Welcome to the Biannual Bulletin from the Center for Addiction Research! The biannual bulletin contains news stories and summaries provided by CAR members about the great work they are doing. Thank you to those who shared stories for this edition! To have your work included in the next issue, coming in late July 2024, please send a brief summary/story accompanied by pictures or graphics (if available) to Jen Rowe (roweji@ucmail.uc.edu) any time prior to July 15th. Thank you!

CAR Biannual Bulletin

January 2024

Member Research Updates

2024 Next Bulletin Release Date:
- Late July

2024 Next Deadline for Submitting Stories:
- July 15th

UC cocaine research disrupts traditional theory

For more than 50 years, the conventional wisdom in the field of research in cocaine use has been that people take cocaine based on the theory of the drug providing positive reinforcement to the user.

New research out of the University of Cincinnati shows that a pharmacological equation disproves that concept and could spark a major shift in that field of research.

The study was published in the journal Scientific Reports.

Andrew Norman, PhD, professor in the Department of Pharmacology and Systems Physiology at the UC College of Medicine and corresponding author of the study, says that in 1968, the first paper on cocaine self-administration was published showing that it was an example of operant behavior theory, a method of learning that uses rewards and punishment to modify behavior. It suggests that certain things like food or drugs motivate the behavior according to schedules of reinforcement.

“The theory maintains that the more reinforcing a drug is, the faster users take it,” Norman says. “Interestingly, animals that self-administer cocaine slow down intake as doses get higher, implying that higher doses are less reinforcing, which doesn’t make sense. But at really lower unit doses, the actual number of presses the animal does goes up as you increase the dose.”
It was believed, Norman says, this means that low cocaine doses produce positive reinforcing effects, but high doses produce more rate-limiting effects, so low doses were believed to provide more useful information. He says his research shows that this is not correct.

“We came along in 1998 and formulated this pharmacological-based theory that explained injection intervals, or the time between injections of cocaine” says Norman.

Norman took a different approach by developing an equation with that can be measured quantitatively and it accurately describes the behavior. He says there is none of the elements of “reinforcement” or “wanting” or “liking” that is the basis of the traditional research approach to cocaine self-administration. The study was published in 1999 in Brain Research.

Norman says the recently-published research was led by two students working in his lab, Jhanvi Desai and Luis Tron Esqueda, who suggested they conduct a new experiment building on an explanation of cocaine self-administration that Norman had published in 2001.

Desai and Tron Esqueda revived the research in 2022 after talking with Norman and expressing a desire to design an experiment to test Norman's original idea.

Desai and Tron Esqueda revived the research in 2022 after talking with Norman and expressing a desire to design an experiment to test Norman's original idea.

"When Dr. Norman was discussing his background, he was explaining to us his previous idea, it was more of an experimental design, and we asked him if he had tested that," Tron Esqueda says. When Norman said he had not tested that, Tron Esqueda and Desai saw an opportunity.

"When Dr. Norman had initially explained to us the paradigm it was very clear," Desai says. "We predicted what the data should look like, and when we did the experiments and analyzed the data, we found exactly what we were expecting. The only surprising thing was that it was so obvious to us, so I can't understand why other researchers don't see it the way we do."

A subsequent study Desai conducted which just got published shows another phenomenon. When access to cocaine is terminated rats continue lever pressing for a while, but after the number of presses to get a dose was increased there was a huge increase in the rate of lever pressing for no cocaine, which had never been recognized before.

"The students were right. It was important to do it," Norman says. "The surprising finding was the huge increase in lever pressing behavior when the animals go on these high schedules of lever pressing which we'd never used before, so I'd never seen that. I believe that is why the field was misled for more than 50 years. They interpreted this as the reinforcing effects of cocaine. Jhanvi's paper shows that it's the schedule, not the cocaine that does the 'reinforcing.' It's been misinterpreted all those decades."

"As pharmacologists, we know that drug effects are related to concentration," adds Norman. "The first question a pharmacologist asks is what is the response that is being induced by this drug. In our case, it's the lever pressing behavior. Our big innovation with this latest research is that we calculated what the concentration of cocaine is in the body every second of the session. What we show is that there is a range of cocaine concentrations that drive the behavior."

"We are hoping that it will open up everyone else's eyes to what's actually been seen for multiple decades now," Tron Esqueda says. "It will hopefully start shifting the current idea on how to study cocaine addiction into a newer idea."

"I think it's going to be a paradigm shift of how to approach preclinical cocaine self-administration studies in animal models," Desai says. "This will hopefully be an example of how to design experiments and interpret data appropriately so that the knowledge can be applied to cocaine use in humans."

