The Opioid Epidemic

What Does it Mean for Nurses?

ABSTRACT

The United States is facing a major crisis with the current opioid epidemic. Tens of thousands of individuals are dying each year due to abuse and misuse of heroin and prescription opiate drugs. Nurses play an integral role in these aspects of health care and offer solutions by providing education; preventive measures; treatments, including medication-assisted treatments (MATs); and ongoing recovery options for individuals with opioid use disorders. Nurses provide education, issue prescriptions and dispense medications, and provide overall physical and mental health care to patients struggling with this "disease of the brain," and with the signing of the Comprehensive Addiction and Recovery Act, advanced practice RNs will soon be able to include MATs related to buprenorphine as part of their treatment plan. The current article explores the anatomy, physiology, and genetics of addiction and how they relate to the pharmacological MATs used to treat opioid use disorders. [*Journal of Psychosocial Nursing and Mental Health Services, 55*(1), 18-23.]

The United States is in crisis. In 2015, more than 27 million U.S. citizens reported current use of illicit or misuse of prescription drugs, to the extent that approximately 8 million individuals required treatment (Center for Behavioral Health Statistics and Quality, 2016). Today, more Americans die each year as a result of drug overdoses (both illegal and prescription) than are killed in motor vehicle accidents (Xu, Murphy, Kochanek, & Bastian, 2016). In fact, in 2015, more than 33,000 individuals died due to an overdose of heroin or prescription opiate drug (Centers for Disease Control and Prevention, 2016), with deaths due to heroin-related causes surpassing those due to gun homicides (Drug Enforcement Agency, 2016).

On an average day in the United States, 650,000 opioid drug prescriptions are dispensed, which is enough to allow each citizen one full bottle of opiate drugs in a given year (QuintilesIMS Institute, 2016). The opioid epidemic has contributed to a growing annual economic impact of approximately $193 billion based on crime, violence, abuse, and the associated health care costs related to substance use and misuse disorders (U.S. Department of Justice National Drug Intelligence Center, 2011). These overwhelming statistics present a national health concern and an opening for nurses, of all practice disciplines and degrees, to intervene using their holistic skills to assess, educate,

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and prescribe treatments, including pharmacological agents, as indicated, to improve the care of individuals with opioid use disorders.

Prior to assuming his position as U.S. Surgeon General, Dr. Vivek H. Murthy (2016, p. v) worked with countless nurses, who he reports inspired him to "do something about the addiction crisis in America." In November 2016, the first ever report of its kind, *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*, was published by the U.S. Department of Health and Human Services. Building on the foundation that substance misuse and abuse is a neurobiological disease of the brain, the report focuses on interventions for recovery from substance use disorders involving counseling and psychotherapy, community education, social support, and medication-assisted treatments (MATs). Nurses play an integral role in these aspects of health care and offer solutions by providing education; preventive measures; treatments, including MATs; and ongoing recovery options for individuals with opioid and substance use disorders.

A DISEASE OF THE BRAIN

To understand the pharmacological treatments available for opioid use disorders, the anatomy and functions of the human brain as they relate to opioid addiction must first be explored. There are three major areas of the brain associated with substance use disorders: (a) the basal ganglia, (b) amygdala, and (c) prefrontal cortex (**Figure**). Opioid agents have a powerful effect in producing pleasurable feelings that alleviate stress and anxiety, compromising executive function capabilities and fueling the overwhelming drive to seek and compulsively use these substances. **Table 1** illustrates the ways in which these brain regions and their associated networks and neurochemicals are involved in substance and opioid use disorders.

