Monográfico

The necessary paradigm shift in the study of addiction: Inconsistencies and fallacies of the brain disease model of addiction

El necesario cambio de paradigma en el estudio de la adicción: inconsistencias y falacias del modelo de enfermedad cerebral de la adicción

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Received: 14/02/2022 · Accepted: 11/03/2022

Cómo citar este artículo/citation: Pedrero Pérez, E. J. (2022). The necessary paradigm shift in the study of addiction: Inconsistencies and fallacies of the brain disease model of addiction. *Revista Española de Drogodependencias*, *47*(1), 118-143. https://doi.org/10.54108/10008

Abstract

The Brain Disease Model of Addiction (BDMA) has been the dominant paradigm since its official proclamation by the National Institute of Drug Addiction (NIDA) a quarter of a century ago. However, all its principles have been repeatedly falsified and none of the benefits proposed by its authors have been achieved. Its survival is based on the unconditional support of the pharmaceutical industry and on the management of funds that NIDA allocates as a priority to studies that verify its hypotheses, as well as disregard for all research that questions its principles. Following Popper, the correct procedure is not verificationism, but the falsification principle, which forces the discarding of refuted hypotheses. And, following Kuhn, when a scientific paradigm does not meet the requirements, it must be replaced by another that surpasses the discarded one. This article reviews the inconsistencies of the BDMA and the fallacies on which its hegemony, now firmly questioned, has been based.

Keywords

Paradigm, Verificationism, Falsificationism, Brain disease model of addiction, Biopsychosocial model, Medicalization, Addictive behaviors.

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Resumen

El Modelo de Enfermedad Cerebral de la Adicción (BDMA, por sus siglas en inglés) es el paradigma dominante desde su proclamación oficial por el National Institute of Drug Addiction (NIDA) hace ahora un cuarto de siglo. Sin embargo, todos sus principios han sido falsados en reiteradas ocasiones y ninguno de los beneficios propuestos por sus autores ha sido alcanzado. Su vigencia se sustenta en el apoyo incondicional de la industria farmacéutica y en el manejo de fondos que el NIDA destina prioritariamente a estudios que verifican sus hipótesis. Siguiendo a Popper, el procedimiento correcto no es el verificacionismo, sino el principio de falsación, que obliga a desechar las hipótesis refutadas. Y, siguiendo a Kuhn, cuando un paradigma científico no cumple los requerimientos debe ser sustituido por otro que supere al desechado. Este artículo repasa las inconsistencias del BDMA y las falacias en las que se ha sustentado su hegemonía, ahora firmemente cuestionada.

Palabras clave

Paradigma, Verificacionismo, Falsacionismo, Modelo de enfermedad cerebral de la adicción, Modelo biopsicosocial, Medicalización, Conductas adictivas.

INTRODUCTION

The Brain Disease Model of Addiction (BDMA) is the dominant paradigm in the conceptualization of addiction and its treatment. It is based on the assertion that drugs change irreversibly the structure and functioning of the brain, so that the problem manifests itself beyond the person's will and has a chronic and, consequently, incurable course (Volkow, & Koob, 2015). However, and despite its unquestionable hegemony, this model faces serious scientific conflicts, insofar as many of its postulates have been refuted and the contestation in the scientific field is solid, consistent and of growing magnitude. Its defenders have accumulated much evidence in favour of their proposals, following a verificationist criterion, but at the cost of ignoring, disregarding or despising all those that falsify them, something unacceptable since the formulation of the criterion of scientific demarcation proposed by Popper (falsificationism; Popper, 1935). Therefore, it is possible that we are already in an incipient change of scientific paradigm, as described by Kuhn (1962).

The question of whether addiction is a disease or not is at the heart of a long-standing controversy and is an ongoing unresolved debate. Both the WHO and the NIDA state categorically that it is, while other authors insistently question this conceptualization. This controversy is difficult to resolve due to a serious problem that hinders any scientific approach: to position oneself on one side or the other, it is necessary to know what the disease is. And we currently lack a definition of disease that can be universally accepted.

What is a disease?

In different disciplines, there is often recourse to definitional proposals that, supported by some theoretical framework, are proposed as provisional conceptual

frameworks that facilitate research. But this does not happen in the case of disease: the main medical diagnostic manuals (e.g., Harrison or Farreras) deal directly with the classification and description of diseases without first defining what it is that they classify (Peña, & Paco, 2002).

