as one of the brain's master control systems, regulating wakefulness, attention, autonomic function and the transition between sleep and consciousness.

Normally, the ARAS allows the brain to move smoothly between states. During the day it maintains alertness and filters out unimportant sensory information. At night it reduces this activity, allowing the brain to disengage from the outside world and enter restorative sleep.

Increasing evidence suggests that dysfunction of this system may contribute to the neurological manifestations of ME.

If neuroinflammation, impaired cerebral blood flow or structural dysfunction affects the ARAS, the brain can lose its ability to make this transition normally. Instead of switching cleanly from wakefulness to sleep, patients become trapped in a paradoxical state that many describe as *'tired but wired'*. The body is profoundly exhausted, yet the brain remains abnormally alert.

At the same time, the ARAS normally acts as a filter, preventing every sight, sound and sensation from reaching conscious awareness. When this filtering mechanism breaks down, ordinary sensory stimuli become overwhelming. Light, noise, movement and even internal bodily sensations may be interpreted by the brain as threatening, preventing normal sleep and contributing to sensory overload and post-exertional malaise.

The ARAS is also closely connected to the brainstem centres that regulate heart rate, blood pressure, breathing and vascular tone.

Dysfunction of this network therefore offers a unifying explanation for several of the cardinal features of ME. The same abnormality that prevents restorative sleep may also contribute to orthostatic intolerance, inappropriate adrenaline release, palpitations, tachycardia and the inability to maintain stable blood pressure.

Importantly, this model complements rather than replaces current theories involving the thalamus. The ARAS and the thalamus function as part of the same neurological network. The ARAS provides the activating signals that allow the thalamus to regulate the flow of information to the cerebral cortex. If the ARAS becomes dysfunctional, the thalamus cannot perform this filtering role efficiently. The result may be the combination of insomnia, sensory hypersensitivity, cognitive dysfunction, autonomic instability and profound fatigue that characterises ME.

Dysautonomia: The Brain Cannot Switch Off

Normal sleep requires a coordinated reduction in sympathetic activity with increased parasympathetic (vagal) tone. Multiple studies demonstrate that this transition is impaired in ME. Sympathetic activation persists throughout the night, heart-rate variability is reduced, and many patients exhibit impaired cardiovascular reflexes. In some, abnormalities of baroreflex function may further impair the brain's ability to regulate blood pressure and heart rate during sleep, perpetuating nocturnal autonomic activation and fragmented sleep.

Endocrine Dysfunction is a Major Contributor to Insomnia in ME

The hypothalamic-pituitary-adrenal axis regulates: cortisol rhythm; melatonin timing, and the circadian rhythm. Many studies demonstrate dysregulation of these systems in ME. DeBellis, (2021), found evidence of autoimmunity involving the hypothalamic-pituitary axis. Many patients therefore lose their normal sleep-wake rhythm despite overwhelming exhaustion.

The Glymphatic System

Recent research has highlighted the importance of the glymphatic system - the brain's waste-clearance network in ME. (Marshall-Gradisnik, 2026). Deep sleep is thought critical for optimal glymphatic clearance. During sleep, cerebrospinal fluid removes inflammatory mediators, metabolic waste and potentially neurotoxic proteins. Recent research suggests glymphatic dysfunction in ME may contribute to persistent neuroinflammation and cognitive impairment. Severe insomnia

may therefore perpetuate disease activity rather than merely accompany it.

Neuroinflammation

Evidence increasingly demonstrates neuroinflammation within the central nervous system of ME patients. (Younger, Hyde, Sheibenbogen). One proposed contributor is increased bradykinin signalling. Within the Scheibenbogen–Wirth model, mitochondrial calcium dysregulation may contribute to this pathway. Bradykinin signalling increases BBB and vascular permeability and may amplify neuroinflammation, acting as a megaphone for the body's symptoms, especially that of pain. It also exacerbates the neuroinflammation, which, in turn, has a detrimental impact on the dysfunctional hypothalamus, the brainstem nuclei, further dysregulates the autonomic nervous system, and disrupts sleep architecture, causing it to be further fragmented, shallow and non-restorative.

In ME, the Brain Cannot Switch Off:

Key Message for Clinicians

ME-related insomnia should be regarded as a potential manifestation of:

Brainstem hypoperfusion
↓
ARAS dysfunction
↓
Thalamic dysregulation
↓
Hypothalamic/autonomic dysfunction
↓
'Tired but wired' insomnia
↓
Loss of glymphatic clearance during deep sleep
↓
Accumulation of neuroinflammation and worsening neurological dysfunction

Decisions regarding withdrawal of effective hypnotic medication should therefore be based on the recognised neurological pathophysiology of ME rather than on assumptions that the insomnia is behavioural or psychological. For patients, prolonged sleep deprivation will usually worsen neurological dysfunction, dysautonomia and overall disease severity, causing the patient to be trapped in a chronic vicious cycle of symptoms.