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Letter From the Editor

William Ellsworth

Readers,

I hope you enjoy the fourth issue of the IYNA Journal! We greatly appreciate your continued (or new) readership.

Drug abuse and addiction is one of the most misunderstood disorders in neuroscience. Unfortunately, it is also one of the most important. Our understanding of drugs lays the bedrock for everything from our public policy on narcotics to our methods of treating addicts.

This understanding, of course, is derived from research. In the research section, Eva Kitlen, Jacob Umans, Kyle Ryan discuss the intriguing relationship between marijuana and Alzheimer’s, and Jacob Umans and Meenu Johnkutty depict cell culture as a research method.

Drug addiction is a disease in and of itself, and can lead to many wide-ranging effects. In the disease section, Christian Gonzalez profiles alcoholic neuropathy, Kento Arendt discusses drug-induced insomnia, and Megumi Sano describes Fetal Alcohol Syndrome.

Drug-related diseases are certainly not going unchecked; researchers are developing a litany of techniques to combat this process. In the new technology section, Mallika Pajjuri writes about Probuphine, and Dhanya Mahesh analyzes the role smartphone apps play in fighting addiction.

Finally, drugs and society are inextricably intertwined. Society influences our choices with drugs, which in turn influences our public policy, which then influences society. In the neuroscience and society section, Jack Ross-Pilkington describes the opioid epidemic, Alexander Skvortsov outlines the different types of addiction, Norhan Algharabawy covers Tramadol, and Neelu Paleti discusses rehabilitation.

As always, it is critical that we recognize all of our dedicated writers for helping us make this issue the success that it is. You can find all of their names and positions on our Contributors page. If you have any questions, comments, or suggestions for us, please feel free to contact
us at info@youthneuro.org. We hope you enjoy our fifth issue as much as we enjoyed writing it!

Best Regards,

William Ellsworth
Editor-in-Chief, IYNA Journal
Update from the Directors

Board of Directors

Hello readers,

This month, the IYNA has undergone tremendous changes. Ever since we were founded back in March 2016, we have strived towards our goal: to promote neuroscience and enthusiasm amongst young adults. This month, we’ve decided to move one step further:

International Expansion:

As you may already be able to see by our name change, the YNCA has decided to rename itself to the IYNA (International Youth Neuroscience Association) due to our decision to expand internationally. The decision to expand came from our desire to reach as many students interested in neuroscience as possible. The IYNA already has members in over 10 countries. If you are interested in establishing an IYNA chapter in your country, contact us via our website or our email: info@youthneuro.org.

Myelin Initiative:

We at the IYNA are proud to announce the initiation of the MYELIN (Modern Youth Education, Leadership, and Inquiry in Neuroscience) initiative. We have partnered with the Synapse Project, another youth neuroscience organization centered in England, in order to develop a set of curricula in neuroscience for use in schools. These will focus on a wide range of topics, from experimental techniques to aging. If you are interested in participating in this project, please email info@youthneuro.org.

Non-profit Expansion:

In accordance with our mission, the IYNA plans to establish itself as an official tax exempt agency, under the provisions of section 501(c)(3) of the Internal Revenue code. We are currently in the process of raising the funds necessary for this incorporation, as well as the incorporation and application itself.

Best Regards,

Jacob Umans and Nicholas Chrapliwy
Presidents

Alexander Skvortsov and Janvie Naik
Executive Vice Presidents

Shreyas Parab
Treasurer

Kyle Ryan
Outreach Director
Basics of Neuroscience V: Addiction

Alexander Skvortsov

Introduction
In society, drug abuse and addiction is often perceived as solely the result of poor life choices. As a consequence of this view, addicts--who are certainly suffering enough already--are stigmatized by society. Such a perspective flies in the face of neuroscience. A plethora of research has shown that neural changes underlie the process of addiction; in turn, differences in neural circuitry can underlie differing susceptibilities to addiction. Thus, while poor individual choices certainly play a role, differences in our brains can lead to altered risk for addiction. How is neural circuitry involved in addiction? How do different drugs affect the brain in different ways? What is the role of neurotransmitters in all of this? We answer these questions and more in our fifth edition of Basics of Neuroscience.

Overview

An addiction is a condition of dependency that often manifests in response to chronic overuse of narcotic substances or activities. Drug addictions affect approximately 23 million people in the United States alone [1], and many more worldwide, especially in developing countries. Individuals suffering from addictions must endure a long and tenuous path to escape this burden. Approximately 50% of people find themselves experiencing relapses, recurrences of use of the addictive entity, after recovering from an addiction [1].

As described in our article on types of addiction, addictions can form in response to nearly all neuromodulating substances or activities that result in positive emotional response. Development of addictions to both of these categories, both substance and activity, operates within similar neural structures and processes.

Manifestation

To fully comprehend addiction, one must first understand how pleasure is perceived by the brain. Throughout all neural function, information is carried, and simultaneously processed, through neural circuits, or complex chains of neural pathways that regulate themselves. A neural circuit that is especially involved in the regulation of pleasure is the anterior cingulate circuit, which runs parallel to the corpus callosum (a bundle of neurons that joins the two cerebellar hemispheres),
and is heavily implicated in motivation [3]. The anterior cingulate circuit runs through a chunk of the brain known as the ventral striatum, which contains a part of the limbic system called the nucleus accumbens. The ventral striatum receives some input from the amygdala and hippocampus, which are involved with memory and learning (see Basics of Neuroscience IV for more information on this), potentially indicating some entanglement of memory processing and pleasure. In addition to this, another structure called the ventral tegmentum, sends dopaminergic neurons, or those that release the neurotransmitter dopamine, into the ventral striatum[2]. Finally, parts of the prefrontal cortex, such as the anterior cingulate cortex, the orbitofrontal cortex, and the medial frontal cortex, complete the circuit and finalize the sensation of pleasure. It is the prefrontal cortex that will inevitably make executive decisions concerning drug use. In short, substances and activities result in pleasure, whether directly or indirectly, through “flooding the nucleus accumbens with dopamine. The hippocampus lays down memories of this rapid sense of satisfaction, and the amygdala creates a conditioned response to certain stimuli.” [1].

As this process is repeated multiple times, associations form between the addictive entity and the pleasure causing release of dopamine solidify and strengthen through LTP (discussed in Basics of Neuroscience IV), the brain starts to replace the feeling of amiability towards an entity with that of desire, resulting in a motivational drive to pursue said entity. Ultimately, the prefrontal cortex is then influenced by this motivational drive to pursue the addictive entity, making it difficult to resist this urge.

An additional effect known as tolerance compounds the addiction. Because addictive entities provide an extremely accelerated shortcut to a feeling of reward, they flood the brain with a level of dopamine higher than that obtained through natural causes. This overwhelms dopamine receptors, resulting in a lowered rate of dopamine production, creating a dependence on the addictive entity. In addition, the brain becomes less sensitive to the addictive entity, requiring a higher quantity to produce the same effect.

References


Classifications of Addictions

Alexander Skvortsov

Addiction is a pain that many people know all too well. It is the immense, never ending struggle of battling monstrous, undefeatable impulses. Addictions can create such a feeling of desire that even the most strong-willed person cannot resist. In fact, many people unaffected by addiction assume that those addicted to a substance or activity are simply weak; however this is simply false. Addiction is much more than a mundane lack of willpower. According to Dr. George Koob, director of NIH’s National Institute on Alcohol Abuse and Alcoholism, “The brain actually changes with addiction, and it takes a good deal of work to get it back to its normal state. The more drugs or alcohol you’ve taken, the more disruptive it is to the brain.” [1]. This article will explore what addiction is, how it works, and the differences between addiction and temptation.

Overview

The word addiction is defined by the American Society of Addiction Medicine as “a primary, chronic disease of brain reward, motivation, memory and related circuitry.” An addiction is, as follows, a disease characterized by a strong impulse to use a given substance or to partake in a given activity. Addictions work primarily through the reward, motivation, and habitual response areas of the brain, and are based in chemical restructuring of the brain.

A way to easier understand exactly how potent addiction is lies in one of its synonyms: dependence. The word dependence brings up a feeling of insecurity, weakness, and subservience. As a child is dependent on a parent, so is an addicted individual to their item of choice.

A commonplace misconception regarding addictions is that of exclusivity to chemicals. While addictions to drugs are the most destructive, and so receive the most attention from researchers, addiction can be divided into 2 general categories: substance and behavioral.

Substance Addictions

Substance addictions are dependencies developed to a brain-modulating substance, or drug. Drug addictions almost always begin by choice- the affected individual must make a conscious decision to take their first shot, smoke their first cigar, or inject their first dose of heroin. This can
result in a powerful first high, which prompts the individual to repeat the drug intake. As they continue this process, their tolerance rises, increasing the threshold of substance necessary for the high to occur. As a result, the individual can often proceed to consume greater and greater quantities of the drug, inevitably resulting in an addiction. Every chemical substance can be addicting, with the most common drug addictions being alcohol, tobacco, marijuana, cocaine, heroin, and methamphetamines.

A relatively new threat lies in prescription drugs. Those very same medicines, antidepressants and antibiotics that are engineered specifically to help make our lives easier, can end up destroying lives at alarming rates. A study by the Foundation for a Drug Free World found that prescription drug overdoses have overtaken those of Heroin, Methamphetamine, and Cocaine combines, forming an alarming 45% of overdose deaths[2].

