

## In the Lab

# How Mom's Scent Can Keep Fear in the Family

## New study shows babies can learn maternal fears through smell

**JACEK DEBIEC, M.D., PH.D., HAS LONG** been intrigued by studies showing that anxious children often have anxious parents. Until recently, genetics were thought to play a primary role, but Debiec's latest research suggests that fear can also be a learned behavior, and mothers can pass their fears onto their newborns through smell.

Debiec began the research during his fellowship at New York University and continues it in his new lab at U-M's Molecular and Behavioral Neuroscience Institute. His team trained rats to be afraid of peppermint by giving them electric shocks every time they came in contact with it. The rats then had pups and were re-exposed to the peppermint scent in the presence of the pups. The mothers trained to be afraid of peppermint expressed fear in their offspring's presence. One week later, the pups were exposed to the peppermint without their mothers present, and they showed fear in reaction to the scent. As Debiec, now an assistant professor in the Department of Psychiatry, points out, newborn pups don't see or hear.

"But somehow they acquire maternal fear," he says. "It prompted us to hypothesize that it's probably the smell they're picking up."



Infants also do not typically form lasting memories. To facilitate attachment to the mother, aversive learning in pups is physiologically suppressed. But Debiec says the maternally transmitted fear learning is so strong, it overcomes these confines. His findings, published in the *Proceedings of the National Academy of Sciences*, have gone viral. The study has been featured in numerous publications in the U.S., as well as more than 100 internationally. Debiec says the infant-mother bond resonates, and studies that offer insight into the "mysterious" minds of infants will "naturally attract attention."

Moving forward, Debiec will work with other U-M researchers to develop a human study on the effects of trauma from maternal fear on infants. He will collaborate with Maria Muzik, M.D., an assistant professor of psychiatry, and Kate Rosenblum (Ph.D. 2000), an associate professor of psychiatry. The team hopes to explore the mechanisms of social buffering. They will also examine the oxytocin pathways in the infant brain

controlled by the maternal presence to better understand resilience and ways to augment it through drugs or behavioral interventions if it's malfunctioning.

Muzik, who studies mothers who experience depression and trauma and their infants, believes the most important takeaway from Debiec's research is that treatment can make a positive difference and help heal both generations. Debiec echoes this thought, stressing that the findings present an opportunity to engage in preventive measures and treat mothers struggling with mental illnesses to help prevent distress in the child.

"The positive message is that early interventions do work," Debiec says, adding that many obstetricians currently screen expectant mothers to look for signs of mental distress, and he hopes this practice becomes more widespread among pediatricians seeing new mothers. "You can possibly screen and design interventions very early, consequently preventing the fear and anxiety that often manifests itself as the baby grows."

# App Helps Care Providers ‘Hear’ Bipolar Mood Swings

## SUCCESSFULLY TREATING BIPOLAR DISORDER DEMANDS PATIENT CARE

teams to swiftly stabilize moods that can swing from the lows of depression to the highs of mania with little warning. Answering the call for improved monitoring of these mood states, U-M researchers are developing a smartphone app that can detect subtle changes in bipolar patients’ voices and signal the need for care.

Results of a pilot study on the app, called PRIORI, showed that it could detect elevated and depressed moods in patients with Type 1 bipolar disorder and a history of frequent depressive and manic episodes. PRIORI automatically records and analyzes patients’ speech qualities during any phone calls they make, including to their care teams. Only the patient’s side of the conversations is recorded, and researchers see just the computer analysis results of those recordings, which are stored in secure servers that comply with patient privacy laws. A specially trained clinician conducts weekly mood assessments to establish a benchmark for the patient’s mood and correlate the acoustic features of speech with their mood state. Further research is needed, but the app may also prove useful in the treatment of other disorders, that could include schizophrenia, post-traumatic stress disorder and Parkinson’s disease, researchers say.

