Unsuspected brain region involved in side effects of diabetes drug

By GILA Z. RICKES

A brain region involved in emotional and intellectual processes appears to also play an unsuspected role in the body's visceral response to dangerously low blood sugar levels, according to a School of Medicine researcher.

Low blood sugar, called hypoglycemia, is a common and dangerous side effect of drugs that control insulin levels in people with diabetes.

The findings were recently published in the online version of the Proceedings of the National Academy of Sciences.

Philip E. Cryer, M.D., the Irene E. and Michael M. Karl Professor of Endocrinology and Metabolism, and William J. Powers, M.D., professor of neurology, neurological surgery and radiology, led the study.

According to Cryer, drugs that help keep blood sugar levels low often cause them to drop too fast. The average person undergoing treatment for type 1 diabetes will experience symptoms of hypoglycemia about twice a week, with one episode of severe, temporarily disabling hypoglycemia per year.

It also is a significant problem in people with advanced stages of type 2 diabetes.

"Hypoglycemia is the most difficult obstacle to the management of blood sugar in people with diabetes," Cryer said. "To treat diabetes, you have to lower glucose levels, but we haven't figured out how to do so without the potential of triggering dangerously low levels."

The symptoms of hypoglycemia, which include shakiness, According to Cryer, drugs that keep blood sugar levels low often cause them to drop too fast. The average person undergoing treatment for type 1 diabetes will experience symptoms of hypoglycemia about twice a week, with one episode of severe, temporarily disabling hypoglycemia per year.

It also is a significant problem in people with advanced stages of type 2 diabetes.

"Hypoglycemia is the most difficult obstacle to the management of blood sugar in people with diabetes," Cryer said. "To treat diabetes, you have to lower glucose levels, but we haven't figured out how to do so without the potential of triggering dangerously low levels."

The symptoms of hypoglycemia, which include shakiness, according to Cryer, drugs that help keep blood sugar levels low often cause them to drop too fast. The average person undergoing treatment for type 1 diabetes will experience symptoms of hypoglycemia about twice a week, with one episode of severe, temporarily disabling hypoglycemia per year.

It also is a significant problem in people with advanced stages of type 2 diabetes.

"Hypoglycemia is the most difficult obstacle to the management of blood sugar in people with diabetes," Cryer said. "To treat diabetes, you have to lower glucose levels, but we haven't figured out how to do so without the potential of triggering dangerously low levels."

The symptoms of hypoglycemia, which include shakiness,
Oltmanns installed as Edgar James Swift Professor

BY GERRY EVEREDING

Thomas F. Oltmanns, Ph.D., a leading researcher on the cognitive and emotional factors behind personality disorders, was installed as the inaugural Edgar James Swift Professor in Arts & Sciences March 16 in Holmes Lounge.

The chair is named for the turn-of-the-century psychologist who founded the University's first stand-alone psychology department in 1924.

Oltmanns joined the University in 2003 as a professor of psychology in Arts & Sciences with a joint appointment as professor of psychiatry in the School of Medicine.

"Tom is very well respected in his field, and he already has begun some excellent work here," said Edward S. Marcus, Ph.D., executive vice chancellor and dean of Arts & Sciences. "He's a very interactive guy who will stimulate our faculty in lots of areas. He provides added leadership to a clinical psychology program here that is already strong and growing."

He earned a bachelor's degree from the University of Wisconsin in 1972 and a doctorate from the State University of New York at Stony Brook in 1976. He then began his career as an assistant professor at Indiana University and became a full professor in 1985. He moved to the University of Virginia in 1986 as a professor of psychology and psychiatry.

"Our search committee was especially impressed by the breadth of Oltmanns' work at Virginia, where he maintained a major lab and had a significant role in the clinical training program in psychology," said Henry D. Boulding III, Ph.D., the James S. McDonnell Distinguished University Professor and chair of psychology. "Our department is thrilled to have recruited him."

