Sleep Can Protect Memories From Associative Interference

BY MARY JO M. DALES
Editorial Director

BOSTON — Sleep strengthens declarative memory, a finding that could one day be exploited to combat cognitive declines associated with dementia and neurologic disorders, Dr. Jeffrey M. Ellenbogen reported at the annual meeting of the American Academy of Neurology.

Sleep previously has been shown to improve motor, visual, and perceptual memories in humans, but this study is one of the first to substantiate a role for sleep in protecting declarative or consciously discussed memories from associative interference, said Dr. Ellenbogen of Harvard Medical School, Boston.

For the study, 48 healthy individuals, aged 18-30 years, were evaluated. No participants took any medications, and all had normal sleep patterns. Subjects were placed in one of four groups, and all were asked to remember 20 words, each of which was paired with an associated word cue.

All groups were tested for their abilities to remember the associated words 12 hours after learning the list. No one in the study was sleep deprived, but the subjects in two groups slept before testing and those in the other two groups did not.

The individuals who slept remembered 94% of the associations; those who did not sleep remembered 82% of the words. Those differences fell just short of statistical significance ($P = .06$).

The differences were marked, however, in the remaining two groups subjected to associative interference. For this part of the study, both groups also learned the same list of 20 word associations.

Again, one group slept and the other did not, and both groups were tested at 12 hours. But 12 minutes before they were tested on the list of words, both groups were subjected to associative interference. They were asked to learn a second list of 20 additional words related to the same word cues. Subjects who had slept and were introduced to the second list of words were able to recall 76% of the word associations from the first list. The subjects who had not slept were able to remember just 32% of the words. The difference in performance was highly significant (P less than .0001).

Sleep is ultimately a brain state that may hold the keys to understanding the neurobiology of memory consolidation, he said. The next step in his research will be to look at the relationships between sleep disorders, cognitive impairment, and neurologic disorders. Dr. Ellenbogen's research was supported by the National Institutes of Health and the University of Pennsylvania's Nassau Undergraduate Research Fund. ■

Depressive Symptoms, Not Hostility or Anxiety, Link to CAD

Depressive symptoms appear to correlate with the development of coronary artery disease, but hostility and anxiety may not, Jesse C. Stewart, Ph.D., and his associates reported.

Several studies have linked various negative emotions with the development of coronary artery disease in initially healthy subjects. But teasing out the relative contributions of depression, anxiety, and hostility has been difficult because they tend to overlap. Dr. Stewart and his associates of the University of Pittsburgh assessed a wide range of such symptoms in a prospective cohort study of subclinical atherosclerosis in healthy subjects aged 50-70 years.

The 324 subjects underwent ultrasonographic assessment of carotid intimal medial thickness (IMT), a noninvasive measure of subclinical atherosclerosis, as well as tests evaluating emotional factors, including the Beck Depression Inventory, the Beck Anxiety Inventory, the Cooke-Medley Hostility Scale, and the State-Trait Anger Expression Inventory.

During 3-year follow-up, only mild to moderate depressive symptoms correlated with the decreasing carotid IMT that signals progression of subclinical atherosclerosis. Hostility symptoms of anxiety, the experience of anger, and the expression of anger showed no correlation with carotid IMT change.

This study is the first ever to report an association between depressive symptoms and carotid IMT change, the investigators said (Arch. Gen. Psychiatry 2007;64:225-33).

The exact mechanism underlying this association is unclear, but depression is known to affect physiologic pathways also involved in atherosclerosis, such as autonomic nervous system dysfunction, hypothalamic-pituitary-adrenal axis dysregulation, inflammatory processes, and altered platelet function, they said.

A post hoc analysis of the data showed that IMT worsening was associated with somatic-vegetative symptoms of depression such as fatigue, sleep disturbance, loss of appetite, and anhedonia, but not associated with more cognitive-affective depressive symptoms such as sadness, pessimism, discontent, or indecisiveness.

