ADDICTION

JOHN FALCON

Over the decades there have been many attempts to find "the cure" for addiction. It really depends on how you define "cure". Many people stop their compulsive addictive behavior and never go back, changing their lives forever. Others have long periods of relapse and recovery. In either case, even if the person stops using completely, there is often an enduring struggle to remain sober and clean or to stop the compulsive behaviors. Because of their biological/psychological make-up and personal history, many people need to take greater care to avoid relapsing. Because it is a lifetime journey, they are never "cured", but they can develop This process is a day-at-a-time approach, and recovery can be achieved: millions of people around the world are living that mindset today. There has been extensive research to understand addiction, to explore where it comes from, and to learn how to manage it. We will look at how society views addiction and how that view is limited in the face of neuroscience. We will also consider the question as to whether addiction is a brain disorder/syndrome or a matter of choice, and finally, we will look at treatment and the variety of approaches used to achieve long-term recovery.

SUBSTANCE USE

Definitions of substance use disorders and addiction have changed substantially over the years. We have gone from addiction to dependency and now substance use/addiction. The term substance use disorder was introduced by the American Psychiatric Association (APA) in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), and refers to the recurrent use of alcohol or other drugs that causes clinically and functionally significant impairment, such as health problems, disability, and failure to meet major responsibilities at work, school, or home (American Psychiatric Association, 2013). Depending on the severity, the disorder is classified as mild, moderate, or severe. This terminology can be confusing, and affects how we view individuals and how we treat them. The term addiction is used to indicate the most severe, chronic stage of substance use disorder, in which there is a substantial loss of self-control, as indicated by compulsive drug taking despite the desire to stop taking the drug. In the DSM-5, the term is synonymous with the classification of severe substance use disorder (American Psychiatric Association, 2013).

SOCIETAL VIEW

The prevention and treatment of substance use disorders has been a challenge for society, which includes communities, families, and the workplace. Why don't substance users seek treatment? Research shows that shame and stigma are the number one reasons. Studies of public opinion from around the world have found that the stigma attached to people with substance use disorders appears to be more severe and persistent compared to other mental illnesses, and people reported having greater fear for and more negative attitudes toward substance use problems compared to other stigmatized conditions such as depression, schizophrenia, or homelessness (Room, 2005).

Society tends not to see substance use and loss of control as a brain condition or syndrome, but rather an act of choice and voluntary. Australia, for example, has a history of attributing weakness to people with substance use and mental health issues. This attitude needs to change to reduce the shame and stigma so that people who need treatment will seek it. Looking at substance use as a brain disorder can increase the likelihood that people affected will seek treatment and have better outcomes (Volkow, 2018; Volkow, Koob, & McLellan, 2016), which will have a flow-on effect on society in general.

SUBSTANCE USE: THE LEVELS

What is substance use and its connection with the brain? How do we assess people with substance use disorders? What does that mean in terms of an integrative treatment approach, and when we look at craving management, how do we maintain recovery in the face of the brain function and relapse cues?

We start with the idea that at some point substance use is a brain condition. In the past two decades, this view has increasingly been supported by research. Yet, because many of the behaviors that users display can be impulsive, compulsive, and sometimes aberrant, some argue that substance use is not tied to neurobiology, but is a behavior of choice. This argument negates what happens in the brain's reward system, however; ingrained attitudes that people's actions are a product of self-determination and personal responsibility challenge the scientific evidence of the brain syndrome.

Substance use disorder has been segregated from the rest of health care and as a result is treated very differently from other chronic conditions such as anxiety or depression. Biological markers of disease states need to be considered. In the disease/condition model, there is an *organ*, which in substance use is the midbrain; the *defect* is the cause (e.g., genetics, trauma, mental health issues, stress); and then there are the *symptoms* such as loss of control, "bad behavior", criminality, and so forth (McCauley, 2009). From a physiological perspective, addiction to alcohol and other drugs (and compulsive/pathological behavior) is considered a brain disease whereby drug actions on brain circuitry result in changes in the control of behavior (Tomberg, 2010). The cycle of addiction, as seen in severe use, is a drug reinforcement circuit (reward and stress) that includes the extended amygdala (the central nucleus of the amygdala, the bed nucleus of the stria terminalis, and the transition zone in the shell of the nucleus accumbens). A drug- and cue-induced reinstatement (craving) neurocircuit is composed

of the prefrontal (anterior cingulate, prelimbic, orbitofrontal) cortex and basolateral amygdala, with a primary role hypothesized for the basolateral amygdala in cue-induced craving (Galanter & Kaskutas, 2008). A drug-seeking (compulsive) circuit is composed of the nucleus accumbens (NAcc), ventral pallidum, thalamus, and orbitofrontal cortex (OFC), and is important to the craving mechanism.

