Eur. J. Psychiat. 2019;33(4):143–151

THE EUROPEAN JOURNAL OF PSYCHIATRY

www.elsevier.es/ejpsy

REVIEW ARTICLE

A systematic review on Substance Addiction: medical diagnosis or morality flaw?

P. Cabral Barata[a,*], **C.F.P. Oliveira**[a], **S. Lima de Castro**[a], **A.M.P. Rocha da Mota**[b]

[a] *Psychiatry Department, Hospital Prof. Dr. Fernando da Fonseca, E.P.E., IC 19, 2720-276 Amadora, Portugal*
[b] *Psychiatry Department, Centro Hospitalar Psiquiátrico de Lisboa, Av. do Brasil, 53, 1749-002 Lisboa, Portugal*

Received 16 November 2018; accepted 2 July 2019
Available online 26 July 2019

KEYWORDS
Addiction;
Volition;
Free-will;
Self-determination;
Substance use;
Morale

Abstract
Background/Objectives: There continues to be a debate on whether Substance Addiction (SA) is best understood as a brain disease or a moral condition. We aim to review the current evidence about substance use disorder and to answer two questions: ''should Substance Addiction be conceptualized as a medical disorder, a morality flaw or an intermediate construct?'' and ''can individuals with substance use disorders be held responsible for their behaviour and, if so, to what extent?''.
Methods: Systematic review of scientific literature (search of scientific articles in PubMed/MEDLINE database and use of a psychiatry textbook) related with SA and its relationship to free will.
Results: Besides the psychiatry textbook, 38 studies met the inclusion criteria. Much of the scientific knowledge related with SA is in its early stages. Several risk factors were found to influence SA's development. SA's neurobiology includes several brain circuits and neurotransmitters. Drug consumption involves a series of voluntary acts; howbeit, its development is associated with enduring changes in brain function related to automatized behaviour. SA can be a major cause of morbidity and mortality.
Conclusions: Significant scientific evidence has been found not to consider SA as a simple morality flaw. Exclusively defining it as a medical diagnosis may be too short for its complexity, as a search for a broader multi-faceted perspective may be warranted. These individual's willpower and self-determination is not entirely preserved nor totally disrupted, and their accountability is a complex and not clear matter. Additional research is needed to further characterize SA and its mechanisms.

* Corresponding author.
E-mail address: p.barata9@gmail.com (P. Cabral Barata).

https://doi.org/10.1016/j.ejpsy.2019.07.001

Introduction

Substance dependence (or Substance Addiction) can be defined as a chronically relapsing disorder characterized by compulsion to seek and take the drug, loss of control in limiting intake[1–7] and emergence of a negative emotional state (e.g. dysphoria, anxiety, irritability) when access to the drug is prevented.[1,2,4,6,7] Moreover, the current medical consensus is that the key feature of substance addiction is compulsive drug use despite significant negative consequences.[3,8–11] The occasional but limited use of a potentially addictive drug should be distinguished from escalated drug use and the emergence of a chronic drug-dependent state.[1,2,4,5,7,12,13]

Nevertheless, there continues to be a debate on whether addiction is best understood as a brain disease or a moral condition.[6,8,14–16] This dispute, which may influence the access to treatment, as well as the stigma attached to addiction, is often motivated by the question of whether and to what extent we can fairly hold addicted individuals responsible for their actions.[8,14,15,17] Besides, the diagnosis of addiction is very coloured by the negative moral and social values entailed with the illness. It is difficult to perceive that people with drug use disorders have a disease; acts of will or volition are usually not accepted as diseases, because volition is an act of choice or free will.[3,15,16,18] However, it has been argued that, if there is a common aetiology for addiction, it should be one that is basic and fundamental to the healthy functioning of a human being – a disorder of volition.[6,18,19] Even though mental illness is often relevant to legal matters, addictive illness – as a subset of mental illness – has had a less favourable legal reception, historically, and only recently have such problems been seen as something other than a form of moral weakness or depravity.[14]

While the issue of whether addiction is a disease has a medical and philosophical importance, it is of vital significance for the person with a substance use disorder who still suffers from the disease of addiction.[3,6,15,18] Recognizing that addiction is a disease should encourage research into treatments that are effective and that address this population's significant brain dysfunction, allowing them to receive the treatment that is required from the medical community.[3,15,16,18]

Through this study, we aim to answer two questions:

1. Should Substance Addiction be conceptualized as a medical disorder, a morality flaw or an intermediate construct?
2. Can individuals with substance use disorders be held responsible for their behaviour and, if so, to what extent?

Besides answering those main questions, we also aim to review the current evidence about substance use disorder risk factors, neurobiology and its consequences.

Methods

This review was performed according to the PRISMA guidelines,[20] thus providing a comprehensive framework which objectively assesses indications of quality of included studies.

The characteristics of the studies eligible for the review included being related to the thematic of addiction, regarding its neurobiology, risk factors, consequences and also addiction's relationship to free will and self-determination. Further criteria adopted were: (a) publication date between 1980 and 2017, (b) written in English, Spanish or Portuguese language, (c) published in a scholarly peer-reviewed journal. The studies were excluded if they did not relate to any of the specific subjects of addiction considered in the review (neurobiology, risk factors, consequences and relationship to free will/self-determination).