In general, any person has an intuitive understanding of what a disease is, but this cannot be assumed in a scientific framework. A glance at any medical dictionary clearly shows that articulating a satisfactory definition of disease is surprisingly difficult (Scully, 2004). According to formulations from several decades ago, disease was defined as "*the sum of the abnormal phenomena displayed by a group of living organisms in association with a specified common characteristic or set of characteristics by which they differ from the norm for their species in such a way as to place them at a biological disadvantage*" (Campbell et al., 1979; p. 757). More recent formulations omit a definition of disease, conceptualizing it as simply the absence of health; for example, Bircher (2005) suggests that "*health is a dynamic state of well-being characterized by a physical, mental and social potential, which satisfies the demands of a life commensurate with age, culture, and personal responsibility. If the potential is insufficient to satisfy these demands the state is disease*" (p. 336). As can be seen, it is easy to describe a myriad of life situations in which there is a transitory or evolutionary decline in personal capacities that can hardly be considered "disease", for example, pregnancy or aging. Moreover, this definition contradicts the WHO proposal in the preamble to its constitution (WHO, 1948), according to which health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. Thus, health and disease are each defined by the absence of the other, which inevitably leads to circular reasoning.

A definition of disease is attributed to the WHO (although it has not been possible to find the primary source; Jaén, 2016): alteration or deviation from the physiological state in one or more parts of the body, due to generally known causes, manifested by characteristic symptoms and signs, and whose evolution is more or less foreseeable. Nor is this definition admissible, since, for example, suffering gender violence, grieving or an infinite number of situations of daily life should be considered "diseases". Some authors attempt to study this question without succeeding in formulating a definition, even a tentative one, of what illness is (Amzat, & Razum, 2014; Ereshefsky, 2009; Powell, & Scarffe, 2019; Scully, 2004). Other authors, surprisingly, consider that endowing the concept of disease with a definition is irrelevant and that clinicians "should feel free" in their clinical practice (Hesslow, 1993). Finally, for other authors something is a disease when clinicians so decide by consensus and advocate a pragmatic and atheoretical use of the disease concept (Heilig et al., 2021). In this scenario, it is not strange that there are proposals that allow themselves to exploit the vague concept of disease, applying it to more and more life situations such as obesity and overweight as 'food addiction' (Volkow, & O'Brien, 2007), or even to old age, which, according to some authors, "*will result in new approaches and business models for addressing aging as a treatable condition*" (Zhavoronkov, & Bhullar, 2015).

Such indefiniteness has made it possible that the most diverse disease proposals have been appearing, especially in psychiatry, the most scientifically soft medical discipline. If in other areas of medicine consensus is mainly used to establish cut-off points in objective biological test results, in psychiatry this consensus is oriented to proclaim what is or is

not a mental disorder in the absence of biomarkers (Meana, & Mollinedo-Gajate, 2017). However, lacking specific tests that ratify psychiatric diagnoses, these are strongly exposed to interests outside the scientific field: the members of the panels that formalized the DSM-5 presented conflicts of interest with the pharmaceutical industry in percentages that approached 100% of cases and reached it in some specific panels, widely aggravating a problem already present in the creation of the DSM-IV (Cosgrove, & Krimsky, 2012). This has led to expand the catalogue of diagnostic categories and to favour more lax criteria to formalize the diagnoses, which has been denounced as favouring overdiagnosis, pathologization of daily life, increased harm in people with problems and greater social stigmatization by labeling as 'mentally ill', something especially serious when it affects children (Coon et al., 2014), and, all this, only to favour the interests of the pharmaceutical industry and physicians with few ethical scruples (Moynihan et al., 2013).

On the other hand, this indefinition has led in recent years to different proposals for the consideration of mental disorders (not diseases) (Ceusters, & Smith, 2010; Kotov et al., 2017; Menon, 2019; Messas et al., 2018; Nielsen, & Ward, 2018). The boldest bet is represented by the Research Domain Criteria Project (RDoC), created with the explicit intention of dispensing with the current classifications based on symptom lists (nineteenth-century, according to the then Director of the US National Institute of Mental Health; Insel, 2013; available on his blog http://www.nimh.nih.gov/about/director/2013/transforming-diagnosis.shtml until recently removed; can be consulted modified at http://psychrights.org/2013/130429NIMHTransformingDiagnosis.htm), to, instead of starting with a definition of the disorder from symptoms (top-down diagnosis), look for its neurobiological foundations (bottom-up diagnosis), so that RDoC starts with the understanding of the relationships between behavior and brain to subsequently link them to clinical phenomena (Insel et al., 2010). This approach, based on the assumption that mental disorders are ultimately brain disorders, aims to evidence the neurological processes underlying manifestations of psychological distress, so that biomarkers for mental disorders can be made available. However, and even though it has been ongoing for more than a decade now, and has sparked intense research activity, at the present time the achievements are very limited (Ross, & Margolis, 2019; Vilar et al., 2019).