Thus, natural and artificial rewards (food, sex, drugs of abuse) have been shown to activate this dopaminergic pathway, also known as the mesolimbic dopamine pathway, causing an increase in dopamine levels within the NAcc. From an evolutionary perspective, this brain reward circuit has ensured survival by giving priority to essential actions such as reproduction (Tomberg, 2010). It is the interaction with these survival mechanisms that separates substance users who use for social and recreational reasons from people described as addicted. There is a clear delineation of how people use alcohol and drugs and the mechanism by which various drugs alter the activity of this neuroanatomical system. To illustrate the levels of use, we need to understand the effects on the reward system and the development of treatment.

How neuroscience research offers new opportunities for prevention and treatment depends in part on an appreciation of the current definitions of substance use. A clear definition and evidence supporting the research findings into acquired disease of the brain are needed to avoid misunderstandings. Clarity and understanding will help to reduce addiction and its damaging effects on individuals and society. If this is to happen, health professionals—and society—must consider an overarching approach and not a one-size-fits-all approach.

The brain does not care what drug (alcohol, tobacco, marijuana, or ice) or which compulsive behavior (gambling, sex, codependency, video gaming) is being used. The brain's reward system goes into action, and for some, it becomes a matter of survival. Susceptibility to the drug or compulsive behavior varies because for various reasons people differ in their vulnerability to it. Many genetic, environmental, developmental, and social factors contribute to the determination of a person's unique susceptibility to using drugs in the first instance, sustaining drug use, and undergoing the progressive changes in the brain that characterize addiction (Demers, Bogdan, & Agrawal, 2014; Volkow & Muenke, 2012). When considering what level a substance user is at - mild, moderate, or severe - all these issues need to be considered in a comprehensive assessment. The proposed treatment also needs to be integrative in its approach.

The *mild* user (previously called the experimental user) uses the drug with no significant ill effects and with no marked withdrawal or tolerance. This person can use alcohol and drugs and return to their normal life. The practice can be precarious, however, because even early, voluntary use can interact with environmental and genetic factors and result in addiction in some people, yet not in others. The concept of behavioral addiction is still controversial. While some people exhibit manageable behavioral self-regulation—even in the so-called behavioral addictions like over-eating, pathologic gambling, and video-gaming—in others these disorders often manifest as compulsive behaviors with impaired

self-regulation (Volkow, Kloob, & McLellan, 2016). Addiction used to be seen as a continuum of use, or stages of use, but the theory no longer has much value because not everyone who uses experimentally becomes an addict. They may use at a young age, perhaps out of curiosity or because their friends are doing it and they feel pressured into using. This is related to a lack of development in the prefrontal cortex, which is responsible for decision-making and impulse control. Therefore, they may move on to the next level for a variety of reasons: because of the availability of drugs and alcohol within the community, whether friends use drugs or alcohol, the family environment (including physical or emotional abuse, mental illness, or alcohol or drug use in the house), or mental health conditions such as depression, anxiety, or ADHD (The Recovery Village, n.d.).

The next level of substance use is the moderate level. Here we see people starting to have some social and physiological issues because of their use. They may increase their use and use more regularly to medicate life issues. They may begin to avoid social commitments and school and work obligations. They may experience withdrawal symptoms and use to compensate stress and worry. They may be concerned by their use but nevertheless develop binge and intoxication behaviors that activate the reward system, which increases dopamine release. All these symptoms plus stigma can influence what they do next.

