

Sleep Loss Tied to Impaired Glucose Tolerance

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RANCHO MIRAGE, CALIF. — Healthy young adults who are chronic “short sleepers”—getting an average of about 5 hours of sleep a night—must secrete 30% more insulin than other adults to achieve a normal glucose curve.

The finding, which points to a potentially important connection between sleep, diabetes risk, and obesity, was just one of a series of observations made during detailed sleep studies conducted at the University of Chicago in recent years and presented by Eve Van Cauter, Ph.D., a professor of medicine at the university.

Sleep deprivation leads to decreased levels of the satiety hormone leptin, increases in the hunger hormone ghrelin, and impaired glucose tolerance, Dr. Van Cauter and associates discovered when they created a “sleep debt” in healthy adults by restricting the number of hours they slept, she said at a conference on sleep in infancy and childhood sponsored by the Annenberg Center for Health Sciences.

“In 1 week of sleep restriction, we brought volunteers to a prediabetic state. That was kind of a frightening thought,” she said in describing one of her early studies into the metabolic and endocrine consequences of too little sleep (*Lancet* 1999;354:1435-9).

One of the first consequences of sleeplessness is appetite dysregulation, the study showed. “Essentially, the accelerator for hunger [ghrelin] was pushed and the brake for satiety [leptin] was released,” she explained. “The leptin levels are screaming ‘More food! More food!’”

Sleep-deprived volunteers—even those receiving consistent and adequate amounts of energy via intravenous glucose—become famished, particularly craving high-carbohydrate foods such as candy, cookies, potato chips, and pasta.

“We have two studies suggesting that if you have a sleep debt, you might be less able to control hunger,” she said at the meeting.

To study glucose tolerance and sleep, Dr. Van Cauter and her associates recently recruited 44 lean, healthy young adults, half of whom were chronic short sleepers who averaged 5 hours, 16 minutes of sleep a night, and half of whom averaged 7 hours, 52 minutes of sleep per night. The subjects were stratified by diabetes risk according to their ethnicity and family history of the disease.

“We found a clear relationship between sleep duration and insulin sensitivity. The short sleepers had lowered insulin sensitivity and the longer sleepers had higher insulin sensitivity, but the relationship was really only significant in those with a low ethnicity-based diabetes risk,” she said.

Further statistical tests revealed significant differences in insulin sensitivity associated with both ethnicity-based diabetes risk and sleep duration. For young healthy subjects in their 20s who were considered to be at low risk for diabetes, the impact of sleep deprivation on insulin sensitivity was profound, placing them in a risk category similar to that of Mexican

Americans or 61- to 80-year-olds.

Dr. Van Cauter noted that sharply rising curves in the prevalence of obesity in the United States since the 1960s mirror reverse curves in the amount of sleep Americans get—the smallest amount in the industrialized world.

“I’m not saying that sleep curtailment, which is an increasingly prevalent behavior, is the cause of rising rates of obesity, but certainly, it hasn’t helped,” she said.

An ongoing study is attempting to de-

termine whether sleep recovery can improve glucose tolerance among chronically sleep-deprived patients who already have impaired insulin sensitivity. Chronic short sleepers between 35 and 41 years old spend 10 hours per night in a darkened sleep laboratory for 8-10 nights.

