

# The Sleeping Brain: Harnessing Glymphatic Clearance of Brain Waste

## Why do we need to sleep?

While it is clear that sleep is vital to the survival of all mammals, the biological function puzzled researchers for decades.<sup>1-3</sup> Sleep requires that we enter into a state of significantly compromised awareness, making us vulnerable to a range of threats. The fact that sleep is critical for both humans and animals, despite these inherent risks to survival, suggests that sleep must serve a fundamental biological function beyond just rest and conserving energy.<sup>1,2</sup> Another unknown has been why sleep is restorative and conversely, a lack of sleep impairs brain and cognitive function.<sup>3</sup>

## How do our brains detoxify and clear brain waste?

In addition, the mechanisms by which neurotoxins and metabolic waste were removed from the brain as well as how brain fluid balance was maintained, were poorly understood until recently. In peripheral tissue, the lymphatic system maintains fluid levels, supports immune function and transports metabolic waste to the general circulation for metabolism and degradation by the liver.<sup>3</sup> Brain tissue, however, lacks conventional lymph vessels, despite cerebral metabolism being highly active and the fragility of neurons and brain tissue.<sup>3</sup>

It was clear that an alternative mechanism needed to exist to protect the brain, neurons and central nervous system (CNS) from toxic waste products. This system was not, however, identified until as recently as 2012 with the discovery of a complex network of fluid channels and mechanisms within brain tissue that serve as the brain's waste clearance system.<sup>1-3</sup> This was named the glymphatic system based on similarities to the lymphatic system and the glial aquaporin-4 (AQP-4) water channels which are a core component of the brain waste clearance system.<sup>1,2</sup>

The glymphatic system is critical for brain homeostasis and neurological health as it is responsible for the efficient clearance of metabolic waste from the brain and brain tissue, including soluble proteins associated with neurodegenerative disease such as amyloid- $\beta$  and tau.<sup>2,3,5-11</sup> In addition to brain waste removal and cleansing, the glymphatic system has a replenishing function in the brain and CNS as it helps distribute molecules such as glucose, amino acids, lipids, growth factors, and neuromodulators, which are important for normal brain function to brain tissue.<sup>1,2,4</sup>

## The link between sleep and brain waste clearance.

An intriguing discovery about the glymphatic brain waste clearance system is that it appears to be 90% more active during sleep, while being profoundly suppressed during wakefulness.<sup>2,3</sup> The glymphatic system is thus sleep-dependent, representing a compelling new explanation for the fundamental biological function of sleep.<sup>2,3</sup> We need to sleep in order to establish a state whereby the glymphatic system can efficiently clear the brain and CNS of all the metabolic waste and unwanted soluble proteins that were produced while awake and replenish with clean cerebrospinal fluid. Without sleep, brain metabolic waste and neurotoxins would accumulate in the brain and CNS, potentially leading to brain fog, neurological and cognitive dysfunction and may contribute to migraine headaches and some mood disorders.<sup>2,9-13</sup>

The discovery of the glymphatic system and that sleep is the key driver for its efficient function, highlights the importance of maintaining regular good quality sleep, especially slow-wave deep sleep in order to support both short and long-term brain health, cognitive health and memory.<sup>3,4,10,11</sup>

*\*References available on request.*