Caffeine is incredibly prevalent, and not often thought of as addictive. It is generally considered safe for relatively common consumption, and is consumed by a vast majority of Americans: about 90%. As a matter of fact, the per capita daily caffeine consumption is above 250mg of caffeine, more than in 12 ounces of coffee [3][4]. Caffeine can be found in many drinks, including coffee, some teas, most soft drinks, dark chocolates, and several over-the-counter (OTC) medications. Research shows that large doses of caffeine, especially those over 200 mg daily, can result in a negative mood, increased anxiety, and other detracting effects [3]. The hypothesis that caffeine is addictive is supported by the phenomenon of caffeine withdrawal symptoms. Abstinence from doses as small as 100 mg can result in withdrawal symptoms, which include, but are not limited to, headaches, fatigue, difficulty concentrating, irritability, depression, anxiety, flu-like symptoms, and sleepiness [3]. Severity of withdrawals from caffeine varies. Approximately 70% of caffeine-dependent individuals experiencing a caffeine withdrawal have reported impairment in their functional lives [3].

Another rare, yet tragic result of substance addiction is neonatal abstinence syndrome (NAS). Cases of NAS result from abuse of opiate substances by an expecting mother during pregnancy. If drug use continues through the pregnancy, the baby might be addicted to the drug at birth [5].

**Behavioral Addictions**

The second, underestimated form of addiction is that of behavioral addictions. There is evidence to support that any and all stimulating activities can be addictive. Behavioral addictions work the same pathways and processes as substance addictions [6]. As stated above, the difference lies in that the addicting entity is an activity/experience rather than a chemical neuromodulating substance. This means that while substance abuse can directly create addictions, behavioral addictions do so through indirectly through activation of primarily dopaminergic neurotransmitters (more on that in our Basics of Neuroscience article on how addictions mechanically work). Behavioral addictions can be based on a myriad of activities, and can be linked to a variety of
emotional effects, including material acquisition, adrenaline release, distraction. Most addictions work through a combination of several of these effects.

Material acquisition is the gain of property. The most basic behavioral addiction based on material gain is that of shopping. Shopping addictions generally develop as the affected individual spends more and more money on superfluous material possessions. With time, the individual starts to derive more pleasure from the process of acquiring goods than with the goods themselves, and can find themselves locked in a perpetual shopping spree. While going to the mall with friends is a perfectly healthy, normal way to spend time, using shopping as a way to escape stress can lead to, or be a sign of, a shopping addiction.

A second type of addiction linked to material acquisition is gambling. Gambling takes many forms, such as casino games, online fantasy sports, slot machines, and other activities in which money is invested, and can be lost or gained due primarily to chance. Gambling is also linked to adrenalinic addictions, or those related to the release of adrenaline. While gambling, an individual will often feel an immense thrill due to suspense and excitement. Unfortunately, gambling rarely pays off—many perpetual gamblers find themselves in financial crises.

Another major adrenalinic addiction, although less distinct as an addiction, is addiction to risky, dangerous activities. These activities will alert the nervous system of danger, releasing in a pleasurable rush of adrenaline.

Yet another addiction linked to adrenaline is the condition of video game dependence. Many thriller action games can be littered with emotional, stressful obstacles which, when overpowered, result in a sudden rush of adrenaline. These video games include various shooters and rpgs, as well as horror themed games.

As with gambling, video games do not fit neatly into one category. Video games can also be associated with the class of addictions primarily associated with distractions. Video games can provide a dull, white-noise distraction from hard, stimulating work, resulting in their prominent use by procrastinators. One can often find himself resorting to a video game as a way to escape the boredom of doing hard, menial work, whether physical or mental. As a result, an addiction forms, easily solidified and amplified by the use of video games for hours upon hours.

The other major addiction used as a distraction is an internet addiction. This includes social media as well as web surfing and other internet usage. This is similar to video game addictions, and often serves as an escape from work. A major feature of internet addictions is an obsession with connecting with other people through the internet. Although keeping in touch with your friends online is totally normal, some individuals find themselves only communicating with other people through the web.
References


Neuroscience and Society: Opiates
Jack Ross-Pilkington

Abstract
Opiates are a drug of contradictions. They come from the beautiful poppy plant, but create a ugly reality for users. They activate the same cells that alleviate pain, but they cause a great deal of anguish. Opiates destroy communities and lives and families, but addiction rates keep rising. To know opiates, and to fight their unlawful use, one must first know what they are and what they do to people.

Inside the brain, there are inhibitory receptors that modulate pain and calm the body. These are called opioid receptors. There are four main types: Delta, Kappa, Mu and Zeta [1]. Zeta receptors are involved in development, while Kappa, Mu and Delta are involved in reducing stress [2]. These receptors are beneficial and necessary for survival [3]. However, when you extract, process, and ingest sap from the poppy plant, certain chemicals attach to and activate the opioid receptors [4]. These chemicals are called opiates. The most common type of opiate is heroin.

As long as there have been organized societies, there have been opiate addicts. The first reference to opiates comes from ancient Sumer - a civilization that also invented writing and the wheel [6]. The Sumerian word for “poppy” is the same as the word for joy [7]. The ancient Greeks used opium as well. In The Odyssey, Homer mentions a drug given by Helen (the daughter of Zeus) to Telemachus (the son of Odysseus), which many believe is opium [8]. In many societies, opium was viewed as a medicine because of its painkilling properties [9]. Given that opium was addictive, knowledge of the preparation and use of opium was restricted to priests and doctors[10]. However, because it was impossible to totally regulate opioid use, illegal use put a strain on society[11].

Despite the ancient origins of opiate addiction, it remains a problem to this day. Around the world, 13.5 million people use opiates. That’s more than the population of New York, LA and Chicago combined [12]. Heroin users alone account for 9 million people [13]. One area where opioid usage has become a major problem is the northeastern US. Overdoses are disturbingly common. For example, Massachusetts, the overdose death rate is twice the national average [14]. Middlesex County alone had over 1,500 overdose deaths from 2000 to 2014 [15]. This increase is not just reflected in the statistics. There seems to be an almost infinite amount of horror stories coming from the epidemic. A man in Niagara Falls, NY was alleged to have left a 5-year-old boy unattended in a Dairy Queen. He was later found on the floor with a syringe in his arm[16]. A couple in Cincinnati collapsed in a McDonald’s in front of their child [17]. A man in Philadelphia was filmed injecting himself while on a bus [18]. These stories put a human face on the growing tragedy.
When we are faced with problems, it is natural to look for solutions. While it is impossible to completely eliminate heroin addiction, it is possible to reduce it. One option is to use buprenorphine or methadone, which has been shown to reduce cravings and criminal behavior [19]. However, some in the addiction recovery industry believe that these drugs are habit-forming [20]. As a result, only about half of addiction treatment centers use these medication [21]. One way to reduce the death toll is to create an intranasal version of Naxelone, a drug that reduces the harm of overdose[22]. But by far the most promising (and the most controversial) idea is harm reduction. The concept is simple - allow addicts to do heroin in a supervised environment, with clean needles, and with a safe dosage [23]. This aims to reduce overdose deaths and the spread of HIV-AIDS [24]. However, critics say that it condones or even encourages addiction [25].

Though there is no consensus regarding a solution to addiction, it is time for a national discussion on a solution to this problem. Too many lives have been lost, too many families have been torn apart, and too many communities have been reduced to nothing. The time for apathy is over. The time for action is now.

References


Rehabilitation: The Uphill Battle

Neelu Paleti

As a crisp apple-scented breeze swayed the auburn leaves on maple trees, one could feel the autumn season starting to set in. For a particular teenage boy, this meant the start of high school football season. But this excitement only lasted for a few days, after which he was met with a terrible head collision on the field. Post-surgery, this boy was prescribed seemingly innocuous drugs in order to improve his condition, but instead they did just the opposite. What started as a slight overdose gradually turned into a constant addiction, as he could not turn down his body's desire for more. Soon enough, glaring physical symptoms, including fatigue, slow reaction, and impaired coordination, forced him to withdraw from his favorite sport. From this point, it was simply a race to the bottom, as he sought no help to his continuous addiction to drugs. Through a combination of denial, shame, or sheer ignorance, the boy made a choice to steer clear of rehabilitation, and this decision just may have cost him his life.

Introduction to Rehabilitation

The situation described above is not uncommon for a countless number of people around the country and beyond. What starts out as a prescription medication turns into an undeniable addiction, sometimes beyond a person's awareness. The first step to curing any condition is the acceptance of the problem. However, in the case of victims of drug addiction, many are not even conscious of the damage being done.

In order to change such circumstances, rehabilitation is often prescribed as an ongoing process in order to identify the problem and treat the source with sensitivity and care. Out of the 23.5 million people needing treatment for drug or alcohol abuse in the U.S., only about 2.6 million are able to receive proper attention from experts in the field (National Institute on Drug Abuse, 2016). This large discrepancy is often a result of multiple factors, but ultimately the necessary help is not distributed ideally. Rehabilitation is often a crucial step in treatment, because patients are able to seek help, speak their minds, and finally embark on a journey to remove addiction from their lives. Without this step, many are left to suffer on their own, without proper guidance. In order to decrease the injuries and deaths resulting from substance abuse, it is imperative that society closes this gap and deliver essential help to the millions in need.

What are the steps involved?

Rehabilitation is a continuous process that often varies greatly from person to person. While some may still be in denial of their condition, others may just need encouragement to stop abusing drugs. Regardless of the stage, it is important for people to seek help as soon as possible, before emotional and physical changes become unmanageable.
The entire process starts with admission into a type of rehabilitation center that suits the patient well. This could be chosen from a variety of centers, including inpatient, outpatient, and dual diagnosis, depending on the severity of substance abuse, among other factors (12 keys rehab, n.d.). Inpatient care tends to focus on intensive, residential care, while outpatient care is relatively independent and guidance-based, and finally dual-diagnosis deals with situations regarding multiple disorders at once (12 keys rehab, n.d.). After several meetings with counselors and administrators, the source of the problem is then identified and addressed in future plans. After designing a personal approach to rehabilitation, the patient then works with staff to undergo a detox, one of the hardest parts of the entire process. This is a period during which all dosage of drugs and alcohol is gradually reduced and finally prohibited, and food and drink is moderated to fit the regulations of a healthy lifestyle (12 keys rehab, n.d.). As this continues, individual counseling begins, where conversations about life and progress are held to motivate individuals to follow the detox plan. Throughout the rest of rehabilitation, much of the responsibility of growth and change is shifted to the shoulders of the patients. This change in authority provides patients with a sense of choice and control, which further encourages and sustains good decision-making. Much of this process is paired with occasional counseling and family support, which eventually guides people along the best path, as they receive another chance, free from substance abuse (12 keys rehab, n.d).

