This Is (Actually, Accurately) Your Brain on Drugs

**WHRY Explores How Cannabis May Affect Men and Women Differently**

Jessica usually smokes cannabis five days a week, mostly at the end of the day, often while reading.

“Why do some people drink alcohol?” she said. “It’s a way to come down after a hectic day. I treat it more like a beer with dinner.”

But one morning late this winter, she smoked a cigarette rolled with government-grown cannabis while lying with her head inside a scanner that recorded images of a radioactive tracer’s path through her brain.

“Cannabis has been illegal and impossible to study,” said Jessica, a 25-year-old graduate student. “The more we know about it, the more we understand how it affects us. It’s not something that’s going to go away.”

Even as the federal government treats the possession and use of cannabis as illegal for any purpose, 29 states now allow medical use of the drug, and nine states have authorized it for recreational purposes. This new and rapidly evolving legal landscape arrives with many unknowns, not the least of which is how, precisely, this popular illicit drug affects people’s brains and behavior.

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Women’s Health Research at Yale was founded in 1998 with initial funding from The Patrick and Catherine Weldon Donaghue Medical Research Foundation. Women’s Health Research at Yale is a program within Yale School of Medicine. Yale University is a 501(c)(3) nonprofit organization.
Jessica, not her real name, was one of the first subjects participating in a study funded by Women’s Health Research at Yale using a new brain scanning technique to examine for the first time how smoking cannabis affects the brains of women and men.

About half of all Americans have tried cannabis, with 22 million reporting they have used it at least once in the last month. Use of the drug is particularly common among adolescents and young adults, whose brains are still developing.

And newer generations of cannabis users are consuming the drug with a potency that has greatly increased over the years. In confiscated samples of cannabis, the average content of tetrahydrocannabinol (THC), the major psychoactive ingredient, climbed from 4 percent in the early 1990s to 12 percent in 2014.

Varieties available in flower form at Connecticut dispensaries — sold with a doctor’s certification to patients with qualifying diagnoses such as cancer, glaucoma, AIDS, Parkinson’s disease, multiple sclerosis, epilepsy, and post-traumatic stress disorder — can have THC contents well above 25 percent. Concentrated forms such as oils and resins approach and exceed 90 percent THC. Other varieties are lower in THC and higher in other compounds, such as cannabidiol (CBD), which has been used to calm anxiety and suppress seizures, particularly in children, without a psychoactive effect.

Greater potency carries the potential for greater problems. About 4 million Americans meet the diagnostic criteria for a marijuana use disorder, meaning that due to their marijuana use they suffer from difficulties with health or the ability to meet responsibilities. The disorder can involve dependence — in which a user who stops taking the drug experiences withdrawal symptoms such as irritability, anxiousness, depression, and sleeping problems — and addiction, defined as the inability to stop even when use causes significant health and social problems in the user’s life.

As recipients of WHRY’s Wendy U. and Thomas C. Naratil Pioneer Award, the researchers expect to find a faster neurochemical reward response in women that makes women more susceptible to addiction and opens the door to the development of gender-sensitive addiction prevention programs and treatments.

“With so little research on this topic, I don’t think we know very much at all,” said Dr. Kelly Cosgrove, Associate Professor of Psychiatry, Radiology and Biomedical Imaging, and Neuroscience. “The first thing we need to do is nail down exactly how cannabis affects brain chemistry.”

Cosgrove, the study’s lead investigator, helped develop the brain scanning methodology in studies of tobacco smoking and alcohol dependence. She saw a clear parallel in adapting the technique to explore how cannabis works inside the brain and to eventually help design better, targeted treatments for people who develop dependence or addiction.

“You can never completely stop using a drug if it has a strong influence on your brain chemistry,” she said. “It’s very important to understand the brain’s response to cannabis use so that we can develop better treatments.”

Cosgrove and her team are investigating how cannabis affects the brain using a mathematical model to take images from PET and MRI scans and create unique videos, shown in segments here, that depict dopamine activation before, during, and after smoking cannabis.

“The first thing we need to do is nail down exactly how cannabis affects brain chemistry.”

In the brain, dopamine is the primary neurotransmitter helping brain cells...
CANNABIS FACTS

Cannabis is the most commonly used illicit drug in the United States (22.2 million people have used it in the past month) according to the 2015 National Survey on Drug Use and Health.