The brain disease model of addiction (BDMA) has required the transgression of all nosological principles of medicine and, even so, its success outside the scientific field is undeniable. For if addiction is a disease, what kind of disease is it? In past decades addiction was considered a mental illness, but if the mind is simply a concept, can concepts become sick? Advances in the understanding of brain function prompted a change to the term brain disease, but did this solve the problem?:

> "*Addiction does not meet the criteria specified for a core disease entity, namely the presence of a primary measurable deviation from physiologic or anatomical norm. Addiction is selfacquired and is not transmissible, contagious, autoimmune, hereditary, degenerative or traumatic. Treatment consists of little more than stopping a given behaviour. True diseases worsen if left untreated. (...) At best, addiction is a maladaptive response to an underlying condition, such as depression or a nonspecific inability to cope with the world. (…) The study on the neurobiology of (…) looked at*

the brains of people with addiction after they had damaged them by their behaviour -brains were not examined in their premorbid state. This is analogous to saying that the sequelae of a traumatic brain injury were themselves the cause of said brain injury (...) Medicalizing addiction has not led to any management advances at the individual level. The need for helping or treating people with addictions is not in doubt, but a social problem requires social interventions". (Holden, 2012).

Addiction "is" a disease?

The concept of addiction as a mental illness did not emerge from the natural accumulation of scientific discoveries, but, initially, as an intuitive explanation for behaviors (apparently) lacking rationality; its ubiquity is a different kind of social construction under historically and culturally specific conditions, promulgated by particular actors and institutions, and internalized and reproduced through certain discursive practices (Reinarman, 2005a). Similarly, and in a certain historical and cultural context of the nineteenth century, African slaves who ran away from their masters were considered mentally ill, as they suffered from a disease called drapetomania that was cured by whipping (Willoughby, 2018). More recently, homosexuality was "rescued" from sin and made a "treatable" disease (Pattison, 1974).

However, the concept reaches an unusual boom in the 1960s and 1970s, in the context of the "War on Drugs", unleashed in the United States, representing, rather than a scientific approach, an ideology of a political nature (Vrecko, 2010). As a result of this political appropriation of the problem, there were significant biases in research and its sources of funding, as well as the imposition of certain language standards and the rejection and prohibition of approaches focused on harm reduction, which were based on the assumption that people use drugs, something politically inadmissible (Reinarman, 2005b).

But it was in 1997 that the then director of NIDA, Allan Leshner, published an article that, in fact, came to be the proclamation of the "dogma" of addiction as a brain disease (Leshner, 1997). His main thesis was that "drug addiction is a chronic, relapsing disease resulting from the prolonged effects of drugs on the brain" (p. 45) and the advantages attributed to this new approach (as focused on brain structure and function) were mainly the following:

1. It would make it possible to reduce the stigma associated with addiction, insofar as the disease, and not the addict's will, was the cause of persistent use.
2. The fundamental evidence that it is a disease is the changes observed in brain functioning, caused by the addictive chemicals, as a consequence of prolonged consumption.
3. Addiction is essentially similar to other chronic diseases, such as diabetes.
4. Consideration as a brain disease would allow the development of useful drugs to treat addiction.

Nearly a quarter of a century later, none of these supposed benefits have been achieved.

Does the disease model reduce the stigma of addicts?

Regarding stigma, as some authors claim, it is surprising that labeling something as a disease (especially if such a disease affects the brain) can reduce stigma, noting that, in fact,

it has markedly exacerbated it (Barry et al., 2014; Fraser et al., 2017). It has increased social rejection, perception of danger and pessimism towards treatments, tending to make the problems chronic, without reducing the feeling of guilt of those affected (Loughman, & Haslam, 2018). As other authors state, "*in the public mind, there may be a very thin line between a diseased brain, a deranged brain, and a dangerous brain. The public may have greater sympathy for a person with a diseased brain, but may be no more inclined to have that person as a friend, neighbor, or employee*" (Erickson, & White, 2009; p. 343).