How effective is rehabilitation?

Treatment of any kind depends on numerous different variables, and rehabilitation is just as vulnerable to these as any other treatment options. The process in its entirety works wonders for some, while barely motivating others to change at all. However, for the majority of people, rehabilitation and further treatment gives patients a sense of purpose and a path carved out to follow. People who possess the desire to change but lack the tools to do so can greatly benefit from rehabilitation, because the combination of detoxes, counseling, and community support ensure a positive environment for change.

However, some instances illustrate that it is possible to improve the rehabilitation process to achieve even greater success. In the current world, one of the biggest problems in rehabilitation is accommodating every single addict with a counselor and rehabilitation center (National Institute on Drug Abuse, 2016). The reality is that even if 100% of people abusing drugs were to file for help, the aid may not be immediately available due to the lack of resources. Keeping this in mind, it might be useful to consider other options, such as online therapy or larger group counseling sessions.

Along with population size, one of the largest problems associated with rehabilitation is the frequency of relapses. A major portion of substance abuse stories portray an endless cycle of quitting and relapsing to previous behaviors. Regardless of the time spent in rehabilitation centers, about 50-90% of people eventually relapse after a period of recovery (DARA Thailand, 2008). Such numbers convey the importance of having programs to supplement the work done inside rehabilitation centers. With proper funding and planning, the level of assistance offered to patients beyond the borders of a care center could maximize the efforts done inside the building to a much greater level. So, while the state of rehabilitation is sufficient for now, future models with changes applied to the size management and relapse prevention could enhance results to a much greater degree.
What are the responsibilities placed on the society?

Substance abuse is a prevalent issue within the confines of our own society, and it requires great attention from the community. This is an issue that is unfortunately associated with most age groups, including teenagers, so it is a widespread problem affecting a great portion of the population (Age and Substance Abuse, 2008). There are many times when victims of drug addiction fail to speak up and ask for help, simply due to the societal stigma against such people. People do not plan of becoming addicts, yet the society does not fail to place a label next to their name. So, in order to reduce such instances, being open-minded and considerate towards such people could possibly benefit at least one victim. In addition, not all people exposed to substance abuse will come asking for help, simply due to shame or ignorance. Such people may need help, so extending out a hand for them when in need could help greatly. Notifying people of your presence and looking out for close ones can always be a great contribution, as well, since not all have the courage to speak up. As a society, it is our responsibility to support the people of our communities, and we can support this cause by being mindful of the situations that brought them to this point.

References


Tramadol: A Medication or a Drug of Abuse?
Norhan Algharabawy

Introduction
Today, the term “drugs of abuse” often evokes alcohol, tobacco, marijuana, or perhaps cocaine. Lesser known, but also potentially dangerous, is the drug known as Tramadol. Originally developed as a painkiller, its addictive properties turned it into a drug of abuse.

What is tramadol?

Tramadol is an opiate pain reliever that is used to treat moderate to moderately severe pain. When it is taken orally, the pain relief occurs within an hour. Tramadol was considered to be safer than other opiate analgesics like morphine, and it was first approved by the FDA in 1995. It was not classified as a controlled substance then, but it was reclassified as a federally controlled drug in 2014 due to evidence of abuse and withdrawal symptoms.

What are the side effects of tramadol as a medicine?

Tramadol has several side effects as a medication including nausea, vomiting, constipation, dizziness, drowsiness, headache, loss of appetite, and dry mouth. There’s also a risk of seizures and convulsions, and this risk is higher in abusers.

What are the effects of tramadol as a drug of abuse?

Tramadol increases activity of the neurotransmitters serotonin and norepinephrine just like some antidepressants, resulting in mood-elevating properties. When tramadol is taken without a doctor’s prescription, it leads to insomnia, causing workers who have to complete two consecutive shifts to take it. Despite its “benefits” to abusers, it also increases the risk of seizures and convulsions due to elevated brain activity. Abusing tramadol leads to psychological dependence, which means that the abuser will suffer from craving the drug and anxiety if they can’t take it. It also causes physical dependence, which means that upon discontinuing use of Tramadol the abusers will face
withdrawal symptoms such as gastrointestinal pain, depression, diarrhea, numbness in the extremities, ringing in the ears, hallucinations, paranoia, agitation, and confusion.

**How bad is a tramadol overdose?**

The effects of tramadol overdose are quite dangerous, the most dangerous are coma, slow or irregular heartbeat, slow breathing or difficulty in breathing and seizures. There are other effects which are less dangerous, like decreased pupil size, extreme drowsiness, cold clammy skin, and loss of consciousness.

**A note on addiction.**

In conclusion, addiction is one of the easiest disorders to avoid. If a certain medication is not prescribed, then individuals can simply avoid taking it. Addicts start their drug-abusing habits in a variety of ways—whether out of peer pressure or innate desire. With mood-elevating drugs, just one time is enough to initiate a downward spiral of addiction and abuse.
The Twenty-Four Hour Counselor: An Overview of Smartphone Applications to Combat Drug Addiction

Dhanya Mahesh

The number of alcoholics is increasing steadily: according to the National Institute on Alcohol Abuse and Alcoholism, 17.6 million people “suffer from alcohol abuse or dependence” (Wilcox, 2015). Despite this, teenagers or adults rarely seek counseling or therapy for their addictions, alcohol or otherwise. The creation smartphone apps designed to combat addiction has helped fill this void; with 68% of adults in the United States owning a smartphone (Mediati, 2015), such applications can provide instant assistance for addicts.

As of right now, there are many different addiction-combating applications on various markets including the Apple App Store and the Google Play Store. Each application contains its own method of helping those struggling with addiction with varying benefits and drawbacks.

For example, recoveryBox, an application for the iPhone, allows users to track the good or bad choices they made throughout the day and send a report to their counselor at the end of the day. This application is not limited to alcoholism and offers services for caffeine, cocaine, and marijuana addictions as well (Peters, 2014). According to reviews on the iOS App Store, the application is effective and is highly rated (Hess, 2016).

Another application developed by the Center for Health Enhancement Systems Studies, A-CHESS, made for the Android platform, takes counseling one step further and allows users to video chat with counselors and have group discussions (“Using a smartphone app to intervene”, 2012). It even uses GPS systems to alert users when they are near risky locations, such as bars for alcoholics. There is also a Panic Button designed for users who are feeling the urge to relapse. After pressing the Panic Button, the application will send users encouraging text messages and direct them to the application’s other features such as “guided relaxation, discussion board, or a recording of their own recovery motivational story” (Isham, 2012). According to researchers, “Participants using the A-CHESS app were 65 percent more likely to abstain from drinking in the year following their release from a treatment center, compared to others who left the center without
support from the app” (Thompson, 2014). Such applications have the potential to support those who feel reluctant to have an in-person discussion with a counselor or want their addiction to remain as private as possible.

While such applications have received a generally positive response, there have been a few criticisms. For example, an application developed by Tel Aviv University tracks users’ behaviors and mannerisms throughout the day and sends this information to therapists in order to help therapists more effectively and accurately diagnose mental illnesses (“Smartphone App May Help Treat Mental Illness”, 2014). While it may give patients more independence and potentially allow important information to be shared with a qualified counselor (“The Rise of Smartphone Apps”, 2016), it also has the potential to invade users’ privacy. Jesse Singal of the New York Magazine argues that in a country where mental illness is not fully recognized as a legitimate disorder, the notion of “tracking the mentally ill” may lead to a lack of privacy and discrimination for those affected. Also, the application may lead to professionals cutting down in-person intervention time by letting the application do the work and “ushering [patients] out the door” (Singal, 2014). Singal also argues that many of the application’s detections could be uncovered during in-person counseling sessions, thereby eliminating the need for a smartphone based application (Singal, 2014).

Overall, many of the applications proposed have varying benefits and drawbacks. The most common benefits across most of these applications are an instant connection to counselors, support groups, psychiatrists, and therapists, as well as “the potential to be really cost effective and...to reach populations that are more difficult to get to or...would not be receptive to meeting with somebody in person” as Nancy Barnett from Brown University says (Peters, 2014). For example, researchers at UCLA are using these methods to target a group of young Korean smokers near Los Angeles who would not otherwise actively seek qualified help (Peters, 2014).

The most common drawbacks are the lack of privacy associated with such applications and the applications’ inability to replace multiple in-person counseling sessions. Barnett, from Brown University, hopes that people will think of such applications as “bridges or as an adjunctive kind of help” to in-person professional help instead of a full treatment (Peters, 2014).

As the development of such applications are still in the beginning stages, they are not yet cost effective and may not be completely useful in treating addictions. For example, A-CHESS costs approximately 10,000 dollars and its use is not advised for serious alcoholics (Thompson, 2014). But with the release of Apple’s ResearchKit, an “open source software framework designed for medical and health research” (Apple Press Info, 2015), the effectiveness and the reach of such applications are projected to become better. Researchers at the Clinical Neuroscience Institute in Spain believe that patients will introduce such applications in their lives and actively use them to fight their addiction (Barrio et al., 2016) and are very interested in such products (Schulte et al., 2016). Researchers at the University
College at London have carried out a full study of such applications which they believe will help them create a better model that fully helps addicts as much as possible (Garnett, 2016). With such projects being carried out, it is likely that more effective and far reaching applications will be available for addicts in the near future.