—Mary Ann Moon

EVIDENCE-BASED PSYCHIATRIC MEDICINE

Neurocognitive Effects of Sleep Apnea

The Problem

You have a patient with an obvious high body mass index. His spouse tells you that he snores and experiences brief episodes of apnea. Polysomnographic recordings confirm a diagnosis of obstructive sleep apnea (OSA). You try to educate him to the sequelae of OSA.

The Question

What is known about the potential neurocognitive consequences of OSA?

The Analysis

First, we searched the Cochrane Database of Systematic Reviews (www.cochrane.org/reviews) but found no review articles on this topic. We then performed a Medline search that combined "sleep apnea" and "cognitive, or cognition."

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The Evidence

OSA is characterized by repetitive and transient upper-airway obstructions during sleep. Obstructions can be complete (apnea) or partial (hypopnea). OSA affects medical disorders such as hypertension, coronary artery disease, and diabetes mellitus (Cleve. Clin. J. Med. 2007;74:72-8). OSA also affects psychiatric disorders such as depression and anxiety, and—in children—hyperactivity and lowered IQ (Int. Rev. Psychiatry 2005;17:277-82). OSA has been estimated to occur in 2%-3% of children and adults (Curr. Opin. Pulm. Med. 2005;11:494-500).

Our search yielded a recently published review article (Acta Neurol. Scand. 2007;115:1-11). The authors first reviewed a number of studies showing common cognitive deficits in attention, concentration, vigilance, memory, and learning ability secondary to OSA. They then focused on the effects of OSA on executive functions, which they defined as a person's ability to respond in an adaptive manner to situations and to engage successfully in independent, purposive, and self-serving behavior. Executive functions are important in behavioral inhibition; set-shifting; self-regulation of affect; memory; and analysis/synthesis.

In all, 40 studies were included. The number of patients ranged from 8 to 199 (median, 24). Of these studies, 19 had fewer than 24 patients. Ages ranged from 40 to 65 years (median, 49 years). Education ranged from 9 to 15 years (median, 13 years), but only half of the studies reported education levels. The proportion of men ranged from 47% to 100%, and in 83% of the studies the patient group consisted of more than 75% men.

A control group was included in 31 of these studies. In 15 studies, a healthy control group was used, although only nine studies confirmed health by polysomnography; in six studies, heavy nonapneic snorers or patients with dementia, chronic obstructive pulmonary disease, or carbon monoxide poisoning were used; and in 10 studies, OSA patients receiving continuous positive airway pressure (CPAP) treatment were compared with OSA patients receiving placebo or conservative treatment.

The duration of CPAP treatment ranged from 1 week to 12 months (median, 8 weeks), with a median compliance with therapy of 5.3 hours per night. Twelve different standardized neuropsychological tests of executive functions were used. The number of tests applied varied from one or two tests in 20 studies to nine tests in three studies. Patient samples were mostly heterogeneous with respect to OSA severity.

In studies comparing healthy controls with OSA patients, the domains of executive function impairment were working memory, phonologic fluency, cognitive flexibility, and planning. CPAP treatment was shown to improve cognitive flexibility and planning, but deficits of working memory persisted after CPAP treatment, and only one study reported improvement in phonologic fluency. (The authors thought that it would be misleading to compare OSA patients with other patient groups, such as dementia patients, because cognitive defects are common sequelae of both groups.)

The Conclusion

The best available evidence shows that obstructive sleep apnea negatively affects numerous cognitive/executive functions, such as working memory (a system for temporarily storing and managing information required to carry out complex tasks, such as learning, reasoning, and comprehension); phonologic fluency (the ability to access verbal memory and retrieve words rapidly); cognitive flexibility (the ability to manage more than one aspect of a task at one time); and planning. Only some of these impairments—cognitive flexibility and planning—are reversible with CPAP.

These conclusions should be tempered by the limitations of the study. Of the 40 studies, 19 had fewer than 24 patients, and only one-half of the studies indicated patient education level. Level of education is an important variable affecting cognitive test performance, because high intelligence may protect against OSA cognitive impairment. Also, samples consisted mainly of men, and study groups were heterogeneous in terms of severity; the number of patients in different severity groups was not reported.

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