“This is tremendously exciting not only as a technical achievement, but also as an illustration of what the marriage of mental health research, engineering and innovative research funding can make possible,” says Melvin McInnis, M.D., the Thomas B. and Nancy Upjohn Woodworth Professor of Bipolar Disorder and Depression and a professor of psychiatry. “The ability to predict mood changes with sufficient advance time to intervene would be an enormously valuable biomarker for bipolar disorder.”

McInnis conducted this research with U-M colleagues Emily Mower Provost, Ph.D., an assistant professor of electrical engineering and computer science, and Satinder Singh Baveja, Ph.D., a professor of electrical engineering and computer science, and Zahi Karam, a computer science research fellow. The team hopes to eventually create software that will learn to detect the changes that precede the transitions to bipolar mood states. They will also work to develop strategies for notifying app users and care providers about mood changes, so appropriate intervention can take place.



## Redesigning Random Assignment

### RESEARCHERS OFTEN FIND

the odds are against them when recruiting patients for random assignment clinical trials that test a new treatment. In a study published in the journal *Stroke*, a U-M team showed a promising new approach that reduces the “random” in clinical trials and preserves the ability to compare treatments. Instead of 50-50 odds, response-adaptive randomization, or RAR, increases the chance over time that patients will receive the best-performing treatment.

The research team — led by William Meurer, M.D., M.S., an assistant professor of emergency medicine and neurology — asked people to imagine they had suffered a stroke, showed them a video describing a study and asked whether they would participate. Half of the people saw a video describing a classic randomized study, and half saw one of an RAR study. Only 54 percent of patients invited to take part in the standard trial said they would volunteer. But 67 percent said they would enroll in the RAR study.

“It shows we might increase recruitment for acute stroke studies using a response-adaptive randomization design,” Meurer says. “This could be especially important in emergency situations, when patients or their loved ones have just minutes to consider options.”

## In the Clinic

# School's in for Surgery Patients

## Pre-surgery training program improves patient outcomes and care delivery

### THE UNIVERSITY OF MICHIGAN

is no longer training only its surgeons to prepare for good outcomes in the operating room; it is also training patients. From pulmonary calisthenics to aromatherapy to smarter snacking, surgical patients at the U-M are learning how to improve their chances of healing through the Michigan Surgical Home and Optimization Program, or MSHOP. Researchers say better prepared patients will also help surgeons be more successful in treating patients.

"Much as an athlete trains for competition, patients should train for surgery," says Michael Englesbe, M.D., an associate professor of surgery at the U-M and principal investigator of the MSHOP project. "The program is designed to help surgeons and patients make better decisions about surgery, to identify high-risk patients and train these patients to improve their medical outcomes following surgery."

Training leading up to the operation focuses on four areas — move, breathe, eat and relax — and MSHOP addresses these areas through patient support and education. This includes encouraging quitting tobacco and practicing breathing exercises that help improve pulmonary function and decrease



Michael Englesbe

post-op pneumonia. The program is also designed to modify patients' nutrition, exercise and stress levels for faster healing, reduced infections and optimized immune function — among other benefits.

The program also aims to improve health care delivery. MSHOP provides doctors and patients with new technology to predict surgical complications and make better decisions about procedures. Physicians can now use a risk assessment app on their smartphones to help determine if surgery will go well for their patients, particularly for those who are elderly and frail. Applying technology most physicians already use, the app makes it easier for them to integrate the data into their fast-paced routines. MSHOP will also use analytic morphomics, a method developed at U-M that uses diagnostic imaging to measure factors like fragility and overall health and assess surgical risk.

Since implementing MSHOP in early 2013, U-M has seen a savings of \$2,518 per case and has reduced time in the hospital after surgery by 30 percent. The project, a collaborative effort between U-M, the Michigan Surgical Quality Collaborative and Blue Cross Blue Shield of Michigan, has earned a \$6.4 million Health Care Innovation Award from Centers for Medicare & Medicaid Services to continue developing the program. The award project is led by Englesbe, and co-principal investigators U-M Health System Chief Medical Officer Darrell A. Campbell Jr., M.D., and Stewart C. Wang, M.D., Ph.D., a U-M professor of surgery.

