



## CNRC RESEARCHERS FIND LINK BETWEEN SLEEP DISRUPTION AND OBESITY IN MICE

Disruption to regular sleep cycles may contribute to the dramatic increase in obesity in the United States, but the biological mechanism underlying this has remained a question.

In a recent study, researchers at the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine have found that disruption of circadian rhythm, or sleep disruption, affects regulation of a hormone called leptin—a key hormone involved in weight regulation. The study appeared in the journal *Cell Metabolism*.

“Our findings uncover a mechanism by which circadian disruption may promote obesity even in people who are eating a healthy diet,” said Dr. Loning Fu, assistant professor of pediatrics at the CNRC. “They suggest that avoiding frequent disruption of the sleep cycle may be important for avoiding obesity and maintaining a normal body weight.”

Researchers found that frequent sleep disruption leads to changes in how the brain senses leptin—a so-called “neuroendocrine dysfunction.” In particular, it disrupts the proper levels of leptin in the blood. Leptin is produced by fat tissue, and its levels increase when fat storage increases (i.e. in obesity). Additionally, like many other hormones, its levels vary over the normal 24-hour circadian cycle. Leptin normally interacts with a brain center called the arcuate nucleus, where it acts to decrease food intake and stimulate energy expenditure. Thus, leptin decreases fat mass, in a normal feedback loop that helps to maintain stable body weight.

If the brain loses its sensitivity to leptin, the brake on fat storage is lost and excess fat accumulates. This is called leptin resistance, which is a hallmark of obesity in humans.

This study showed that frequent disruption of circadian rhythm in mice inhibits leptin function in the arcuate nucleus, even when blood leptin levels are very high. This results in an increase in fat storage and the development of obesity, even in mice eating a normal healthy diet, Fu said.

“Previous reports have described the phenomenon of leptin resistance in obese humans and mice, and also have found that circadian disruption causes weight gain in both



## SUMMER CAMP FOR OVERWEIGHT KIDS SHOWS LONG-TERM SUCCESS

Kamp K'aana, a fun-based weight management camp for overweight and obese children ages 10 to 14, is about to celebrate its 10th anniversary, and researchers at the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine report that it's having a long-term impact on participants.

Developed by Baylor, Texas Children's Hospital and Camp Cho Yeh and now managed by the YMCA, Kamp K'aana is a two-week, sleep away camp that includes physical activities such as swimming, horseback riding, pedal cars, soccer, basketball, lake fun, paint ball, ropes courses, a rock wall and zip lining.

In addition, for one hour a day, children receive a lesson from health educators using a curriculum designed by a multi-disciplinary team of experts on how to achieve a healthy lifestyle. A healthy meal that includes a new fruit or vegetable is served each day. Parents take part in education sessions on the first and last days of camp. Additionally, families attend two follow-up reunions three and six months after camp to reconnect and reinforce lessons learned.

“Overweight and obese children are known to have low self-esteem,” said Dr. William Wong, professor of pediatrics at the CNRC who developed the program and is one of the recent study's authors. “The summer camp program offers a nurturing environment and activities that promote confidence. We strongly believe that unless children can feel good about themselves, they are not going to have any motivation to achieve a healthy lifestyle that could last for a lifetime.”

# GUT MICROBIOME COMPOSITION HELPS WITH UNDERSTANDING OF CHRONIC ABDOMINAL PAIN IN CHILDREN

For many years, all bacteria were considered to be bad for one's health, but we now know that there is such a thing as good bacteria. In particular, good bacteria in the gut are very important in helping our immune system develop and remain healthy. Researchers at the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine are conducting studies to understand how the bacteria in the gut and the DNA within the bacteria, together known as the gut microbiome, work in children with chronic abdominal complaints. Three separate studies were recently published on this topic.

Dr. Robert J. Shulman, professor of pediatrics at Baylor and the CNRC, and colleagues focused on understanding the gut microbiome of children between 7 and 12 years, the ages during which chronic abdominal problems first appear. In their first study, published in *Microbiome*, they focused on examining the gut microbiome composition in healthy children and compared it to adults.

The study, conducted by Shulman, Dr. Emily Hollister and colleagues, showed that even in children between 7 and 12 years of age, the composition of the gut microbiome was not the same as the composition in adults, contrary to what was previously thought.

"This appears to be an age when the gut microbiome is still transitioning into 'adulthood,'" said Shulman.

Researchers also found differences in the composition of the gut microbiome in children who had chronic abdominal pain problems compared with healthy children of the same age and gender.

"So we wondered whether or not treatment would be affected by the gut microbiome composition," said Shulman.