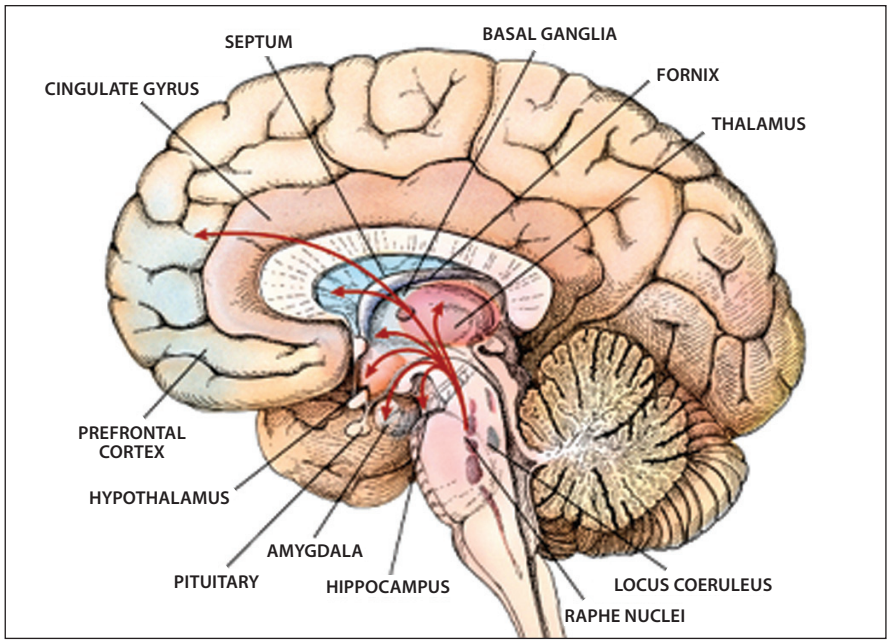

Figure. Schematic of the brain.
Photo courtesy of and reprinted with permission from C. Donner (2013).

Genetics also play a role in understanding opioid use disorders and potential MATs. It is well known that heritability accounts for approximately 50% of the risk factors for addiction, whereas environmental influences account for the remaining 50%. In recent years, various genes have been identified and are thought to have some impact on the risks associated with and pharmacological treatments for substance use disorders.

The pharmacodynamic μ-opioid receptor gene is associated with the risk of abuse and addiction, thus caution should be used in prescribing opioid agents to individuals with the G allele (Dinarvand et al., 2014). These individuals may require higher-than-average doses of opioid agents for pain relief, which in turn may lead to dependence, addiction, or both. Similarly, catechol-O-methyltransferase (COMT), another pharmacodynamic gene, is associated with the breakdown of dopamine in the prefrontal cortex, which affects reward-seeking behaviors, impulsivity, and cognition (Shield, Thomae, Eckloff, Wieben, & Weinshilboum, 2004). Individuals with the met allele of COMT tend to have higher than normal levels of dopamine, which is associated with better cognitive performance as well as increased anxiety and reactivity (Smolka et al., 2005). Individuals with the val allele of COMT tend to have reduced levels of dopamine in the prefrontal cortex, resulting in decreased executive functioning and impulsivity (Malhotra et al., 2002). Therefore, individuals with the met/met or val/met variants of COMT may be susceptible to opioid misuse and addiction as well as other psychiatric illnesses.

It is also important to understand the pharmacokinetic genetic polymorphisms as they relate to drug–drug interactions. Most psychotropic medications are either common inducers or inhibitors of cytochrome P450 (CYP) system enzymes in the liver. Understanding the genetic polymorphisms can lead to improved drug dosing by lowering the dosage

TABLE 1

REGIONS OF THE BRAIN ASSOCIATED WITH OPIOID USE DISORDERS

Brain Region	Associated Areas	Neurochemical Involvement	Impact on Health and Survival	Impact in Opioid Use Disorders
Basal ganglia	Nucleus accumbens Dorsal striatum	Increases • Dopamine • Opioid activation • Glutamate	• "Reward center" • Feelings of pleasure • Motivation and engagement	• Binge and intoxication • Reward-seeking behaviors • Habit formation
Amygdala	Hypothalamus	Decreases • Dopamine (D2) Increases • Norepinephrine • Corticotropin releasing factor	• "Fight or flight" • Regulates stress and anxiety	• Withdrawal symptoms (especially irritability and anxiety) • Regulation of pituitary gland
Prefrontal cortex	Nucleus accumbens Dorsal striatum	Increases • Glutamate	• "Executive function" ("Stop and Go Center") • Overall cognition • Decision making • Organization • Time management	• Preoccupation and anticipation • Emotional dyscontrol • Impulsivity • Poor decision making

for patients with poor metabolism and increasing the dose or offering more frequent medication dosing for patients with ultra-rapid metabolism.

Many opioid medications and treatments are substrates of the pharmacokinetic genes CYP2D6, CYP3A4, and CYP2B6 responsible for the metabolism of the drug. In addition, methadone is metabolized by even more CYP enzymes. For instance, tobacco is a potent inducer of the CYP1A2 gene, which also metabolizes methadone. If a smoker is stabilized on methadone and stops smoking, the result can be a dangerous increase in the methadone level (Wahawisan, Kolluru, Nguyen, Molina, & Speake, 2011), which may lead to overdose or even death. Similarly, grapefruit juice is a potent inhibitor of the CYP3A4 gene, which also metabolizes methadone, leading to decreased absorption of approximately 50% within 4 hours of consumption (Benmebarek et al., 2004) and decreased methadone level.

