

PENN PSYCHIATRY PERSPECTIVE

Perelman School of Medicine at the University of Pennsylvania | Department of Psychiatry

Ideas, Suggestions, and News!

We welcome your news and announcements about your activities for stories in *Penn Psychiatry Perspective*, the eNewsletter of the University of Pennsylvania Department of Psychiatry. Our goal is to offer useful and interesting news to readers and highlight our many outstanding faculty, programs, and services. Please submit your recommendations to psychweb@mail.med.upenn.edu.

In this Issue

Departmental Goings-On.....1-2

News and Announcements.2-4

Awards and Honors.....4-5

Upcoming Events.....5

Departmental Goings-On

Antipsychotic Drugs Linked to Increased Mortality Among Parkinson’s Disease Patients



Daniel Weintraub, MD was the first author of a new study examining an association between the use of antipsychotic drugs and early death in Parkinson’s patients. At least half of Parkinson’s disease patients experience psychosis at some point during the course of their illness, and physicians commonly prescribe antipsychotic drugs, such as quetiapine, to treat the condition. The study suggests that these drugs may do significantly more harm in a subset of patients. The study was led by Dr. Weintraub and senior author Helen C. Kales, MD from the University of Michigan and the Ann Arbor VA Medical Center. It was published online on March 21, 2016 in *JAMA Neurology*.

The research team’s analysis of about 15,000 patient records in a VA database found that Parkinson’s patients who began using antipsychotic drugs were more than twice as likely to die during the following six months, compared to a matched set of Parkinson’s patients who did not use such drugs.

In a March 21, 2016 Penn Medicine news release, Dr. Weintraub acknowledged the potential dangers, “I think that antipsychotic drugs should not be prescribed to Parkinson’s patients without careful consideration. Treatment with antipsychotics should be reserved for those cases where the potential benefits exceed the risks.”

These findings are not the first to link antipsychotic drugs to increased mortality. Since 2005 the U.S. Food and Drug Administration (FDA) has mandated “black box” warnings on antipsychotic drug packaging, noting the apparently increased risk of death when these drugs are used in dementia patients. For the new study, Dr. Weintraub’s research team examined the possibility that antipsychotic drug use is associated with higher mortality not just in Parkinson’s dementia patients, but in all Parkinson’s disease patients. Psychosis in Parkinson’s, although it is associated with dementia and later-stage disease, can occur even in the early stages of illness and in the absence of dementia. “It happens not uncommonly earlier in the course of the illness,” Dr. Weintraub said.

For the study, the researchers examined records from a large Veterans Affairs database, comparing a group of 7,877 Parkinson’s patients who were prescribed antipsychotic drugs at any time during 1999-2010 to an equal-sized “control group” of Parkinson’s patients who did not use antipsychotic drugs.

The analysis revealed that in the 180 days after they first took antipsychotic drugs, patients in the first group died in much larger numbers, compared with the matched control patients during the same periods. Overall the Parkinson’s patients who used antipsychotics had 2.35 times the mortality of the non-users. The relative risk seemed

Continued on page 2

Antipsychotic Drugs Linked to Increased Mortality Among Parkinson's Disease Patients

Continued from page 1

to vary by the specific drug - for example, 2.16 times higher for quetiapine fumarate compared with non-treatment, 2.46 for risperidone, 2.79 for olanzapine, and 5.08 for haloperidol. First-generation or "typical" antipsychotics, which include haloperidol, collectively were associated with about 50 percent greater relative mortality risk, compared to more recently developed "atypical" antipsychotics such as risperidone and quetiapine.

Researchers still do not fully understand why these drugs are linked to higher mortality in certain patient groups. "In this study we looked at the dataset for clues," said Dr. Weintraub, "but the most common cause of death listed was 'Parkinson's disease' - so there really wasn't anything that pointed to a specific cause or mechanism."