Studies were identified by searching papers according to their relevance via PubMed/MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed), using the following keywords: ''substance addiction and will''. After performing the initial literature search, the first 400 study titles and abstracts (seriated according to ''best match'') were screened for eligibility by the first author. Full texts of all potentially relevant studies were subsequently retrieved and further examined for eligibility: 38 studies were suitable for the inclusion in this review.

Besides the mentioned studies, one textbook of Addiction Psychiatry was also included in the review, due to its close relationship to the main subject of the study and to the author's noteworthy work in the field of addiction.

The PRISMA flow diagram (Fig. 1) provides more detailed information regarding the selection process of the bibliography.

In order to accomplish this study, ethical approval was obtained from the Ethical Committee of the main investigator's institution.

Results

In addition to the use of an Addiction textbook, the search in Pubmed/MEDLINE database resulted in 38 scientific articles meeting the inclusion criteria. The results shall be divided in 4 subjects: Addiction risk factors, Neurobiology of Addiction, Addiction Consequences and Addiction and free will.

Addiction risk factors

Some individuals are more susceptible to addiction than others due to a range of risk factors.[1,6,8] The probability of initial use and the probability of progression towards a pathological pattern of use are influenced by biological factors, environmental factors, the nature of the addictive agent and the interaction between them.[1,6,21] While ''environmental'' factors, generally speaking, have a stronger effect on initiation, genetic factors play a larger role in the transition from regular use to the development of addiction.[13,22]

Gender

Men are more likely to have problems with addictive drugs.[10] However, women are more sensitive to the reinforcing properties of drugs, are thought to progress to addiction quicker than men and are currently having more opportunities of access to addictive substances.[12]

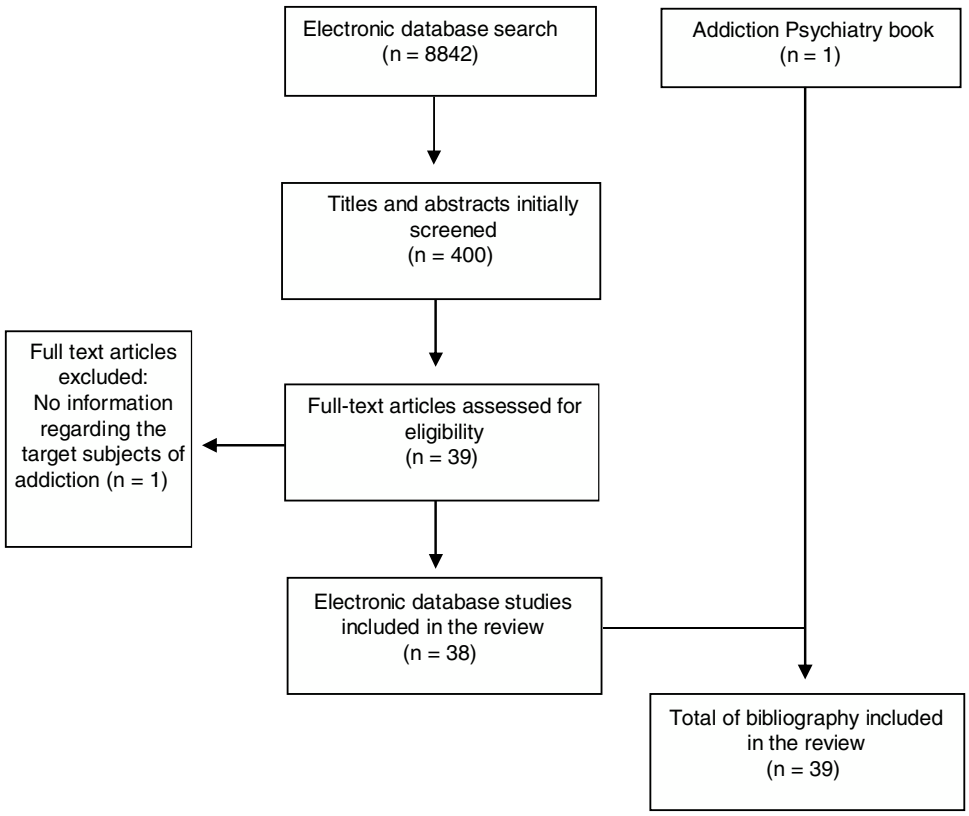

Figure 1 PRISMA flow diagram of the study selection process.

Genetics

There has been found unequivocal evidence of genetic variations contributing to the development of substance use disorders.[13] It has been estimated that genetic and epigenetic factors account for between 40% and 60% of a person's vulnerability to addiction.[1,10,11,23]

Genetic contributions can be substance-specific or reflect a more general vulnerability to addiction.[22,23] Genes that have been studied operate at many levels: genes for metabolic enzymes (e.g., aldehyde dehydrogenase, monoamine oxidase A, catechol-O-methyl transferase)[1,13,15,22,24]; genes encoding molecular targets for the various psychoactive drugs [e.g., dopamine, γ-aminobutyric acid (GABA), glutamate, opioid, nicotinic and cannabinoid receptors][13,22–25]; circadian genes[5]; and genes influencing other aspects of addiction neurobiology, like learning or behavioural disinhibition/impulsivity.[15,23] The strongest specific genetic contributors to dependence are related to the pharmacologic responses to nicotine and alcohol; they include discrepancies between nicotinic receptor genes, nicotine metabolizing genes and alcohol metabolizing genes.[13]

Psychological factors

Individuals take drugs for a variety of reasons: to feel good, to feel better, to do better, and because others are doing it.[1,10]