Oltmanns publishes on topics involving cognitive and emotional factors in psychopathology, including schizophrenia, obsessive-compulsive disorder and personality disorders. The National Institute of Mental Health funds his research on the assessment of personality disorders.

Oltmanns supervises students in the clinical training program and teaches undergraduate courses on abnormal and clinical psychology. His abnormal psychology textbook, now in its fourth and eighth editions, are used at universities around the world.

While most of his profession is spent doing research and teaching, he is also a licensed clinical psychologist who provides therapy in patient care.

He specializes in cognitive behavioral therapy for the treatment of people with obsessive-compulsive disorder.

He has held editorial roles for the journal of Abnormal Psychology, the Journal of Personality Disorders and Psychological Bulletin.

A joint appointment as professor of psychology in Arts & Sciences with a joint appointment as professor of psychiatry in the School of Medicine.

Bankruptcy fallout to be examined at conference

The United States' recent economic slowdown has been punctuated by some of the largest bankruptcies in history, including Enron and WorldCom. Leaders in academics and prominent practitioners will examine the fallout from these bankruptcies at the Faculty of Thomas F. Oltmanns, Ph.D., signifying him as the holder of the Edgar James Swift Professorship in Arts & Sciences. Oltmanns is a leading researcher on the cognitive and emotional factors behind personality disorders. Swift founded the University's first stand-alone psychology department in 1924.

Titled "Bankruptcy and Reorganization: Current Issues and Future Outlook," the conference will focus on how bankruptcy law should be structured to address corporate failures on employees. It will be held April 2 at the School of Law.

"How policy and the law are shaped in this area affects not only corporate accountability and performance, but also raises concerns about fairness and equity, particularly when it comes to the impact of corporate failures on employees," said Elizabeth Warren, the Leo Gottlieb Professor in Law and the School of Arts & Sciences.

At an installation ceremony March 16 in Holmes Lounge, Chancellor Mark S. Wrighton placed a medallion around the neck of Oltmanns to honor his appointment to the chair.

Efforts at manipulating the audience without the public's knowledge or consent, the conference will examine the fallout from these bankruptcies at the E

Edgar James Swift Professorship in Arts & Sciences. Oltmanns is a leading researcher on the cognitive and emotional factors behind personality disorders. Swift founded the University's first stand-alone psychology department in 1924.

"How policy and the law are shaped in this area affects not only corporate accountability and performance, but also raises concerns about fairness and equity, particularly when it comes to the impact of corporate failures on employees," said Elizabeth Warren, the Leo Gottlieb Professor in Law and the School of Arts & Sciences.

At an installation ceremony March 16 in Holmes Lounge, Chancellor Mark S. Wrighton placed a medallion around the neck of Oltmanns to honor his appointment to the chair.

Efforts at manipulating the audience without the public's knowledge or consent, the conference will examine the fallout from these bankruptcies at the E

Edgar James Swift Professorship in Arts & Sciences. Oltmanns is a leading researcher on the cognitive and emotional factors behind personality disorders. Swift founded the University's first stand-alone psychology department in 1924.
every animal — including humans — is home to "friendly" gut bacteria that help digest food and perform other important functions. Now, a tiny, transparent fish is offering biologists a new window into understanding and treating human digestive problems.

School of Medicine researchers have shown for the first time that zebrasfish can be raised in a germ-free environment. Because zebrasfish are transgenic until they reach adulthood, they provide researchers with unique opportunities to watch the gut develop with and without the beneficial effects of symbiotic bacteria.

To untangle the complex interactions between humans and their friendly gut bacteria, we need simple animal models that can function as living test tubes," said principal investigator Jeffrey I. Gordon, M.D., the Dr. Robert J. Glaser Distinguished University Professor and head of the Department of Molecular Biology and Pharmacology. "These models are key to identifying the genes and chemicals that allow friendly bacteria to enhance our health."

A study, recently published in the online version of the Proceedings of the National Academy of Sciences, also is the first to describe which bacteria normally reside in the zebrasfish gut.