It's use is more prevalent among men than women — a gender gap that widened in the years 2007 to 2014.

Women's substance use tends to progress more quickly from first use to addiction.

Rates of marijuana use among middle and high school students have dropped or leveled off in the past few years after several years of increase. However, the number of young people who believe regular marijuana use is risky is decreasing.

In 2016, 9 percent of 8th graders reported marijuana use in the past year and 5 percent in the past month.

Among 10th graders, 24 percent had used marijuana in the past year and 14 percent in the past month.

Rates of use among 12th graders were higher still: 36 percent had used marijuana during the year prior to the survey and 23 percent used it in the past month; 6 percent said they used marijuana daily or near-daily.

Source: The National Institute on Drug Abuse

Communicate with one another, it can create a sense of euphoria or of simply feeling good. The release of dopamine is what produces the good feeling when someone enjoys eating, having sex, acing a test, winning a race, hugging a baby — all of the activities the body naturally rewards.

But there can be too much of a good thing, particularly when it comes to ingesting substances. The “good feeling” associated with drugs such as nicotine and cocaine arrives in part from a release of dopamine in the brain, which diminishes with repeated use and can push people to seek the drug over and over again because the intensity and duration of the “good feeling” subsides over time. This pursuit of that feeling or effect can damage the user’s health and happiness.

In studying cigarette smokers, Cosgrove and other researchers in the Yale Specialized Center of Research (SCOR) to Develop Gender-Sensitive Treatment for Tobacco Dependence discovered that men smoke more often for the rewarding effects of nicotine, and women smoke more often to cope with stress or otherwise improve their mood.

“We’re starting to treat men and women cigarette smokers differently,” Cosgrove said. “Men are more likely to respond to nicotine replacement therapy, for example. We are pursuing development of new medications targeted to help women. And that’s because of the research we’re doing.”

Now Cosgrove wants to make a similar impact by informing people about the risks of using the cannabis of the 21st century and providing data-driven assistance for people who develop a cannabis use disorder.

“For example, if we find sex differences in marijuana smoking, it could lead to a different treatment regimen,” she said. “Maybe women and men need different clinical interventions. We won’t know unless we continue to study the issue.”

Making Movies of the Mind

In order to determine how the brains of women and men react differently to drugs, researchers need the right tools and a way to analyze the data they obtain.

In studies exploring the effects of nicotine, alcohol, cocaine, and cannabis on the brain, Cosgrove uses images created by positron emission tomography (PET).

A PET scan allows researchers and medical practitioners to track chemical activity in the body that could be evidence of disease or — as with the cannabis study — of dopamine release. In this procedure, a team operating a PET scanner injects a safe radioactive drug, known as a tracer, into a subject or patient. The tracer is known to collect in the specific areas of chemical activity under study, and the radioactivity shows up visually as bright spots on the recorded images to aid diagnosis or provide useful data to researchers about how psychological processes or disorders affect brain activity.

For example, when men smoke cigarettes while in a PET scanner, dopamine gets released in a part of the brain called the ventral striatum, which is associated with reward and reinforcement. For women, dopamine tends to collect in the dorsal striatum, which is more associated with habit and learned behaviors like those in response to a negative mood.

This fits with other research revealing that men smoke more for the rewarding effects of nicotine and women smoke more to affect mood and are cued by other aspects of the habit than the craving for nicotine.

Traditionally, researchers using PET scans to detect the effect of a particular drug on dopamine activity in the brain first administer the drug, then place the subject in the PET scanner, wait 90 minutes, and calculate the average over that time of how much of the tracer binds to the dopamine receptors they are targeting.
About 10 years ago, Dr. Evan D. Morris, Professor of Radiology and Biomedical Imaging, Psychiatry, and Biomedical Engineering, began looking at what valuable information might be hiding in that average.

“What happens if a phenomenon we’re looking for happens in a short period of time?” Morris said. “What if there is a spike in the data and not a simple straight line? Can we detect these things? We needed a more sophisticated mathematical method.”