This was the focus of another study, published in *Alimentary Pharmacology and Therapeutics*, with Dr. Bruno Chumpitazi as lead author. There have been a number of different treatments that people have employed to try to help children with chronic abdominal pain. Recently, one of these has focused on changing their diet by removing certain types of sugars and carbohydrates. This is referred to as the low FODMAP (Fermentable Oligo-Di-Monosaccharides and Polyols) diet.

The study found that those children who did not improve when fed the low FODMAP diet had a lower abundance of bacteria capable of breaking down sugars and those who did respond to the diet had a higher abundance of bacteria that could digest the sugars.

"The FODMAP diet is not easy to follow so this opened up the potential to be able to identify which kids would respond to the diet so that those kids could be put on the diet and those kids unlikely to respond need not. We could personalize this treatment," said Shulman.

In the final study, published in the *Journal of Parenteral and Enteral Nutrition*, Shulman, Dr. Zev Davidovics,



and colleagues studied children who had short bowel syndrome. Some infants have to have a large portion of their intestines removed because they are born with congenital problems or have had diseases that cause irreversible damage to the intestines. This radically upsets the normal functioning of the intestine and many children have to receive specialized or intravenous nutrition to maintain their health. One of the problems these individuals are susceptible to is having bacteria leak from their intestine into their bloodstream, causing infections.

This preliminary study showed what kind of changes occurred to the gut microbiome in individuals with short bowel syndrome to better understand why certain bacteria are able to leak into the bloodstream. They found that the gut microbiome differed in children who had short bowel syndrome compared to healthy children. Those with short bowel syndrome had a higher percentage of bacteria that are known to cause disease in people.

"The condition of short bowel syndrome appeared to promote the growth of bacteria that are potentially disease causing as opposed to those bacteria that are most associated with health," said Shulman.

The next stage of Shulman's research is to look at the connection between chronic abdominal pain problems in children and low grade inflammation in their intestines. They suspect that this low grade inflammation might be related to alterations in the gut microbiome composition.

The microbiome studies are being done in collaboration with the Texas Children's Hospital Microbiome Center under the direction of Dr. James Versalovic with the assistance of Drs. Ruth Ann Luna, Tor Savidge, and Numan Oezguen. Dr. Hollister also is a faculty member of the Microbiome Center and Dr. Chumpitazi is a member of the pediatric gastroenterology, hepatology and nutrition section of Baylor College of Medicine. Dr. Davidovics is an assistant professor of pediatrics at the University of Connecticut School of Medicine.

The work was supported in part by R01 NR05337, UH3 DK083990, and K23 DK101688 from the National Institutes of Health, the USDA/ARS No. 6250-51000-057-02S, and P30 DK56338 which funds the Texas Medical Center Digestive Disease Center.

## SLEEP DISRUPTION AND OBESITY (CONTINUED FROM PAGE 1)

species. Our study is one of the first to connect these very different observations by showing that circadian disruption directly causes leptin resistance,” she said.

This points to the importance of our body’s internal function in weight control, in addition to external variables like diet and physical activity.

“Current diet and exercise programs for overweight individuals, especially for school children, are often inefficient for maintenance of long-term weight loss because the role of endogenous physiology in weight control is not taken into consideration,” Fu said. “Our discovery may lead to the design of more efficient programs for body weight control by decreasing the risk of both external and internal obesity risk factors for all age groups. However, adolescents may benefit most from our discovery because, compared to adults, adolescents experience a higher risk of lacking hormonal stability and often experience sleep disruption.”

Others who contributed to this study include Nicole Kettner, Sara Mayo and Jack Hua, all of the CNRC; David Moore of the department of molecular and cellular biology at Baylor College of Medicine; and Choogon Lee of Florida State University.

Support for the research came from the National Institutes of Health and the U.S. Department of Agriculture.



## SUMMER CAMP (CONTINUED FROM PAGE 1)

A recent study on the program, published in the *Journal of Pediatric Gastroenterology*, looked at long-term (11 month) outcomes of weight and BMI.

Previous studies had already determined the success of the program in the short and intermediate term. At two weeks postcamp, there was a reduction in weight and body mass index (BMI) and fat mass among participants, with an increase in lean body mass, indicating that the campers were losing body fat and increasing muscle. They also had improved self-esteem and quality of life scores. After three months, the new weight status was maintained on average and the self-esteem scores further improved.

The long-term study found that, on average, the reductions in BMI percentile and BMI z-score, which are measures of body weight that take into account height and age, remained significantly improved compared with initial measures. Some campers continued to have not just maintenance of BMI percentile or z-score but further improvement.

“We know that a two-week camp is not enough to move from obesity to healthy weight, but our hope has been that it is a jumpstart,” said Dr. Sarah Barlow, associate professor of pediatrics at Baylor and director of the Center for Childhood Obesity at Baylor and Texas Children’s Hospital and a study co-author. “The campers have a positive experience of healthy living that motivates them to bring those

skills home. And this study shows that this experience was successful.”