The problem is aggravated when, as has happened in Spain, approaches such as 'dual pathology' are encouraged, so that addicts are not only sick because they abuse drugs, but also present one or more other "mental illnesses" (Szerman et al., 2013). Promoted by professionals with strong links to the pharmaceutical industry, and with their enthusiastic support, they focus their proposal on making equivalent the terms diagnosis and disease, which is inadmissible in the whole field of medicine, but most especially in psychiatry, unable to provide objective evidence to support diagnoses (Double, 2002) and using the concept of 'comorbidity', inappropriate in psychiatry (Lilienfeld et al., 1994; Maj, 2005a,b). We have not found studies that explore the benefits (and harms) derived from the expansion of this model of 'dual pathology', dominant in Spain in the last two decades. And yet, the monopolization of training and exchange events, through the generous support of the pharmaceutical industry, has led many professionals to uncritically assume that this is the correct and unquestionable paradigm. Some studies denounce that this approach further stigmatizes patients and prevents them from being received normally in mental health services, to the extent that professionals "expect" certain behaviors that are difficult to manage and refuse to work with this type of patient (Guest, & Holland, 2011).

In any case, the false dichotomy between "vice" as a moral deficit or brain disease, which advocates of BDMA (and 'dual pathology') wield as an alibi, is largely overcome, with new ways having been proposed to understand and transmit to the population scientifically valid explanations capable of reducing stigma (Heather, 2017; Sussman, 2021).

Are observable changes in brain structure and function caused by drugs proof that it is a disease?

The main argument put forward by BDMA advocates that addiction is a brain disease is the functional and structural changes that occur in the brains of people with addictive behaviors. These would be, according to them, irreversible neuroadaptations of various brain structures caused by drugs (Koob, & Volkow, 2016). NIDA funding has been devoted over the past two decades to accumulating evidence of differences between people with addictive behaviors and people who do not exhibit substance addiction. However, none of the countless studies that have sought to verify such postulates have been able to find evidence that such changes are caused by drugs; they have simply found associations between addiction and certain brain configurations, as befits cross-sectional studies. We do not have longitudinal studies that can report causal relationships.

Moreover, the observed differences are not exclusive to addiction: many of them are also observed in people who are victims of poverty (Lipina, & Posner, 2012), as acknowledged by BDMA advocates themselves

(Tomasi, & Volkow, 2021). Since there is a clear association between poverty and associated stress, on the one hand, and drug use and addiction, on the other (Kim et al., 2013; Silverman et al., 2019), it cannot be asserted that the changes associated with addiction are not, in fact, prior to drug use and due to the conditions associated with economic and stimular poverty. Chronic poverty is associated with early onset of consumption, higher probability of establishment of addictive behaviors and lower possibility of recovery (Matto, & Cleaveland, 2016).

Moreover, the brain changes attributed to addiction are practically the same as those observed in real-life situations that can hardly be considered as diseases: for example, social attachment and romantic love (Burkett, & Young, 2012) Even more: the pathways involved in the craving associated with addiction are essentially the same as those involved in romantic rejection (Fisher et al., 2010). Some authors go so far as to consider that romantic love should be considered as a natural addiction (Fisher et al., 2016), although perhaps, it would be more parsimonious if instead of "pathologizing love" one tended to "naturalize addiction". In any case, other studies show that the changes attributed to addiction are largely the same as those observed in all reward-oriented behaviors (Blum et al., 2012), although including some toxic effects specific to each substance (Fernandez-Serrano et al., 2011).