The first author is John F. Rawls, Ph.D., a postdoctoral fellow in Gordon's laboratory.

Gordon's team believes zebrasfish provide a nice complement to ongoing mouse research for several reasons. First, the zebrasfish genome is organized in ways similar to those found in the mammalian gut, and an international effort to sequence the zebrasfish genome is almost complete.

Zebrasfish are also less than one centimeter long during development, so it is easy to raise large numbers at once. And finally, unlike mice, it is possible to watch the gut develop and function in zebrasfish.

After months of trial and error, the team finally succeeded in raising zebrasfish that survived until late juvenile stages.

The researchers discovered that several biological processes were disturbed in germ-free zebrasfish. These impairments were similar to those the team had documented previously in germ-free mice. For example, the ability to process nutrients was compromised, as was the zebrafish's immune system.

To begin to decipher the mechanisms underlying the observed abnormalities, the researchers determined the genetic profile of three groups of fish: a group raised under conventional conditions with bacteria; a group raised in a germ-free environment; and an additional group that had been colonized with normal gut bacteria.

The comparison revealed 212 genes with different levels of expression in germ-free fish compared with the other two groups that had been exposed to bacteria.

The researchers found 66 zebrasfish genes analogous to genes regulated by friendly bacteria in the mouse intestine. The team then began compiling a list of bacterial species that reside in the zebrasfish gut.

"We need to determine which members of the microbiome community could be responsible for specific biological processes," Rawls said. "Using a molecular approach, we were able to identify a large number of types of bacteria that exist within the zebrasfish digestive tract."

The team then systematically re-colonized germ-free animals with selected mixes of bacteria. Using representatives from each two microbial types of zebrasfish, the team found that some host responses are quite specific for a given type of bacterium. For example, a type of bacterium that helps digest specific dietary components of evolution could provide new approaches for supporting and healing the digestive system.

"Results from our studies of pharmacogenetic correlations will be distributed to the medical community to help improve the practice of medicine," Gordon said. "Our goal is to identify the best way to use the results to benefit adult physiology and to benefit adult physiology.

"The use of powerful new germ-free animals is that you can define how a single species, or combinations of bacterial species, function to help complete animal development and to benefit adult physiology," Gordon said.

The team plans to use its germ-free zebrasfish to characterize the chemicals produced by gut bacteria.

According to Gordon, the chemical messengers developed by symbiotic gut bacteria over the course of evolution could provide a source of new molecules for the development of new drugs.
McDonough to address 'Equity, Education and Environment'

By Barbara Rea

It is a commonly held belief that commerce and ecology are diametrically opposed, that one cannot exist without the other, either pro-business or pro-environment. 

William McDonough has debunked this myth through a career that balances ecological and socially conscious practices. He will be in Steinberg Auditorium at 2 p.m. on Monday, April 5.

McDonough holds an undergraduate degree from Dartmouth College in Environmental Studies and a master’s degree from the University of Virginia’s Darden Graduate School of Business Administration. 

He has received many honors and awards from his profession, including being named a fellow of the American Institute of Architects and a fellow of the University of Virginia’s School of Architecture.

McDonough’s designs are based on a way of thinking that he calls “The Next Industrial Revolution.” He states in this way: “It is time to stage a second Industrial Revolution: one that measures progress by the number of ecosystems we work across the skylines and that measures prosperity by how low raw materials and energy use are.” 

McDonough states that his designs are based on a way of thinking that he calls “The Next Industrial Revolution.” He states in this way: “It is time to stage a second Industrial Revolution: one that measures progress by the number of ecosystems we work across the skylines and that measures prosperity by how low raw materials and energy use are.” 

McDonough has earned a silver medal for his work in 1989, a silver medal in 1990, and a gold medal in 2004 for his work. 

He earned an undergraduate degree from Dartmouth College in Environmental Studies and a master’s degree from the University of Virginia’s Darden Graduate School of Business Administration. 

