WHOLE HEALTH: CHANGE THE CONVERSATION

Advancing Skills in the Delivery of Personalized, Proactive, Patient-Driven Care

Neuroplasticity and Sleep Clinical Tool

This document has been written for clinicians. The content was developed by the Integrative Medicine Program, Department of Family Medicine, University of Wisconsin-Madison School of Medicine and Public Health in cooperation with Pacific Institute for Research and Evaluation, under contract to the Office of Patient Centered Care and Cultural Transformation, Veterans Health Administration.

Information is organized according to the diagram above, the Components of Proactive Health and Well-Being. While conventional treatments may be covered to some degree, the focus is on other areas of Whole Health that are less likely to be covered elsewhere and may be less familiar to most readers. There is no intention to dismiss what conventional care has to offer. Rather, you are encouraged to learn more about other approaches and how they may be used to complement conventional care. The ultimate decision to use a given approach should be based on many factors, including patient preferences, clinician comfort level, efficacy data, safety, and accessibility. No one approach is right for everyone; personalizing care is of fundamental importance.
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Introduction

Why do we sleep? After all, it seems such a waste of time to spend one-third of our lives unconscious and immobile. However, if we consider sleep from an evolutionary perspective, it becomes clear that sleep is vital for most species on Earth. Even bacteria demonstrate alternating periods of increased and decreased metabolic activity based on the day-light cycle, governed by genes known as “clock genes.” Plants such as four o’clock’s and morning glories open their flowers by day and close by night. Sleep is essential to survival. Deprive a laboratory rat of sleep and it will die, just as quickly as if it is deprived of food and water.

Neuroplasticity is defined as change in the brain’s structure and function due to experience. The brain was once thought to become immutable after a critical period of development in early childhood. Now we know that the brain is constantly changing in response to experience and disease. Given the fundamental importance of sleep in the biology of all life, it should come as no surprise that sleep has major effects on the brain through neuroplastic mechanisms. This clinical tool is offered as a means for clinicians to gain a better understanding of these mechanisms, with the intention that with this understanding can come enhanced care of people with sleep disorders, not to mention a greater appreciation of why sleep is vital to Whole Health.

Four Key Neuroplastic Mechanisms

1. **Long-term potentiation (LTP)** is a neuroplastic mechanism that is due to the strengthening of existing synapses. LTP is a very dynamic process that occurs over seconds to minutes. Reading this document may result in LTP for an insight that is captured in short-term memory. If someone were to ask you what you just read, you would be able to tell her. If asked the next day, or a week later, your recall would not be as good. Although the information and ideas were held in your short-term memory, there was no persistent change in brain function or structure, so information was lost.

2. **Synaptogenesis** is a neuroplastic mechanism that results in structural and functional reorganization of the nervous system. It too is dynamic and occurs over a time course of minutes to hours. Some of the material in this document may stick in your memory, where it interacts with other memories and internal psychological states. If what you read today “sticks with you,” it does so because it stuck in your mind via increased numbers of strengthened synapses in the brain.
3. **Axonal sprouting, myelination, and dendritic arborization** are longer-term processes that involve complex learning and skill acquisition. These processes occur over much longer time frames than LTP and synaptogenesis; they can take days to weeks—even months. Once formed, these effects are particularly long lasting. Achieving this degree of learning usually involves repetition over time. But once learned this way, something is not easily forgotten. Think of learning to ride a bike or playing a C-sharp scale on the piano.

4. **Neurogenesis**, also referred to as adult neurogenesis, is a process whereby stem cells activate, differentiate into neurons, migrate, and then integrate into existing neuronal networks. The full process takes about two months. Neurogenesis occurs most robustly in infancy and childhood, but it also occurs in adults—in restricted areas of the adult brain—throughout life. In addition, neurogenesis occurs after damage to the brain, e.g., after stroke or spinal cord trauma. Because most of the new neurons the body generates cannot find a neuronal network to plug into, they die. Those that arise naturally in specific zones in the brain under the right physiological conditions may survive. Their role is one of the great controversies of neurobiology. Many factors affect the rate of birth and survival of these baby neurons, and one of the most important is sleep.

