

## How is prescription opioid misuse related to chronic pain?

Health care providers have long wrestled with how best to treat the more than 100 million Americans who suffer from chronic pain.<sup>38</sup> Opioids have been the most common treatment for chronic pain since the late 1990s, but recent research has cast doubt both on their safety and their efficacy in the treatment of chronic pain when it is not related to cancer or palliative care.<sup>29</sup> The potential risks involved with long-term opioid treatment, such as the development of drug tolerance, hyperalgesia, and addiction, present doctors with a dilemma, as there is limited research on alternative treatments for chronic pain. Patients themselves may even be reluctant to take an opioid medication prescribed to them for fear of becoming addicted.

Estimates of the rate of opioid misuse among chronic pain patients vary widely as a result of differences in treatment duration, insufficient research on long-term outcomes, disparate study populations, and different outcome measures (e.g., dependence versus OUD or addiction). One study assessing current criteria for OUD in a large number of chronic pain patients receiving opioids found that 28.1 percent had mild OUD, 9.7 percent had moderate OUD, and 3.5 percent had severe OUD (addiction).<sup>39</sup>

To mitigate addiction risk, physicians should adhere to the [CDC Guideline for Prescribing Opioids for Chronic Pain](#). Before prescribing, physicians should assess pain and functioning, consider if non-opioid treatment options are appropriate, discuss a treatment plan with the patient, evaluate the patient's risk of harm or misuse, and co-prescribe naloxone to mitigate the risk for overdose (see NIDA's webpage on [naloxone](#)). When first prescribing opioids, physicians should give the lowest effective dose for the shortest therapeutic duration. As treatment continues, the patient should be monitored at regular intervals, and opioid treatment should be continued only if meaningful clinical improvements in pain and functioning are seen without harm.<sup>29</sup>

### CNS Depressants

## What are CNS depressants?

CNS depressants, a category that includes tranquilizers, sedatives, and hypnotics, are substances that can slow brain activity. This property makes them useful for treating anxiety and sleep disorders. The following are among the medications commonly prescribed for these purposes<sup>40</sup>:

- **Benzodiazepines**, such as diazepam (Valium<sup>®</sup>), clonazepam (Klonopin<sup>®</sup>), and alprazolam (Xanax<sup>®</sup>), are sometimes prescribed to treat anxiety, acute stress reactions, and panic attacks. Clonazepam may also be prescribed to treat seizure disorders and insomnia. The more sedating benzodiazepines, such as triazolam (Halcion<sup>®</sup>) and estazolam (Prosom<sup>®</sup>) are prescribed for short-term treatment of sleep disorders. Usually, benzodiazepines are not prescribed for long-term use because of the high risk for developing tolerance, dependence, or addiction.
- **Non-benzodiazepine sleep medications**, such as zolpidem (Ambien<sup>®</sup>), eszopiclone (Lunesta<sup>®</sup>), and zaleplon (Sonata<sup>®</sup>), known as z-drugs, have a different chemical structure but act on the same GABA type A receptors in the brain as benzodiazepines. They are thought to have fewer side effects and less risk of dependence than benzodiazepines.
- **Barbiturates**, such as mephobarbital (Mebaral<sup>®</sup>), phenobarbital (Luminal<sup>®</sup>), and pentobarbital sodium (Nembutal<sup>®</sup>), are used less frequently to reduce anxiety or to help with sleep problems because of their higher risk of overdose compared to benzodiazepines. However, they are still used in surgical procedures and to treat seizure disorders.

## How do CNS depressants affect the brain and body?

Most CNS depressants act on the brain by increasing activity at receptors for the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). Although the different classes of CNS depressants work in unique ways, it is through their ability to increase GABA signaling—thereby increasing inhibition of brain activity—that they produce a drowsy or calming effect that is medically beneficial to those suffering from anxiety or sleep disorders.<sup>40</sup>

## What are the possible consequences of CNS depressant misuse?

Despite their beneficial therapeutic effects, benzodiazepines and barbiturates have the potential for misuse and should be used only as prescribed.<sup>40</sup> The use of non-benzodiazepine sleep aids, or z-drugs, is less well-studied, but certain indicators have raised concern about their misuse potential as well.<sup>41</sup>

During the first few days of taking a depressant, a person usually feels sleepy and uncoordinated, but as the body becomes accustomed to the effects of the drug and tolerance develops, these side effects begin to disappear. If one uses these drugs long term, he or she may need larger doses to achieve the therapeutic effects. Continued use can also lead to dependence and withdrawal when use is abruptly reduced or stopped (see "[Understanding Dependence, Addiction, and Tolerance](#)"). Because CNS depressants work by slowing the brain's activity, when an individual stops taking them, there can be a rebound effect, resulting in seizures or other harmful consequences.<sup>40</sup>

Although withdrawal from benzodiazepines can be problematic, it is rarely life threatening, whereas withdrawal from prolonged use of barbiturates can have life-threatening complications.<sup>42</sup>

Therefore, someone who is thinking about discontinuing a CNS depressant or who is suffering withdrawal after discontinuing use should speak with a physician or seek immediate medical treatment.