Overall it is clear that most of the benefits of such applications can potentially help users to a certain extent. A teenager who is addicted to cigarette smoking can hit a panic button when he feels the urge to smoke and within seconds be introduced to a support group or a counselor who will calmly and patiently help him. A recovering alcoholic can get a reassuring and motivating text message reminding her of her progress every time she drives by a bar. Even though there are currently privacy issues, and applications may not be able to replace human interaction, these applications have the potential to help millions of people with just a few clicks of a button.

References


Probuphine: Synopsis of a New Technology in the Face of Opioid Abuse

Mallika Pajjuri

Introduction

Opium and its derivatives including morphine and oxycodone have been subject to scrutiny in the past few years as a result of their drastic effects upon society. It has ingrained itself in the lives of millions of people since its introduction in the Neolithic Era, and using it became a common practice in countries such as India and Greece. In popular media, opium has been romanticized as a slumber-inducing drug, placing its users into a nebulous haze, luring users in with its earth-transcending effects into the sublime. However, opium abuse has turned from a glamorized endeavor to a widespread epidemic, affecting 2.1 million people across the United States (Volkow, par. 2). Delineated by the recently infamous image of Rhonda Pasek, a grandma who overdosed on heroin while sitting in the passenger seat of a car, the usage of opioid derivatives is a burgeoning problem worldwide, yet researchers have yet to find an extremely effective treatment process. Most current treatment processes merely revolve around aiding the recovery. However, a novel subdermal implant, called Probuphine, has increased in global popularity, and its effectiveness is positively rerouting our knowledge about opioid addiction treatment.

How Opium Affects the Brain

In 1973, using a radioactive, synthetic opiate called naloxone, researchers were able to identify a specific opiate receptor within the human brain, allowing for scientists to further understand the processes of opiate abuse. Opiates, classified as depressants, tend to mimic naturally occurring opiate-like molecules in the brain called endorphins, activating endorphin receptors within neurons [i]. However, this artificial activation of endorphin receptors during opiate addiction is overproduced, and, to compensate for this overproduction, the brain halts its excretion of pain-reducing neurotransmitters, often causing opiate abusers extreme chronic pain.
As it is a depressant, opium tends to affect a person drastically, allowing them to function in a sluggish, heavy manner, often sedating or relaxing the user. Immediately following opiate usage, users enter a trance of pure euphoria, feeling intense pleasure and acknowledging their extreme well being, but the detrimental side effects, such as slowed breathing, impaired coordination, and slurred speech, engulf the pleasures [2]. In reference to long term effects, opiate abusers, using drugs such as Vicodin and OxyContin, are at the risk of mental impairment, sadness, and depression since the brain signals the stop of endorphin release, depriving users of the neurotransmitter's “feel-good” benefits. Both female and male users can exhibit loss of sex drive, infertility, and constipation as well. Female opiate abusers, on the other hand tend to over time acquire irregular menstrual cycles.

The Science Behind Probuphine

Probuphine is a fairly novel treatment alternative for opiate abuse as it is the first buprenorphine implant approved by the US Food and Drug Administration. With a lasting period of six months, probuphine is designed to provide a constant dosage of buprenorphine to the patient. This method is extremely unique within itself, since buprenorphine is a partial opioid agonist: it partially activates mu opioid receptors, but still restricts the effects of opioid abuse [3]. Since it is a partial opioid agonist, it effectively aides rehabilitation patients, fulfilling their cravings while lowering their dependency on these drugs.
Probuphine’s Effects Upon the Drug Rehabilitation Processes

Probuphine, after many tests, has been acknowledged one of the most highly effective and relatively convenient opiate abuse treatment options [4]. It does not require the treatment of dependent patients in a primary care setting since acquiring and utilizing one merely involves visiting a physician’s office [5]. In addition, according to a study conducted by JAMA Internal Medicine, Probuphine patients fared better when utilizing the technology for the complete six months rather than diminishing usage in the middle of the time period [6]. Thus, Probuphine’s existence in the treatment realm will likely continue to expand and eventually become a widespread treatment option.

References


A Synopsis of Alcoholic Neuropathy

Christian Gonzalez

Introduction
In 1787, English physician John Coakley Lettsom observed a patient with leg paralysis and hyperesthesia. The patient that was described by Lettsom was the first description of symptoms of a disease that would later be known as alcoholic neuropathy. Later on, in 1822, neuropathy was described in alcoholics as well. By the late 1800s, the symptoms that these physicians and doctors were observing became to be known clinically as alcoholic neuropathy (Mawdsley & Mayer, 1965). Alcoholic neuropathy is a neurological disorder that causes paresthesia (abnormal tingling) and sensory and motor abnormalities, as a result of axonal degeneration of motor and sensory neurons. This is due to either chronic alcoholism or vitamin deficiency, and is closely associated with Korsakoff’s syndrome and Beriberi. (“Types of Peripheral Neuropathy,” n.d.).

Overview and Symptoms
Alcoholic neuropathy typically manifests itself through two different classes of physical symptoms: sensory symptoms and motor symptoms. Some of the most common sensory symptoms include nerve pain, numbness, heat intolerance, and muscle cramps. Additionally, patients may often experience abnormal tingling sensations known as paresthesia (“Types of Peripheral Neuropathy,” n.d.). The acuteness of sensory symptoms depends substantially upon the severity of the disease in a patient. In alcoholic neuropathy, sensory symptoms are the first physical signs that a patient will typically exhibit; these symptoms can be used as diagnostic and prognostic indicators and are useful to neurologists. After sensory symptoms are displayed by a patient with alcoholic neuropathy, the individual will usually begin to encounter motor symptoms. In the case of motor symptoms, a patient may experience difficulty urinating, constipation, diarrhea, and muscle cramps. In addition to overall muscle weakness, the patient may also be burdened with a lack of coordination known as ataxia as a result of cerebellar degeneration, in addition to muscle spasms, atrophy, dysphagia (difficulty swallowing), and dysarthria (difficulty speaking) (“Alcoholic neuropathy,” 2015).

Causes
The etiological origin of alcoholic neuropathy is the result of excessive alcohol consumption. With respect to the precise mechanism leading to the symptoms and pathology of the
disease, however, the root cause is disputed. The two most likely causes are alcohol’s toxic effect and malnutrition linked to alcohol consumption. Malnutrition results from the phenomenon by which high alcohol consumption disrupts daily habits and patterns in alcoholics but not normal people. Living an unstructured life can lead to alcoholics eating abnormally, resulting in malnutrition due to irregular eating and loss of appetite. Regardless of the cause of symptoms in alcoholic neuropathy, though, the eventual pathological progression of the disease is the result of damage to peripheral nerves. When nerves are damaged, a patient will have motor and sensory symptoms associated with the progression of alcoholic neuropathy. In addition to alcohol consumption, vitamin deficiencies have also been linked to the development of the disease. Specifically, some of the more common deficiencies linked to alcoholic neuropathy are thiamine, retinol, pantothenic acid, pyridoxine, biotin, cobalamin, folic acid, and niacin (“Alcoholic neuropathy,” 2015).

Diagnosis

When trying to reach an accurate diagnosis of alcoholic neuropathy, physicians will typically examine a patient’s family history for a background of alcoholism and study their symptoms. Unfortunately, many symptoms of Alcoholic Neuropathy are similar to those displayed in other diseases that result from axonal degeneration. If a patient has both sensory and motor symptoms, along with nutritional and vitamin deficiencies, however, then it is much easier to tell that the patient has alcoholic neuropathy rather than another similar condition. Some of the diseases that alcoholic neuropathy is commonly misdiagnosed as include ALS, Beriberi, CMT, Diabetic Neuropathy, and Guillain Barre (“Alcoholic Neuropathy: Background,” n.d.). Besides nutritional deficiencies, other ways that neurologists differentiate between alcoholic neuropathy and other diseases include the use of EGD, EMG, medical imaging, and nerve conduction studies (“Alcoholic neuropathy,” 2015).

Pathophysiology

The progression of alcoholic neuropathy typically presents itself through nerve damage followed by sensory and motor symptoms that can be useful in diagnosing the disease. As discussed above, excess alcohol consumption and vitamin deficiencies result in axonal degeneration, which makes the beginning stages of alcoholic neuropathy less thoroughly understood compared to other stages during its pathology. When axonal degeneration takes place, a process called demyelination occurs that results in a decrease in the travelling speed of action potentials across neurons from the loss of saltatory conduction. This nerve damage underpins the pain that patients with alcoholic neuropathy experience. Low levels of thiamine contribute to the onset of the disease, as decreased thiamine contributes to neurons being unable to maintain normal levels of adenosine triphosphate (ATP) necessary for usual functioning. Additionally, acetaldehyde can have toxic effects on peripheral nerves leading to damage observed in the disease as well (Mawdsley & Mayer, 1965).
Treatment

There is currently no available cure for alcoholic neuropathy. Fortunately, patients have a variety of treatment options to lessen the severity of their symptoms that stem from the pathophysiology of their condition. Difficulty walking and issues with mobility can be aided by physical therapy. Additionally, pain experienced during alcoholic neuropathy can be treated with a number of drugs such as vitamin supplements, amitriptyline, gabapentin, and capsaicin. These drugs alter some of the many physical processes that result in the symptoms of the disease. Managing overall symptoms in the disease is also best done through improving nutrition. Specifically, being alcoholically abstinent can help patients lessen the progression of the disease and prevent many of the symptoms associated with alcoholic neuropathy (“Alcoholic Neuropathy: Background,” n.d.).