Desai, who was an undergraduate neuroscience student in the UC College of Arts & Sciences when she joined the Norman lab, says this project has shifted her career goal from being a medical docdtor to enrolling in the combined research-directed MD/PhD program in the UC College of Medicine.

"This is my first research experience," she says. "UC is a top research university and there is really good mentorship, good resources and the research we do here is top level."

UC News story by Bill Bangert:
UC cocaine research disrupts traditional theory

Read the study from Scientific Reports:
The ascending limb of the cocaine unit dose–response function in rats as an experimental artifact

Read another related story from Medical Xpress:
Research challenges traditional theory of mechanisms of cocaine self-administration

Overdose treatment boxes available at rest area

Ohio Healing Communities Study

Intervention facilitated by the Ohio Healing Communities Study, co-Principal Investigator and CAR Director, Dr. T. John Winhusen.

IRONDALE — As part of its daily mission to save lives whenever needed, the TEMS Joint Ambulance District has been working with others to make it possible for non-medical personnel to do the same.

Clark Crago, director of the ambulance service, said the agency has installed a special box in each of the restrooms of the rest area near state Routes 7 and 213 with materials anyone can use to help a person suffering from an opioid overdose.

Inside each NaloxBox are nasal sprays containing two doses of 4 milligrams each of naloxone. Commonly sold as Narcan, the drug is used to reverse the effects of an opioid overdose.

The rest area was chosen because such overdoses have occurred there in the past, but Crago and other officials hope to install NaloxBoxes at other public places.

Installed in June with the cooperation of the Ohio Department of Transportation, the boxes are the first in the state to be offered at a location outside of the turnpike, noted Ashley Wilson, a community engagement facilitator for the HEALing Communities Study.

Funded by the National Institutes of Health and Substance Abuse and Substance Abuse and Mental Health Services Administration, the study is aimed at significantly reducing opioid overdose deaths.

Its goal has been to identify methods that are most effective in preventing and treating opioid overuse and reduce deaths by overdose by 40 percent during the next three years.

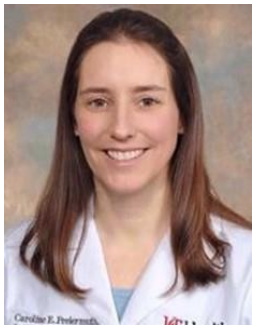
Its scope includes communities in Kentucky, New York and Massachusetts as well as Ohio, where its efforts have been supported by Gov. Mike DeWine's RecoveryOhio program.

Involving 19 randomly selected counties in various parts of the Buckeye State, the study involves Ohio State University, the University of Cincinnati, Case Western Reserve University, Ohio University, University of Toledo, Wright State University and the Nationwide Children's Hospital.

"The drug epidemic has touched the lives of many Ohioans and we know that no community is immune," said Aimee Shadwick, director of RecoveryOhio. By providing naloxone at rest areas, we want more Ohioans to have timely access to naloxone. We can save lives and give people a chance to access treatment and recovery services."

Read the full story:
Overdose treatment boxes available at rest area

UC receives grant to explore alternatives to opioids in the ED



The Department of Emergency Medicine has been awarded a $1.4M federal grant from the Emergency Department Alternatives to Opioids Demonstration Program (ED-ALT) through the Substance Abuse and Mental Health Services Administration to expand the use of available evidence-based options for pain management in the emergency department (ED), focusing on pain relief and empowering people with tools to use for pain management while minimizing the risk of potential harms from opioid exposure.

Led by **Caroline Freiermuth, MD, MS**, Emergency Medicine Endowed Chair to Benefit the Acute Treatment of Mental Health and Substance Use Disorder, the overarching goal of this project is to provide alternatives to opioids for the management of pain in the ED and post-discharge by implementing Integrative Health approaches and expanding local injectable anesthetic initiatives. “Although the overall goal of the grant is to decrease the amount of opioids used, it is our hope that physicians and others in the ED become better educated and expand their armamentarium of options to treat pain to ensure patients receive the care they deserve while minimizing side effects and exposure to opioids,” says Freiermuth. **Richard Ryan, MD**, professor and vice chair of operations, Sanjay **Shewakramani, MD,** Medical Director, West Chester Hospital and Osher Center for Integrative Health Academic Advisory Council Member, and **Patrick Minges, MD**, assistant professor, will also be key personnel on the project from the Department of Emergency Medicine.

