NEW CLUES: PREDICTING OPIOID MISUSE IN PATIENTS ON LONG-TERM PAIN THERAPY

An estimated 20 percent of all patients presenting with non-cancer related pain at a physician’s office are prescribed opioids, but which of these patients, especially those who use the medicine long-term to control chronic pain, are likely to become addicted? Understanding the characteristics of such patients could arm doctors with important insight that could change the face of today’s opioid epidemic.

“We know the number of people who take prescription opioids and then turn to heroin is on the rise,” said R. Kathryn McHugh, PhD, assistant professor of psychology in the Department of Psychiatry at Harvard Medical School and an associate psychologist with the Division of Alcohol and Drug Abuse at McLean Hospital. “Our research asks ‘can we predict which patients will progress to misuse of opioids before it happens?’ and if so, what can we do to prevent that from happening.”

Dr. McHugh said one factor appears to be a person’s ability to manage his or her own emotions.

In a recent study in *The Journal of Pain*, Dr. McHugh and colleagues looked at 51 people who were receiving opioid treatment for chronic pain. Participants were, on average, 50

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years old. Researchers looked at medical records and examined subjects for pain sensitivity. They also tested their tolerance of their own emotions—did the subjects feel they could handle emotions such as anger or anxiety?

“What we found was that those who were misusing their medication, for instance, by taking more than prescribed, had much less tolerance of their own distress,” said Dr. McHugh.

“Some studies suggest as much as 30-40 percent of people who are taking opioids for chronic pain will eventually misuse their medications.”

“When they can’t handle how they are feeling, they just want to make it go away, so they are more likely to take an extra pill.”

Neither the level of the participant’s pain nor the severity of their depression or anxiety mattered as much as their ability to tolerate distress, said Dr. McHugh.

Findings of another study, presented in June at the annual meeting of the College on Problems of Drug Dependence, suggest a patient’s ability to delay gratification—or hold off getting a reward in order to get a larger reward in the future—also may play a role in opioid misuse.

The study involved 139 participants who were in treatment for opioid use disorder and used prescription painkillers or heroin. Although some of these participants had been prescribed opioids for pain, many first started using opioids by getting them from friends or family.

“People who are more susceptible to a substance use disorder are more impulsive and less likely to delay gratification,” said Dr. McHugh. This impulsivity makes people more likely to engage in behaviors, even when they know they are risky.

There were also differences depending upon the type of drug that was misused. The research found heroin users were much more impulsive and less likely to be restrained in seeking gratification than those who misused opioid pills.

While more research in this area is needed, studies like Dr. McHugh’s could eventually lead to the development of screening tools to help clinicians identify those at higher risk.

“Some studies suggest as much as 30-40 percent of people who are taking opioids for chronic pain will eventually misuse their medications,” she said. “Clinicians need all the tools they can get to predict which subset of patients will do well and which will not.”
By 5pm, Kathy Stafford’s busy day with the kids was winding down and she would reach for a glass of wine. But as time went on, one glass in the early evening wasn’t enough.

“I found myself wanting and having a glass of wine well before 5pm,” says the mother of two whose battle with alcohol lasted five years. “Alcoholism is a progressive illness and that is the way it went for me. I would drink against my will, knowing that if I did, I would feel better. And that scared me.”

Kathy’s husband called her primary care doctor who suggested detoxification at McLean Hospital. That led her to Fernside, McLean’s premier drug and alcohol treatment program. Located on a mountain ridge with a view of Boston in the distance, Fernside offers exceptional clinical care and puts into practice the innovative research findings from McLean’s renowned addiction program.

“We have all the research at our disposal including up to date, high level expertise to address the full spectrum of psychiatric conditions,” explained Rocco Iannucci, MD, director of Fernside. “This allows us to offer the absolute best practices for treating those who are struggling with addiction and co-existing psychiatric disorders, and for those who want to tackle substance problems using state-of-the-art, evidence-based practices.”

Recently, for example, Fernside instituted gender-specific programs—women’s and men’s recovery groups based on protocols developed at McLean—after McLean researchers found evidence these groups led to increased patient engagement. Integrated group therapy, another evidence-based psychotherapy developed at McLean, was put into place after researchers found it to be beneficial for those with both substance use disorder and bipolar disorder.

Kathy enrolled in Fernside’s 28-day program just before Thanksgiving of 2013.

“I was so afraid when I went in. I didn’t know what to expect,” recalled Kathy. “But it was such a comfortable, warm environment. I felt safe. It did not feel like I was in a hospital. I was actually glad to be there getting help.”

Fernside offers nine private rooms and a range of therapy including motivational enhancement therapy, cognitive behavior therapy, dialectical behavior therapy, mindfulness-based cognitive therapy, acceptance and commitment therapy, and medication-assisted therapies, in addition to the groups described above.

It also offers a comprehensive mind and body recovery program that includes yoga, individualized fitness plans, nutrition education, smoking cessation, and expressive art and music therapies.

“I am so grateful for the skills that this program provided me to live a healthier and happier life without alcohol.”