MEDICATION-ASSISTED TREATMENTS FOR OPIOID USE DISORDERS

Many individuals, including policymakers, authorities in the criminal justice system, and treatment providers, have viewed MATs for substance use disorders as substituting one addictive substance for another. These individuals have adhered instead to an abstinence-only philosophy that avoids the use of medications, especially those that activate opioid receptors. Such views are not scientifically supported; research demonstrates that MATs lead to better treatment outcomes compared to behavioral treatments alone (National Institute on Drug Abuse, 2012). One of the major keys to treating opioid use disorders with MAT is to provide patients with an adequate dose of the medication and an adequate duration of treatment, which is long enough to offer the best chance of maintaining abstinence, often >1 year. **Table 2** lists MATs approved for the maintenance of abstinence in individuals with opioid use disorders.

MATs for opioid use disorders used in conjunction with counseling and behavioral therapies have been associated with many positive outcomes. The objective of MAT is to provide a holistic, whole person approach to treating opioid use disorders to improve the overall physical and emotional health and well-being as well as to restore the individual's ability to function as a productive member of society. When offered as part of the overall treatment plan, MAT has been shown to increase abstinence from opioid use/abuse, decrease drug-related mortality, increase engagement and retention in treatment, reduce criminal activities, lower risk of communicable diseases (e.g., hepatitis, HIV/AIDS), and decrease health care costs (Connery, 2015; Substance Abuse and Mental Health Services Administration [SAMHSA], 2015). MAT interventions also suppress withdrawal symptoms, extinguish cravings, and block the reinforcing effects of the abused opioid agents.

Although the three major U.S. Food and Drug Administration–

TABLE 2

U.S. FOOD AND DRUG ADMINISTRATION–APPROVED OPIOID USE DISORDER MEDICATION-ASSISTED TREATMENTS

Drug	Distribution	Indication(s)	Mechanism of Action	Dosing Frequency	Pregnancy/DEA CDS Class	Abuse/ Diversion
Methadone	• SAMHSA certified • OTPs	Detoxification Maintenance	Synthetic full μ-opioid agonist Inhibits NE & 5HT	Daily—oral tablet or liquid Initial 10 mg to 30 mg Typical 60 mg to 120 mg	Category C Can nurse infant DEA CDS II	Yes
Buprenorphine	• Currently only licensed physician with waiver[a] • Outpatient	Treatment induction	Opioid partial agonist	Daily—sublingual tablet or film Initial 2 mg to 4 mg Increase by 2 mg to 4 mg	Category C Use caution DEA CDS III	Yes
Buprenorphine with naloxone	Same as buprenorphine	Maintenance	Opioid partial agonist/opioid antagonist	Daily—sublingual tablet or film Typical 8 mg to 16 mg Maximum dose 24 mg	Category C Use caution DEA CDS III	Yes
Naltrexone	• Practitioners licensed to prescribe • Outpatient	Prevention of relapse	Opioid antagonist Cannot begin treatment until opioid free for 7 to 10 days	Daily—oral tablet Typically 50 mg to 100 mg Monthly—intramuscular injection 380 mg/4 cc	Category C Avoid nursing infant Not controlled	No
Naloxone	• First responders • Pharmacies • Prescribing practitioners • Outpatient	Acute opioid overdose	Opioid antagonist	As needed for overdose Subcutaneous injection Nasal spray	Can be used in pregnancy Not controlled	No

Note. DEA = Drug Enforcement Agency; CDS = controlled dangerous substance; SAMHSA = Substance Abuse and Mental Health Services Administration; OTP = opioid treatment program; NE = norepinephrine; 5HT = serotonin.

[a] Nurse practitioners and physician assistants may receive waiver under the Comprehensive Addiction and Recovery Act (2016).

approved medications for opioid abstinence have all shown efficacy, there are subtle differences that make each unique and may offer benefit to one patient versus another.