At this level (moderate use), users may not consider what is happening in the brain, so psychoeducation needs to be utilized to increase their awareness. This process involves the same molecular mechanisms that strengthen synaptic connections during learning and memory formation. During intoxication, drug-induced activation of the brain's reward regions is enhanced by conditioned cues in areas of increased sensitization. During withdrawal, the activation of brain regions involved in emotions results in negative mood and enhanced sensitivity to stress. During preoccupation, the decreased function of the prefrontal cortex leads to an inability to balance the strong desire for the drug with the will to abstain, which triggers relapse and reinitiates the cycle of addiction. The compromised neurocircuitry reflects the disruption of the dopamine and glutamate systems and the stress-control systems of the brain that are affected by corticotropin-releasing factor and dynorphin (Volkow, Koob, & McLellan, 2016). When use is increased and the reward system is activated, users may pursue that reward with some negative effect. There may be some ambivalence in their thinking that they can use like others and that there is no problem; stigma and shame may also be present. This is a fine edge for them and for treatment providers in helping them to participate in treatment.

The *severe* use level is characterized by an increase in a psychological need to use. Tolerance develops in that they need more of the drug to get the same high, or reward. In a person with addiction, the reward and motivational systems become reoriented through conditioning to focus on the more potent release of dopamine produced by the drug and its cues. As a result, with severe use, the person no longer experiences that same degree of euphoria (tolerance). In addition to resetting the brain's reward system, repeated exposure to the dopamine-enhancing effects of most drugs leads

to adaptations in the circuitry of the extended amygdala in the basal forebrain; these adaptations result in increases in a person's reactivity to stress and lead to the emergence of negative emotions (Davis, Walker, Miles, & Grillon, 2010; Jennings et al., 2013). Many times, the use of drugs, as well as drug seeking, become actions for survival. The user doesn't experience the same high, so they keep using to get the same effect. This was once called "chasing the dragon".

Some of the factors that contribute to severe use are a person's susceptibility to using drugs, sustained use, and changes in the brain that characterize addiction. Other factors are genetics, family history, early exposure, high-risk environments, social stressors, easy access to drugs, and other mental health issues. Many people at this level of severe use frequently use more, and they may also attempt to quit, but physical tolerance and shame increase their vulnerability. Many users cannot face life without the drug and cannot control their use. They continue to harm themselves and many do not recognise they have a problem. Their brain has been highjacked; their neurobiological changes are distinct and profound.

The behaviors during the three stages of addiction change as a person transitions from drug experimentation to *severe use/addiction* as a function of the progressive neuroadaptations that occur in the brain. At this point using is not a choice, and society needs to understand that users are cellular-adapted, not bad people, and just saying "no" or "being responsible" when they use is not that easy. These tips do not help them but further enhance their ambivalence about seeking help. When addressing *severe use/addiction* there are implications for treatment that need to be considered.

TREATMENT

Approaches to substance use disorder have been controversial over the years because of the different perspectives: is it a choice or is it a disease? Are users in denial, or are they naturally ambivalent to change due to what is happening to their brain? A better understanding of the brain disease model of addiction may help to moderate some of the moral judgment attached to addictive behaviors and foster more scientific and public health-oriented approaches to prevention and treatment (The Recovery Village, n.d.; Volkow, Koob, & McLellan, 2016).

To moderate the moral judgment of addiction, a disease/condition/syndrome approach helps in prevention and treatment. There are many evidence-based interventions aimed at prevention that are supported by neurobiological research. What this research shows is that onset occurs predominantly during a risk period: adolescence. Adolescence is a time when the still-developing brain is particularly sensitive to the effects of drugs, a factor that contributes to adolescents' greater vulnerability to drug experimentation and addiction. The studies show that children and adolescents with evidence of structural or functional changes in frontal cortical regions or with traits of novelty-seeking or impulsivity are at greater risk for substance use disorders (Castellanos-Ryan, Rubia, & Conrod, 2011; Nees et al., 2012; Quinn & Harden, 2013).

This research can be used to describe early-warning signs that would become useful to tailor

prevention strategies and develop treatment programs. According to research related to the brain disease model of addiction, preventive interventions should be designed to enhance social skills and improve self-regulation. Bessel van der Kolk, a clinician, researcher, and teacher in post-traumatic stress, coined the term "limbic therapy" (van der Kolk, 2014) for his approach to treatment. His work integrates developmental, neurobiological, psychodynamic, and interpersonal aspects of the impact of trauma and its treatment, whereby the therapist needs to work with clients to regulate their emotional responses and their craving, utilizing limbic approaches, such as expressive therapies, mindfulness, and meditation.