Drs. Weintraub, Kales, and colleagues are now conducting a follow-up study that might shed more light on that mechanism. They will examine the same VA database, looking not at mortality but at "morbidity" - disease diagnoses, injuries, and other new episodes of ill-health - among Parkinson's patients taking antipsychotic drugs, who survive for six months, comparing them with the same matched controls.

For the present, Drs. Weintraub and Kales suggest that neurologists, psychiatrists, and other physicians should prescribe antipsychotics to Parkinson's patients only after looking for other possible solutions, such as treating any co-morbid medical conditions associated with psychosis, reducing the dosage of dopamine replacement therapies, and simply managing the psychosis without antipsychotics using behavioral and cognitive techniques.

Dr. Weintraub cautioned, "Patients should not be left on these drugs long-term without re-evaluation."

The study was also covered in *HealthDay* (via Philly.com) and *ScienceDaily*.

Dr. Weintraub is Associate Professor of Psychiatry and Neurology in the Department of Psychiatry and Institute on Aging at Penn. Other co-authors of the study from the Departments of Psychiatry and Neurology at Penn were **Jayne Wilkinson, MD** and **Eugenia Mamikonyan, MS**. Drs. Weintraub and Wilkinson are also affiliated with the Corporal Michael J. Crescenz VA Medical Center in Philadelphia. Senior author Dr. Kales is from the University of Michigan and the Ann Arbor VA Medical Center. Other co-authors were Claire Chiang, PhD, Hyungjin Myra Kim, ScD, and Barbara Stanislowski, MPH, MSW from the Ann Arbor VA Medical Center and Connie Marras from the University of Toronto.

View the March 22, 2016 *Penn Medicine* news release at - http://www.uphs.upenn.edu/news/News_Releases/2016/03/weintraub/

News and Announcements

In the News

Penn Department of Psychiatry faculty are highly acclaimed experts in their chosen fields, often contacted by local, national, and international media outlets for their knowledge about topics of immediate interest. In this section, we provide just a brief sample of the many recent interactions that our faculty have with the press. (For a more complete listing, please visit - <http://www.med.upenn.edu/psych/news.html>.)

Debate Over Addyi Flares Anew



C. Neill Epperson, MD was quoted in a March 1, 2016 *MedPage Today* article reporting that a review of eight clinical trials testing flibanserin (Addyi) concluded the drug performed on the low end of the clinical efficacy range used to gain U.S. Food and Drug Administration (FDA) approval. Addyi is the first and only drug on the market to treat hypoactive sexual desire disorder (HSDD) in women. The analysis appeared in *JAMA Internal Medicine*. Taking into account this finding, many women's health experts argue that the drug earned its approval and should remain in the treatment arsenal. Others, however, do not support the FDA's approval of the medication, given their reading of the evidence.

Dr. Epperson is a skeptic. She told *MedPage Today*, "The effect was not large, and the side effects of Addyi are not minimal. We'll need to see if the side effects are enhanced in the average population among people who typically aren't as healthy as those participating in a randomized controlled trial." "I have my doubts about the medication and how effective it's going to be, but I'm glad we have an option," Dr. Epperson said.

Dr. Epperson is Professor of Psychiatry and Obstetrics and Gynecology and Director of the Penn Center for Women's Behavioral Wellness (PCWBW) in the Department of Psychiatry at Penn.

View the March 1, 2016 *MedPage Today* article at - <http://www.medpagetoday.com/OBGYN/GeneralOBGYN/56481>

What Alcohol Does to the Aging Brain



David W. Oslin, MD was interviewed in a March 4, 2016 *Philadelphia Inquirer* article about his research on alcohol abuse and dementia. He examined dementia in a VA nursing home in a 2003 study, still one of the few investigations of the topic. Ten percent of the patients had alcohol-related dementia, compared with 16.5 percent who had Alzheimer's disease, 29 percent with vascular dementia, and 44 percent with some mixture of dementias. "These folks end up being under the radar or labeled with Alzheimer's disease," he said.