Methadone

Methadone can only be dispensed by opioid treatment programs (OTPs) certified by SAMHSA and approved by the designated state authority. Under federal regulations, it can be used in individuals younger than 18 at the discretion of an OTP physician (SAMHSA, 2015). In addition, individuals who choose methadone to maintain abstinence must be committed to appearing at the OTP on a daily basis until they "earn take-home doses," through the accompanying contingency management program. Methadone is extensively metabolized by multiple enzymes by the liver's CYP450 system; thus, the risk of drug–drug interactions is a concern. Although advanced practice RNs (APRNs) with controlled dangerous substance (CDS) II prescriptive authority can prescribe methadone for management of chronic intractable pain, APRNs cannot prescribe methadone for opioid abstinence.

Buprenorphine

Buprenorphine, as opposed to the combination of buprenorphine/naloxone, is the preferred formulation for induction of MAT as well as for patients who have hepatic impairment or women who are pregnant (SAMHSA, 2016). Buprenorphine is less extensively metabolized in the liver than methadone; therefore, there is less potential for drug–drug interactions. One advantage to buprenorphine MAT is that it can be prescribed in outpatient settings by practitioners who hold a waiver certifying their training in opioid use disorders and the prescribing and monitoring of buprenorphine. At this time, SAMHSA, in collaboration with numerous nursing organizations, is in the process of developing the training modules to allow APRNs to be waivered to prescribe buprenorphine as part of the Comprehensive Addiction and Recovery Act (CARA) signed into law in July 2016, which expands the provider base to increase the availability of MAT for individuals with opioid use disorders.

Although the three major U.S. Food and Drug Administration–approved medications for opioid abstinence have all shown efficacy, there are subtle differences that make each unique and may offer benefit to one patient versus another.

Buprenorphine/Naloxone

This combination formulation is used for detoxification and/or maintenance of abstinence for individuals 16 or older. Caution must be used when prescribing this formulation as the naloxone component can precipitate opioid withdrawal, although, this may also deter patients from misuse by injection. Other considerations are listed above under buprenorphine.

Naltrexone

This MAT produces no opioid-like effects and is not subject to abuse. Naltrexone prevents other opioid agents from binding to opioid receptors so that they have little to no effect. It also interrupts the effects of any opioid drugs, precipitating opioid withdrawal in patients with opioid dependence. Naltrexone, in any of its delivery systems, can be administered only after a complete detoxification from opioid agents. The extended-release monthly injectable is recommended to prevent relapse to opioid agents. APRNs with prescriptive authority can offer this MAT in any setting in which they work.

Naloxone

Although not technically a MAT for abstinence from opioid agents, naloxone is an important medication in the arsenal to combat the opioid epidemic. Naloxone works by displacing opioid agents from receptors in the brain, thereby blocking their effects on breathing and heart rate (SAMHSA, 2016). The sole purpose of naloxone is to prevent death due to opioid overdose. It essentially extends the time available for family, friends, or first responders to maintain life while transporting a victim of opioid overdose to a facility with more comprehensive treatments. It is not intended as a method to treat opioid addiction. In signing CARA (2016), President Obama has pledged to expand the availability of naloxone in the community in an effort to reduce the thousands of deaths related to opioid overdose in the United States.

COMPREHENSIVE ADDICTION AND RECOVERY ACT OF 2016: WHAT'S IN IT FOR NURSES?

On July 22, 2016, President Obama signed the CARA into law. The Treatment Expansion and Modernization Act of CARA temporarily expands the eligibility to prescribe buprenorphine-based drugs as MAT for substance use disorders. Nurse practitioners and physician assistants, who complete a minimum of 24 hours of specified training and have a col-

laborating physician who is eligible to prescribe buprenorphine, may be eligible to receive a waiver through October 2021, which will allow them to prescribe, administer, and/or dispense buprenorphine in an outpatient office setting to treat up to 30 patients with opioid use disorders. This is an important step for APRNs and the patients they treat with opioid use disorders, as it will allow APRNs to practice to the fullest extent of their education and training and offer their expertise as holistic providers in combatting the opioid epidemic facing the United States.

SUMMARY

The United States is facing a major crisis with the current opioid epidemic. Tens of thousands of individuals are dying each year due to abuse and misuse of heroin and prescription opiate drugs. Although nurses have provided education, issued prescriptions and dispensed medications, and provided overall physical and mental health care to patients struggling with this "disease of the brain," APRNs have not been able to include MATs related to buprenorphine as part of their treatment plan. The signing of CARA will provide the opportunity for APRNs who choose to use MAT with buprenorphine to obtain a waiver and include this treatment in the comprehensive, holistic care they provide to their patients with opioid use disorders.

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