### Stimulants

## What are stimulants?

Stimulants increase alertness, attention, and energy, as well as elevate blood pressure, heart rate, and respiration. Historically, stimulants were used to treat asthma and other respiratory problems, obesity, neurological disorders, and a variety of other ailments. But as their potential for misuse and addiction became apparent, the number of conditions treated with stimulants has decreased.<sup>43</sup> Now, stimulants are prescribed for the treatment of only a few health conditions, including attention-deficit hyperactivity disorder (ADHD), narcolepsy, and occasionally treatment-resistant depression.<sup>44-46</sup>

## How do stimulants affect the brain and body?

Stimulants, such as dextroamphetamine (Dexedrine<sup>®</sup>, Adderall<sup>®</sup>) and methylphenidate (Ritalin<sup>®</sup>, Concerta<sup>®</sup>), act in the brain on the family of monoamine neurotransmitter systems, which include norepinephrine and dopamine. Stimulants enhance the effects of these chemicals. An increase in dopamine signaling from nonmedical use of stimulants can induce a feeling of euphoria, and these medications' effects on norepinephrine increase blood pressure and heart rate, constrict blood vessels, increase blood glucose, and open up breathing passages.<sup>47</sup>

## What are the possible consequences of stimulant misuse?

As with other drugs in the stimulant category, such as cocaine, it is possible for people to become dependent on or addicted to prescription stimulants. Withdrawal symptoms associated with discontinuing stimulant use include fatigue, depression, and disturbed sleep patterns. Repeated misuse of some stimulants (sometimes within a short period) can lead to feelings of hostility or paranoia, or even psychosis.<sup>31</sup> Further, taking high doses of a stimulant may result in dangerously high body temperature and an irregular heartbeat. There is also the potential for cardiovascular failure or seizures.<sup>47</sup>

## Cognitive Enhancers

The dramatic increases in stimulant prescriptions over the last 2 decades have led to their greater availability and to increased risk for diversion and nonmedical use.<sup>48</sup> When taken to improve properly diagnosed conditions, these medications can greatly enhance a patient's quality of life. However, because many perceive them to be generally safe and effective, prescription stimulants such as Adderall<sup>®</sup> and Modafinil<sup>®</sup> are being misused more frequently.

Stimulants increase wakefulness, motivation, and aspects of cognition, learning, and memory. Some people take these drugs in the absence of medical need in an effort to enhance mental performance.<sup>49</sup> Militaries have long used stimulants to increase performance in the face of fatigue, and the United States Armed Forces allow for their use in limited operational settings.<sup>50</sup> The practice is now reported by some professionals to increase their productivity, by older people to offset declining cognition, and by both high school and college students to improve their academic performance.

Nonmedical use of stimulants for cognitive enhancement poses potential health risks, including addiction, cardiovascular events, and psychosis. The use of pharmaceuticals for cognitive enhancement has also sparked debate over the ethical implications of the practice. Issues of fairness arise if those with access and willingness to take these drugs have a performance edge over others, and implicit coercion takes place if a culture of cognitive enhancement gives the impression that a person must take drugs in order to be competitive.<sup>49,51</sup>

## Future Research Directions

There are a handful of psychedelic drugs being researched and used for mental health treatments. These drugs carry a risk, and must be administered under medical supervision. Information on these human studies can be found on [clinicaltrials.gov](#). These include:

- **Ketamine**, a dissociative drug, which has been approved by the FDA under the name esketamine for treatment resistant depression
- **MDMA**, a synthetic drug chemically similar to both stimulants and hallucinogens, which is being studied under an FDA [breakthrough therapy](#) designation for post-traumatic stress disorder
- **Psilocybin**, extracted from certain types of mushrooms, is being studied under a [breakthrough therapy](#) designation for treatment-resistant depression

## Are prescription drugs safe to take when pregnant?



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Some prescription medications taken by a pregnant woman can cause her baby to develop dependence, which can result in withdrawal symptoms after birth, known as neonatal abstinence syndrome (NAS). This can require a prolonged stay in neonatal intensive care and, in the case of opioids, treatment with medication (see "[Sex and Gender Differences in Substance Use Disorder Treatment](#)" in NIDA's [Substance Use in Women Research Report](#)). Women should consult with their doctors to determine which medications they can continue taking during pregnancy.

Opioid pain medications require particular attention; rising rates of NAS have been associated with increases in the prescription of opioids for pain in pregnant women. NAS associated with opioid use (heroin or prescription opioids) increased fivefold from 2000 to 2012, with a higher rate of increase in more recent years.<sup>52,53</sup>