Alongside of emotional regulation, we need to consider behavioral therapy. The brain condition/ disease model of addiction has also fostered the development of behavioral interventions to help restore balance in brain circuitry affected by drugs (Litten et al., 2015). Strategies to assist clients to avoid situations need to be part of the treatment to improve executive functioning and help them self-regulate and manage strong urges and craving.

As well as behavioral approaches, clients can help to prevent relapse while the brain is healing and normal decision-making is restored through self-direction and self-discipline. This would take time and practice and would develop neuroplasticity in the brain (adaptation, plasticity, learning, and memory). Research has shown that nerve cells in the brain are able to compensate for diseases like addiction and adjust their activities in response to new situations or to changes in the environment. This is called neuroplasticity. Prolonged (self-)administration of drugs induces gene expression, neurochemical, neurophysiological, and structural changes in many brain-cell populations. These region-specific changes correlate with addiction, drug intake, and conditioned drug effects, such as cue- or stress-induced reinstatement of drug seeking (Korpi et al., 2015).

Medication can also assist patients with opioid-use disorder, and maintenance therapy with agonists or partial agonists such as methadone or buprenorphine can be essential in helping to control symptoms of withdrawal and cravings (Bell, 2014). Opioid antagonists such as extended-release naltrexone may be used to prevent opioid intoxication (Sullivan et al., 2013). Naltrexone and acamprosate have been efficacious in the treatment of alcohol-use disorders, and other medications can help in the recovery from nicotine addiction (Müller, Geisel, Banas, & Heinz, 2014).

Alternatives to medication to prevent relapse and reduce vulnerability to craving can also be applied. If we apply the five theories of addiction, namely: the pathology of motivation and choice (Kalivas & Volkow, 2005); stress and allostasis (Koob & Le Moal, 2001); the pathology of learning and memory (Everitt & Robbins, 2005, 2016; Hyman, 2005); incentive-sensitization of reward (Robinson & Berridge, 2001), and genetic vulnerability (Schuckit, Li, Cloninger, & Deitrich, 1985), we can begin to address what alternative approaches can be applied alongside medication treatments (McCauley, 2015).

Taking motivation and choice first, we know that drug taking can damage the OFC, causing the loss of a crucial behavioral guidance system with the result that responses are impulsive and inappropriate.

There are deficits in self-regulation, the inability to properly assign value to rewards (such as money vs. drugs), and a tendency to choose small & immediate rewards over larger but delayed rewards (McCauley, 2015). There are useful strategies to combat this disruption to effective functions in the OFC, the anterior cingulate cortex, and the prefrontal cortex—that deal with failure of executive functioning due to moderate and severe use. These include: medical/craving/psychiatric stabilization, abstinence, peer support (small, single-gender, long-term), agency-building exercises, service work, working with newcomers in 12-step support groups, and purposeful, meaningful goals.

More holistic, psychosocial, and spiritual aspects of the recovery process can be applied. For example, amino-acid therapy for reward deficiency syndrome, developed by Kenneth Blum and colleagues (Blum et al., 2016), promoting pro-dopamine regulation to induce dopamine homeostasis. Blum's work includes Molecular neurobiology of addiction recovery: The 12 steps program and fellowship (Blum et al., 2013).

Strategies for dealing with stress (the anti-reward system), can also include natural amino acids such as GABA (gamma-aminobutyric acid), serotonin, glutamine, and 5-HTP (5-Hydroxytryptophan). This approach was developed by Julie Ross, a world leader in the use of nutritional therapy for the treatment of mood problems, eating disorders, and addictions, and aims to restore neuron imbalances due to addiction as well as moods (Ross, 2003). And strategies for dealing with the glutamate (memory) component of addiction include: being aware of triggers, avoiding triggers as much as possible (e.g., avoiding old places, drug-using friends, etc.), self-talk in moments of craving, frequent monitoring, and medication (McCauley, 2015).

