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Specific Changes in the Brain Associated With Sleep Deprivation Described in New Study

ScienceDaily (Nov. 4, 2010) — Researchers at the Allen Institute for Brain Science and SRI International have published the most systematic study to date of the effects of sleep deprivation on gene expression in the brain. The findings have implications for improving the understanding and management of the adverse effects of sleep deprivation on brain function.

The study, available in *Frontiers in Neuroscience*, has created an extensive and detailed map of gene activity, known as gene expression, in the mouse brain across five behavioral conditions including sleeping, waking and sleep deprivation. Activity of approximately 220 genes responding to these conditions was examined in detail, down to the cellular level, throughout the brain. Additionally, seven brain areas were examined by DNA microarray analysis, which reports the expression levels of tens of thousands of genes and allows a genome-wide analysis of the consequences of sleep deprivation.

"Although most people experience occasional sleep deprivation and recognize its impact on their mood and behavior, there is little scientific understanding of how sleep loss actually affects brain function," said Thomas Kilduff, Ph.D., senior director of the Center for Neuroscience at SRI International. "This pioneering study documents how extending wakefulness affects gene expression in specific brain regions and describes a 'molecular anatomical signature' of sleep deprivation. Our findings may contribute to treatments that will help improve sleep quality and reduce problems arising from sleep deprivation."

By comparing which genes were turned on and where in the brain across the different conditions, the researchers discovered that the majority of the neurons in the forebrain were affected in diverse ways by sleep deprivation, painting a dynamic picture of the molecular consequences of sleep deprivation on higher cognitive functions. Affected forebrain regions include the neocortex, amygdala and hippocampus, which mediate cognitive, emotional and memory functions that are impaired by sleep deprivation.

Detailed analysis of 209 brain areas revealed a novel set of genes not previously associated with sleep deprivation, including genes associated with the stress response, cell-cell signaling, and the regulation of other genes. One gene, neurotensin, has been implicated in schizophrenia and is similarly induced by antipsychotic drugs. These genes may provide potential targets for therapeutic intervention to alleviate the effects of sleep deprivation.

"These data illustrate the complex and dynamic relationship between sleep and sleep deprivation, neuroanatomical pathways and gene expression," said Ed Lein, Ph.D., senior director of neuroscience at the Allen Institute for Brain Science and senior author of the study. "The breadth and level of detail provided by these data will be a unique resource for the scientific community, and to that end we have made the data set publicly available online in its entirety."

The resulting open data resource is one of a growing collection of public online resources provided by the Allen Institute, which was founded by philanthropist Paul G. Allen to advance brain research.

Sleep deprivation leads to a range of cognitive, attention and emotional deficits, including irritability and impaired memory, coordination, and concentration. These effects, which can compromise health, performance and safety, are common among those who work extended hours, including military and medical personnel, and others suffering from chronic sleep loss. Sleep deficits have also been linked to the development of some chronic diseases and disorders, including diabetes, depression, obesity and cardiovascular disease.

The control of sleeping and waking and the consequences of sleep deprivation are believed to be associated with gene activity changes in brain regions involved in sleep regulation and higher level functions. Understanding these changes in gene activity is a critical step toward advances in the treatment of sleep disorders and mitigation of the effects of sleep deprivation.

The data in this study are publicly available via the ALLEN Brain Atlas data portal (www.brain-map.org) as the "Sleep Study." This online dataset comprises a substantial collection of data detailing where specific genes are expressed, or "turned on," throughout the mouse brain for five conditions of sleeping and waking. Specifically, it includes searchable image-based gene expression data for approximately 220 sleep-related genes, genome-wide microarray data for seven sleep-associated brain areas, and a 3D viewing tool for visualizing changes in gene expression across different conditions.

This public resource is a unique resource for sleep researchers worldwide and holds promise for accelerating progress toward understanding and effective treatment of sleep disorders.

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Journal Reference:

1. C.L. Thompson et al. **Molecular and anatomical signatures of sleep deprivation in the mouse brain.** *Frontiers in Neuroscience*, 2010; DOI: [10.3389/fnins.2010.00165](https://doi.org/10.3389/fnins.2010.00165)

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