KEY TERMS

Hyperesthesia- Increased physical sensitivity in response to stimuli
Paresthesia- Abnormal tingling sensation from nerve damage
Ataxia- Loss of coordination of voluntary muscle movements
Cerebellar Degeneration- Deterioration of neurons in the cerebellum that results in difficulty with balance and coordination
Dysphagia- Difficulty swallowing
Dysarthria- Condition characterized by difficulty speaking as a result of neurological injury
Thiamine (Vitamin B1)- Vitamin important for proper heart, muscle, and nerve function
Retinol (Vitamin A)- Vitamin important for proper immune function, development, growth, and vision
Pantothenic Acid (Vitamin B5)- Vitamin important for synthesis and metabolism of carbohydrates, fats, and proteins
Pyridoxine (Vitamin B6)- Vitamin important for glucose and protein metabolism, myelin formation, and the synthesis of the neurotransmitters norepinephrine and serotonin
Biotin (Vitamin H or B7)- Vitamin important for synthesis of fatty acids and glucose
Cobalamin (Vitamin B12)- Vitamin important in formation of red blood cells
Folic Acid- Vitamin used to treat anemia; important for synthesis of nucleic acid
Niacin (Vitamin B3)- Vitamin used to treat high levels of cholesterol and triglyceride, niacin deficiency, and lowers heart attack risk
EGD- Esophagogastroduodenoscopy; a test used to examine the esophagus and stomach lining
Electromyography- Technique for assessing muscle health; also known as EMG
Saltatory Conduction- Action potential propagation along neuronal axons via myelin sheath
Adenosine Triphosphate (ATP)- The energy currency for intracellular energy transfer in cells
Acetaldehyde- Toxic byproduct of alcohol metabolism involved in alcoholic neuropathy
Amitriptyline- Tricyclic antidepressant used to treat alcoholic neuropathy
Gabapentin- Anticonvulsant drug used to treat alcoholic neuropathy and epilepsy
Capsaicin- Active ingredient of chili peppers
References


Drug Induced Insomnia
Kento Arendt

Introduction
Drug induced insomnia is the inability to sleep caused by the use (or, in some cases, the quitting) of a certain drug. Though insomnia may seem like a minor problem compared to the other detrimental effects drugs can have on the human body, it should not be ignored. A lack of sleep has been repeatedly proven to drastically slow down brain function. Everything from memorization to simple motor abilities are impacted by insomnia. It is important to know which drugs can cause insomnia, so that we can remain healthy while also getting enough sleep.

A Quick Note on Sleep
Sleep--everyone does it, and for good reason. While we lack concrete explanations of why humans need sleep, there are multiple theories. One theory, called the Inactivity Theory, is based on the presumption that animals have a higher chance of survival in dangerous conditions when they remain still and unnoticeable. Based on the Inactivity Theory, diurnal animals (those that are active during the day) sleep during the night to protect themselves from nocturnal predators. This theory has clear problems; as logic might imply, the chance of survival of an organism increases when an organism is conscious. Another prevalent theory, the Brain Plasticity Theory, posits that sleep allows the brain to undergo important changes. According to the Division of Sleep Medicine at Harvard Medical School, “sleep is correlated to changes in the structure and organization of the brain ”[i]. During infancy, sleep is a driving force behind brain development. Between infants, young children, teenagers, and adults, infants acquire the most information from living. Sleep allows the brain to change in a way that allows the infants to retain all that new information. This is why infants spend about 13 to 14 hours a day sleeping. Sleep can also affect our emotional state. People suffering from sleep deprivation tend to get angry and become aggressive much easier than those that get at least 8 hours of sleep. Sleep affects our emotions because of how it affects our amygdala (see image below). The amygdala is known as the part of the brain that controls emotions. Though scientists have done years of research on the brain and sleep, there is still much to be discovered. One thing that scientists know for sure, though, is that sleep is important and drugs can disrupt it.
Sleep deprivation causes an increase in activity in the amygdala, which controls emotion. Sleep deprived people are more likely to react to an event with a strong emotion, like anger [2].

How Drugs Cause Insomnia

There are several ways that drugs can cause insomnia. Many heart medications are known for causing insomnia. Beta blockers, a class of heart medication, which are used to treat ailments such as high blood pressure, abnormal heartbeat, and angina, increase the chance of random awakenings during the night [3]. Beta blockers work by inhibiting beta-1 adrenergic receptors, which are G-protein coupled receptors responsible for changes in heart rate. G-protein coupled receptors are simply cellular receptors that work by transferring a signal from a ligand (the molecule that is binding to the receptor) to a receptor protein. The receptor protein then transmits the signal to a G-protein, which in turn transmits the signal to other proteins that amplify and further transmit the signal until it reaches the terminal protein that completes the signal’s function.

Melatonin, a hormone created by the pineal gland, helps regulate the sleep cycle, and also plays a critical role in the abovementioned process. The inhibition of beta-1 adrenergic receptors prevents melatonin from binding to the receptors and therefore deregulates the sleep cycle.

Moreover, in the process of inhibiting these beta-1 adrenergic receptors, beta blockers also block the pathway of coenzyme Q10-dependent enzymes. Coenzyme Q10, abbreviated CoQ10, is essential in the production of adenosine triphosphate (ATP). In other, simpler terms, CoQ10 is an ingredient in the process that creates usable energy in the body. So, beta blockers’ blockage of CoQ10 slows down energy production in the body [4]. Through both a decrease in the hormone that regulates sleep and energy production, beta blockers have a high tendency to cause insomnia.

One of the most common diseases in the world is asthma. In the United States, about one out of every one hundred people has asthma. Asthma is characterized by the constriction of a person’s airway when that person is in the presence of a “trigger.” Such triggers can include dust, smoke, and mold. In order to help clear the airways in the event of an asthmatic attack, many doctors recommend the use of the drug Theophylline. Theophylline can actually be found in the human body as well - but only after the consumption of caffeine. The liver metabolizes caffeine into three products, one of which is theophylline. The molecular similarity of caffeine and theophylline can be seen below:
Because of its molecular similarity to caffeine, theophylline can cause many of the same effects, such as increased blood flow and the inability to sleep. Corticosteroids, which are the most frequently prescribed treatment for asthma, can have similar sleep-depriving effects.

SSRIs, a common class of antidepressant, are also known to interfere with sleep. Serotonin is released into the synapse, where it reacts with postsynaptic receptors. These postsynaptic receptors create the signals that make humans feel happy. Presynaptic serotonin reuptake proteins take up serotonin to remove it from the synapse and allow it to be reused. The uptake of serotonin regulates synaptic serotonin levels, which in turn helps regulate how happy people feel - and how people sleep [6]. The amount of serotonin in the synapse is associated with wakefulness and transitions between sleep stages. More serotonin will result in more happiness and more wakefulness. SSRIs work by inhibiting the presynaptic receptors. By inhibiting the uptake of serotonin, SSRIs increase the concentration of serotonin in the synapse. Although the SSRIs have been proven to make people happier, they also make people more sleepless [6]. The irony of this medication is that the less sleep people get, the less happier they are likely to be.

**So, What Should I Do?**

This article only covers the most commonly used drugs that can cause insomnia. There are many more out there. Luckily, all medications are required to have a list of side effects. If restlessness or insomnia are listed as possible side effects, some may choose to find an alternative medication. The importance of proper sleep for proper bodily function can not be emphasized enough. In 2013, the National Highway Traffic Safety Administration estimated that drowsy driving was the cause of about 72,000 crashes, 44,000 injuries, and 800 deaths in the United States alone [7]. Considering these statistics, it is important to avoid driving while taking medications that are known to cause drowsiness. A healthy lifestyle is always important, and sleep is an often-overlooked part to achieving that lifestyle.

References


Fetal Alcohol Syndrome: A Few Drinks Can Hurt

Megumi Sano

Introduction

Ancient Greek and Roman writings show that newlyweds were forbidden to drink on their wedding night. Aristotle (384 - 322 BC) believed in the association between alcohol consumption during pregnancy and congenital abnormalities, describing the children of “drunken women” as “morose and languid” (Mitchell et al.). Fast-forward two millennia: in 1968 France, the first paper was published on the shared abnormalities of 127 children born to alcoholic mothers, identifying alcohol as a teratogen, an agent that can disturb embryo or fetus development (Lemoine et al.). Described as fetal alcohol syndrome five years later (Jones et al.), FAS has been the leading non-genetic cause of mental retardation. Many argue that children born with the syndrome are denied their rights to health and normal development, as interventions may only alleviate but never eliminate their symptoms. Nevertheless, alcohol use has been self-reported by approximately 15% of pregnant women in the United States with rates as high as 20% in recent decades (National Household Survey), which communicates the need for a greater level of awareness.

Overview and Symptoms

Fetal Alcohol Syndrome (FAS) is one of the specific diagnostic categories used under the umbrella term, Fetal Alcohol Spectrum Disorders (FASD). While FASD refers to the range of effects that can occur in an individual who is exposed to alcohol during the nine month prenatal period before birth, FAS indicates the most severe end of the spectrum, with fetal death being the most extreme outcome (Center for Disease Control and Prevention). Recent reports show the prevalence of FASD to be as high as 20 to 70 cases per 1000 live births (May et al.), while that of FAS is 2 to 7 cases per 1000 (Stratton et al.). Symptoms of FAS include a constellation of abnormal facial features, small head circumference, short height, weak immune system, hearing and vision problems, memory problems, and lack of focus or hyperactivity. However, the effects of FAS on the child depend heavily upon the mother’s alcohol consumption in different stages of pregnancy. The general trend is that alcohol consumption leads to more severe brain damage in later stages of pregnancy. For example, children with mothers who consumed alcohol during the first trimester of their pregnancy...
statistically experience more facial malformation and damaged organs. Contrarily, those exposed to alcohol in the second or third trimester may encounter destruction of brain cells and therefore impairment of the final stages of brain development. This may result in more functional problems than physical abnormalities. Symptoms of FAS do not fade after childhood; its long-term consequences feed into adolescence and adulthood and may include social withdrawal, impulsive behavior, and aggression. In fact, very few adults with FAS are able to live and work independently, with significantly higher rates of mental illness, psychosis, sexual and social problems, suicide, and drug and alcohol abuse (Spohr).

