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THE ROLE OF THE LOCUS COERULEUS IN THE REGULATION OF SLEEP-WAKE CYCLES

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The locus coeruleus (LC), a small bilateral nucleus located in the dorsal pons, serves as the brain's primary source of noradrenaline (NE). Despite its compact size, the LC exerts global influence through extensive axonal projections that innervate virtually the entire central nervous system, including the cerebral cortex, hippocampus, thalamus, hypothalamus, cerebellum, brainstem, and spinal cord. Once released, NE acts upon a diverse family of adrenergic receptors (α1, α2, β1), which are G-protein-coupled and produce either excitatory (primarily via α1 and β) or inhibitory (via α2) postsynaptic effects, enabling nuanced regional control.

The aim of this study is to analyze the physiological mechanisms by which the locus coeruleus regulates sleep and to determine how disturbances in these mechanisms contribute to sleep disorders and related conditions.

During slow wave sleep phase (NREM - non rapid eye movement), LC activity decreases; during the rapid eye movement sleep phase (REM), it falls nearly silent. The LC exhibits two fundamental firing modes: tonic (baseline, sustained activity) and phasic (brief, stimulus-evoked bursts). Tonic activity regulates global arousal and vigilance, while phasic responses enhance cortical signal-to-noise ratio–facilitating attentional focus and decision-making. The relationship between LC activity and cognitive performance follows an inverted U-shaped curve, as described by the Yerkes–Dodson law: moderate LC tone optimizes performance, whereas hypo- or hyperactivity impairs function through inattention or anxiety, respectively (Nikolenko et al., 2024).

Physiologically, the LC is integral to sleep–wake regulation, stress responses, and emotional processing. During sleep, complex, sleep-specific LC firing patterns support slow oscillations and spindles, essential for memory consolidation and immune function. Chronic stress induces maladaptive LC hyperexcitability, contributing to hyperarousal, sleep dysregulation and emotional imbalance.

Critically, the LC is among the earliest brain regions affected in neurodegenerative diseases such as Alzheimer's and Parkinson's, where tau or α-synuclein pathology and subsequent NE loss precede cortical damage. Researches show that this early vulnerability disrupts neuroprotection, accelerates neuroinflammation, and impairs protein clearance, making the LC a driver of disease progression (Ross and Van Bockstaele, 2024; Nikolenko et al., 2024).

Disruption of locus coeruleus activity alters normal sleep architecture, impairs the restorative functions of sleep, and contributes to brain inflammation, making the brain more vulnerable to neurodegeneration (Osorio-Forero et al., 2025).

In conclusion, understanding LC's dedicated role in arousal has clinical implications for narcolepsy, disorders of excessive sleepiness, and conditions of hyperarousal like post-traumatic stress disorder and anxiety. These physiological processes provide valuable insight for improving prevention and treatment approaches.