RESEARCH HIGHLIGHT

Less Sleep, Disrupted Internal 24-hour Clock Means Higher Risk of Diabetes and Obesity

Orfeu M. Buxton, Ph.D., Brigham and Women’s Hospital

A study led by Orfeu M. Buxton, PhD, at Brigham & Women’s Hospital reinforces the finding that too little sleep or sleep patterns that are inconsistent with our body’s “internal biological clock” may lead to increased risk of diabetes and obesity. Related findings have been seen in short-term lab studies and in epidemiological studies of nightworkers. However, unlike epidemiological studies, this study provided direct causal support for a role of sleep and circadian rhythms in cardiometabolic disease by examining humans in a controlled lab environment over a prolonged period while reducing the amount of sleep, altering the timing of sleep, and disrupting internal circadian (24-hour) rhythms.

The study was electronically published on April 11, 2012, in Science Translational Medicine.

Researchers hosted 21 healthy participants (11 younger participants and 10 older) in a completely controlled environment at the Harvard Catalyst Clinical Research Center at Brigham & Women’s Hospital (HCCRC @ BWH) for nearly six weeks. Participants were screened to ensure that they were healthy and free of any disorders of sleep, circadian rhythms or metabolism. Before their admission to the HCCRC @ BWH, participants were instructed to spend 10 hours in bed each night and have normal exposure to daylight for a period of three weeks. Once on the research unit, the researchers controlled how many hours of sleep participants got, as well as when they slept, and other factors such as activities and diet.

Participants started by getting optimal sleep (approximately 10 hours per night). This was followed by three weeks of 5.6 hours of sleep per 24-hour period and with sleep occurring at all times of...
Medical Device Development Course
Do you have an idea for a new medical device or ideas on how to improve an existing device? Do you have the engineering expertise to build a device but need more business or medical acumen to move forward? Do you need help anticipating and navigating the regulatory and other key issues associated with creating a medical device or new technology, and bringing an innovation to market? Medical Device Development, will begin with a symposium on October 3, 2012, that will give an overview of the process of developing a medical device. The one-day intensive course, held the next day on October 4, 2012, will cover the process of identifying novel technologies, improving existing medical devices and technologies, and planning and executing pre-clinical and clinical studies through licensing and commercialization. Applications are due by 5pm on August 2, 2012.
http://catalyst.harvard.edu/services/rcdc/device.html

Childhood Obesity Pilot Grant Opportunity
The Harvard Catalyst Community Health Innovation and Research Program (HC-CHIRP), in collaboration with the Programs on Health Disparities Research and Child Health, invites researchers from all Harvard schools and affiliated institutions to apply for funding to support innovative, interdisciplinary research to improve the prevention of childhood obesity in the context of health systems reforms. Funding is available for direct costs of up to $50,000 for one year. Proposals must address one or more of the five substantive categories: 1) Strengthening the capacity of state systems to implement and evaluate evidence-based policy; 2) Reducing the consumption of sugar-sweetened beverages; 3) Policies and interventions in families and early childhood settings; 4) Innovative collaborations with industry; 5) Socio-cultural aspects of the food and physical activity environment. Applications are due by 5pm on August 9, 2012.
http://catalyst.harvard.edu/services/pilotfunding/childhood-obesity.html

Introduction to Clinical Investigation
Introduction to Clinical Investigation course offers an introduction to the skills necessary to embark on a career in clinical research. By providing a survey experience in core competency areas using a mixture of didactic lectures and workshops, attendees will be challenged to move beyond rote repetition of learned material. Participants will enhance their ability to analyze, synthesize, and evaluate data along the translational research continuum of: T1 (first-in-human/proof of concept research); T2 (definitive clinical trials to change the standard of care); T3 (practice-based research); and T4 (population-based research). Applications are due by 5pm on September 6, 2012.
http://catalyst.harvard.edu/services/ici/

Pan-Massachusetts Clinical and Translational Science Award CRC Symposium
The Nursing, Administration and Metabolism & Nutrition Research Directors of Harvard Catalyst, Tufts University, Boston University and the University of Massachusetts-Worcester Clinical Research Centers (CRCs) convened at Harvard on June 8, 2012 for the Pan-Massachusetts Clinical and Translational Science Award (CTSA) CRC Leadership Symposium to identify best practices and commonalities between centers. For the first time since the inception of the CTSA operational leadership came together to compare metrics and organizational tools across the centers with the aim of identifying shareable best practices.