CONCLUSION

When we can accept that moderate to severe use is more than a behavioral disorder or choice, and see it from a scientific perspective as a condition of the brain, then the stigma and shame can be reduced. Treatment needs to be integrative. This means considering the genetics and family influences for prevention strategies, the damage to the cortex, and the imbalance of the midbrain's neurochemistry. Addiction is more than a behavioral disorder. It involves behavioral changes and complications, and cognitive and emotional changes; a comprehensive approach needs to be applied to address relapse and cravings. Utilizing alternative therapies can heal the brain. Support groups like 12-step support groups (Brande, 2018) can foster long-term recovery and SMART Recovery (https://smartrecoveryaustralia.com.au/) can support individuals in changing thinking, beliefs, and behaviors toward recovery.

The good news is recovery is possible for individuals, families and society. Changing our attitudes and fine tuning our treatment to direct it toward the brain, gives us hope.

REFERENCES

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: Author.

Bell, J. (2014). Pharmacological maintenance treatments of opiate addiction. British Journal of Clinical Pharmacology, 77, 253–263. doi:10.1111/bcp.12051

Blum, K., Femino, J., Teitelbaum, S., Giordano, J., Oscar-Berman, M., & Gold, M. (2013). Molecular neurobiology of addiction recovery: The 12 steps program and fellowship (Springer Briefs in Neuroscience). New York, NY: Springer.

Blum, K., Febo, M., Badgaiyan, R. D., Braverman, E. R., Dushaj, K., Li, M., & Demetrovics, Z. (2016). Neuronutrient amino-acid therapy protects against reward deficiency syndrome: Dopaminergic key to homeostasis and neuroplasticity. Current Pharmaceutical Design, 22(38), 5837–5854.

Brande, L. (2018, August 23). About the Alcoholics Anonymous (AA) 12-step recovery program. Retrieved from https://www.recovery.org/topics/alcoholics-anonymous-12-step/

Castellanos-Ryan, N., Rubia, K., & Conrod, P. J. (2011). Response inhibition and reward response bias mediate the predictive relationships between impulsivity and sensation seeking and common and unique variance in conduct disorder and substance misuse. Alcoholism, Clinical and Experimental Research, 35, 140–155. doi:10.1111/j.1530-0277.2010.01331.x

Davis, M., Walker, D. L., Miles, L., & Grillon, C. (2010). Phasic vs. sustained fear in rats and humans: Role of the extended amygdala in fear vs. anxiety. Neuropsychopharmacology, 35, 105–135. doi:10.1038/npp.2009.109

Demers, C. H., Bogdan, R., & Agrawal, A. (2014). The genetics, neurogenetics and pharmacogenetics of addiction. Current Behavioral Neuroscience Reports, 1, 33–44. doi:10.1007/s40473-013-0004-8

Everitt, B. J., & Robbins, T. W. (2005). Neural systems of reinforcement for drug addiction: From actions to habits to compulsion. Nature Neuroscience, 8(11), 1481–1489. doi:10.1038/nn1579

Everitt, B. J., & Robbins, T. W. (2016). Drug addiction: Updating actions to habits to compulsions ten years on. Annual Review of Psychology, 67, 23–50. doi:10.1146/annurev-psych-122414-033457

Galanter, M., & Kaskutas, L. A. (Eds.). (2008). Research on Alcoholics Anonymous and spirituality in addiction recovery. New York, NY: Springer.

Hyman, S. E. (2005). Addiction: A disease of learning and memory. The American Journal of Psychiatry, 162(8), 1414–1422. doi:10.1176/appi.ajp.162.8.1414

Jennings, J. H., Sparta, D. R., Stamatakis, A. M., Ung, R. L., Pleil, K. E., Kash, T. L., & Stuber, G. D. (2013). Distinct extended amygdala circuits for divergent motivational states. Nature, 496(7444), 224–228. doi:10.1038/nature12041

Kalivas, P. W., & Volkow, N. D. (2005). The neural basis of addiction: A pathology of motivation and choice. The American Journal of Psychiatry, 162(8), 1403–1413. doi:10.1176/appi.ajp.162.8.1403

Koob, G. F., & Le Moal, M. (2001). Drug addiction, dysregulation of reward, and allostasis. Neuropsychopharmacology, 24, 97–129. doi:10.1016/S0893-133X(00)00195-0