Dr. Jenna Sullivan, in 2013 the first graduate student to earn a Ph.D. while conducting research in the Yale PET Center, wrote her doctoral thesis after discovering in papers published by others that the amount of time spent in the PET scanner after smoking affected the results.

“Timing mattered,” Morris said. “The information we were seeking was in the data. It was just a matter of getting it out and getting it out reliably.”

Morris and his students developed a mathematical model that reliably extracts the timing data and allows the team to map the dopamine activation before, during, and after a drug’s administration. Currently, Heather Liu, a second-year biomedical engineering graduate student, helps crunch the numbers and create data visualization movies that depict precisely what is happening over time.

“If an effect is short, if it’s subtle, a traditional model won’t capture it at all,” Liu said. “Dr. Morris’ model is unique and gives us the entire curve of dopamine as it is released over time — not just before and after it is released.”

Smoking for Science

When Jessica showed up for her PET scan, she had been asked to abstain from smoking cannabis for 12 hours to maximize any craving. With approval from Yale’s Institutional Review Board to conduct research on human subjects, Cosgrove’s team and the staff at the PET center took a detailed medical history and assessment of cannabis, alcohol, and other drug use.

They tested her blood for levels of hormones and THC.

They performed a physical and neurological examination, including an electrocardiogram of heart function to make sure she had no complicating medical conditions.

They screened her urine to make sure she wasn’t pregnant.

They evaluated her to determine any psychiatric illness and assessed her for depression, anxiety, and impulsivity.

They administered a task designed to assess her responsiveness to rewards.

And they asked her to plunge her hand into freezing water to assess her pain threshold and any possible link to cannabis craving.

Jessica also underwent a magnetic resonance imaging (MRI) scan that the

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**LEGALITY OF CANNABIS IN THE UNITED STATES**

Currently, 29 states allow medical use of cannabis, and nine states have authorized it for recreational purposes. This map includes laws which have not yet gone into effect. Cannabis remains a Schedule I drug under federal law. Image © Wikimedia CC Lokal_Profil

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**ABOUT THE INVESTIGATOR**

Dr. Kelly Cosgrove earned her Ph.D. and B.A. degrees in Psychology from the University of Minnesota. She completed a post-doctoral fellowship at Yale School of Medicine’s SPECT Brain Imaging Laboratory and since 2013 has been an Associate Professor in the Department of Psychiatry.

A trained clinical psychologist, Dr. Cosgrove’s research has focused on understanding the neurochemical, behavioral, and cognitive components of addiction, particularly tobacco smoking and alcohol dependence.
WOMEN’S HEALTH RESEARCH AT YALE

Built to Last

Women’s Health Research at Yale has thrived for 20 years, and the reasons are clear:

As a self-supporting center, WHRY continues to succeed in advancing the study of sex and gender differences and, in turn, improves the study and practice of medicine for the benefit of all people.

Yet another reason for the center’s longevity lies in the careful, deliberate way in which it has widened the scope of its research and added programs to advance its mission.

In the beginning, WHRY Director Carolyn M. Mazure, Ph.D., focused research grants on studies of adults. Over time, those research grants came to include adolescents and younger girls. The formula WHRY followed then and now — start something important, do it well, and then do more — holds today.

Researchers used to map where the PET scan shows activity on a more detailed image of her brain.

After the battery of tests, Jessica lay down on a cushioned table with her head in the round opening of the PET scanner. A nurse infused her with the radioactive tracer through an intravenous tube. And after 30 minutes, she began to puff from a cannabis cigarette, provided through the National Institute on Drug Abuse, with about 3.5 percent THC, exhaling into the bowl-shaped end of a device that sucked in the smoke and filtered it to protect the researchers and the equipment.

After each staggered series of puffs, a researcher asked Jessica to rank on a scale from zero to 10 how high she felt, how good she felt, how anxious she felt, and how much she was craving cannabis.

In a control room, computer monitors displayed the position of Jessica’s head in the PET scanner and began to produce the numbers Liu will apply to Morris’ mathematical model and translate into the videos showing where, when, and for how long the dopamine appears.

For most subjects, the dopamine starts to flow shortly before they begin to smoke. The researchers interpret this as anticipation of the pleasurable effects of the drug.

For this initial study, the team anticipates testing five women and five men. They expect to find a difference between the sexes and then apply for a larger grant to test more subjects, looking for a larger effect and eventually the proof necessary to guide better, more individualized treatments.