While at Fernside, Kathy attended both individualized therapy with a counselor who specializes in alcohol addiction and intense group sessions.

“I went for long walks in the conservation land trails close by, worked out at the gym, did yoga and crafts—all of which aided in changing my daily routine,” said Kathy. “I was able to focus on my recovery.”

She also attended AA meetings nightly, which she was able to continue once she returned home. Now, she is enjoying her 10 and 11 year olds, and is no longer obsessed with thoughts of drinking.

“I have a sense of freedom now,” Kathy explains. “I am so grateful for all the skills that this program provided me to live a healthier and happier life without alcohol.”

For information on Fernside or to make a referral, call 844.425.8964.
LESSONS LEARNED FROM THE BENZODIAZEPINE WITHDRAWAL PROGRAM

Recent studies show more American adults are filling prescriptions for benzodiazepines and are receiving increasing quantities of medication throughout their course of treatment. At the same time, 31 percent of the nearly 23,000 prescription overdose deaths in 2013 involved this class of drug.

“While benzodiazepines have their place in treatment, they have been over prescribed especially in the elderly population and many patients have a hard time tapering off them,” said Olivera Bogunovic, MD, medical director of Ambulatory Services and head of the benzodiazepine withdrawal program within the Division of Alcohol and Drug Abuse at McLean Hospital. “With very rapid inpatient tapering, the relapse rate can be as high as 50 percent.”

Dr. Bogunovic’s Benzodiazepine Withdrawal Program uses a safe and slow taper process with psychiatric support, individualized to each patient. It starts with a full assessment of the patient’s condition and current withdrawal symptoms. The program has treated patients ranging in age from 18 to mid-70s. Some of the patients became addicted to the medication and were abusing it, while others were taking the medication as prescribed but developed side effects and had trouble discontinuing use on their own or with their physician.

“It can take several months or up to one year for a successful taper,” she said. “Our program has been successful because it offers the intense, personalized attention that some patients need to manage symptoms and allows them to break free of the medication.”

Pat, now 34, has successfully gone through the program. In recovery from opioid addiction since 2010, Pat wanted to be free of the Klonopin he had taken for years to control performance-based anxiety in his high-stress job.

“I had to take more and more to get the same level of anxiety relief. I ended up on 20 milligrams a day. I didn’t want to be chained down to this really addictive substance any more,” Pat said. “At the same time, the mental side effects of coming off the drug were really terrifying.”

With the help of Dr. Bogunovic and the rest of his treatment team, Pat added Neurontin to his treatment and over the course of 10 months, slowly tapered off of Klonopin.

“I feel like myself again, and I have so much gratitude,” said Pat. “I recognize how lucky I am to have this amazing team and parents and a girlfriend who are supportive. It’s almost impossible to do this by yourself in a vacuum.”

“Our program has been successful because it offers the intense, personalized attention that some patients need.”

Olivera Bogunovic, MD
More than 400 clinicians from around the world converged on Cambridge, Massachusetts in early May for the McLean Hospital Addictions 2016 conference. Those in attendance included addiction specialists, mental health professionals, and practitioners, representing family and internal medicine, anesthesiology, infectious disease, pediatrics, and emergency medicine.

“This was a hugely successful conference that brought together a variety of professionals who are interested in helping people with substance use and other addiction disorders,” said Christopher M. Palmer, MD, director of the Department of Postgraduate and Continuing Education at McLean. “The wide range of topics allowed for in-depth exploration of contemporary issues in the addiction field.”

The sixth annual conference covered topics such as addiction and suicide, pain management in the context of addiction, medical marijuana, and gambling disorders.

To learn more about McLean’s other Continuing Education offerings, including the next Addictions conference scheduled for May 2017, please visit mcleanhospital.org/conferences.
For more than 20 years, Staci Gruber, PhD, director of McLean Hospital’s Cognitive and Clinical Neuroimaging Core and associate professor of psychiatry at Harvard Medical School, has dedicated her work to uncovering the mysteries of marijuana. As the country continues to debate the pros and cons of the legalization of marijuana and medical marijuana, Dr. Gruber’s work has never been more critical. She recently sat down with McLean Hospital’s news team for an exclusive interview.

What have you discovered about the impact of early marijuana use?
The results have been striking. Data from our studies and other groups have now demonstrated that chronic, heavy marijuana smokers with earlier onset (under the age of 16) show significant changes in brain structure and function relative to those with later onset. They appear to have more difficulty with cognitive tasks, particularly those mediated by the frontal cortex. Interestingly, later onset smokers don’t appear to have the same level of difficulty with frontally-mediated tasks and appear more similar to those who have never smoked.

Does the type of marijuana product used make a difference in your findings?
While we’ve looked at age of onset, frequency, and magnitude of marijuana use and done some work exploring the ways that people use cannabis (smoking, vaporizing, dabbing, edibles, etc.), there’s a lot we still have to learn. We’ve recently begun collecting information on the actual products that our subjects use. So far, we can say that earlier age of onset as well as frequency and magnitude of use are all related to task performance and measures of brain health.