The program is an important example of a healthcare-community partnership—most of the campers heard about the program from healthcare offices. Also significant is that campers in the program to date were predominantly non-white and at least half were low-income, a population that can have difficulty accessing typical intensive nutrition programs.

**Kamp K’aana will be held this year from June 12–25, at the YMCA of Greater Houston Camp Cullen. To be eligible for this specialty camp, children must be in the 95th percentile of BMI for their gender and age. Find more information online at [www.kampkaana.org](http://www.kampkaana.org).**

Others who took part in the study include Alicia Farhat, North Texas Food Bank, Dr. Shreela Sharma, University of Texas School of Public Health, and Dr. Stephanie Abrams, Children’s Gastroenterology MCSG, Long Beach, Calif.

## NUTRITION & YOUR CHILD

is published quarterly by Baylor College of Medicine as a research and information update for the general public and Center volunteers and supporters. Send comments or change of address information to

### Children's Nutrition Research Center

1100 Bates Street  
Houston, TX 77030-2600  
cnrc@bcm.edu  
www.kidsnutrition.org

### Center Director

Dennis M. Bier, M.D.

### Publication Advisors

Janice C. Baranowski, M.P.H., R.D.  
Nancy F. Butte, Ph.D.  
Marta L. Fiorotto, Ph.D.  
Karen W. Cullen, Dr.P.H., R.D.  
Teresia Margareta O'Connor, M.D., M.P.H.  
Stephanie Sisley, M.D.  
Janice E. Stuff, Ph.D., R.D.  
Robert A. Waterland, Ph.D.

### Editors

Dipali Pathak and Dana Benson  
Office of Communications &  
Community Outreach  
Baylor College of Medicine

The Children's Nutrition Research Center is operated by Baylor College of Medicine, in cooperation with Texas Children's Hospital, for the Agricultural Research Service of the United States Department of Agriculture.

## Join a CNRC Nutrition Study!

Houston-area residents are invited to participate in the following nutrition research projects designed to help CNRC scientists learn more about the nutritional needs of children. Free parking is provided. For most studies, financial compensation is provided and transportation may be available.

### FOR MORE INFORMATION ON ANY OF THE FOLLOWING CNRC NUTRITION STUDIES,

contact Marilyn Navarrete at 713.798.7002 or rilynn@bcm.edu.



## VOLUNTEERS

### Adult Volunteers Needed

**H-34291** Healthy, overweight volunteers aged 18 to 65 and volunteers diagnosed with type 2 diabetes within the last three years, also aged 18 to 65, are needed for a metabolic study. These volunteers will help researchers determine whether healthy volunteers, type 2 diabetics and ketosis-prone diabetics make an important compound called arginine in different amounts. Healthy, overweight volunteers should have no chronic medical conditions and all who reply should consume a diet adequate in calories and protein. Women must not be pregnant.

### Baylor Infant Twin Study (BITS)

**H-36097** Do you expect or have twins less than 4 months of age? We are seeking twin infants for a research study being conducted on twins from 4 months through 3 years of age to learn more about infant and child feeding and behavior. Two visits are required at the Children's Nutrition Research Center and other visits are conducted by mailed questionnaires.

### Children's Physical Activity in the Neighborhood H-34292

Researchers at Baylor College of Medicine want to study how neighborhoods influence young children's physical activity. If you enroll, your child will be asked to wear activity monitors and a

location monitor for 3 hours (one time only). Your child will be asked to perform a series of tasks at your home and neighborhood with the assistance of a research staff member. The child's parent has to be with him/her at all times. Study requirements are healthy children ages 3 to 5 years old, family owns a car with child car seat, parent has a valid driver's license.

**Fatty Liver H-31469** 11- to 21-year-old overweight adolescents and young adults with and without liver disease are needed for a research study investigating risk for early heart disease in youth. Study involves body composition, liver scan and blood tests.

**Newborn Colic H-35001** Do you have a baby with fussiness? Gas? Spitting up? Tummy pain? Trouble with bowel movements? Researchers at Texas Children's Hospital and Baylor College of Medicine are seeking infants between 14 and 28 days of age for possible participation in a feeding study. You must be able to read and understand English and have telephone access to be eligible.

**SEEDS H-28013** Ayuda a los científicos aprender sobre las experiencias alimenticias de los niños con su participación en clases educativas y actividades alimenticias con otras familias. Todas las madres serán recompensadas por su tiempo en cada día de pruebas. Las clases se llevarán a cabo en el código postal 77016, 77022, 77039, 77044, and 77093.

**Teen Heart Health H-30665** 13- to 18-year-old adolescents and young adults (normal weight and overweight) with and without type 2 diabetes are needed for a research study investigating risk for heart disease in youth. Study involves body composition, heart scan and blood tests.