The ED will partner closely with the Osher Center for Integrative Health, and Center Director, **Sian Cotton, PhD**, **Mladen Golubic, MD, PhD**, Medical Director, and **Meriden McGraw**, **MS, MPH**, Director of Workplace Mindfulness, to introduce a full menu of integrative health and medicine techniques for novel outpatient follow-up (e.g., acupuncture, yoga), with patients receiving information on mindfulness and stress reduction techniques to use immediately. Mindfulness and resilience training sessions will be offered to ED team members in an effort to decrease burnout and improve well-being through experiencing the benefits of mind-body therapies firsthand and allowing them to be more informed when offering these interventions to patients and families.

Study shows widespread naloxone distribution is not enough

A new study from the College of Medicine finds that widespread community distribution of naloxone through a take-home naloxone (THN) program did not significantly impact the median monthly opioid overdose rates. The study was published in PLOS ONE.

The Naloxone Distribution Collaborative was facilitated from October 2017 through December 2019 by Hamilton County Public Health. Opioid overdose mortality was compared between the period before (October 2015 to September 2017) and during the program (October 2017 to September 2019). Prior to the start of the program, there was little distribution of THN to individuals in Hamilton County.

"Our goal with the Naloxone Distribution Collaborative was to see what happens if we could saturate an entire community and see what impact that might have on the opioid overdose rates,” says Caroline Freiermuth, MD, Class of 2006, Endowed Chair to Benefit the Acute Treatment of Mental Health and Substance Use Disorder in the Department of Emergency Medicine. “We looked to see what impact broad distribution of naloxone had on the community and what we found is that it held opioid overdose death rates steady.”

UC News story by Bill Bangert:
Widespread naloxone distribution not enough to impact overdose death rate

Read the study in PLOS ONE:
Evaluation of a large-scale health department naloxone distribution program: Per capita naloxone distribution and overdose morality

WVXU: Health benefits and risks to recreational marijuana

Issue 2 passed in Ohio on Nov. 7 with more than 55% of the vote, legalizing recreational marijuana for adult use.

The University of Cincinnati's LaTrice Montgomery, PhD, joined WVXU's Cincinnati Edition to discuss the potential health benefits and risks associated with cannabis use. Montgomery studies cannabis use disorder, particularly around young adults using blunts, hollowed out cigars where tobacco is partially or fully replaced with marijuana.

The wide variety of cannabis products makes it difficult for researchers looking to make strong conclusions, Montgomery said.

"I think as legalization increases, it's going to become more and more important for us to get more and more specific about the products that we're talking about in our research as well as the dosage, specific strains, etc. in order to really make strong public health impact statements," said Montgomery, adjunct associate professor in the Department of Psychiatry and Behavioral Neuroscience in UC's College of Medicine and a licensed clinical psychologist. "As we think about legalization here in Ohio, we have to get really thoughtful about the education we provide."

While many people commonly claim that cannabis is not addictive, cannabis addiction or cannabis use disorder is listed in the industry standard handbook in the substance abuse section along with other stimulants like alcohol and cocaine. There are 12 symptoms that describe cannabis use disorder, including cannabis use impairing your ability to go to work or school, withdrawal symptoms similar to nicotine withdrawal and unsuccessful efforts to cut down or control cannabis use.

"Although when we think of cannabis versus opiates and some other drugs you might say, 'Well, cannabis isn't killing anybody and it's not causing all those huge issues,' it does cause impairment," Montgomery said. "It is important for us to know that, and that's why I am glad to see here in Ohio now that there will be at least a portion of the funds dedicated to education around this issue."

UC News story by Tim Tedeschi:
WVXU: Health benefits and risks to recreational marijuana

Listen to WVXU's Cincinnati Edition here:
WVXU: Health benefits and risks to recreational marijuana

UC researcher says toxic substances remain on surfaces, even in homes that ban indoor smoking

It's long been established that secondhand smoke is a detriment to health and linked to cancer.

Now, researchers are looking more closely at thirdhand smoke, which is the presence of toxic tobacco by-products that remain on surfaces such as furniture, décor, walls and floors.

In a new study, published in the Journal of Exposure Science & Environmental Epidemiology, researchers tested the surfaces in smoking households where children reside and found troubling results, says Ashley Merianos, a tobacco researcher at the University of Cincinnati who led the study.

Researchers found nicotine on surfaces in all of the children's homes and detected the presence of a tobacco-specific carcinogen (called NNK) in nearly half of the homes, she says.

The study reported that the NNK levels on surfaces and vacuumed dust were similar, which Merianos says indicates that surfaces and dust can be similar reservoirs and sources of thirdhand smoke exposure for children.

"This is critically important and concerning, since NNK is considered the most potent carcinogen for tobacco-induced cancers," says Merianos, an associate professor in UC's School of Human Services.