In his research, Dr. Oslin looked at very heavy drinkers, men who drank 35 drinks a week for five years or women who had 28 drinks a week. "It's very unlikely that you would get [alcohol-related dementia] from being a social drinker," he noted.

Dr. Oslin is Professor of Psychiatry in the Department of Psychiatry at Penn, Chief of Behavioral Health at the Corporal Michael J. Crescenz VA Medical Center (Philadelphia), and Director of the Veterans Integrated Service Network (VISN) 4 Mental Illness Research, Education and Clinical Center (MIRECC).

View the March 4, 2016 *Philadelphia Inquirer* article at - http://www.philly.com/philly/health/20160306_What_alcohol_does_to_the_aging_brain.html

Preparing for a Mission to Mars: What Astronaut Scott Kelly's Year in Space Can Teach Us



Mathias Basner, MD, PhD spoke to CBS3 (Philadelphia) about his role in simultaneously monitoring Commander Scott Kelly, in space, and his twin brother, retired astronaut Mark, back on earth, to pinpoint how months in space could affect abilities to think, reason, and make decisions. Scott Kelly returned to Earth on March 1 from his year-long mission on the International Space Station. As part of a study by Dr. Basner and Penn Psychiatry colleagues **Ruben C. Gur, PhD** and **David F. Dinges, PhD**, both Kellys were tested for spatial orientation, memory, abstraction, attention, and other brain functions.

"Scott [underwent] cognitive tests in space," Dr. Basner explained. "Mark [did] his on earth at the same time so we can make comparisons." The tests on the International Space Station monitored Scott Kelly's emotion recognition, spatial orientation, and other abilities, allowing him to comment on results and immediately receive vital feedback on whether long-term exposure to "zero gravity" and other factors affected his performance. Dr. Basner hopes that what is learned from Kelly's journey will help fellow astronauts who one day may well make the three-year trip to Mars.

All colleagues in the Department of Psychiatry at Penn, Dr. Basner is Associate Professor of Sleep and Chronobiology in Psychiatry, Dr. Ruben Gur is Professor of Psychology in Psychiatry and Director of the Center for Neuroimaging in Psychiatry, and Dr. Dinges is Professor of Psychology in Psychiatry and Director of the Unit for Experimental Psychiatry and Chief of the Division of Sleep and Chronobiology.

View and listen to the March 1, 2016 CBS3 television (Philadelphia) article and video segment at - <http://philadelphia.cbslocal.com/2016/03/01/penn-med-school-has-special-link-to-returning-astronaut/>

For additional information about the long-term work of Drs. Basner, Ruben Gur, and Dinges in studying astronauts, view the March 10, 2016 article in *Penn Current* at - <http://www.upenn.edu/pennnews/current/2016-03-10/latest-news/penn-researchers-help-evaluate-astronaut-scott-kelly-after-his-record-stay-sp>

Also view the March 30, 2016 *The Daily Pennsylvanian* article at - <http://www.thedp.com/article/2016/03/penn-med-twins-in-space>

Go to Bed!



David F. Dinges, PhD was interviewed in a March 1, 2016 article in *The Scientist* about the short- and long-term impact of sleep deprivation on the human body. The immediate consequences of losing out on sleep may be harbingers of long-term repercussions. The article described the "myriad health burdens" that may result from sleep problems, including emotional distress, cognitive impairment, high blood pressure, obesity, metabolic syndrome, and cardiovascular and neurologic dysfunction.

Referencing past sleep research, Dr. Dinges noted that "epidemiologic studies . . . kept showing over and over again that when people reported sleeping less than six hours per night they were almost always overweight or obese. And it wasn't just obesity." People who slept very little (often less than six hours per night) were more likely to be diabetic or suffer a heart attack as well. "This led to an increasing medical understanding that sleep may be playing a role in things we never thought possible," said Dr. Dinges.