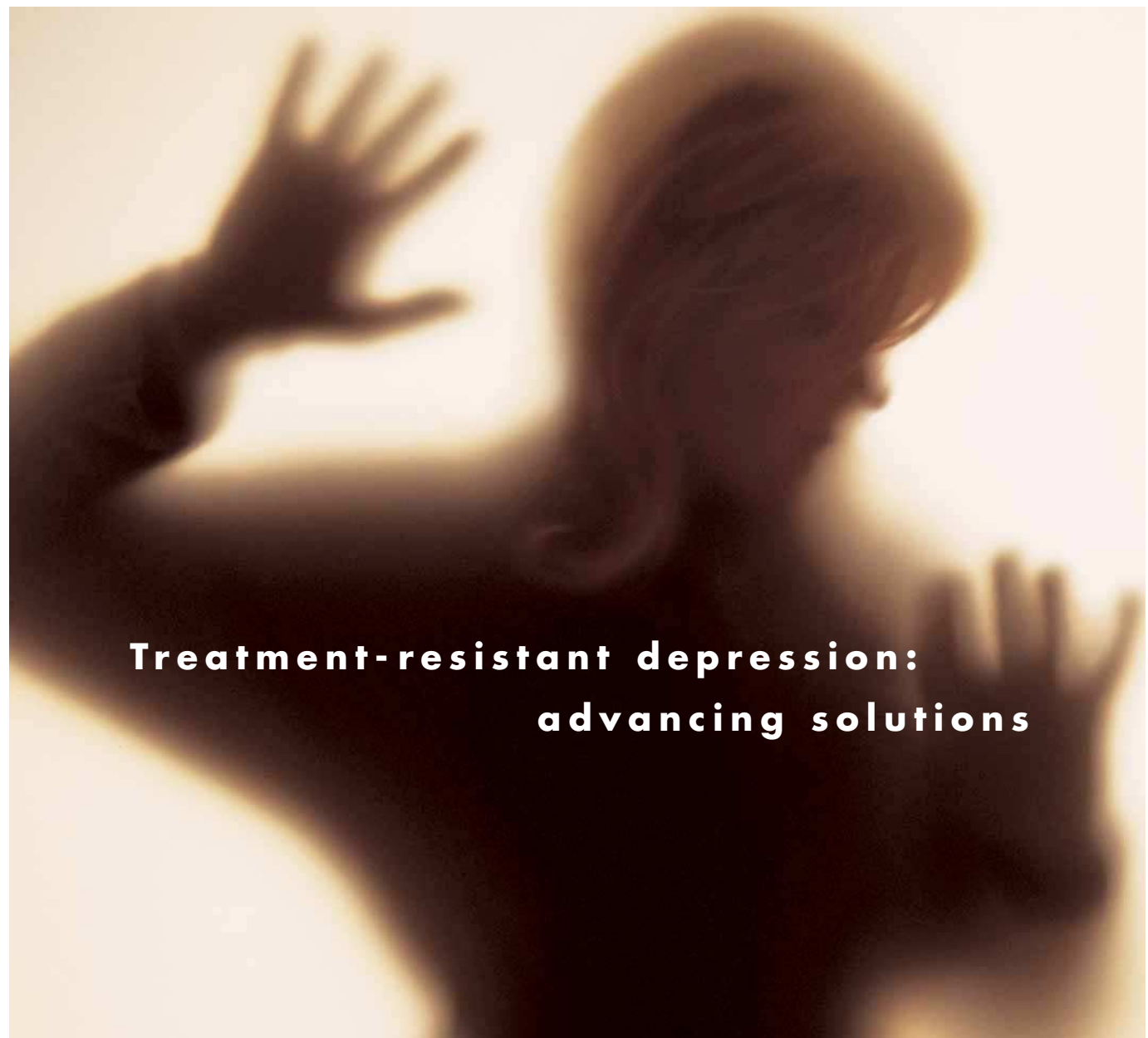
“You have to pay them,” she observed, noting that for many Americans, shortened sleep is a way of life.

Early results suggest that a longstanding sleep debt cannot be recovered in some

short sleepers, who remain awake most of the hours they spend in laboratory-imposed darkness.

However, chronically sleep-deprived subjects who do extend their sleeping time show a rapid and impressive improvement in glucose tolerance, particularly at the 90-minute mark in glucose tolerance tests.

The average improvement of 25 mg/dL “is about what you can get with an antidiabetic drug like Metformin,” she said. “We’re pursuing this vigorously.” ■



Treatment-resistant depression: advancing solutions

The challenge treatment-resistant depression (TRD) poses to physicians and patients is universally acknowledged. Patients with TRD are twice as likely to be hospitalized,¹ make more outpatient visits,¹ consume over six times more healthcare utilization costs,¹ and are at greater risk of suicide than patients who experience sustained efficacy.²

After one or two prior episodes of depression, patients have a 50% to 90% risk of another

episode,³ which is often of longer duration, more severe, and less responsive to treatment.³ Long-term outcomes may be even worse than those reported in clinical trials, with the percentage of patients who get well and stay well falling as low as 35%.²

Given that patients with TRD require long-term or lifelong treatment,⁴ there remains the need for a more tolerable therapy that provides antidepressant and quality-of-life efficacy shown

to improve over time and to be sustained long-term. Despite the many therapeutic options available, the prevalence and implications of TRD highlight the urgency of exploring new therapies with unique mechanisms of action. In collaboration with psychiatry, Cyberonics is committed to search for more effective and tolerable long-term solutions.

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References: 1. Crown WH, Finkelstein S, Berndt ER, et al. The impact of treatment-resistant depression on health care utilization and costs. *J Clin Psychiatry*. 2002;63:963-971. 2. Fava M, Rush AJ, Trivedi MH, et al. Background and rationale for the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study. *Psychiatr Clin N Am*. 2003;26:457-494. 3. Zajecka JM. Clinical issues in long-term treatment with antidepressants. *J Clin Psychiatry*. 2000;61(suppl 2):20-25. 4. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder (revision). *Am J Psychiatry*. April 2000;157(suppl):1-45.

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