Psychiatric disorders have been identified as risk factors for developing substance use disorders. Two psychiatric disorders are noteworthy. Firstly, individuals with attention-deficit/hyperactivity disorder (ADHD) often find that self-medicating with stimulants (e.g. amphetamine) calms them, improves focus and diminishes distractibility.[1] Secondly, people with anxiety disorders and anxiety-related personality traits [such as panic disorder, social anxiety disorder and increased harm avoidance] may use substances to reduce their anxious experiences.[1,24] It is known that a quarter of young male alcoholics suffer from social anxiety disorder.[1]

Certain personality characteristics have also been reported to be associated with a higher risk for various types of addiction – impulsivity, behavioural disinhibition and sensation seeking.[1,7,11,12,26,27] Individuals with these traits seem more likely to use substances for the immediate and easily obtainable desirable changes, at the expense of future consequences.[11,26,27]

Age

Research shows that the earlier a person begins to experiment with drugs or alcohol, the more likely he or she will develop an addiction.[12,21]

Adolescence is a particular vulnerable period due to a number of psychological traits, such as risky and reward-seeking behaviour that adolescents exhibit, but also due to the harmful effect that drugs can have on the developing brain.[12]

Drug use tends to be at a maximum prevalence during emerging adulthood, peaking at ages 21–22. Emerging adults may feel particularly invulnerable to negative life consequences, be self-interested or even hedonistic, and

so, more likely to engage in risky behaviours, being relatively more frequently exposed to addiction-related settings (e.g., raves).[28]

Family and social environment

Home life can heighten a child's risk for later alcohol or drug problems. Several factors play an important role: living with someone (a parent or significant other) who abuses alcohol or drugs, abusive or neglectful parents, childhood adversity and ineffective parenting.[10,22]

Interactions outside the family can involve other risks, for instance: peer influence, academic failure, neighbourhood characteristics, social acceptance or availability of the substances.[10,13,21,22,27,29] The high cost of a substance through taxation can reduce initiation, use, and addiction; this has a stronger influence on teenagers, thus limiting initial use.[13]

The addictive agent

The speed at which different substances enter, act upon, and leave the brain plays a major role in the reinforcing effects and abuse potential of a substance. Smoking or injecting a drug leads to a rapid increase in the onset of a substance's pleasurable effects, making the substance more rewarding and increasing its addictive potential.[1,3]

Neurobiology of substance addiction

The brain controls necessary motivational and cognitive processes, which can be disrupted by substances of addiction.[1,2,5,7,8,10,26,27,30–32] These processes comprise a network of independent and overlapping brain circuits, defining reward, motivation, learning/memory and cognition/decision-making.[1,10,30,31]

However, the science of the neural basis of addiction is still in its early stages,[8,14] and there's not yet a fully convincing theory of how addiction results from the interaction of risk factors, drugs and the brain.[8] Besides, much of the data about the mechanisms of addiction has derived from the study of animal models of addiction on specific drugs.[2,7] There are also disagreements at the theoretical level of what the existing data means to the mechanisms of addiction.[8,32] Nonetheless, a review of the actual knowledge shall be described.

The neurobiological mechanisms of addiction that are involved in various stages of the addiction cycle have a specific focus on certain brain circuits. There are neurochemical changes associated with those circuits during the transition from drug taking to drug addiction, and the way those changes persist influence the vulnerability to relapse.[1–3,7,23,26,27,30,31,33]

Reward

The reward system – a central component for driving incentive-based learning, eliciting appropriate responses to stimuli and the development of goal-directed behaviours[1,10,14,19,32,34] – is a key element of drug addition, changing with the development of addition.[1–3,10,14,25,30,32,34,35]

There is compelling evidence for the importance of the mesocorticolimbic dopamine system in the neurobiology of the positive reinforcing effects of drugs with dependence potential, including the many neural inputs and outputs that interact with the ventral tegmental area (VTA) and the basal forebrain – these brain circuits have been named by some authors as the mesolimbic reward system.[2–4,14,34,35] What is more, specific components of the basal forebrain have also been associated with drug reward: the so-called ''extended amygdala''[2,4,7,34] – comprised of the bed nucleus of the stria terminalis, the central nucleus of the amygdala, the medial amygdala and the transition zone in the shell of Nucleus Accumbens (NAcc).[2,4,34]

Besides neural circuits, neurotransmitters/neuromodulators have also been correlated with the reinforcing effects of drugs with dependence potential, and nine have been identified to have a role in the reinforcing effects of drugs: mesolimbic dopamine,[1–4,7,10,11,15,19,25,26,31–35] opioid peptide, GABA,[1,2,4,15,25,32,34] endocannabinoid,[2,30,32] serotonin,[4,26,34] glutamate,[7,32,33] substance P, norepinephrine and acetylcholine.[34]

Dopamine is known to increase activity levels,[10,19] in addition to providing feelings of pleasure and promoting general well-being and happiness.[1,10,32] Considering the dopaminergic reward system, and in an oversimplification, when there is anticipation of a reward, dopamine is released in the NAcc from the terminals of dopaminergic projections emanating from the VTA.[1,10,14,19,25,30–32]