What do we know about the impact of medical marijuana on brain function?
No studies thus far have assessed the specific impact of medical marijuana on brain-related measures or assessed outcome over extended periods of time. That’s why in 2014 we launched the MIND program (Marijuana Investigations for Neuroscientific Discovery). Our first phase of study involves assessing patients certified for medical marijuana use prior to the initiation of their medical marijuana treatment using a comprehensive battery of measures that captures information regarding their mood, cognitive status, quality of life, sleep, clinical symptoms, and their current use of ‘standard’ pharmacologic agents. We’ve collected data on brain structure and function as well as their most commonly used products and will continue to see them for follow-up visits over the course of 12 months. While our data are very preliminary, early findings are promising, as the majority of our participants report a positive experience with the treatment.

Why is marijuana research so critical at this point in time?
Perception of risk and harm related to marijuana use is at an all-time low among our youth, which may in fact be the result of our ongoing dialogues about medical marijuana. In fact, for the first time in 2015, the National Monitoring the Future study reported that more high school seniors smoke marijuana every day than smoke cigarettes. It is important to let them know that during adolescence and teen years, the brain is still developing and vulnerable to many influences, including drugs. In addition, more potent, concentrated forms of marijuana like shatter, wax, dabs, and budder are increasing in popularity and may be more likely to cause negative effects in those who are still developmentally immature, given the very high levels of THC in these products. My work and that of my colleagues in this field is dedicated to answering many complicated questions that are designed to help policymakers make sound, fact-based decisions.

Dr. Gruber’s work has recently been featured on CNN, Yahoo News, ESPN, and PBS.
RESEARCH ROUNDUP

THE FOLLOWING ARE SOME RECENT PEER-REVIEWED PUBLISHED STUDIES FROM McLEAN HOSPITAL AND OUR RESEARCH COLLEAGUES

Long-term outcomes from the National Drug Abuse Treatment Clinical Trials Network Prescription Opioid Addiction Treatment Study
ncbi.nlm.nih.gov/pmc/articles/PMC4407806

Immediate and persistent effects of salvinorin A on the kappa opioid receptor in rodents, monitored in vivo with PET
Placzek MS, Van de Bittner GC, Wey HY, Lucas SE, Hooker JM. Neuropsychopharmacology June 2015
nature.com/npp/journal/v40/n13/full/npp2015159a.html

Availability of N-methyl-D-aspartate receptor coagonists affects cocaine-induced conditioned place preference and locomotor sensitization: implications for comorbid schizophrenia and substance abuse
jpet.aspetjournals.org/content/353/3/465.long

Neural correlates of adherence to extended-release naltrexone pharmacotherapy in heroin dependence
ncbi.nlm.nih.gov/pmc/articles/PMC4354350

Prolonged hypogonadism in males following withdrawal from anabolic-androgenic steroids: an under-recognized problem
ncbi.nlm.nih.gov/pmc/articles/PMC4398624

Initial response as a predictor of 12-week buprenorphine-naloxone treatment response in a prescription opioid-dependent population
McDermott KA, Griffin ML, Connery NS, Hilario EY, Fiellin DA, Fitzmaurice GM, Weiss RD. Journal of Clinical Psychiatry February 2015
ncbi.nlm.nih.gov/pmc/articles/PMC4352119

Opioid withdrawal, craving, and use during and after outpatient buprenorphine stabilization and taper: a discrete survival and growth mixture model
ncbi.nlm.nih.gov/pmc/articles/PMC4252696

The multi-site prescription opioid addiction treatment study: 18-month outcomes
Potter JS, Dreifuss JA, Marino EN, Provost SE, Dodd DR, Rice LS, Fitzmaurice GM, Griffin ML, Weiss RD. Journal of Substance Abuse Treatment January 2015
ncbi.nlm.nih.gov/pmc/articles/PMC4250351
INSIDE:
BRINGING YOU THE LATEST ADVANCES
in substance use treatment and research from McLean Hospital and Harvard Medical School

On the Road

McLean Hospital and its addiction specialists will be participating in a number of conferences throughout the rest of 2016 and early 2017.

If you plan to attend any of these meetings, we hope to see you! To schedule a time to meet with us, please call 844.425.8964.

Cape Cod Symposium on Addictive Disorders
September 8-11, 2016
Hyannis, MA

Canadian Psychiatric Association Annual Conference
September 22-24, 2016
Toronto, Canada

Moments of Change
September 26-29, 2016
Palm Beach, FL

ABCT Annual Convention
October 27-30, 2016
New York, NY

Employee Assistance Professionals Association Annual Conference
October 31-November 3, 2016
Chicago, IL

American Academy of Addiction Psychiatry
December 8-11, 2016
Bonita Springs, FL

Nevada Psychiatric Association, 22nd Annual Psychopharmacology Update
February 15-18, 2017
Las Vegas, NV

American Society of Addiction Medicine
April 6-9, 2017
New Orleans, LA

American Psychiatric Association Annual Meeting
May 20-24, 2017
San Diego, CA

National Association of Addiction Treatment Providers
May 21-23, 2017
Austin, TX

West Coast Symposium on Addictive Disorders
June 1-4, 2017
La Quinta, CA