After a day of medical and psychological tests, smoking for science, Jessica reported feeling relaxed. A little sleepy, but satisfied she helped contribute to a better understanding that can help people.

“Men and women should be treated equally, but biologically we are separate,” Jessica said. “Who knows what’s going to be uncovered. It’s why we need to keep looking.”

The Women’s Health Research at Yale Pilot Project Program is supported in part by The Rice Family Foundation, The Werth Family Foundation, The Community Foundation for Greater New Haven, the Maximilian E. and Marion O. Hoffman Foundation, the Seymour L. Lustman Memorial Fund, The Seedlings Foundation, and The Eppley Foundation for Research.

That philosophy also guided the center’s approach to its mentored training programs. In part with the help of multi-year grants from the National Institutes of Health, WHRY prepared graduate students and junior faculty members for careers in women’s health and sex/gender research. The graduates of this program have gone on to obtain significant research positions to further this crucial work at Yale and at other institutions.

Once WHRY established a program to train graduates and junior faculty, the center began its Undergraduate Fellowship, a hands-on mentoring program providing a “scientific home” for students to explore subjects in women’s health research under the tutelage of Yale faculty. Starting three years ago with five students, the program has expanded to encompass a total of 16 fellowships.

Through careful planning and judicious expansion, WHRY has been able to enlarge its vision, reach, and influence in each of its 20 years. That particular combination — vision, reach, and influence — explains why WHRY has earned the dedication of thoughtful and generous donors who see the value and results and are determined to help us do even more.

With my thanks to all who have brought us to this point and who will, now, take WHRY into its future,

Barbara M. Riley
Philanthropy Chair
Happy 20th Anniversary, WHRY!

The Celebration Continues

“As a 30-year survivor of ovarian cancer, I know firsthand the importance of advancing medical research on women’s health. It is one of the many reasons I am so proud to work with Women’s Health Research at Yale and so grateful for this center’s leadership in this important field. As I continue to represent Connecticut’s Third District in Congress, WHRY helps provide me with the necessary data-driven information to make sure that we all can live healthier and happier lives.”


“Thanks to WHRY, we are making excellent progress in guiding medical school curriculum reform so that our physicians and scientists investigate and account for important sex and gender differences. With your leadership, more and more medical institutions will continue to integrate these concepts into education and care to reduce health disparities and provide optimum interventions.”

— Njeri Thande, M.D., Assistant Professor of Medicine (Cardiology), Yale School of Medicine, Co-Director of the Homeostasis integrated course for first year medical students

“When I first joined the Yale faculty in 2011, I had spent six years purifying the protein created by the BRCA2 gene that, when mutated, leads to breast and ovarian cancer in women. But we don’t know which types of mutations put women at higher risk for cancer and which aren’t dangerous. WHRY gave me my first grant at Yale, helping me to obtain larger external grants and launching my work into how these mutations function to better guide treatment and save lives.”

— Ryan Jensen, Ph.D., Associate Professor of Therapeutic Radiology, Yale School of Medicine

Thank You for Your Support

Women’s Health Research at Yale is pleased to acknowledge the many important gifts from our Society of Friends, who support our shared mission to improve the health and well-being of everyone. In the constantly changing landscape of research and health care, we are so fortunate to have committed allies who appreciate the need to provide reliable resources to secure the advancement of research in women’s health.

We value each and every gift. Thank you for your continued generous support. 🎉

A complete list of all our friends for the 2017-18 year can be found on our website, www.yalewhr.org, on August 1.

JOIN THE PARTY!

If Women’s Health Research at Yale has touched your life, we want to hear from you! Please write to share your thoughts and help celebrate our 20th anniversary year: rick.harrison@yale.edu

It’s only through gifts like yours that the center can inspire and prepare the next generation of researchers, such as WHRY Undergraduate Fellows Dikshitha Balaji (left) and Kaveri Curlin (center).
Getting Under the Skin

**WHRY Finds Clues to Better Treat a Cancer Common in Women**

Squamous cell carcinoma, or SCC, can grow rapidly, cause pain, and is more common in women than men.