**Etiology**

Often, the main cause of FAS is misunderstood. It is believed by many to be excessive alcohol consumption by pregnant mothers. However, the term “excessive” is unnecessary, as there is no particular threshold of alcohol use for the child to develop symptoms of FAS. Any pregnant woman drinking alcohol during pregnancy has a significantly higher risk of giving birth to a child with FAS than those who entirely avoid alcohol. It is also important to acknowledge that alcohol concentration and therefore the type of alcohol consumed does not determine manifestation of the disorder, much less the severity of the disorder. There are many other factors, such as the mother’s digestive system, contributing to the severity of FAS; outcomes of alcohol consumption during pregnancy are unique to the individual. In terms of biological mechanisms, the primary reason behind alcohol’s destructive influence on the fetus’s development is the difference in abundance and efficiency of the enzymes responsible for breaking down alcohol in the liver of the mother and fetus.

**Diagnosis**

Currently, there is no approved medical test for diagnosing FAS. Doctors will normally look for the following signs: 1) abnormal facial features which may include thin upper lip, smooth philtrum, and small eye openings, 2) growth problems indicated by height and weight, and 3) central nervous system problems which may be classified into structural, neurological, and functional (“Centers for Disease Control and Prevention,” 2014). Structural problems of the central nervous system mainly refer to reduced head circumference or significant changes in brain structure, while examples of peripheral nervous system problems include poor muscle control that indicate impaired nerve transmission. Some of the major functional problems are cognitive deficits, executive functioning deficits, motor functioning delays, problems with attention, impaired social skills, and impaired hearing and vision. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) is presently aiming to create a new set of criteria for recognizing alcohol-related neurodevelopmental disorder (ARND), which is a diagnostic term on the milder end of FASD. In turn, the diagnostic criteria specific for FAS, which is on the more severe end of the spectrum, also need further improvement as doctors are fully dependent upon them to make consequential diagnostic decisions. Interestingly, although doctors may also check for prenatal exposure to alcohol through a questionnaire by the mother, this is not a requirement. In other words, if the child meets all the
other three criteria listed above, confirmation of the mother’s alcohol consumption during pregnancy is not necessary for diagnosis, despite it being the main cause of FAS.

Pathophysiology

Alcohol is the most common human teratogen, meaning that it has the potential to induce physical and behavioral effects on the fetus. There is an unimpeded bidirectional movement of alcohol between maternal and fetal tissue, resulting in equal alcohol concentrations after the mother’s consumption. Since an enzyme called alcohol dehydrogenase (ADH) in the fetal liver shows less than 10% of the activity it shows in the adult liver, the fetus cannot detoxify alcohol on its own and experiences intensified impacts by the same alcohol concentration. Moreover, the amniotic fluid surrounding the fetus may act as an alcohol store, decreasing metabolism and further prolonging alcohol’s harmful effects. Although some molecular mechanisms are still unknown, research suggests an array of potential mechanisms including disruption of cellular differentiation and growth, interference with DNA and protein synthesis, decrease in serotonin levels, and inhibition of cell-to-cell adhesion. One of the most frequently proposed of these mechanisms is the blockage of N-methyl-d-aspartate (NMDA) receptors. Alcohol interacts with a number of neuronal membrane receptors including NMDA receptors which play an important role in neuronal plasticity during development and later in life. Chronic blockage of these receptors may lead to adaptive upregulation during periods of withdrawal, increasing either receptor number or the release of glutamate, the excitatory neurotransmitter that usually activate these receptors. As a result, NMDA receptors are overactivated and this eventually leads to excitotoxic cell death. This chain of processes can occur during fetal development (Irdus & Thomas) and it is this cell loss that hugely contributes to symptoms of FAS.

Currently, neuroimaging is also used to identify damaged parts of the brain and their relationship with neurocognitive and behavioral symptoms in children with FAS. While one paper indicated an association between decreased volume of the caudate nucleus and impaired cognitive performance and verbal learning (Fryer et al.), another has concluded a correlation between reduced palpebral fissure length and neurocognitive impairment (Yang et al.). These studies help to enhance our understanding of the bigger picture without solely focusing on molecular pathophysiology.

Treatment

Although there are currently no cures available for FAS, early intervention and treatment services may support the child’s development and alleviate its negative effects on quality of life. Parents and guardians have the option of choosing between a wide range of services including behavior therapy, speech therapy, parent training, and alternative educational pathways, which may not only reduce the child’s functional symptoms but also create a suitable environment for each individual’s learning capabilities. In addition, some medications for the pregnant mother have shown potential therapeutic properties including antioxidants which mitigate the effects of alcohol exposure on the imbalance of the intracellular reduction-oxidation state (Joya et. al, 2015). These can be taken as food supplements during the prenatal period by the mother. However, discouraging
alcohol consumption during pregnancy is the most effective approach to reducing risks of FAS and securing the basic human rights of innocent children.

Further Reading

National Organization on Fetal Alcohol Syndrome [www.nofas.org](http://www.nofas.org)


**KEY TERMS**

**Adaptive upregulation** - An increase of a cellular component such as the number of receptors to a molecule in response to molecular stimulus which enhances the cell’s sensitivity to the molecule.

**Alcohol dehydrogenase (ADH)** - A group of enzymes that facilitate the interconversion between alcohols and aldehydes or ketones with the reduction of nicotinamide adenine dinucleotide (NAD+).

**Alcohol-related neurodevelopmental disorders (ARND)** - A complex range of disabilities in neurodevelopment and behavior, adaptive skills, and self-regulation in the presence of confirmed prenatal alcohol exposure. Unlike those with FAS, children with ARND do not have abnormal facial features or growth problems.

**Antioxidant** - Any agent that inhibits oxidation by removing oxidizing agents.

**Caudate nucleus** - The upper of the two gray nuclei of the corpus striatum in the cerebrum.

**Cell-to-cell adhesion** - The process by which cells interact and attach to a surface, substrate, or another cell, mediated by interactions between transmembrane glycoproteins.

**Excitotoxic cell death** - The death of neurons arising from prolonged exposure to glutamate and the associated excessive influx of ions into the cell.

**Fetal Alcohol Syndrome (FAS)** - A congenital syndrome associated with alcohol consumption by the mother during pregnancy and characterized by physical and mental abnormalities.

**Fetal Alcohol Spectrum Disorders (FASD)** - A group of conditions that can occur in an individual whose mother drank alcohol during pregnancy. This includes fetal alcohol syndrome (FAS), alcohol-related neurodevelopmental disorder (ARND), partial fetal alcohol syndrome (pFAS), and neurobehavioral disorder associated with prenatal alcohol exposure (NP-PAE).

**Glutamate** - An excitatory neurotransmitter involved in learning and memory.

**N-methyl-d-aspartate (NMDA) receptor** - An ionotropic glutamate receptor that allows positive charged ions to flow into the cell when activated by glutamate or glycine.
**Palpebral fissure** - The elliptic space between the medial and lateral canthi of the two eyelids; the distance between the inner and outer corners of the eye.

**Phi-lfur** - The vertical groove between the base of the nose and the border of the upper lip.

**Serotonin** - A neurotransmitter involved in the control of pain perception, the sleep-wake cycle, and mood.

**Teratogen** - Any agent that can disturb the development of an embryo or fetus and may cause birth defects and congenital disorders.

References


Study Summary: A Molecular Link between the Active Component of Marijuana and Alzheimer’s Disease Pathology
Eva Kitlen, Jacob Umans, Kyle Ryan

Background
Alzheimer’s disease is one of the leading causes of death among the elderly, and the affected population is ever increasing. This growing number of patients has resulted in a rising demand for improved treatments and innovative research. Alzheimer’s is thought to result primarily from the aggregation of amyloid plaques (made from Aβ in brain regions important for memory and cognition). A decrease in acetylcholine levels may also play a role; the activity of AChE is thought to be related to this pathology. For one, AChE is involved in the breakdown of acetylcholine, so excessive AChE activity could be related to the drop in acetylcholine levels seen in Alzheimer’s. In addition, recent studies have shown evidence suggesting that AChE facilitates the aggregation of Aβ tangles. These results indicate that AChE activity is central to the pathology of Alzheimer’s; thus, inhibiting AChE could lead to treatments for the disease.

Presently, drug treatments focus on the relationship between AChE activity and Aβ aggregation. Specifically, researchers have looked at the PAS (peripheral anionic binding site) of AChE known to bind to Aβ. However, new research has reported a link between Alzheimer’s and the endocannabinoid system, leading researchers to investigate whether THC, the active compound in marijuana, can bind to the PAS site and decrease the activity of Aβ.

Eubanks et al. investigated the molecular link between THC and the pathology of Alzheimer’s in “A Molecular Link between the Active Component of Marijuana and Alzheimer’s Disease Pathology,” a study published in Molecular Pharmaceutics in 2006. They found that THC is a better inhibitor of amyloid β-peptide formation than current drugs because it competitively inhibits AChE. This review aims to give a concise overview of this study’s methodology and findings as well as an analysis of its implications.

Methods: A Brief Overview
The researchers determined the extent to which THC inhibited AChE by performing assays using a spectrophotometer to analyze enzyme kinetics.

A thioflavin T based fluorometric assay was used to quantify the aggregation of Aβ. All solutions used contained Aβ, but had varying concentrations of AChE and THC. T-tests were used to determine the significance of the results of the fluorometric assay.
Results

Prior to examining the real reaction, the researchers used an in silico (computer-based) method to gather data on the interaction between THC and amyloid beta. This simulation found that THC can bind to AChE just as effectively as the best existent PAS binders (medications that bind to the PAS to block AChE activity).