Moving forward, 12,500 patients will be enrolled in the program, first at UMHS and then at 40 hospitals in Michigan. A field-tested and optimized model will be available for implementation across the country at the project's conclusion.



## Diabetes Drug Risks May Trump Benefits

### MEDICATION SHOULD DO

more than treat the complications of a condition. It should also improve the quality of a patient's life. But for many people with type 2 diabetes, the burdens of taking medication to manage blood sugar outweigh the benefits, according to research led by U-M, the VA Ann Arbor Healthcare System and University College London.

Published in the *JAMA Internal Medicine*, the study suggests that once moderate levels of glucose control are achieved, intensifying treatment to achieve a certain blood sugar goal offers little additional benefit for most patients. However, the costs, risks and side-effects increase substantially. Because the benefits of treatment also

decline with age, the negative effects of most treatments are likely to eclipse any positive effects for patients over age 75. The findings exclude the 15-20 percent of people with type 2 diabetes who have very high blood glucose levels and need more aggressive treatment to prevent associated diabetes complications, such as kidney, eye and heart disease.

"If you're a patient with fairly low complication risks, but are experiencing symptoms from low blood sugar, gaining weight or find frequent insulin shots to be disruptive to your daily life, then the drugs are doing more harm than good," says Sandeep Vijan, M.D., a professor of internal medicine at U-M and lead author of the study.

The study recommends treatment

plans that factor in age, degree of blood glucose elevation, and the safety and side effects of taking medication, rather than focusing solely on glucose goals. This will allow doctors and patients to base their medication decisions on individual circumstances and preferences.

"These are important decisions because type 2 diabetes is a chronic disease that requires lifelong treatment," says senior author Rodney Hayward, M.D., professor of internal medicine and of health management and policy at the U-M and senior research scientist at the Center for Clinical Management Research at the VA Ann Arbor Healthcare System.

Both Vijan and Hayward are members of the Institute for Healthcare Policy and Innovation at U-M.

## Statins Fail to Prevent Pulmonary Flare-ups

**STATINS DO NOT IMPROVE CLINICAL** outcomes for chronic obstructive pulmonary disease (COPD) or acute respiratory distress syndrome (ARDS), according to research performed at the UMHS and hospitals across the U.S. and Canada. Though statins are primarily used to lower cholesterol, previous studies have suggested that people with lung diseases do better when taking them because they may also reduce inflammation. For patients with COPD and ARDS, inflammation contributes to worsening lung function

and complications such as hospitalization, the need for ventilator support and death. The National Heart, Lung and Blood Institute initiated two separate studies to investigate the effects of statins on the two lung diseases. Both studies were stopped early because there was very little chance of showing that statins would improve any clinical outcome for either lung disease. COPD patients taking statins experienced no reduction in the frequency of flare-ups or other adverse events. ARDS patients on statins showed no reduction in

death or days free of the ventilator.

Jeffrey L. Curtis, M.D., a critical care specialist at the U-M and chief of pulmonary and critical care medicine at the VA Ann Arbor Healthcare system; MeiLan Han, M.D., M.S., associate professor of internal medicine and medical director of U-M's Women's Respiratory Health Program; and Fernando J. Martinez, M.D., adjunct professor in the Division of Pulmonary & Critical Care Medicine, co-authored a paper published in the *New England Journal of Medicine* about the findings.

## In the School

# The Learning Cycle

## U-M launches first-of-its-kind academic program

**THE UNIVERSITY OF MICHIGAN IS** developing programs in an emerging academic field in which health care systems are the teachers — and the students.

In July, the U-M announced the expansion of its Department of Medical Education, renaming it the Department of Learning Health Sciences. The new department focuses on the study of learning as it applies to all levels of health care. Newly appointed department chair Charles P. Friedman, Ph.D., will develop academic programs based on the concept of a learning health system — in which health professionals, care teams, institutions and large-scale systems come together to share resources, data and best practices to study and improve health and health care. Meanwhile, the department will continue its rich tradition in clinical simulation technology and interprofessional education.