**Sleep, Sleep Deprivation, and the Hypothalamic Pituitary Axis (HPA)**

The hypothalamic pituitary axis is a key element in the translation of the autonomic nervous system (ANS) both systemically and through both feed-forward and feedback mechanisms, into the brain. The ANS is divided into the sympathetic (SNS) and parasympathetic nervous systems (PNS). The SNS is key to survival in crisis situations.
Activation of the SNS results in the release of epinephrine, norepinephrine, and cortisol. These neurotransmitters prepare the body for immediate life-saving action—flight or fight—and cause elevations of blood pressure, heart rate, serum glucose, immune suppression, and diversion of blood flow away from the internal splenic organs and toward the muscles. Every process of the body and brain that is necessary for long-term health is suspended temporarily in the name of short-term survival. This is the body’s way of preparing for war.

Sleep deprivation is interpreted by the body as a stress. This results in SNS activation, triggering the release of catecholamines and serum cortisol. This leads to multiple systemic effects, such as elevations of serum glucose, blood pressure, and heart rate, and it results in brain effects as well. Through a feed-forward mechanism, the effects of SNS activation result in increased activation of the amygdala, a key nucleus in the limbic system of the brain and an important regulator of SNS activity. This means that activation of the SNS will become more likely to occur in the future. Since SNS activation results in sleep disruption, a vicious feed-forward loop can ensue in which insomnia becomes entrenched. In addition, elevations of cortisol to sustained high levels may result in decreased dendritic arborization and even death of neurons in vulnerable areas of the brain.

The effect of cortisol on neurogenesis is dose-dependent. At low levels, cortisol primarily stimulates central nervous system mineralocorticoid receptors that are very sensitive to cortisol. This results in increased neurogenesis. Indeed, many of the factors that increase neurogenesis do so through low-level cortisol stimulation. Higher levels of cortisol result in activation of glucocorticoid receptor activation. This is toxic to neurons and decreases neurogenesis, impeding changes that promote a good night’s sleep.

**Hippocampal Neurogenesis and HPA Regulation**

Hippocampal neurogenesis is neurogenesis in a portion of the temporal lobe involved with memory. It is a key control point for regulation of the HPA. Although neurogenesis is a process that takes weeks, new neurons have the lowest thresholds to LTP and as such are the pinnacle of neuroplasticity. In the hippocampus, they appear to be involved with the transition of short-term, hippocampal-dependent memory into long-term, consolidated memory. They also play a key role in decreasing emotionally driven activation of the amygdala and in interrupting the feed-forward activation of the SNS in response to stress such as sleep deprivation.

Hippocampal neurogenesis is enhanced or inhibited by multiple behavioral factors (see Table 1).
Table 1. Behavioral Factors that Enhance or Inhibit Neurogenesis

<table>
<thead>
<tr>
<th>Neurogenesis is increased by...</th>
<th>Neurogenesis is decreased by...</th>
</tr>
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<tbody>
<tr>
<td>Sleep</td>
<td>Sleep loss</td>
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<tr>
<td>Exercise</td>
<td>Stress</td>
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<tr>
<td>Environmental novelty</td>
<td>Depression</td>
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<td>SSRIs</td>
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An Integrated Model of the Neurobiology of Stress and Sleep

An integrated model of this process places sleep in the center of a variety of self-care practices that promote emotional and physical health. Engaging in practices such as breathwork and yoga can increase parasympathetic nervous activation, decreasing the negative effects of chronic SNS activation that result in myriad negative effects on Whole Health, including insomnia.

And our understanding continues to expand. In addition to the neuroplastic effects of sleep summarized here, recent reports have brought to light a novel effect of sleep on maintaining brain health. During sleep, small extracellular channels develop; these channels appear to facilitate the flow of extracellular fluid from the brain. One effect of this is to decrease the accumulation of beta-amyloid in the brain. When beta-amyloid accumulates in neurons in the brain they die. This one of the key steps in the development of dementia.

It is clear that the biological effects of sleep are multiple and are fundamental to our health.

Suggestions for Further Reading


Article from Seed Magazine on the work of Elizabeth Gould on neurogenesis and the neurobiology of stress:
http://seedmagazine.com/content/article/the_reinvention_of_the_self/

Whole Health: Change the Conversation Website

Interested in learning more about Whole Health? Browse our website for information on personal and professional care.

http://projects.hsl.wisc.edu/SERVICE/index.php
Whole Health: Change the Conversation
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References