Dopamine is also released after the use of addictive drugs.[1,4,10,11,14,15,25,31–33,35] When some drugs like cocaine are taken, they can release two to ten times the amount of dopamine – when compared to the effects on the brain's pleasure circuit produced by natural rewards, such as food and sex.[10,25] If one keeps taking drugs, the brain adjusts to the overwhelming surge in dopamine (and other neurotransmitters), causing a breakdown in the natural process of brain reward by producing less dopamine and/or by reducing the number of dopamine D_2 receptors, causing low dopamine function, high cravings[7,10,25] and a reduced ability to perceive pleasure from natural rewards.[7,10,27] It is important, though, to note that not all drugs evoke the same dopaminergic processes or effects; consequently, a broad theory of dopamine and addiction is unsatisfactory.[25,30,32]

Motivation and drive, cognitive control, memory and learning

In long-term drug users, reductions in the activity of the orbitofrontal cortex (regions related with motivation and compulsive behaviours) and of the cingulate gyrus (region related involved with inhibitory control and impulsivity) can be verified,[1,2,31,32] implicating the loss of control and compulsive drug intake that characterizes addiction.[1,31,32]

Because dopamine cells fire in response to salient stimuli and facilitate (conditioned) learning, their activation by drugs will be experienced as highly prominent, driving the motivation to take the drug, further strengthening conditioned learning and thus producing automatic behaviours,[1,15,31] regardless of natural or more adaptive objectives such as career or family.[7]

Addictive drugs specific mechanisms of action

Alcohol and opioids primarily act on mesolimbic dopaminergic pathways, whereas cocaine blocks the action of three of the major neurotransmitter system transporters: dopamine, serotonin and norepinephrine. Even acting through different mechanisms, alcohol, opioids and cocaine increase the release and synaptic availability of dopamine.[25]

The pleasurable effects of alcohol have been connected to its capacity of promoting the release of endogenous opioids.[25,32] It is believed that the binding of the endogenous opioid peptide β-endorphin (and opioid drugs) to the μ-opioid receptors of the GABAergic interneurons in the VTA (who have the function of inhibiting the VTA dopamine neurons projecting to the NAcc) depolarizes their membranes, inhibiting the release of GABA; this inhibition of GABA subsequently increases the release of dopamine in the NAcc (because the VTA dopamine neurons are disinhibited, which stimulates the release of dopamine).[1,25,32,35]

Cocaine increases the availability of dopamine in the synapse by binding to the dopamine transporter and inhibiting reuptake of dopamine from the synapses, increasing dopamine content in the synaptic cleft.[10,25,30,32,35]

In the case of marijuana, the evidence gathered from neuroimaging shows that it's chronic use is accompanied with both functional and structural faulty changes in various regions of the brain, and one study has reported an increase in the density of cannabinoid-1 receptors in the caudate and putamen of recent consumers, indicating that the drug can indeed impact the neurochemistry of the cannabinoid system. Although the relationship between marijuana and addiction is not clear,[30] cannabinoid-1 receptors activity has been positively associated with drug reinforcement.[32]

Integration of the processes: dependence, withdrawal and craving

Three neurobiological circuits have been identified that have empirical value for the study of the neurobiological changes associated with the development and persistence of drug dependence: (A) a drug-reinforcement (''reward'' and ''stress'') circuit, comprised of the extended amygdala; (B) a drug- and cue-induced reinstatement (''craving'') circuit, comprised of the prefrontal cortex and basolateral amygdala; and (C) a drug-seeking (''compulsive'') circuit, composed of the NAcc, ventral pallidum, thalamus and orbitofrontal cortex.[2] A schematic explanation of these circuits can be found in Fig. 2.

The neural substrates and neuropharmacological mechanisms for the negative motivational effects of drug withdrawal may involve disruption of the same neural systems implicated in the positive reinforcing effects of drugs. Examples of these disruptions are decreases in reward neurotransmitters, hypothesized to contribute significantly to the negative motivational state associated with acute drug abstinence and long-term biochemical changes that contribute to the clinical syndrome of protracted abstinence and vulnerability to relapse.[2,32] Different neurochemical systems involved in stress modulation may also be engaged within the neurocircuitry of the brain stress systems in an attempt to overcome the chronic presence of the drug and to restore normal function despite the presence of the substance, which will have an impact upon acute withdrawal. Therefore, during the development of dependence, it might not only occur a change in function of neurotransmitters associated with the acute reinforcing effects of drugs, but also recruitment of the brain stress system and dysregulation of the antistress system. This activation of the brain stress systems may also contribute, alongside reward neurotransmitters disruption, to the negative emotional state associated with acute abstinence.[2]

Addiction consequences

Addiction as a prototypical psycho-biological illness can pose severe implications in biological, psychological and social spheres, and the negative effects of substance use and addictive disorders are a major cause of morbidity and mortality in our society.[18]

The repeated use of drugs induces not only physical but also psychological dependence, representing a severe financial burden on the health-care system. The social costs of addiction include interactions with the legal system (because of behaviours focusing on obtaining illicit drugs), substantial loss of productivity at work, and multiple incarcerations secondary to criminal behaviours.[30]

Drug use and addiction have well-known negative consequences for physical and mental health, as well as implications for public health – since drug use, directly or indirectly, is a recognized major vector for the transmission of serious infectious diseases, particularly acquired immunodeficiency syndrome, hepatitis, and tuberculosis, besides contributing to violence.[3] Additionally, the use of illicit drugs is accompanied by severe neuropsychological impairments that appear to be secondary to functional and structural changes in various brain regions, including both cortical and subcortical regions of the human brain. There's also a well-known documented link between different substances use and adverse cerebrovascular effects.[30]