The symposium opened with a powerful keynote presentation by a team of a PI, Research Nurse and Dietitian who together, are safely testing the hypothesis that chronic antigen exposure during peanut oral immunotherapy (OIT) will induce beneficial changes in the specific immune response in children. The MGH-based keynote speakers represented the crucial collaboration between investigators and CRC nurses and nutritionists to create the right environ-
CRC updates

HCCRC Metabolism & Nutrition Research Presented at Translational Science 2012

Joanna Radjewski, MS, RD, and Ellen J. Anderson, MS, RD, Directors of Metabolism & Nutrition Research at Beth Israel Deaconess Medical Center and Massachusetts General Hospital, respectively, presented “Nutrition Workload Levels Across Harvard Catalyst Clinical Sites” at the Translational Science 2012 meeting in Washington, D.C. to their gathered peers from across the CTSAs.

They presented the HCCRC nutrition workload project which established a common matrix for comparability of services across the Harvard Catalyst CRC sites. The April 2012 presentation was attended by research dietitians from CTSAs across the United States and physicians interested in nutrition services that facilitate individual research projects. Session participants discussed the specialized role of nutrition services in research and how best to communicate research dietitian expertise. In addition, the session presented an opportunity to share the challenges faced with the NIH’s new grant structure and requirements.

The Translational Science Annual Meeting welcomed individuals engaged in clinical and translational research in-

HCCRC METABOLISM AND NUTRITION RESEARCH DIRECTORS

Nutrition Directors from Harvard Catalyst Clinical Research Centers, from left to right, Joanna Radjewski, MS, RD, LDN, Nicolle Quinn, MS, RD, LDN, Janis Swain, MS, RD, and Ellen Anderson, MS, RD, LDN. Photo: Kerry Foley

Open House at MIT

The Harvard Catalyst Clinical Research Center @ MIT held an open house on May 30th to introduce the MIT community to its new home. Attended by over 50 people, the open house offered tours of the new facility’s biomedical and nursing areas, behavioral testing rooms, and testing observation rooms. Visitors also engaged in informal Q&As about the research services available to all members of and collaborators with the MIT community. The HCCRC@MIT offers assistance with behavioral and biomedical aspects of human research studies, including staff and facilities for nursing needs and advanced behavioral and neuropsychological testing of adults and children. Anyone interested in using the HCCRC@MIT services and facilities for upcoming studies is welcome to email crc-info@mit.edu, call 617-253-6331, or visit http://crc.mit.edu/ for more information.

Unit Coordinator Wins Spirit Award

The Harvard Catalyst Clinical Research Center @ BIDMC cheered on Claire Migliero, HCCRC @ BIDMC Scheduler, as she received the Spirit Award at BIDMC. Claire was awarded because of her positive outlook, enthusiasm, and accountability to the CRC. Her presence at the CRC made a significant impact and was celebrated by both her colleagues and the investigators that work there.

SPIRIT OF CLINICAL RESEARCH

Claire Migliero, center, won the Spirit Award at Beth Israel Deaconess Medical Center. Celebrating with her are colleagues (from the left) Audrey Nathanson, RN, Santiago Mandi, RN, and Linda Godfrey-Bailey, MSN, ACNS, BC. Photo: BIDMC News
LESS SLEEP: CONTINUED FROM PAGE 1

day and night on a 28-hour “day”: subjects got up 4 hours later each day, like travelers moving four time zones west each day. Thus, during this period, there were many days when participants were trying to sleep at unusual times within their internal circadian cycle—the body’s “internal biological clock” that regulates sleep-wake and many other processes within our bodies. The study closed with the participants having nine nights of recovery sleep at the usual circadian time. While awake, participants were allowed to read, write, play board or card games, view movies, do arts and crafts, and perform mild stretching (exercise was not allowed). During the entire study, participants were monitored by technicians either through closed-circuit cameras or direct observation to ensure they stayed awake when they weren’t scheduled to sleep.