Korpi, E. R., den Hollander, B., Farooq, U., Vashchinkina, E., Rajkumar, R., Nutt, J., . . . Dawe, G. S. (2015). Mechanisms of action and persistent neuroplasticity by drugs of abuse. Pharmacological Reviews, 67(4), 872–1004. doi:10.1124/pr.115.010967

Litten, R. Z., Ryan, M. L., Falk, D. E., Reilly, M., Fertig, J. B., & Koob, G.F. (2015). Heterogeneity of alcohol use disorder: understanding mechanisms to advance personalized treatment. Alcoholism, Clinical and Experimental Research, 39, 579–584. doi:10.1111/acer.12669

McCauley, K. (2009). Pleasure unwoven: A personal journey about addiction [Video]. Retrieved from https://addictioneducationsociety.org/dr-kevin-mccauley-pleasure-unwoven/

McCauley, K. (2015, May). The brain and recovery: An update on the neuroscience of addiction. Paper presented at the Third Annual Idaho Conference on Alcohol and Drug Dependency, Boise State University, ID. Retrieved from http://attendicadd.com/2017/speakers_notes/B3_F5_Brain_and_

Recovery_McCauley.pdf

Müller, C. A., Geisel, O., Banas, R., & Heinz, A. (2014). Current pharmacological treatment approaches for alcohol dependence. Expert Opinion on Pharmacotherapy, 15, 471–481. doi:10.1517/14656566.2014.876008

Nees, F., Tzschoppe, J., Patrick, C. J., Vollstädt-Klein, S., Steiner, S., Poustka, L., . . . IMAGEN Consortium (2012). Determinants of early alcohol use in healthy adolescents: The differential contribution of neuroimaging and psychological factors. Neuropsychopharmacology, 37, 986–995. doi:10.1038/npp.2011.282

Quinn, P. D., & Harden, K. P. (2013). Differential changes in impulsivity and sensation seeking and the escalation of substance use from adolescence to early adulthood. Development and Psychopathology, 25, 223–239. doi:10.1017/S0954579412000284

Robinson, T. E., & Berridge, K. C. (2001). Incentive-sensitization and addiction. Addiction, 96(1), 103–114. doi:10.1080/09652140020016996

Room, R. (2005). Stigma, social inequality and alcohol and drug use. Drug and Alcohol Review, 24, 143–155. doi:10.1080/09595230500102434

Ross, J. (2003). The mood cure. New York, NY: Penguin.

Sullivan, M. A., Bisaga, A., Mariani, J. J., Glass, A., Levin, F. R., Comer, S. D., & Nunes, E. V. (2013). Naltrexone treatment for opioid dependence: Does its effectiveness depend on testing the blockade? Drug and Alcohol Dependence, 133, 80–85. doi:10.1016/j.drugalcdep.2013.05.030

The Recovery Village. (n.d.). Stages of Addiction. Retrieved from: https://www.therecoveryvillage.com/drug-addiction/stages-of-addiction/

Tomberg, C. (2010). Alcohol pathophysiology circuits and molecular mechanisms. Journal of Psychophysiology, 24, 215–230. doi:10.1027/0269-8803/a000035

Van der Kolk, B. (2014). The body keeps the score. New York, NY: Viking.

Volkow, N. D. (2018, March 23). What does it mean when we call addiction a brain disorder? Scientific American. Retrieved from https://blogs.scientificamerican.com/observations/what-does-it-mean-when-we-call-addiction-a-brain-disorder/

Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiological advances from the brain disease model of addiction. The New England Journal of Medicine, 374, 363–371. doi:10.1056/nejmra1511480

Volkow, N. D., & Muenke, M. (2012). The genetics of addiction. Human Genetics, 131, 773–777. doi:10.1007/s00439-012-1173-3

John Falcon is a psychologist and addiction specialist. He has been a psychiatric nurse, counsellor, and psychologist in the behavioral health field for over 30 years, with a focus on addictions. He is currently an academic teacher at the Australian College of Applied Psychology in Sydney, Australia, has been a support officer with the Higher Education Leadership Institute (https://heli.edu.au/), and is a clinical supervisor in private practice.