Disruption of social and occupational functioning may be related to acute substance intoxication, withdrawal states or psychotoxicity due to long-term substance exposure. In some cases, addictive illness may lead to some degree of work impairment caused by cognitive dysfunction, lessened judgement or erratic behaviour. This outcome tends to be a late-stage phenomenon after pre-existing conditions like family, marital, emotional or physical problems.[14]

Patients with substance use disorders have a significantly increased risk for suicide.[14] Up to 40% of patients seeking treatment for substance dependence report a history of suicide attempts.[36] Many suicide attempts occur while intoxicated.[14] Substance dependent individuals who search for treatment are at elevated risk for suicide attempts for various reasons, since they frequently present depressive symptoms and a number of severe life stressors, namely interpersonal relationship loss or conflict, occupational or financial problems. Major depression, bipolar disorder, borderline personality disorder and post-traumatic stress disorder are also

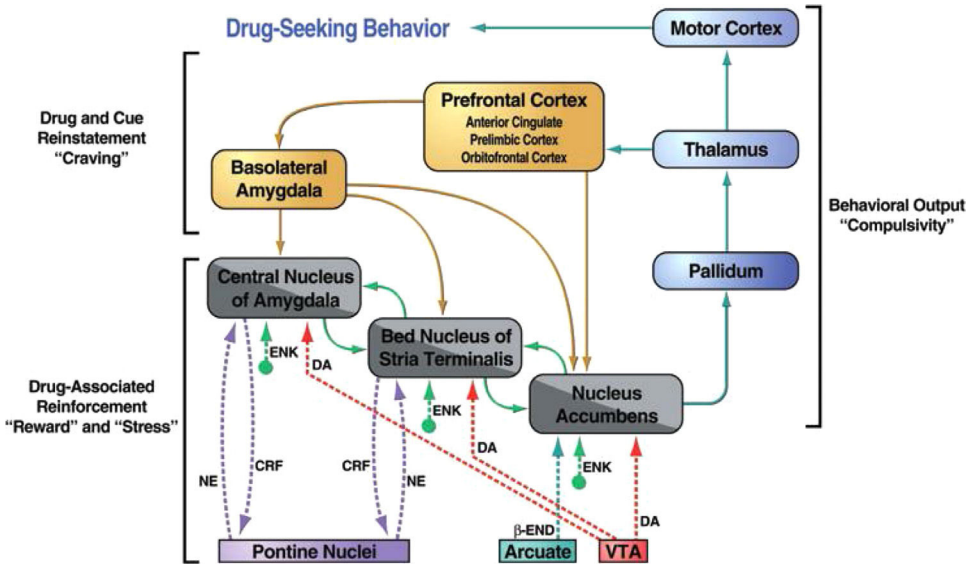

Figure 2 Key common neurocircuitry elements in drug-seeking behaviour of addiction. Three major circuits can be distilled from the literature. (a) *A drug-reinforcement* (''reward'' and ''stress'') circuit, comprised of the extended amygdala, which is hypothesized to mediate integration of rewarding stimuli or stimuli with positive incentive salience and aversive stimuli or stimuli with negative aversive salience. Multiple modulator neurotransmitters are hypothesized, including dopamine and opioid peptides for reward and corticotropin-releasing factor and norepinephrine for stress. The extended amygdala is hypothesized to mediate integration of rewarding stimuli or stimuli with positive incentive salience and aversive stimuli or stimuli with negative aversive salience. During acute intoxication, valence is weighted on processing rewarding stimuli, and during the development of dependence aversive stimuli come to dominate function. (b) *A drug- and cue-induced reinstatement* (''craving'') neurocircuit is comprised of the prefrontal cortex and basolateral amygdala with a primary role hypothesized for the basolateral amygdala in cue-induced craving and a primary role for the medial prefrontal cortex in drug-induced craving, based on animal studies. Human imaging studies have shown an important role for the orbitofrontal cortex in craving. (c) *A drug-seeking* (''compulsive'') circuit is composed of the NAcc, ventral pallidum, thalamus and orbitofrontal cortex. The NAcc has long been hypothesized to have a role in translating motivation to action and forms an interface between the reward functions of the extended amygdala and the motor functions of the ventral striatal–ventral pallidal–thalamic–cortical loops. The striatal–pallidal–thalamic loops reciprocally move from prefrontal cortex to orbitofrontal cortex to motor cortex, leading ultimately to drug-seeking behaviour. Note that for the sake of simplicity, other structures are not included, such as the hippocampus (which presumably mediates context-specific learning, including that associated with drug actions). Also note that dopamine and norepinephrine both have widespread innervation of cortical regions and may modulate function relevant to drug addiction in those structures. DA, dopamine; ENK, enkephalin; CRF, corticotropin-releasing factor; NE, norepinephrine; β-END, β-endorphin. [Reproduced with permission from Koob, 2006; © 2006 American Psychiatric Association. Journal Compilation © 2006 Society for the Study of Addiction.]

linked to suicidal behaviour in people with addictive disorders.[36]

A particularly relevant consequence linked to addiction is the frequency of disinhibitory and impulsive behaviours.[11,26] Disinhibition and impulsive states typically involve diminished consideration of negative consequences and lack of awareness of the impact of one's own actions, namely moral and legal implications (e.g. physical aggression towards other, driving while intoxicated). There is a well-documented link between substance use and crime: approximately 70% of those arrested for violent crimes test positive for substances,[11] and studies demonstrate that rates of drug-related and violent crimes are reduced after addiction treatment.[14]