The article highlighted Dr. Dinges' interest in discerning the variable responses among individuals to sleep deprivation and the causes for these differences. He and others have looked for genes related to vulnerable phenotypes, but they have yet to identify any that can explain the different responses to sleep deprivation. Dr. Dinges is also keen on finding a biomarker that can predict the degree of vulnerability someone has to sleep loss. Such a test could be useful to the military

Continued on page 4

Go to Bed! Continued from page 3

or to transportation agencies, where people have jobs in which they may operate under poor sleep conditions. Dr. Dinges told the publication, "We'd really like to know, how can one person tolerate this so much better than another?"

Dr. Dinges is Professor of Psychology in Psychiatry and Director of the Unit for Experimental Psychiatry and Chief of the Division of Sleep and Chronobiology in the Department of Psychiatry at Penn.

View the March 1, 2016 article in *The Scientist* at - <http://www.the-scientist.com/?articles.view/articleNo/45375/title/Go-To-Bed-/>

New Painkiller Rules for Doctors Aim to Stem Drug Use, Deaths



Charles P. O'Brien, MD, PhD was interviewed in a March 20, 2016 article on Philly.com about the new guidelines of the Centers for Disease Control and Prevention (CDC) for opioid prescribing. Responding to the increasing recognition of the dangers of prescription painkillers for patients, the CDC issued detailed recommendations on their use. The CDC's "Guideline for Prescribing Opioids for Chronic Pain" unrelated to cancer is aimed at primary care doctors.

Dr. O'Brien told the reporter that most doctors have little or no training in addiction, let alone prescription opioids. He said that the first thing he teaches medical residents is to respect the addiction potential of opioids. That doesn't mean not to use them, but to understand when they are appropriate and what to expect, like withdrawal. "Physical dependence is a normal adaptation; you take a drug and your body adapts to it and changes. When the drug stops, your body reacts to that change," Dr. O'Brien said.

"Addiction is getting a high, doctor-shopping, doing all those things. It's pathological." Genetic differences, Dr. O'Brien added, influence who goes from the first to the second.

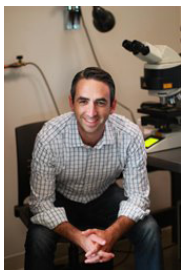
Dr. O'Brien is the Kenneth E. Appel Professor of Psychiatry and Founding Director of the Center for Studies of Addiction in the Department of Psychiatry at Penn.

View the March 20, 2016 Philly.com article at - http://www.philly.com/philly/news/20160320_New_painkiller_rules_for_doctors_aim_to_stem_drug_use__deaths.html

Awards and Honors

Regional, National, and International Honors

Dr. Kayser Honored by Sloan Foundation and by March of Dimes



Matthew S. Kayser, MD, PhD was recognized by two major organizations for his research. Dr. Kayser specializes in issues related to sleep and mental health. His lab works on how neural circuits give rise to complex behaviors and how dysfunction of neural processes can cause mental illness. His particular focus is in understanding how sleep contributes to sculpting brain circuits during development and in other times of life.

Dr. Kayser was named a 2016 Alfred P. Sloan Research Fellow in Neuroscience, one of three Penn faculty who received a Sloan Fellowship this year. In all, 126 U.S. and Canadian researchers received Sloan Research Fellowships in 2016. The Alfred P. Sloan Foundation has granted yearly fellowships since 1955 to early-career scientists and scholars whose achievements and potential identify them as the next generation of scientific leaders. To qualify, candidates must be nominated by their peers and selected by an independent panel of senior scholars. Each Fellow receives a \$50,000 award to further his or her research.

Dr. Kayser also received a 2016 March of Dimes Basil O'Connor Starter Scholar Research Award. This award supports young scientists just embarking on their independent research careers whose research interests are aligned with the mission of the March of Dimes – "to improve the health of babies by preventing birth defects, premature birth and infant mortality." The award is \$150,000 for two years.