When women seek treatment for this skin cancer commonly found on lower legs, they face a large menu of options. Potential interventions include scraping or cutting away the cancerous growth and burning what remains with an electric needle. A physician might opt to inject a drug locally into the tumor to cause destruction. Sometimes a cream or lotion can remove a very superficial cancer. More aggressive methods include simple excisions in which a surgeon cuts out the affected skin. Or even more involved procedures in which the cancer is removed one layer at a time and examined under a microscope to make sure no damaged cells are left behind. Some patients undergo a therapy to kill the cancer cells with high-energy radiation. If the cancer has spread to the lymph nodes — structures that help rid the body of harmful substances — or far-away organs, a physician might recommend systemic chemotherapy.

Treatment decisions are paramount because choosing a more aggressive treatment for a mostly indolent, or slow-growing, skin cancer can unnecessarily leave a patient with painful open sores at the site of removal. Choosing a conservative treatment for a cancer that ultimately proves aggressive through recurrence or by spreading to a new location could require a more invasive treatment later with worse health outcomes.

Now, Dr. Christine J. Ko, a Professor of Dermatology and Pathology at Yale School of Medicine, has identified a promising method to predict the growth rate of SCC and better guide treatment decisions.

In Ko’s clinical practice, her extensive training and experience diagnosing all kinds of skin cancers in the laboratory often leave her questioning present diagnostic criteria and systems of classification.

Currently, Dr. Ko and her colleagues have no absolute way to determine if a sample of SCC viewed under a microscope might be keratoacanthoma, a less aggressive form that can go away on its own, or a more aggressive and dangerous variety with potential to spread. Certain clues are sometimes helpful to predict aggressive behavior — tumor size, growth of cancer cells around nerves or into blood vessels, cancer cells that look less like normal tissues — but many tumors lack those features. And it remains difficult to predict long-term outcome in most cases.

“When a pathologist determines if a sample is or isn’t SCC, it involves a visual examination with individual interpretation.”
“The public often thinks that the diagnosis of cancer is black and white,” Ko said. “But genetic analysis of tumors is showing us that there is definitely a gray zone. A growth may be not quite benign but not quite malignant. We need to be able to clearly differentiate in order to determine the best management and treatment.”

In a study funded by WHRY with co-funding from the Yale Comprehensive Cancer Center and published last year in the Journal of the American Academy of Dermatology, Dr. Ko and her co-authors found evidence that sequencing the precise order of the code embedded in a specific gene could serve as a biological marker to better classify SCC.

“When a pathologist determines if a skin sample is or isn’t squamous cell carcinoma, it involves a visual examination with a certain amount of individual interpretation,” Ko said. “We need more objective criteria. If we knew 100 percent of the time that the presence of specific mutations were markers of an aggressive form of SCC, then we could be more sure of the diagnosis and recommend the best course of treatment for that patient. Conversely, absence of those mutations could predict a slower growing course and the appropriateness of a more conservative therapy.”

The “Guardian of the Genome”

About one million cases of squamous cell carcinoma are diagnosed in the United States each year, an increase of about 200 percent over the last 30 years. Caused mainly by exposure of the skin to ultraviolet light from the sun, SCC is most often cured when detected early and treated properly. But every year as many as 8,800 Americans die from the disease. And others are left disfigured or in pain.

Dr. Ko and her colleagues noticed that female patients over 70 often had multiple lesions on their legs with many features in common with slow-growing keratoacanthoma. She designed a study seeking to determine whether samples of such lesions obtained from the lower legs of female patients would be similar genetically to keratoacanthoma, which most dermatologists today still consider a form of SCC. Her evaluation focused on attempting to detect mutations in a gene called TP53, known as “The Guardian of the Genome” for its role in protecting DNA from mutations.

Most cancers, including SCC, have many mutations, permanent changes in the sequence of the genetic code through replication error or unrepaired damage. In fact, between 60 and 90 percent of SCC tumors show changes in the TP53 gene, specifically in the DNA-binding region that plays an important role in DNA replication and repair. A minority of keratoacanthomas have TP53 mutations, and if they are present, they are in a different region of the gene.

Ko’s team studied samples that all met criteria for SCC as previously diagnosed by a pathologist. The researchers used ultra-deep sequencing to read the DNA code, a method involving increased precision in correctly detecting mutations.