Acute and extended drug use causes pervasive changes in brain function at all levels (molecular, structural and functional) involving abnormalities in brain metabolic activity, receptor availabilities, gene expression and responsiveness to environmental cues.[1–3,7,23,26,30,31] Impaired control in addiction suggests the involvement of key frontal structures in neurobiological processes relevant to addiction and impulsivity (such as the orbitofrontal cortex and anterior cingulate gyrus), as both acute and chronic substance administration may lead to frontal lobe impairment – sharing similarities with disinhibition traits seen in frontal lobe injuries. Specifically, alcohol, cocaine and opioid use may acutely depress prefrontal cortical activity.[11] This risk is particularly high for adolescents because the prefrontal cortex, which guides thoughtful decision making, does not fully develop until the mid-20's.[21] Being ''addicted'' can imply the loss of self-determination (in other words, to have control over one's life and actions or to act in accord to one's own values and beliefs).[37,38]

The faulty memory access and abnormal volition seem to be a common denominator for addiction disorders and these drug-induced pathological changes are associated with enduring behaviours that persist despite negative biopsychosocial consequences.[30]

Addiction and free will

Humans use psychoactive substances for a variety of reasons, including reducing anxiety, obtaining pleasure, relieving pain or stress, increasing energy and enhancing sociability. Consumption of psychoactive drugs begins with a choice. A choice to change feelings, perceptions, or thoughts.[39]

Drug use is initially voluntary, but the repeated exposure to addictive substances has been shown to create enduring changes in brain structure and function that are thought to underlie the transition to addiction.[12,15,28] People with substance use disorders verbalize their understanding of the potential negative consequences of beginning the addictive behaviour, recognizing that the addiction has caused harm and do not appear to suffer from lack of willpower in other life domains.[18]

Self-determination is defined as being in charge of one's own life.[37] Having agency is to have control over one's actions that is partly constitutive of autonomy, which is defined as the ability to act in accord with one's reasons, motives, and values. Having agency, also, does not necessarily depend on normally functioning neurocircuitry and, if an anomaly is found, it does not automatically deprive individuals of their capacity for autonomous decision-making and control over their action.[38] On the other hand, compulsion-like desire to consume is usually only experienced as not belonging to oneself, mainly, at the presence of withdrawal symptoms, or when the person is staying abstinent and is triggered by a particular circumstance. These experiences are also explained with neuroscientific correlates demonstrating higher excitability of parts of the brain usually involved in automatized behaviour.[8,37]

Socrates suggested that healthy individuals with healthy minds would not deliberately behave illogically or self destructively – if they did not act in their best interest, they would not be acting deliberately, and this would be abnormal.[18] The ''addict'' behaviour seems to be based only on acts of will or volition with negative consequences, which could be addressed as a moral condition and not a brain disease. Nevertheless, people with substance use disorders do have a volitional disorder based on cognitive impairment caused by impaired memory access, and there is substantial evidence for a disease model, but the disease model does not resolve the question of voluntary control. At the same time, none of the current views conceives that the person with substance use disorder should be absolved of all responsibility for self-control.[8]

Those who argue that addiction is best conceptualized as a choice, a moral condition, a lack of willpower or a personality flaw are based on the concept that drug seeking and drug taking involve a series of voluntary acts that often require planning and flexible responses to changing conditions.[8,17] They worry that medicalization will lead people with substances use disorders to excuses for their actions, rather than full engagement with treatment and rehabilitation.[8] It has been shown that, in heroin use disorder, financial concerns, values regarding parenthood, fear of arrest and many other factors which influence decisions in general, often bring drug-oriented behaviour to a halt, indicating that the desire of taking the substance is not irresistible – however, one should keep in mind that this substance use disorder is a multi-determined pattern of behaviour and it probably differs across individuals in terms of severity and causal influences.[17] Another argument supporting this point of view is that the specific behavioural consequence of all the neurobiological changes associated with chronic drug use has not yet been determined. Furthermore, no scientific model satisfactorily explains addictive behaviours nor provides any explanation that defines a common cause for the various behaviours called ''addictive''.[12,18]

Legal concerns

The link between crime and substance use is well documented: approximately 70% of those arrested for violent crimes test positive for substances; alcohol use frequently precedes or accompanies marital violence; and child abuse and neglect have been associated with substance use.[11]

There is still doubts about to what extent the person with substance use disorder should be held responsible for becoming addicted, for certain addictive behaviours, and for maintaining sobriety after initial diagnosis and treatment of addiction. The altered volition that characterizes addicted and the voluntariness of drug seeking does not necessarily mean that all free will is suspended and does not equate to involuntary behaviour.[14] Therefore, alterations in volition do not imply that all moral and/or legal responsibilities for personal choices are nullified. Generally, it is agreed that a person who is intoxicated is not insane. Hence, voluntary intoxication at the time of criminal activity will generally not relieve a person of criminal responsibility.[11]

In what respects to common civil competencies, like signing in to a hospital voluntarily or consenting to other medical procedures, to make a will, or to manage personal financial affairs, addictive disorders can cause impairment by cognition or judgement deficits or another co-occurring mental illness. It is important to clarify how the substance-related illness was diagnosed, how do specific symptoms result in compromise of competency, and which criteria for competency are compromised by those symptoms.[14]