Encouraged by the results of the computer modeling, the researchers used in vitro (outside of the human body) studies in order to further analyze the effects of THC and AChE activity. Their analysis found that THC is a competitive inhibitor of AChE, meaning that THC prevents acetylcholine from binding to its substrate. Although the strength of inhibition is not particularly high, it is comparable to typical PAS binders.

Typically, competitive inhibitors bind directly to the active site, but the researchers noted that THC may block the active site rather than binding to it because it binds to the PAS. To test this hypothesis, the researchers conducted further kinetics analysis while looking at propidium, a non-competitive inhibitor of AChE. They found that THC and propidium cannot bind to AChE simultaneously, showing that THC does not bind to the AChE active site.

To test how THC inhibits Aβ activity, the researchers used thioflavin T (a fluorescent dye, abbreviated ThT) to conduct a fluorometric assay analyzing the interaction between THC and Aβ. In this test, the researchers found that while propidium cannot fully prevent AChE-induced aggregation, THC is able to completely block it. It is possible that ThT also binds to the PAS site. Furthermore, researchers used control experiments to verify that results were a result of Aβ inhibition.

Implications

THC has long been known as the main psychoactive chemical substance in the drug, marijuana. Therapeutic applications for THC have been found not only for Alzheimer’s, but also other health issues like glaucoma and chronic pain. This study expands upon the benefits of THC and focuses on the biochemical explanations for these benefits. The researchers propose that THC can actually affect the progression and pathology of Alzheimer’s. Because the results show that THC binds to AChE PAS and reduces the aggregation of Aβ plaques, the progression of Alzheimer’s could in theory be slowed with a combination of other variations that as mentioned have therapeutic effects.

This study brings up an important question that society needs to think about and answer: Is it acceptable to use marijuana, a known hallucinogen, to treat Alzheimer’s disease? As research develops, society will need to draw the line at which the side effects of a medication make their use unjustified. A similar conundrum has already been observed with opioids—though they serve as powerful analgesics, there is a risk of addiction and abuse. Doctors continue to use such drugs, believing that the benefits they provide to patients outweigh the risk of addiction. However, it still remains unknown whether medical marijuana will become accepted as well? At the same time, this study also emphasizes that even drugs traditionally seen as harmful could hold within them the potential to serve as therapeutic agents in disease treatment and save lives.

Abbreviations and Terminology to Know
Aβ-Amyloid Beta
A protein known to create plaques, a key feature in Alzheimer’s pathology

AChE-Acetylcholinesterase
Acetylcholinesterase is an enzyme that breaks down Acetylcholine in the synapse. Decreases in acetylcholine levels are known to be linked to Alzheimer’s disease.

Enzyme Kinetics
The study of how enzymes interact with their substrates and other molecules, including reaction rate, inhibition, and binding sites

Fluorometric assay
Based on fluorescence, or light, coming from molecules bound to fluorescent dyes
Example: Researchers use fluorescent molecules attached to antibodies to identify the location and amount of certain cellular proteins

PAS (Peripheral Autonomic Binding Site)
One part of the AChE enzyme known to bind to Aβ

THC (Δ⁹-Tetrahydrocannabinol)
The psychoactive ingredient of marijuana, which binds to the brain’s endogenous cannabinoid (endocannabinoid) receptors

Thioflavin T (ThT)
A fluorescent dye that can bind to Aβ, used to detect its presence and aggregation

Disclaimer: Neither the authors of this article nor the IYNA are in any way supportive of recreational, unmedicated, or otherwise unauthorized drug use; we are simply attempting to explore their therapeutic potential in order to give our readers a more holistic perspective on drugs

References
Research Methods: Cell Culture

Jacob Umans and Meenu Johnkutty

Introduction

Though it may sound like neurons listening to Beethoven or admiring a work by Picasso, cell culture is the process of raising cells in vitro, or outside the human body. Cell culture is a powerful method which allows researchers to define the medium in which cells grow, and modify it with great precision. In drug research, this can be especially valuable, as traditional in vivo methods of research are highly unethical, and in the case of giving humans drugs to study their effects in the brain outright illegal.

Cell Culture: A Brief Overview

To conduct cell culture experiments in human subjects, the first step is to obtain cells to grow. Naturally, obtaining cells that grow is a problem, since most neuronal cell lines exist in Go, a phase in the cell cycle in which cells do not divide. Although this is difficult, primary cell cultures most accurately model the in vivo activity of human neurons. One way researchers can get around this difficulty is to use cell lines derived from immortalized neuronal tumor lines. These lines may be able to more readily divide than neurons; however the differences between these lines and normal human cells make it difficult to apply these findings to real life. It is possible to use growth factors or other chemicals to allow for the better modeling of neurons, but this technique still has its limitations.

Several different analytical tools can be used in the laboratory setting. Flow cytometers measure different properties of cells through the use of automated machines, which can detect dye fluorescence levels (these dyes can be used to tag proteins, to identify protein concentration) and identify cell size. A related technology, FACS, fluorescence-activated cell sorting, can actually divide cells into different tubes based on their fluorescence at a given wavelength. This allows researchers to identify a subset of cells based on their protein-expression levels. Immunofluorescence utilizes antibodies conjugated with colored dyes in order to visualize the locations of certain protein under a special microscope.

Live-cell imaging, as the name suggests, uses time-lapse microscopy to catch the living cell in action through the measurement of cell growth rate and development. In order to conduct this analysis, the images are often transferred to a computer where specific programs are used to analyze
the data. All of these tools allow researchers to study the inner workings of the microscopic world and predict how novel drugs will affect target cells.

**Experimental Design**

Though cell culture varies tremendously among different studies, some principles in cell culture research remain the same. First, cell culture environments must contain several elements which allow the cell to properly respond to the drug or treatment being tested. For example, all cells must have a substrate or medium which supplies essential nutrients like amino acids, carbohydrates, vitamins, and minerals. In addition, all cell cultures should be housed in physically and chemically suitable environments. Factors like pH, osmotic pressure, and temperature must be regulated, unless they are being manipulated for the experiment.

As in all other types of experiments, studies based on cell culture must be conducted in a rigorous, repeatable manner. Aside from the independent variable, all other variables must be kept controlled in order to ensure that the validity of the data obtained. One important factor to consider when conducting cell-culture research is contamination. If bacteria, fungi, or other microbes enter the medium in which the cells are suspended, it is proper to avoid collecting data on the contaminated cells. For this reason, cell-culture research is conventionally done in a laminar flow hood by researchers wearing gloves in order to avoid all contamination.

When using human cells, there are strict ethical guidelines that researchers must follow. Researchers hoping to experiment on human cells must first obtain official approval by an Institutional Review Board (IRB). Such a board considers the merits of the research and its effects on the subjects. Once approved, researchers must ensure that the subjects give informed consent to participate in the research, and avoid any undue harm.

**Cell Culture and Drug Research**

One of the major applications of cell culture is in drug research. In order to find treatments and cures for the world’s most pressing diseases, cell cultures are or have been used. One of these pressing issues is Fetal Alcohol Syndrome, a devastating pediatric disorder resulting in mental retardation in infants, which is caused by excessive alcoholic consumption during pregnancy (see our article on Fetal Alcohol Syndrome in the disease section for more information on this disorder). In an effort to investigate the extent of damage done to fetal brains during gestation, researchers used cell cultures in order to determine the role ethanol had to play on the development of glia, the collection of cells which provide support and protection for neurons. The researchers used immunofluorescence within their cell cultures in order to show the differences between the healthy control glia and the glia exposed to ethanol. The researchers found that ethanol exposure altered the development of astrocytes, a subpopulation of glia. They also posited that one of the targets of ethanol toxicity is the corpus callosum, the bridge between the left and right cerebral hemispheres.
Since the corpus callosum plays an integral role in the delivery of information from both hemispheres, the researchers proposed that the neurodevelopmental abnormalities linked to Fetal Alcohol Syndrome could be linked to the deterioration of glia observed post-ethanol exposure in their cell cultures [1].

iPS Neurons: A New Frontier

One emerging field that shows incredible promise involves Induced Pluripotent Stem Cells (iPSCs). Fibroblasts, or other cells, are cells taken from human subjects, then “reprogrammed” to act as a pluripotent stem cell (or one that can differentiate into all other cell types). Following this, iPS cells can be induced to differentiate (specialize) into neurons much like embryonic stem cells do in the developing brain. Such protocols have remarkable specificity--researchers have managed to turn iPS cells into a wide variety of neuron types to model disease. This technique is especially powerful because it allows researchers to look at individual variation, and directly observe events similar to those occurring in early neural development.

One lab utilizing this technology has analyzed iPS-derived neurons from patients with schizophrenia and healthy controls. Such an experimental setup allowed his lab to gain a view of the developing brain that would not be feasible in an in vivo study. With this design, his lab identified specific differences in the development and gene expression of neurons from healthy subjects and schizophrenic patients. The researchers found that genes related to the cytoskeleton and oxidative stress had altered transcription levels. They also found that cells from schizophrenic patients had abnormal migration patterns. This study provided the researchers with valuable data regarding how the schizophrenic brain functions [2].

One nascent field even within the area of iPS cells is the growth of mini-brains. Mini-brains are three-dimensional cell cultures that more accurately represent the early embryonic development of the human brain. Named by The Scientist as one of the biggest scientific advancements of 2013, organoids allow researchers to study an in vitro system that can recapitulate the biological and gene expression levels of the developing brain in vivo, a feat that seemed almost unattainable [3]. Already, advancements have already been made with the aid of organoids. Using a forebrain organoid platform, scientists were able to model Zika, a fetal developmental disease often transmitted to pregnant mothers through mosquitos. Quantitative analysis revealed that both the African and Asian strains of Zika lead to infection, cell death, and reduced proliferation - trademark signs of microcephaly, a condition where infant heads are abnormally small due to defects in brain development [4].