His talk also is part of the “The University of Virginia’s School of Architecture.”

His talk also is part of the “The University of Virginia’s School of Architecture.”

McDonough is the principal architect of the first large-scale recycling building in the United States, the McDonough Braungart Design Chemistry LLC, a product and process firm that designs profitable and environmentally intelligent products and systems.

McDonough and Braungart have created a book that will teach in a cradle-to-cradle cycle. 

McDonough holds teaching appointments with the University of Virginia’s Darden Graduate School of Business Administration and at his alma mater, the University of Virginia’s School of Architecture.

McDonough has received many honors and awards from his profession, including being named a fellow of the American Institute of Architects and a fellow of the University of Virginia’s School of Architecture.

His talk also is part of the “The University of Virginia’s School of Architecture.”

McDonough has earned a silver medal for his work in 1989, a silver medal in 1990, and a gold medal in 2004 for his work. 

He earned an undergraduate degree from Dartmouth College in Environmental Studies and a master’s degree from the University of Virginia’s School of Architecture.

His talk also is part of the “The University of Virginia’s School of Architecture.”

McDonough is the principal architect of the first large-scale recycling building in the United States, the McDonough Braungart Design Chemistry LLC, a product and process firm that designs profitable and environmentally intelligent products and systems. 

McDonough and Braungart have created a book that will teach in a cradle-to-cradle cycle. 

McDonough holds teaching appointments with the University of Virginia’s Darden Graduate School of Business Administration and at his alma mater, the University of Virginia’s School of Architecture.
Carlin to perform concert March 28

BY LIAM OTTEN

R enowned pianist Seth Carlin, professor of music and director of musical performance in Arts & Sciences, will perform music of Bach, Ravel and Schumann in Mabee Center, the Feb. 28, 3 p.m. Margaret Bacchus, Maurice Rawl and Robert Schumann in Mabee Center, the Feb. 28, 3 p.m. Margaret Bacchus, Maurice Rawl and Robert Schuman.

For Carlin, the concert will represent a personal milestone as he prepares for the remainder of his concert season, when he will perform Bach and Schumann.

"In the past, I’ve dedicated my career to performing music of the type of instrument for which it was actually written," Carlin said. "I have come to the thinking that today’s piano accompaniments are still a broad range of music, including Schumann and Ravel.

On this recital, I’m playing a work by Bach because of my own love for the great music, despite the fact that in recent decades we have lost the clarity of his keyboard works frequently have been readapted."

The harpsichord was the preferred historical instrument for Bach’s time, and the Baroque period, followed by the harpsichord in the Classical period of Haydn and Mozart. The modern piano did not reach its current form until about 1860.

Carlin and begin his pro-

fessional career with Bach’s Partita in B-flat Major, BWV 1012. He will perform Ravel’s Miroirs, a set of five piano pieces inspired by the popular Alborada del gracioso.

The program will conclude with the prelude and piano music of Bartók, a well-known composer who wrote music that reflects the influence of Middle Eastern, Russian, and Jewish folk music.

"Many of his compositions, figures of commerce and all else and even philosophical oppo-

sitions to one another."

"The unexpected discovery that the NanoSIMS can provide new insight into how the brain functions during such basic, primitive responses and demonstrates an important link between cognitive processes and innate, physiological responses," Zinner said.

The researchers then planned to "develop our hypothesis of how such low blood sugar levels ultimately lead to hypoglycemia unawareness.

"We’re realizing, to quote a friend who is a health services researcher, ‘the warnings are not being heard, let alone acted on.’"

The researchers report that the warning system does not work by Bach because of my own love for the great music, despite the fact that in recent decades we have lost the clarity of his keyboard works frequently have been readapted."

The harpsichord was the preferred historical instrument for Bach’s time, and the Baroque period, followed by the harpsichord in the Classical period of Haydn and Mozart. The modern piano did not reach its current form until about 1860.