Coercive treatment models in addiction

There's still the conceptual idea that if the evidence demonstrates that the neurobiological changes in addiction impair the ability to avoid drug use, and the individuals with substance use disorders cannot make decisions concerning their addiction-related actions, they should, therefore, be subjected to coercive treatment. The standard criteria for decision-making capacity require the person to communicate a choice, understand the relevant information, appreciate the situation and its consequences, and demonstrate reasoning regarding treatment options. As Uusitalo described in his article, people with substance use disorders are capable of acknowledging their medical condition and likely consequences of treatment options, maintain their actions intentional and are probably goal-oriented. What is problematic in addiction is the lack of capacity to appreciate and to be motivated to have a life without addiction. Nevertheless, supportive environment can have a powerful effect in facilitating these changes. The evidence illustrated in

Uusitalo paper indicates that individuals, regardless of their addiction severity, retain a capacity to overcome addiction-related compulsive urges. So, the coercive treatment of addiction cannot be ethically justified. This conceptual approach supports the idea that addiction should not be viewed as autonomy negating, and individuals should not be forced into therapy, but supported in identifying and training their own will and capacity for self-control.[38]

Discussion

The neurobiological changes identified in addiction clearly do not point in the direction of conceptualizing it solely as a moral condition, since human cognitive and motivational processes can be biologically disturbed by substances of addiction.

Long-term drug users have drug-induced changes in the activity of the cortical regions related with motivation, compulsive behaviours, inhibitory control and impulsivity, which helps explaining the loss of control and compulsive drug intake that characterizes addiction. The motivation to take drugs is driven by conditioned learning: a product of dopamine cells firing in response to salient stimuli (drugs), experienced as highly prominent, further strengthening conditioned learning and thus producing automatic behaviours. Some may say that brain disease theories of addiction seem to employ a narrow, empirical and conceptual scope in explaining human action, which might have unwelcome implications on addiction treatment, eventually reducing it to ''simple'' biological events, emptying the individual's responsibility in their own treatment and devaluing the importance of their motivation for change. On the other hand, these theories also demonstrate that the occurrence of addiction is influenced by one's history and life-environment, and that many substance use circumstances are will-dependent. For example, it is known that drug-related cues in the environment can act as potent triggers for cravings; therefore, an environment free of such cues might help people with substance use disorders to avoid cravings and overcome their addiction.

In substance use disorders, we come across complex interactions between the biological systems and the environment that people interact with, raising questions on how should psychiatry look at addiction: is it more than a medical diagnosis? Should a broader multi-faceted perspective be considered instead? It may be too simple to classify it as a medical diagnosis and nothing else.

Although several will-independent risk factors for drug addiction have been identified (e.g. genetic vulnerabilities), as well as significant drug-induced neurobiological changes, these probably do not excuse the individuals with substance use disorders of their responsibilities. Consumption of psychoactive drugs begins with a choice, as drug use is initially voluntary, and it is the repeated exposure that creates enduring changes in brain structure and function that are thought to underlie the transition to addiction. Patients with substance use disorders are able to acknowledge the potential negative consequences of following the addictive behaviour, admitting that the addiction has caused harm and do not seem to lack willpower in other life spheres. What is more, drug seeking and taking involves several voluntary acts that usually demand planning and flexible responses to shifting settings.

One might say that, in addiction, the individuals' willpower and self-determination is not entirely preserved nor totally disrupted. Patients with substance use disorders have the potential of understanding their medical condition and of choosing – especially when help is shown to be available – to change their life-goals. However, and particularly when exposed to substance-related cues, they are biologically vulnerable and have a deficit in their ability to inhibit their consumption urges.

Although impaired volition related to disinhibition and addictive behaviours has been studied from multiple perspectives, additional research is needed to further characterize the mechanisms of impairment. Such findings may have important implications in multiple legal and psychiatric domains, as many doubts remain.

Limitations

Our study has several limitations. Not all 8842 articles in the initial search were screened, but only the first 400 according to ''best match''; the search in Pubmed database was not done through the controlled vocabulary thesaurus Medical Subject Headings, which could have improved the appropriateness of the retrieved studies; and the languages were limited to Portuguese, English and Spanish (although it could also be considered a strength).

Conclusion

There is significant scientific evidence not to consider substance addiction as a simple morality flaw. However, questions arise while defining it solely as a medical diagnosis, for an intricate plot exists when science tries to analyze substance use disorders: a quest towards a broader multi-faceted perspective may be a suitable option of conceptualizing such riddle. The willpower and self-determination of individuals with substance use disorders is not entirely preserved nor totally disrupted, and their responsibilization is a complex and not clear matter, as it is critical to be aware that changes in volition do not imply that all moral and/or legal responsibilities for personal choices are nullified. When evaluating their own responsibility for their actions, it is important to clarify how was the substance use disorder diagnosed, how did specific symptoms result in compromise of competency, and which criteria for aptitude were compromised by those symptoms. Substantial – yet incomplete – scientific data exists, in what regards substance use disorder risk factors, neurobiology and its consequences; additional research shall be useful to further characterize this pathology, paving the way for more perspicuous scientific and philosophical answers.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Conflicts of interest

None to declare.