Additional findings include:

- Children living in lower-income households had higher levels of NNK and nicotine found on home surfaces.
- Children living in homes that did not ban indoor smoking had higher levels of NNK and nicotine found on surfaces.

Merianos says that NNK and nicotine were still detected in homes with voluntary indoor smoking bans, which highlights the persistence of thirdhand smoke pollutants on surfaces in children's homes.

"This research highlights that home smoking bans do not fully protect children and their families from the dangers of tobacco," she adds.

Merianos is a prolific researcher and has extensive training and experience in the epidemiology and prevention of substance use with an emphasis on tobacco, as well as quantitative statistical methods and clinical and translational research in the pediatric health care setting.

She is also a research affiliate member of Cincinnati Children's Hospital Medical Center, the Thirdhand Smoke Research Consortium and the American Academy of Pediatrics Tobacco Consortium.

UC News story by Angela Koenig:
UC tobacco use researcher cited as expert in a national news feature on vaping in the office

Read the study in Journal of Exposure Science & Environmental Epidemiology:
Contamination of surfaces in children's homes with nicotine and the potent carcinogenic tobacco-specific nitrosamine NNK

UC tobacco use researcher cited as expert in a national news feature on vaping in the office

According to a Daily Mail article, recent studies find that 76 percent of e-cigarette users reported vaping at work.

"There may be confusion about whether vapes are covered by tobacco-free policies in work environments if there is no written policy addressing vaping, especially since these products became available on the market after combustible tobacco products," UC's Ashely Merianos says in the article.

Some studies show that second hand vape fumes have the potential to be as dangerous as secondhand smoke; and researchers, the article states, are beginning to warn of the dangers, which likely prompted a new law in Alabama banning residents from vaping in cars with children under 14 present.

Even if there is no tobacco-free law that prohibits tobacco use in the work place, Merianos said it is encouraged that employers enact a strict, comprehensive tobacco-free policy that covers combustible tobacco products and non-combustible tobacco products, including vapes.

Merianos is a prolific researcher and has extensive training and experience in the epidemiology and prevention of substance use with an emphasis on tobacco, quantitative statistical methods, and clinical and translational research in the pediatric healthcare setting. She is also research affiliate member of Cincinnati Children's Hospital Medical Center and the Thirdhand Smoke Research Consortium.

UC News story by Angela Koenig:
UC researcher says toxic substances remain on surfaces, even in homes that ban indoor smoking

Read the story from Daily Mail:
Is it now time to get annoyed with co-workers vaping in the office? Six in 10 US workers say their colleagues are at it - despite mounting evidence they're as bad as cigarettes

Center for Addiction Research 2023 Summer Speaker Series Impact

To view the recordings and presentation slides, please visit the 2023 Summer Speaker Series webpage. The 2022 Summer Speaker Series and 2021 Summer Speaker Series recordings and presentation slides are also available.

Increased total number of post-event evaluations with eighty-five TY.

Highest percentage of attendees each session completing post-event evaluations.

CAR website	# Users Visited
April 14 – 30, 2023	126
May 2023	193
June 2023	316
July 2023	264
August 2023	208
Total	1107

Increased CAR awareness and drove another 1107 new users to the CAR website.

The success of the SSS has driven, 5400 new users to the CAR website since March 31, 2021.

Increased the number of individuals receiving the CAR newsletter by 82 additions.

CAR Member Recognition

Congratulations to Dr. Teresa Reyes, PhD, Professor in the Department of Pharmacology and Systems Physiology and CAR Member for being named Senior Associate Dean for Basic and Translational Research!

The announcement below was made by Dean Filak in October.

The Senior Associate Dean for Basic and Translational Research is an extremely important leadership position in the College of Medicine. Dr. Reyes will join with Brett Kissela, MD, MS, Executive Vice Dean and Senior Associate Dean for Clinical Research, to co-lead the college's Office of Research and provide strategic oversight for our research agenda, which at the close of FY2023 included more than $140 million in NIH-sponsored research holdings. With her extensive research and programmatic leadership experience, her success in obtaining NIH and foundation funding and her commitment to mentoring students and trainees, I believe Dr. Reyes will thrive in this position taking the college's research program to the next level by building on the many successes of her predecessor, Melanie Cushion, PhD.

Dr. Reyes is a Professor in the Department of Pharmacology and Systems Physiology. She joined the College of Medicine faculty in 2015, coming to Cincinnati from the University of Pennsylvania, Perelman School of Medicine. Prior to that she was on faculty at The Scripps Research Institute in Jupiter, Florida. She received her doctorate in Psychology from the University of Wisconsin, Madison and completed a postdoctoral fellowship at the Salk Institute for Biological Studies in La Jolla, CA.

