The conservation of sleep across all animal species suggests that sleep serves a vital function. Sleep deprivation reduces learning, impairs performance in cognitive tests, prolongs reaction time, and is a common cause of seizures. However, after decades of effort, still one of the greatest mysteries in biology is why sleep is restorative and, conversely, why lack of sleep impairs brain function.

In this article, the researchers show that the restorative function of sleep may be a consequence of the enhanced removal of potentially neurotoxic waste products that accumulate in the awake central nervous system. Several degradation products of cellular activity, such as Ab oligomers and amyloid depositions, have adverse effects on synaptic transmission and cytosolic Ca2+ concentrations can trigger irreversible neuronal injury. Using real-time assessments of tetramethylammonium diffusion and two-photon imaging in live mice, the investigators show that natural sleep or anesthesia are associated with a 60% increase in the interstitial space, resulting in a striking increase in convective exchange of cerebrospinal fluid with interstitial fluid. In turn, convective fluxes of interstitial fluid increased the rate of b-amyloid clearance during sleep. Thus, the restorative function of sleep may be a consequence of the enhanced removal of potentially neurotoxic waste products that accumulate in the awake central nervous system.

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