Dr. Kayser is Assistant Professor of Psychiatry and Neuroscience in the Department of Psychiatry at Penn.

View the February 26, 2016 Penn News release on the Sloan Research Fellowships at - <https://news.upenn.edu/news/three-penn-researchers-awarded-2016-sloan-fellowships>

For more about the March of Dimes Basil O'Connor Starter Scholar Research Award, visit - <http://www.marchofdimes.org/glue/materials/basil-oconnor-boc-starter-scholar-research-award-request-for-proposals.pdf>

Department's Drug and Alcohol Abuse Teaching Program Ranks High

The Department of Psychiatry's teaching program in Drug and Alcohol Abuse ranked in 7th place nationwide in the 2016 *U.S. News & World Report* survey of medical schools and their specialty programs. As specified by the publication, these programs are for students interested in curbing substance abuse, and they incorporate behavioral science, treatment, and prevention techniques for patients with addictions.

Upcoming Events

2016 Annual Meeting of the Organization for the Study of Sex Differences (OSSD) To Be Held at Penn

The Penn Center for Research on Sex and Gender in Health and the Penn Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Program will be hosting the 2016 Annual Meeting of the Organization for the Study of Sex Differences (OSSD) at the Inn at Penn on May 23-26, 2016. The OSSD is an international scientific membership organization that seeks to enhance knowledge of sex/gender differences by facilitating interdisciplinary communication and collaboration among scientists and clinicians of diverse backgrounds. This meeting is ideal for Penn faculty and trainees who are interested in learning more about the role of sex differences in human health. The local hosts of the meeting are **Tracy L. Bale, PhD** and **C. Neill Epperson, MD**.

ALL REGISTRANTS SHOULD ATTEND THE BANQUET, WHICH FEATURES OUR VERY OWN TONY "TORO" ROSTAIN AND THE HOUSE BAND. COME DANCE TO GREAT TUNES.

EARLY BIRD REGISTRATION ENDS APRIL 24, 2016

Sessions for this year include:

- Sex Differences in Developmental Origins of Metabolic Disease
- Sex Differences in Sensorimotor Control
- Sex Differences in the Gut Microbiome
- Sex Differences in Bones and Joints
- Sex Differences in Multiple Sclerosis
- Sex Differences in Stress Responses
- Sex, Inflammation and Stroke
- Sex Differences in Memory Decline
- Sex Differences in Cardiovascular Disease
- Sex Differences in Circadian Rhythms
- Sex Differences in Addiction
- Sex Chromosomes and Sex-Linked Genes in Cancer
- Research Methods for Studying Sex

For more information about the program and registration details, visit the Meeting website at - <http://www.ossd.wildapricot.org/2016-meeting>

Department of Psychiatry Grand Rounds

Department of Psychiatry Grand Rounds are held on the designated dates in the designated locations. Please note any changes in time. The next lectures are listed below. For more information about Grand Rounds and the 2015-16 schedule, please visit - <http://www.med.upenn.edu/psych/rounds.html>

May 5, 2016

Elizabeth Weller Memorial Lecture

Karen D. Wagner, M.D., Ph.D.

Marie B. Gale Centennial Professor and
Vice Chair

Director, Child and Adolescent Psychiatry
Department of Psychiatry and Behavioral
Sciences

University of Texas Medical Branch at Galveston

Location: BRB II/III Auditorium

Time: 12:00PM

May 19, 2016

Edward A. Strecker Award Lecture

Peter F. Buckley, M.D.

Dean, Medical College of Georgia
Georgia Regents University

Location: BRB II/III Auditorium

Time: 12:00PM

May 26, 2016

Brandon A. Kohrt, M.D., Ph.D.

Assistant Professor

Department of Psychiatry & Behavioral Sciences
Assistant Research Professor
Duke Global Health Institute
Duke University School of Medicine

Location: BRB II/III Auditorium

Time: 12:00PM