The main metabolic challenge was the response to a standardized meal in each of the three conditions: a well-rested baseline, following prolonged exposure to a prior history of circadian disruption and sleep restriction, and after recovery/realignment. Crucially, the metabolic tests were conducted at the same internal circadian time of day, so these meals were all in the biological “morning”, the time we are at our metabolic best. In an earlier study by Frank Scheer and colleagues also conducted in the BWH CCI/CRC, meals eaten during the biological night, or during acute circadian misalignment common in nightworkers, can lead to a pre-diabetic state. This current study thus controlled for circadian phase to instead test the independent effects of prior circadian disruption. The researchers also tested resting metabolic rate (the amount of calories of fuel burned at rest, without exercise), and a variety of fasting and 24-hour hormonal profiles.

The researchers saw that prolonged sleep restriction with simultaneous circadian disruption led to increased glucose concentrations in the blood after the identical meals. This was because of unexpectedly poor insulin secretion by the pancreas. Increased glucose concentration and poor insulin secretion could lead to an increased risk for diabetes. Results were similar in both age groups and showed no differences due to sex. Fortunately, all subjects recovered when they had a chance to catch up on sleep with their circadian rhythms back in synch.

Furthermore, the exposure to prolonged sleep restriction with simultaneous circadian disruption decreased the participants’ resting metabolic rate. According to the researchers, a decreased resting metabolic rate could translate into a yearly weight gain of over 10 pounds if diet and activity are unchanged.

These results support the findings from studies showing that, in people with a pre-diabetic condition, night workers are much more likely to progress to frank diabetes than day workers. Since night workers often have a hard time sleeping during the day, they can face both circadian disruption working at night and insufficient sleep during the day. The evidence is clear that getting enough sleep is important for health, and that sleep should be at night for best effect.

This research was supported by a National Institute on Aging Program Project grant (Charles A. Czeisler, PI); additional support came from National Heart, Lung and Blood Institute; National Center for Research Resources; Center for Clinical Investigation of the Harvard Clinical and Translational Science Center; Joslin Diabetes and Endocrinology Research Center Service Specialized Assay Core; the National Space Biomedical Research Institute; and Natural Sciences and Engineering Research Council of Canada.

Orfeu M Buxton, Sean W Cain, Shawn P O’Connor, James H Porter, Jeanne F Duffy, Wei Wang, Charles A Czeisler, Steven A Shea. Adverse Metabolic Consequences of Chronic Sleep Restriction Combined with Circadian Misalign-

SYMPOSIUM: CONTINUED FROM PAGE 2

ment for new clinical and translational discoveries. Principal Investigator Wayne Shreffler, MD, PhD, Director, Food Allergy Center and Section Chief, Pediatric Allergy & Immunology, along with Clinical Research Nurse Catherine Griffin, PhD(c), RN, ACNP-BC, and Research Dietitian Joshua Holewinski, MS, RD, LDN, together presented on 'Implementing PNOIT at the MGH CRC'. This study at Massachusetts General Hospital targets pediatric study subjects with a diagnosis of peanut allergy and a history of clinical symptoms – a delicate population who need the combined nursing and nutritional resources, technology and expertise to minimize the risks of exposure to controlled dosages of peanut flour. Their presentation is will be available soon on the Harvard Catalyst portal website.

The Nurses, Administrators and Nutritionists first gathered in functional group roundtables to discuss the breakout topics but later combined for a robust discussion culminating in a thoughtful compilation of the key initiatives each center implemented to adapt and grow their resources and services to meet investigator needs while faced with fixed budgets. Symposium attendees planned to reconvene, by institutional group, to discuss the ideas with the faculty leadership of their CRCs. The next step for the pan-Massachusetts group is to work with operational leaders from the CTSAs of the New England region to convene a larger gathering in 2013.