Out of the 30 samples sequenced, 20 had no TP53 mutation at all. This about the investigator

Dr. Christine J. Ko earned her M.D. from New York University and her B.A. from Princeton University. She is currently a Professor of Dermatology and Pathology at Yale School of Medicine.

Her research into skin cancer has targeted clinical subsets of cutaneous squamous cell carcinoma, including keratoacanthoma.

SQUAMOUS CELL CARCINOMA

Dr. Ko did not find mutations in a common cancer-causing gene in 20 of 30 samples previously diagnosed as squamous cell carcinoma. This research offers a new path toward identifying forms of squamous cell cancer that are slow-growing so as to require substantially less invasive treatments and provide the biological basis for ensuring better outcomes.
result is particularly striking because sequencing often involves reading samples more than 500 times, but Ko’s team looked at the DNA samples an average of 2,000 to 3,000 times to reduce potential errors.

“It was surprising that 20 out of 30 tumors didn’t have a *TP53* mutation if they are really conventional SCC,” Ko said. “These results are more in keeping with the tumors being closer to keratoacanthoma. And it’s not likely we missed mutations, because they should have been detected with the ultra-deep sequencing.”

In addition, Ko reviewed each tumor microscopically, intentionally unaware of the results of the DNA sequencing so as to avoid influencing her evaluations. She visually categorized 16 of the tumors as having similar features, resembling an early form of keratoacanthoma. Fourteen of the tumors remained classified as conventional SCC, which keratoacanthoma mimics in its growth stage. Of 14 tumors she classified as SCC, 10 had mutations, none of which were in areas of the gene known to be highly mutated in conventional SCC, and two of 10 were in a region like mutations found in keratoacanthoma.

All 16 she classified as resembling an early keratoacanthoma did not have a *TP53* mutation.

Ko and her colleagues concluded that the absence of a *TP53* mutation and the presence of keratoacanthoma-like mutations in these samples suggested that the lesions might more accurately be diagnosed as keratoacanthoma in early and growth stages. This type of skin cancer can grow rapidly but ultimately does not have an aggressive course.

“We were able to show that these lesions, classified as squamous cell carcinoma before the study, either lack *TP53* mutations or have mutations in *TP53* that are different from previously described mutations in SCC,” Ko said. “These results point toward an effective way to predict slow-growing, less aggressive behavior in skin cancer and direct appropriate treatment and management for patients.”

Ko envisions that with more data on the particular *TP53* mutations associated with indolent and aggressive SCUs, *TP53* sequencing tests could be developed as an inexpensive commercially available method to aid in diagnosis and treatment plans.

She expressed confidence in achieving her goal by studying more of these tumors, collecting more data on the specific mutations in tumors with known aggressive vs. indolent behavior, and reaching a better understanding of how particular gene mutations can guide treatment decisions.

“What really is a skin cancer?” Ko said. “What, if left alone, would harm the patient? We know a bit more now, and we are making progress every day.”

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**WHRY Investigator Elected to National Academy of Sciences**

Women’s Health Research at Yale congratulates Dr. Akiko Iwasaki on being elected to the National Academy of Sciences for her outstanding research achievements.

Dr. Iwasaki, Waldemar Von Zedtwitz Professor of Immunobiology and Molecular, Cellular and Developmental Biology and a Howard Hughes Medical Institute Investigator, focuses her work on the mechanisms of immune defense against viruses at the mucosal surfaces.

Ever since receiving the first of two research grants from WHRY in 2003, Iwasaki’s lab has earned significantly larger funding from the National Institutes of Health for studies that have established groundbreaking insights into the transmission, treatment, and possible prevention of herpes.

Iwasaki hopes to soon have a treatment in clinical trials to benefit the millions of people suffering from this disease, a majority of whom are women. Her other research explores challenges in confronting influenza, rhinovirus, human papillomavirus, and Zika.

Iwasaki joins 31 other faculty members from Yale School of Medicine who have been elected to the National Academy of Sciences, one of the highest honors available to scientists in the world.

She received her Ph.D. and B.Sc. from the University of Toronto and her postdoctoral training from the National Institutes of Health before joining the Yale faculty in 2000.
Picking Up the Pace
By Rick Harrison

Have you heard the news?