References

1. Nutt D, Nestor LJ. Addiction. Lundbeck I. Oxford: Oxford University Press; 2013. p. 90.
2. Koob GF. The neurobiology of addiction: a neuroadaptational view relevant for diagnosis. Addiction. 2006;101 Suppl. 1:23–30.
3. Leshner AI. Addition is a brain disease, and it matters. Science. 1997;278:45–7.
4. George O, Le Moal M, Koob GF. Allostasis and addiction: role of the dopamine and corticotropin-releasing factor systems. Physiol Behav. 2012;106:58–64.
5. Logan RW, Williams WP III, McClung CA. Circadian rhytms and addiction: mechanistic insights and future directions. Behav Neurosci. 2014;128:387–412.
6. Karasaki M, Fraser S, Moore D, Dietze P. The place of volition in addiction: differing approaches and their implications for policy and service provision. Drug Alcohol Rev. 2013;32:195–204.
7. Edwards S, Koob GF. Escalation of drug self-administration as a hallmark of persistent addiction liability. Behav Pharmacol. 2013;24:1–12.
8. Hyman SE. The neurobiology of addiction: implications for voluntary control of behavior. Am J Bioeth. 2007;7:8–11.
9. Peoples LL. Will, anterior cingulate cortex, and addiction. Science. 2002;296:1623–4.
10. Blum K, Cshen ALC, Giordano J, Borsten J, Chen TJH, Hauser M, et al. The addictive brain: all roads lead to dopamine. J Psychoactive Drugs. 2012;44:134–43.
11. Leeman RF, Grant JE, Potenza MN. Behavioral and neurological foundations for the moral and legal implications of intoxication, addictive behaviors and disinhibition. Behav Sci Law. 2009;27:237–59.
12. Torregrossa MM, Corlett PR, Taylor JR. Aberrant learning and memory in addiction. Neurobiol Learn Mem. 2011;96:609–23.
13. Bierut LJ. Genetic vulnerability and susceptibility to substance dependence. Neuron. 2011;69:618–27.
14. Gendel MH. Substance misuse and substance-related disorders in forensic psychiatry. Psychiatr Clin North Am. 2006;29:649–73.
15. Nutt D. Addiction: lifestyle choice or medical diagnosis? J Eval Clin Pract. 2013;19:493–6.
16. Richter L, Foster SE. Effectively addressing addiction requires changing the language of addiction. J Public Health Policy. 2014;35:60–4.
17. Henden E. Heroin addiction and voluntary choice: the case of informed consent. Bioethics. 2013;27:395–401.
18. Campbell WG. Addiction: a disease of volition caused by a cognitive impairment. Can J Psychiatry. 2003;48:669–74.
19. Littrell J. How addiction happens how change happens, and what social workers need to know to be effective facilitators of change. J Evid Based Soc Work. 2011;8:469–86.
20. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6:1–28.
21. Maguire D. Drug addiction in pregnancy: disease not moral failure. Neonatal Netw J Neonatal Nurs. 2014;33:11–8.
22. Vink JM. Genetics of addiction: future focus on gene × environment interaction? J Stud Alcohol Drugs. 2016;77:684–7.
23. Volkow ND, Koob G, Baler R. Biomarkers in substance use disorders. ACS Chem Neurosci. 2015;6:522–5.
24. Ducci F, Goldman D. The genetic basis of addictive disorders. Psychiatry Clin North Am. 2012;35:495–519.
25. Patriquin MA, Bauer IE, Soares JC, Graham DP, Nielsen DA. Addiction pharmacogenetics: a systematic review of the genetic variation of the dopaminergic system. Psychiatr Genet. 2015;25:181–93.
26. Jentsch JD, Ashenhurst JR, Cervantes MC, Groman SM, James AS, Pennington ZT. Dissecting impulsivity and its relationships to drug addictions. Ann N Y Acad Sci. 2014;1327:1–26.
27. Cox WM, Klinger E, Fadardi JS. The motivational basis of cognitive determinants of addictive behaviors. Addict Behav. 2015;44:16–22.
28. Sussman S, Arnett JJ. Emerging adulthood: developmental period facilitative of the addictions. Eval Heal Prof. 2014;37:147–55.
29. Shmulewitz D, Greene ER, Hasin D. Commonalities and differences across substance use disorders: phenomenological and epidemiological aspects. Alcohol Clin Exp Res. 2015;39:1878–900.
30. Cadet JL, Bisagno V, Milroy CM. Neuropathology of substance use disorders. Acta Neuropathol. 2014;127:91–107.
31. Volkow ND, Fowler JS, Wang G-J, Swanson JM, Telang F. Dopamine in drug abuse and addiction. Arch Neurol. 2007;64:1575–9.
32. Lingford-Hughes A, Watson B, Kalk N, Reid A. Neuropharmacology of addiction and how it informs treatment. Br Med Bull. 2010;96:93–110.
33. Grueter BA, Rothwell PE, Malenka RC. Integrating synaptic plasticity and striatal circuit function in addiction. Curr Opin Neurobiol. 2012;22:545–51.
34. Commons KG. Neuronal pathways linking substance P to drug addiction and stress. Brain Res. 2010;1314:175–82.
35. Badiani A. Substance-specific environmental influences on drug use and drug preference in animals and humans. Curr Opin Neurobiol. 2013;23:588–96.
36. Yuodelis-Flores C, Ries RK. Addiction and suicide: a review. Am J Addict. 2015;24:98–104.
37. Schlimme JE. Addiction and self-determination: a phenomenological approach. Theor Med Bioeth. 2010;31:49–62.
38. Uusitalo S, van der Eijk Y. Scientific and conceptual flaws of coercive treatment models in addiction. J Med Ethics. 2016;42:18–21.
39. Gray MT. Freedom and resistance: the phenomenal will in addiction. Nurs Philos. 2007:3–15.