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In Sleepless Nights, a Hope for Treating Depression

By TERRY SEJNOWSKI

All-Nighters is an exploration of insomnia, sleep and the nocturnal life.

Is there anything good about insomnia? Could there possibly be any upside to a long, torturous sleepless night?

To answer the question, let's look at another condition entirely.

Tags:

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Postpartum depression affects between 5 percent and 25 percent of new mothers. Symptoms — including sadness, fatigue, appetite changes, crying, anxiety and irritability — usually occur in the first few months after child birth. There is a simple way to alleviate postpartum

depression in just a few hours: sleep deprivation.

If a depressed mother stays up all night, or even the last half of the night, it is likely that by morning the depression will lift. Although this sounds too good to be true, it has been well documented in over 1,700 patients in more than 75 published papers during the last 40 years.[1] Sleep deprivation used as a treatment for depression is efficacious and robust: it works quickly, is relatively easy to administer, inexpensive, relatively safe and it also alleviates other types of clinical depression. Sleep deprivation can elevate your mood even if you are not depressed, and can induce euphoria. This throws a new light on insomnia.

This remarkable result is not well known outside a small circle of sleep researchers for three good reasons. First, sleep deprivation is not as convenient as taking a pill. Second, prolonged sleep deprivation is not exactly a desirable state; it leads to cognitive defects, such as reduced working memory and impaired decision making. Finally, depression recurs after the mother, inevitably, succumbs to sleep, even for a short nap. Nonetheless this is an incredibly important observation; it shows that depression can be rapidly reversed and suggests that something is happening in the sleeping brain to bring on episodes of depression. All this offers hope that studying sleep deprivation may lead to new, unique and rapid treatments for depression.

Neuroscientists have been trying to solve this puzzle. The first hint of what may be happening during sleep came from J. Christian Gillin, a former colleague of mine at the University of California at San Diego and the San Diego Veterans Affairs Medical Center.

Scans suggest that something happening in the sleeping brain can bring on episodes of depression.

Using imaging, he found that a small area of the cerebral cortex in the front of the brain — the anterior cingulate cortex — which was consistently overactive in depressed patients, quieted to normal levels of activity after the patients were deprived of sleep. And when the patients were allowed to sleep, the activity in this area returned to the elevated levels.

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Helen Mayberg at Emory University has shown that electrical stimulation of the anterior cingulate cortex, which disrupts normal activity, also reduces depression. Some patients reported feeling immediate relief and calm after the procedure.

This tells us where in the cortex to look, but we also need to understand the changes that occur in the cortex during sleep. As you fall asleep, neurons in the brain stem that project throughout the cortex and keep it activated stop firing. The reduced stimulation from the brain stem disconnects the cortex from sensory input and there is a major shift in the pattern of electrical activity in the cortex. During the early part of the night the cortex is in a state of slow-wave sleep punctuated by brief periods of rapid-eye movement sleep (REM), which become more frequent and longer lasting toward early morning.

One major class of antidepressants, tricyclics, blocks REM sleep, which suggests that sleep deprivation may work against depression the same way. This is consistent with the tendency for depressed individuals to sleep longer than they do when they feel normal. Additional support for this hypothesis comes from genetic studies of families with short REM latency — the tendency to enter REM early in the sleep cycle. This condition disrupts slow wave sleep and extends REM sleep. The risk of depression is much greater if you come from a family with this genetic background. While this is a rare genetic defect that can only account for a small fraction of all depressed patients, these special cases give us valuable clues to conditions that predispose some people to clinical depression.

Despite all we have learned about the brain and sleep states, we still do not have a smoking gun to pinpoint what goes wrong when a mother suffers from postpartum depression, or why sleep deprivation lifts her mood. But what we do know is intriguing and this is driving research that could lead someday to rapid and effective ways to treat depression.

This is exciting news for researchers, and for the millions who suffer from debilitating mood disorders. Insomniacs, though, are unlikely to welcome yet another lost night of sleep, or to be cheered by the notion that a good slumber the night before could have made them feel even worse.

Footnote: [1] *J. Christian Gillin, Monte Buchsbaum, Joseph Wu, Camellia Clark, William Bunney Jr., Sleep deprivation as a model experimental antidepressant treatment: Findings from functional brain imaging, Depression and Anxiety 14 (1), 37-49, 2001*

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