Additional faculty from fields such as information science and economics will be recruited in the coming months to join Friedman in developing the new department. Over the next year, they hope to roll out a doctoral program, and the department will continue its role in the education of U-M's medical students, residents and faculty.

"We will focus on the science underneath the process of learning and how different disciplines can come together to use the process of learning to improve health care," Friedman says. "No such de-



The Clinical Simulation Center, part of the newly renamed Department of Learning Health Sciences, is one of the Medical School's many initiatives focused on learning at all levels.

partment exists in the country because this is a new type of thinking in our field."

The Medical School, and the new department, will collaborate within UMHS as well as across the university with departments and schools that influence health-related professions and information sciences. These areas include the School of Public Health, the School of Information and the Health Informatics program, which develops innovative ways to put information to use in promoting health and improving health care. Friedman says these institutional collaborations will drive learning as an ongoing product of health care delivery and help create the framework for a health system that learns continuously.

For example, a statewide learning health system is being developed through the Center for Healthcare Research and Transformation, or CHRT, a non-profit partnership between the U-M and Blue Cross Blue Shield of Michigan. On July 11, a diverse group of more than 100 professionals involved in health care across Michigan — from physicians to community health workers to leaders in the insurance industry — met to discuss how the learning health system concept can be used to improve health care across the state.

"Communities of interest have formed

to address some very interesting problems," Friedman says. "People around the state are coming together to look at issues like improving disease surveillance and immunization rates, improving continuity of care and ensuring the right information is readily available as patients move around the state."

The new department will continue to reach outside the university and across the state as new communities of interests develop. In this wide-reaching work, the department will create a common health learning infrastructure — rich with technological and policy structure — that can be applied to any number of complex health care problems, at any time and in any place.

"Imagine you need to do 20 loads of laundry in one day," Friedman says. "You could go from house to house in your neighborhood, find 20 people with washing machines, find out when they're going to be home, what type of detergent they use, and then go to each house to distribute the laundry. Or you can go to the laundromat, where everything is waiting for you. What we're building now is the laundromat. It's the infrastructure. It's the platform that supports this.

"I believe in this program," he adds, "and I believe we're putting Michigan ahead of the curve."

## New Director Joins Kresge Hearing Research Institute

### **GABRIEL CORFAS, PH.D., A LEADING**

researcher in the interface between the brain and the ear, joined the U-M as director of the Kresge Hearing Research Institute and as a professor in the Department of Otolaryngology. His appointment began on July 1.

Corfas, an Argentina native, comes to Michigan from Boston, where he served as director of basic research in Otolaryngology at Children's Hospital and as a professor of neurology and otolaryngology at Harvard Medical School. He is a graduate of the Weizmann Institute of Science in Israel and trained at the Washington University School of Medicine and Harvard Medical School before joining the Harvard faculty in 1992. His research focuses on the molecular mechanisms involved in the development, function and maintenance of the nervous system, and their application in understanding and developing therapies for nervous system disorders.

Kresge's 13 faculty-led research teams focus on the basic biology of all aspects of the human ear and sense of hearing, including deafness, tinnitus and head and neck cancer. Its research programs include multi-disciplinary projects in behavior, morphology, physiology, molecular biology and genetics, bioengineering, pharmacology and biochemistry.

Integral to Kresge's efforts are its many training programs for up-and-coming scientists, including a summer program for deaf and hard-of-hearing students, and the Hearing, Balance, and Chemical Senses Program for graduate students and postdoctoral fellows.