Despite the promise shown by this technique, it still has serious limitations at the moment. Presently, researchers have not discovered how to faithfully recreate the development of the vascular system within the brain. As this is incredibly important to later stages of brain development, the use
of mini-brains can only model early stages of brain development (Kelava & Lancaster, 2016). Advancements in mini-brain technology raises serious ethical questions as well: If researchers can grow a full human brain, is it moral to experiment on it? While growing the entire human brain will not be feasible for some time, it is important to consider such ethical considerations when developing mini-brain technology.

With such a wide variety of possible experiments, cell culture is an incredibly powerful tool for neuroscience researchers. New techniques are constantly being developed to better analyze the cells, and the rise of iPS technology will allow researchers to analyze individuals. As the development of new experimental techniques advances, researchers will be able to vastly expand their knowledge of the brain.

**Key Terms**

Contamination: Pathogens entering the cell-culture medium. In cell-culture experiments, researchers should focus on avoiding contamination to ensure the validity of their data

Flow Cytometry: A technique that uses lasers to analyze cell size and fluorescence when stained with specific dyes

Immunofluorescence: An experimental technique used to visualize protein concentrations and distributions within cells

iPS Cells: Induced Pluripotent Stem Cells are human adult cells that are reprogrammed to become pluripotent stem cells.

IRB: Institutional Review Board, an organization dedicated to ensuring that human experimentation follows the appropriate guidelines

Mini-brains: A nascent stem-cell-based technology involving the creation of three-dimensional analogs of the human brain.

Live-Cell Imaging: A microscopy technique that allows the visualization of living cells. It is especially useful in tracking change over time.

Microcephaly: Condition where a baby's head is significantly smaller than normal; linked to defects in brain development.


The Controversy of Smart Drugs
Vivi Lu and Anita Singh

What if someone told you that taking a pill could sharpen your mind? If you could improve your test scores by taking a drug, would you do it?

Although this may sound like a hypothetical moral dilemma, this question is in fact based entirely in reality. Cognitive-enhancing pills, or 'smart drugs', are taken every day by students across the world. The Universities of Zurich and Basel in Switzerland recently found that 13.8% of students admitted to using smart drugs while in school (Borreli).

A smart drug or nootropic is a neuroenhancer used to improve mental abilities such as memory, learning, concentration, or social skills (Chudler). Most who use smart drugs believe that the drugs will boost their concentration and focus, improve their grades, and allow them to function well on little sleep. The different types of smart drugs range from ADHD medication to the increasingly popular Modafinil.

But are smart drugs ethical?

Some argue that they are another form of cheating due to the fact that they attempt to improve mental abilities (Solon). Smart drugs help enhance cognitive abilities beyond those that have been given. Steroids and smart drugs could be seen as equivalents. Enhancing the body is greatly frowned upon and is considered illegal in sporting events. Therefore, abiding by the same rules, smart drugs should not be used to help one take concentrate or take a test. This is the perspective of bioconservatists who argue that smart drugs are causing a division in humanity, especially between those who can and can not afford to buy the drugs (“Transhumanism and Bioconservatism”).

On the other hand, transhumanists support the widespread use of smart drugs and believe that continuing the use of these smart drugs could further human abilities (Solon). Already, a substantial number of people take prescribed drugs which qualify as smart drugs. If smart drugs were banned, people with serious brain disorders would be put at a great disadvantage. In medical ethics, one of the four principles of the Hippocratic oath is nonmaleficence, or the requirement that scientists should not intentionally create harm or injury to the patient, either through acts of
commission or omission ("Medical Ethics"). The ability to use smart drugs could change an impaired person’s life. Refusing to help them would be disobeying the rule of nonmaleficence.

The usage of smart drugs additionally could cause addiction. It is well-known that even the most common of soft enhancers, caffeine, have withdrawal symptoms - throbbing headaches, nausea, irritability, fatigue, etc ("Medicines in My Home: Caffeine and Your Body"). Although there have been no reported cases of smart drug addiction thus far, with the surge in popularity, the possibility is becoming greater and greater. Students relying on the use of smart drugs to maintain or raise their grades could easily develop an addiction (Urschel).

So could smart drugs be the future of the human race or the newest addiction? Like most ethical arguments, the debate of smart drugs provides no easy solution.

References


Ph.D. Interview: Studying Pain and Drug Addiction

Ed Bilsky, Ph.D. interviewed by Kyle Ryan

Recently, I interviewed Dr. Ed Bilsky, founding Director of the Center for Excellence in the Neurosciences, and Co-director of the Center of Biomedical Research Excellence for the Study of Pain and Sensory Function at the University of New England. Dr. Bilsky talks about his background and experience in researching the neurobiology of pain and drug addiction as well as his more recent work with drug discovery and development. Dr. Bilsky also offers his thoughts on the progression of drug addiction and its possible remedies, as well as his thoughts on the progressing and vast field of Neuroscience.

Kyle Ryan (KR): “What is your educational background and what made you interested in conducting research and specifically Neuroscience?”

Ed Bilsky, Ph.D. (EB): “I received a Bachelors of Science in Physics as an undergraduate at Rensselaer. The program required an undergraduate research project. I had just taken a course on alcohol and drug abuse and approached the professor at the end of my sophomore year. As I got into the research, I became fascinated with how the brain worked and how these different drugs acted on the nervous system, including powerful effects that could lead to habitual use/misuse. I decided to get a Masters degree in behavioral neuroscience at Rensselaer and then pursued a Ph.D. in Pharmacology and Toxicology at the University of Arizona. My dissertation research was on opioid pharmacology with connections to the neurobiology of pain and addiction.”

KR: “What aspect of neuroscience does your laboratory focus on?”

EB: “My research laboratory focuses on early stage drug discovery and development, mostly with opioid analgesics and opioid antagonists. We also develop new ways of testing potential analgesics in laboratory animals and try to better understand the pain pathways and how signals are modified by the nervous system.”

KR: “Have you looked at drug addiction and abuse in your lab?”
EB: “We study drug reinforcement and the addictive like behaviors in rats and mice through a variety of experimental protocols. Rats and mice, like pretty much all vertebrates including humans, have primitive systems in their nervous system that reinforce behavior that is important for survival (food, water, sex). They share many of the fundamental receptors, neurotransmitters and basic circuitry that humans have. Not surprisingly, rats and mice will work hard to get infusions of drugs such as heroin, cocaine and even nicotine and alcohol. They, like humans, can associate cues in their environment that are associated with drug effects, and will display behaviors that suggest that the drug effects are producing a positive (rewarding) affective state. They can also become tolerant and physically dependent on certain drugs like opioids and go through withdrawal when the drug is taken away. Ultimately, they can become focused almost exclusively on receiving the drug effects and ignoring natural rewards. We use a lot of different tools to determine the neurochemistry associated with these behaviors and approaches that may be useful in reducing the actions of these drugs of abuse.”

KR: “With all of the current problems that are arising with opioid abuse, what are some alternate options to opioids? Or do effective ones even exist?”

EB: “Opioids are one class of drugs that are used for their analgesic properties. Like all other drugs, they have side effects that have to be carefully monitored and managed. We have know about the abuse potential of opioids for decades if not centuries. There are a number of other drug classes that are used to manage pain, many of which do not have abuse liability. The problem is that they have either incomplete efficacy/effectiveness against more moderate to severe pain, or they have other serious side effects. Aspirin and ibuprofen (Advil) are excellent examples of this. While effective against some types of pain, they do not adequately control severe pain such as that associated with a major surgery or some of the more severe chronic pain states. They also cause ulcers and bleeding of the stomach when taken at high doses for prolonged periods of time.

There are many other non-pharmacological techniques used in treating chronic pain. All of these have to be carefully integrated into a plan for the individual patient. The challenges we face are that in general, integrated care is not well done in our medical system, and insurers do not adequately reimburse for this type of care, particularly when dealing with management of a challenging chronic illness. Examples of non-drug treatments include exercise regimens that are appropriate for the patient, nutrition, physical and occupational therapy, mental health support services, support groups, alternative medicine, etc.”

KR: “How do you foresee the world tackling drug addiction?”

EB: “We ultimately need to get a better understanding of why so many people are attracted to (and susceptible) to the effects of these drugs of abuse (not just the opioids). We need to remove the stigma that is associated with any of the diseases that affect the brain and nervous system, including drug addiction, pain and the various psychiatric disease. Stigma, marginalization and isolation play a huge role in not recognizing the illness early on and not getting people access to the care they need"
before the disease fully sets in. While we do have to have laws and enforcement in place to reduce supply, we should be concentrating efforts on prevention, early recognition and treatment, and better support services, even for those who continue to struggle with the effects of substance misuse, abuse and addiction disorders.”

**KR: “What is the most pressing issue in neuroscience today and can it be tackled in any way?”**

EB: “The neuroscience field is very large and there are so many different diseases of the brain and nervous system that need attention and more research (e.g., Parkinson’s disease, Alzheimer’s disease, etc.). But for sheer numbers and economic burden (as well as the negative effects on the individual, family and community), I think that pain and substance abuse should be our top priorities. We can (and must) tackle these problems. There are programs that do help in preventing and treating these disorders. They need to be more fully implemented/funded by federal, state and local agencies, and the efforts need to be much better coordinated and sustained in order to see positive changes. More research needs to be done to develop and test new treatments, assess progress, and make needed changes on the fly.”

As Dr. Bilsky mentioned, we are at a time in our society where it is necessary for us to focus on prevention and better treatment of drug addiction and abuse. Due to the increasing prevalence of chronic pain, which often is medicated with opioids, we need to place a greater focus on the research and funding of programs that will seek very effective alternatives to opioids that wouldn’t have the addictive qualities that opioids do.
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