Dr. Reyes' lab is focused on how early life environment shapes brain development and cognition, with a focus on understanding neuron-glial interactions. Her work examines a range of environmental influences, including nutrition as well as exposure to inflammation, drugs of abuse and chemotherapeutic medications.

Christine Wilder, MD, associate professor, Department of Psychiatry and Behavioral Neuroscience, and medical director of the department's Addiction Sciences Division, has been appointed to the OneOhio Recovery Foundation Expert Panel.

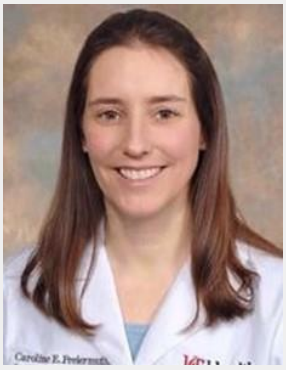
The OneOhio Recovery Foundation is a 501(c)(3) charitable organization charged with statewide distribution of more than $800 million for addiction prevention, treatment and recovery efforts. The Exert Panel is comprised of nine professionals in addiction, pain management, public health and other opioid-related fields and makes recommendations to ensure the foundation addresses the opioid epidemic locally and statewide.

Wilder is an addiction psychiatrist with expertise in supporting pregnant and postpartum women and evaluation science.

CoM Office of Research recognizes Gallery of Awardees for faculty who have been awarded external grants of $100,000/yr.
Congratulations to **Joel G. Sprunger, PhD**, Assistant Professor, Department of Psychiatry and Behavioral Neuroscience.

- Award: National Institute on Drug Abuse
- Project Title: Improving Buprenorphine Retention with Transcutaneous Auricular Neurostimulation for Patients with Co-occurring Posttraumatic Stress Disorder and Opioid Use Disorder
- Project Period: 9/1/2023-8/31/2024

- Summary: This project is relevant to public health because patients with both opioid use disorder (OUD) and posttraumatic stress disorder (PTSD) are at high risk for dropping out of buprenorphine medication therapy and experiencing overdose. This project will first examine how helpful patients with PTSD and OUD find a device that administers therapeutic electrical stimulation to their vagus and trigeminal nerves through the skin around their ears and then complete FDA pre-submission for using the device with this population more broadly. Finally, researchers will study how effective the device is for helping patients with PTSD and OUD stay in buprenorphine treatment by comparing the results of those who received therapeutic stimulation versus those who believed that they had but, in fact, did not.



Congratulations to **Caroline Freiermuth, MD** (**CAR Population Health and Health Services Core Co-Leader and CAR Member**), Class of 2006, who was appointed Emergency Medicine Endowed Chair to Benefit the Acute Treatment of Mental Health and Substance Use Disorder, Department of Emergency Medicine, effective July 1, 2023, to June 30, 2028 by the UC Board of Trustees at its August 22 meeting.

Gold and Silver Apples awarded
Medical Sciences undergraduate students have named the 2023 recipients of Gold and Silver Apple Awards for the best courses this past academic year in the Medical Sciences Baccalaureate Program. The students selected their most impactful courses to recognize the excellent teaching by MedSci instructors. Congratulations to **Dr. Terry, Kirley, PhD**, Class of 1982, professor, Department of Pharmacology and Systems Physiology, **(and CAR Member)** who was the recipient of the Golden Apple in 1000/2000 Level Courses for “History of Medicine and Technology Innovation” and a Silver Apple in 4000 Level Courses for “Fundamentals of Medical Pharmacology”.

Center for Addiction Research (CAR)

University of Cincinnati
College of Medicine
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CAR Director:
Dr. T. John Winhusen

Changing outcomes, saving lives through work on opioid, stimulant, cannabis, and alcohol use disorders

CAR Mission

To accelerate scientific progress in the prevention and treatment of substance use disorders and their consequences by fostering research collaborations across:

- UC departments, colleges, and centers including Cincinnati Children’s Hospital Medical Center
- Local, regional, and state community and governmental partners
- Other academic institutions and industry

The CAR includes three research concentrations (cores):

- Addiction Treatment Development and Testing (ATT)
- Perinatal Addiction/Developmental-consequences (PAD)

University of CINCINNATI
CENTER FOR ADDICTION RESEARCH

- Population Health and Health Services (PHHS)

Find out more about the CAR using the website link below: https://med.uc.edu/institutes/CAR/home