This question used to be easier to answer. These days, there’s just too much coming much too fast.

Over the past year, news cycles have grown more and more attenuated to the point where major stories that would have occupied print and broadcast media for months are quickly shoved aside as soon as the next gigantic development arrives with a breathless, breaking news alert.

In this hectic environment, Women’s Health Research at Yale takes a more measured approach. We play a vital, deliberate role toward achieving equity in how medical science is conducted and translated into practice.

For 20 years, WHRY has developed and promoted treatments and prevention strategies that focus on diseases and conditions disproportionately affecting women and that fully embrace our biological and environmental differences. Because while women and men deserve equal treatment under the law, at work, and in private interactions, we are not all the same when it comes to the biology that determines our sex classifications or in the combination of biology, environment, and experience that forms our gendered self-representations.

For example:

• Drug overdoses have contributed to the lowering of life expectancy in the United States for the second year in a row, and the rate of men dying from prescription pain relief overdose jumped by 404 percent from 1999 to 2016. But the overdose death rate for women over that same period increased by 583 percent.

• If a woman drinks the same exact amount of alcohol as a man, she will likely become more intoxicated (and more rapidly), even if they weigh the same.

• Half of all women over the age of 50 who have osteoporosis will break a bone; 20 percent of postmenopausal women with hip fractures die within a year.

• Among Americans with autoimmune diseases, such as lupus and rheumatoid arthritis, 3/4 are women.

• Of the 5.3 million Americans age 65 and older with Alzheimer’s disease, almost 2/3 are women.

• Depression is more common in women than men and is the greatest cause of disability for women worldwide.

WHRY leads the way in conducting and spurring research that continues to demonstrate how women and men have different risk factors for diseases, how responses to a given treatment can differ by gender, and how prevention strategies often need to be gender-specific.

We’ve learned that women are not just smaller versions of men or a subgroup of the population. Women and girls possess their own unique biology and gender identities and make up more than half of the 7.5 billion people in the world. Now is the time to make sure biomedical research and clinical practice focus on sex and gender to better care for women and girls and to uncover differences that can benefit everyone.

We certainly live in rapidly evolving times. And so we must invest the necessary effort, forethought, and resources to ensure that we are all living the healthiest and happiest lives possible.

Investigator Update

Dr. Martin Kriegel’s work on the origins of and potential new treatments for autoimmune disease has been featured in a pair of recent articles published by high-impact journals.

In Science, Dr. Kriegel and his co-authors demonstrated how normally beneficial bacteria can travel from the small intestines of mice and humans and trigger the body’s natural defenses against disease. The study evolved from Dr. Kriegel’s WHRY-funded pilot project as an Assistant Professor of Immunobiology and provides a new approach toward effectively treating autoimmune diseases such as systemic lupus by targeting the problematic bacteria with antibiotics.

In addition, a study Dr. Kriegel authored with Dr. Sandra L. Wolin, Professor Emeritus of Cell Biology, ran in a recent issue of Science Translational Medicine, describing how a protein found in common bacteria can trigger an autoimmune response. The study, also stemming from Dr. Kriegel’s WHRY-funded work, helps advance the development of individualized treatments for lupus that could target specific disease-causing bacteria at the source of autoimmune reactions.
Women’s Health Research at Yale

Women’s Health Research at Yale is changing the landscape of medical research and practice by ensuring the study of women and examining health differences between women and men to improve the lives of everyone.

What’s Inside:

“Why Didn’t I Know This?” — A New Blog on Women’s Health Research

WHRY Undergraduate Fellow Dhikshitha Balaji has launched the center’s first blog, titled “Why Didn’t I Know This?”

Balaji, who graduated in May with a degree in English Language and Literature, has been sharing her thoughts on women’s health and sex and gender differences, including the history behind the current gap in knowledge and how that gap is narrowing thanks to the latest research at WHRY and elsewhere.

“I want to go to medical school and treat diseases and promote health,” Balaji said. “I believe in the power of knowledge for everyone and in providing people with the most accurate information about their health so they can apply it to their lives.”

To read the blog, visit: https://medium.com/why-didnt-i-know-this

Your Brain on Drugs

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Getting Under the Skin

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