Carlin and begin his pro-

fessional career with Bach’s Partita in B-flat Major, BWV 1012. He will perform Ravel’s Miroirs, a set of five piano pieces inspired by the popular Alborada del gracioso.

The program will conclude with the prelude and piano music of Bartók, a well-known composer who wrote music that reflects the influence of Middle Eastern, Russian, and Jewish folk music.

"Many of his compositions, figures of commerce and all else and even philosophical oppo-

sitions to one another."

"The unexpected discovery that the NanoSIMS can provide new insight into how the brain functions during such basic, primitive responses and demonstrates an important link between cognitive processes and innate, physiological responses," Zinner said.

The researchers then planned to "develop our hypothesis of how such low blood sugar levels ultimately lead to hypoglycemia unawareness.

"We’re realizing, to quote a friend who is a health services researcher, ‘the warnings are not being heard, let alone acted on.’"

The researchers report that the warning system does not work
Making Einstein accessible

Will, known worldwide as one of the leading experts in using experimental and observational data to explain Einstein's theory of general relativity, will receive the Fellow's Award for making Einstein's theory accessible to the public and for making a significant impact on the public understanding of Einstein's theory.

His 1986 book on Einstein's theory and the general relativity and the experiments to test it made The New York Times Christmas Books list in 1986. His essay "Einstein Right-handed" was included in an essay called The American Institute of Physics Science Writing Award, which is given annually to the best popular science book. A second edition was published in 1995, and at last count it had been translated into 10 languages.

Will, who is in semitropical Florida this year but will attend the dinner, has been referred to as one of the best lecturers in physics, engaging, entertaining, and instructive. The United States is considered the bible of scientific innovation.

Correction


St. Louis' Academy of Science to honor Will and Buckley

The Academy of Science of St. Louis will honor two University of Missouri academics during its 10th annual Outstanding St. Louis Scientists Awards Dinner at 6:30 p.m. April 1 at The Westin St. Louis hotel, 111 Sprite St. Clifford M. Will, Ph.D., professor and former chair of the Department of Physics and Astronomy in Arts and Sciences, and James H. Buckley, Ph.D., a former physics professor, are among the eight men and women who are being honored for their exceptional accomplishments in science, engineering and education by furthering understanding of the sciences.

The Fellow's Award, which honors active scientists who excel in communicating to colleagues, future scientists and the general public and who have made a positive impact on the public understanding of science, will be given to Will.

Buckley will receive the academy's Young Scientist Award, which recognizes a scientist under 40 who is at the forefront of scientific investigation.

St. Louis' Academy of Science to honor Will and Buckley

Making Einstein accessible

Will, known worldwide as one of the leading experts in using experimental and observational data to explain Einstein's theory of general relativity, will receive the Fellow's Award for making Einstein's theory accessible to the public and for making a significant impact on the public understanding of Einstein's theory.

His 1986 book on Einstein's theory and the general relativity and the experiments to test it made The New York Times Christmas Books list in 1986. His essay "Einstein Right-handed" was included in an essay called The American Institute of Physics Science Writing Award, which is given annually to the best popular science book. A second edition was published in 1995, and at last count it had been translated into 10 languages.

Will, who is in semitropical Florida this year but will attend the dinner, has been referred to as one of the best lecturers in physics, engaging, entertaining, and instructive. The United States is considered the bible of scientific innovation.

Correction

Diabetes edge childhood leads cutting-edge research
Neil H. White with his wife, Ann, and sons, Michael (far right) and Justin.

Neil H. White leads cutting-edge childhood diabetes research

Enhancing the lives of children


He's a superhero. We should get him a cape.

He has a passion for what he does, and I think it comes across in what he accomplishes.

By DIANE DUKES WILSON


He has devoted his professional career to enhancing the lives of children with diabetes, says Alan Schwartz, Ph.D., M.D., chairman of the Department of Pediatrics. "For more than two decades, Neil has been at the cutting edge of multicenter trials in pediatric diabetes, and his advice is sought worldwide."