## Cardiovascular Center Names New Director

**ON JULY 1, THOMAS WAKEFIELD, M.D.** (Residency 1984, Fellowship 1986), began his four-year appointment as a director of the University of Michigan Samuel & Jean Frankel Cardiovascular Center. He joins directors Kim A. Eagle, M.D., David J. Pinsky, M.D., and Richard L. Prager, M.D., along with chief administrative officer Linda R. Larin, M.B.A., on the CVC leadership team. James C. Stanley, former co-director, is resuming his role as associate chair of the U-M Department of Surgery.

"The Frankel Cardiovascular Center combines advanced patient care, ground-breaking research, outstanding educational opportunities, and a culture of collaboration and respect," Wakefield says. "I am excited about the opportunity to help lead the Cardiovascular Center into the next generation of health care."

Wakefield, head of vascular surgery at the U-M since 2004, is a graduate of the Medical College of Ohio. As a surgeon-scientist, he works with teams at the Conrad Jobst Vascular Research Laboratory to develop new approaches to prevent and treat deadly blood clots. He is also a former president of the American Venous Forum and the Michigan Vascular Society.

Wakefield's career spans 36 years at the U-M. From 2002-2012, he was the S. Martin Lindenauer Collegiate Professor of Vascular Surgery. In 2012 he was installed as the James C. Stanley Professor of Vascular Surgery, a professorship created to honor his predecessor.



## In the Clinic

# U-M Welcomes New Department Chairs



This fall, the University of Michigan welcomed three new department chairs. **CHARLES P. FRIEDMAN, PH.D.**, stepped into his role as chair of the De-

partment of Learning Health Sciences — formerly the Department of Medical Education — on July 1. (Learn more about the new department on page 8. He will also be the Josiah Macy, Jr., Professor of Medical Education. Friedman comes to the Medical School from the U-M School of Public Health and School of Information, where he ran the joint Health Informatics program from its inception. He will continue to hold appointments in both schools.



On Sept. 1, **LONNIE D. SHEA (PH.D. 1997)** began as chair of the Department of Biomedical Engineering, a joint effort between the

Medical School and College of Engineering. Shea was most recently a professor of chemical and biological engineering at the Robert R. McCormick School of Engineering and Applied Science at Northwestern University, where he directed the National Institutes of Health/ National Institute of General Medical Sciences Predoctoral Biotechnology Research Training Program.



**CHARLES A. PARKOS, M.D., PH.D.**, joined the U-M on Sept. 15 as chair of the Department of Pathology and the Carl Vernon Weller Professor in Pathol-

ogy. Previously, Parkos was a professor and vice chair of the Department of Pathology and Laboratory Medicine at the Emory University School of Medicine, where he also served as director of the Division of Experimental Pathology and Medical Science Training Program.

Congratulations to Friedman, Parkos and Shea on their appointments.

## U-M Welcomes Future Leaders of Medicine

### THE MEDICAL SCHOOL CLASS OF 2018 WAS

formally welcomed during a White Coat Ceremony held Aug. 3. The 177 physicians-to-be have arrived at a time of transition for the Medical School and UMHS, with a renovation of the Taubman Health Sciences Library underway, an ongoing initiative to restructure the medical student curriculum and an increasing number of patients covered under the Affordable Care Act. They will learn to work in health care environments that embrace new approaches to population-based care and utilize advanced health information technology.

- Number applying: **5,776**
- Number interviewed: **578**
- Students in the class: **177\***
- Female: **53.1%**
- Male **46.9%**
- Class average Sci GPA: **3.77**
- Class average total GPA: **3.79**
- Class average MCAT **34.81**
- Underrepresented in medicine: **21 (11.9 %)**
- Average age: **24.3**
- Michigan residents: **47.5 %**
- Non-residents: **52.5%**
- Number of states represented: **32**

- Total undergraduate institutions represented: **77**
- Michigan undergraduate institutions represented: **16**

### TOP UNDERGRADUATE FIELDS OF STUDY

- Biology: **18.1%**
- Science (other than biology): **18.1%**
- Biochemistry: **11.3%**
- Chemistry: **9.0%**
- Natural & Physical Sciences: **8.5%**

\* Data subject to change