"We are so very fortunate to have him leading those efforts here at Washington University," says Anthony Pagliara, M.D., an immediate past chairman of the Department of Pediatrics.

Devoted to diabetes

White, the son of an optometrist and elementary-school teacher, grew up with a brother and sister on Long Island in the town of Great Neck. Weekends were spent boating the cool waters of Long Island Sound. White was "a lot of time on the tennis court."

He attended medical school at Albert Einstein College of Medicine in the Bronx, where he became interested in diabetes, while training at Lincoln Hospital, a hospital in the South Bronx that serves an indigent population.

But it wasn't until his residency at St. Louis Children's Hospital in 1975 that White discovered endocrinology. He was fascinated by the interaction of physiology with the management of diabetes in the day-to-day life of children.

"Not only were these physicians interesting people who were incredibly devoted to their patients, but they also were dedicated to me understanding this fascinating disease," White says.

Although Haymon and Pagar left the School of Medicine around the time White began a pediatric endocrinology and metabolism fellowship, he soon met two other University endocrinologists, Julio Santiago, M.D., and Phil Creyer, M.D., the Irene E. and Michael M. Karl Professor of Endocrinology and Metabolism. White joined the faculty as an instructor and began working with Santiago and Creyer on a number of key diabetes studies. After a four-year stint on the University of Michigan faculty, White returned to Washington University in 1991. He was involved in the national Diabetes Control and Complications Trial (DCCT) both here and at the University of Michigan.

Considered one of the most important studies in diabetes research, in 1993 the DCCT determined that strictly controlling blood sugars can prevent or delay the ravaging complications of the disease, such as limb amputation, kidney failure and blindness.

"It was a very exciting year," White says. "It made me see all the feeling that we had conducted for 10 years had really paid off."

He was also involved in the Diabetes Prevention Program (DPP), a large national study that found that people at high risk for type 2 diabetes can sharply lower their chances of getting the disease with diet and exercise.

Additionally, White has conducted studies with psychologist Michael A. Harris, Ph.D., instructor of pediatrics, who specializes in psychosocial interventions in treatment of patients, particularly in diabetes.

White is motivated by the positive comments he receives from his patients and their families as a result of the important breakthroughs in the field of diabetes over the past 20 years.

"I feel strongly that this is a worthwhile endeavor," he says. "And I take a great deal of pride in knowing that I helped this diabetes become survive a very difficult tragedy that could have destroyed us."

In his research and care of patients, White has learned that children with diabetes need not lose out to positive reinforcement — focusing on what they've achieved instead of what they need to do.

He has also discovered that each family is different and he must assess a family's physical, financial and emotional resources before developing a plan to help them manage diabetes.

White's next big study is Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY), which is the first clinical trial to focus on type 2 diabetes in children and teens. To slow the rate at which children are being diagnosed with type 2 diabetes, White believes society needs to first address the alarming amount of obese children.

"I think the wake-up call is getting to this population of at-risk patients before they develop diabetes," he says.

Passionate about patients

In his free time, White attends many Cardinal games and plays in a "very bad game" of golf with his children, Michael, 25, and Justin, 23. He is a nuclear engineer in upstate New York, and Justin will begin graduate school to study trumpet in the fall.

He is married to Ann, a busy volunteer for St. Louis Children's Hospital and occasionally works with her on special projects.

Over the years, White has stayed committed to helping children with diabetes while maintaining his enthusiasm for the outdoors. For the past 21 years, he's been involved with the American Diabetes Association (ADA) camps in Missouri and Michigan, many of those years as medical director.

He has served as president of the local ADA and on many of the association's national committees.

He's also encouraged many families to become involved with the ADA and empowered them in managing the disease.

"He's a superhero," says Ed Clay, executive director of the local ADA. "We should get him a cape."

"He has a passion for what he does, and I think it comes across in what he accomplishes."