The BDMA requires that the observed changes, which are attributed to direct effects of the drugs on the nervous system, be irreversible, to justify the chronicity and frequency of relapses. However, this is not true either: drastic changes in the direction to normality are observed from very early phases of abstinence, which should not be attributed solely to the withdrawal of the toxic effects of drugs, but perhaps mainly to the recovery of healthy eating habits, improved rest, reduction of stress, etc.; these changes being both structural and functional (Bartsch et al., 2007; Forster et al., 2016; Pfefferbaum et al., 2006; Chanraud et al., 2007). Almost all of the structural alterations observed in people with addictive behaviors remit very rapidly when consumption is interrupted and healthy habits are recovered (Agartz et al., 2003; Ende et al., 2005; Wallace et al., 2020; Wang et al., 2013). Although functional recovery occurs after longer or shorter periods of abstinence (Meyerhoff, & Durazzo, 2020), subjects recover cognitive functioning similar to controls after some time of abstinence, irrespective of the drug, or the severity of the previous pattern of abuse, or age (Darke et al., 2012; Fein et al., 2006; Fein, & McGillivray, 2007; Schmidt et al., 2017; Schreiner, & Dunn, 2012; Selby, & Azrin, 1998; Tang et al., 2019).

Some structural features seem to persist after long periods of abstinence: a smaller volume than controls of the orbitofrontal cortex is observed in subjects abstinent (between 2.4 and 4.7 years) to various drugs (cocaine, amphetamines and alcohol). The authors consider that this reflects a long-lasting neuroadaptation that is a consequence of addiction and maintains deficits in decision-making (Tanabe et al., 2009). However, there is nothing to indicate that such a reduced volume is not related to the establishment of the addictive process, and it should then be considered that these would be preconditions that explain a vulnerability that favoured its establishment and not consequences of the addictive behavior itself.

But there is definite proof that the premise according to which addiction is explained

by the direct effect of substances on the nervous system is false: the so-called behavioral addictions share a common pattern of 'disturbances' with substance addictions (Chen et al., 2020; Horvath et al., 2020; Qin et al., 2020; Seok, & Sohn, 2015; Schmitgen et al., 2020; Turel et al., 2014; Yao et al., 2017). What 'substance' explains such similarities?

The whole BDMA set-up has dopamine as its center of gravity. Three decades ago, addiction was explained as the effect of drugs on the dopaminergic reward system (Barnes, 1988). As a result, dopamine came to be conceptualized as the pleasure drug (something that is still heard frequently). Despite the fact that many studies have shown that there is no such relationship, several authors continued to state that "all psychoactive substances with a high potential for abuse are characterized by altering the function of the mesocorticolimbic dopaminergic neurotransmitter system" (Corominas et al., 2007), possibly because this dopaminergic hypothesis of addiction allowed or justified the use of a good number of drugs. However, other authors considered this hypothesis inadequate, since, as has been shown in a good number of investigations, dopamine in the nucleus accumbens is involved in motivational, appetitive and aversive processes, including behavioral activation, effort, approach behavior, sustained task engagement, Pavlovian processes and instrumental learning (Salamone, & Correa, 2012). In fact, the function of dopamine is to warn the organism that a reinforcer is approaching, or a known reward is available. What certain authors consider "altered function of the mesocorticolimbic dopaminergic dopaminergic neurotransmitter system" is simply the effect of learning (Lewis, 2018). Giving up the dopaminergic icon as evidence for pathological effects of drugs has proved very difficult for BDMA proponents. However, one experiment was to definitively put an end to the biologistic misleading.

In 2015 a group of researchers presented a paper (Gu et al., 2015) exploring the importance of smoking expectancies and their impact on dopaminergic function. Essentially, the idea was to form two randomized groups; both groups were provided with a nicotine-containing cigarette. Participants in the first group were informed of this, while the second group were led to believe that the cigarette did not contain nicotine, although it did in fact contain nicotine. If the dopaminergic hypothesis was correct, both groups should show usual dopaminergic activity after nicotine administration. However, the second group, who believed they were not smoking nicotine, did not show the dopaminergic activity that would correspond to the effects of nicotine, which was effectively being administered. Thus, it was clear that the dopaminergic activity is a consequence of the subject's expectations and not of the pharmacological action of the drug. Again, something that was intended to be biological was clearly psychological. Subsequent studies replicated the experiment with identical results (Gu et al., 2016). Nora Volkow herself was forced to respond, unconvincingly, that the Gu et al. study "*illuminates the mechanisms whereby belief can influence nonconscious learned association by modulating how the brain performs risk decisions while under the effects of nicotine*" (Volkow, & Baler, 2015).

In the words of Marc Lewis (2016): "*Medical researchers are correct that the brain changes with addiction. But the way it changes has to do with learning and development -not disease* (...) *Addiction is a habit, which, like many other habits, gets entrenched through a decrease in selfcontrol* (...) *But the severe con-*

sequences of addiction don't make it a disease, any more than the consequences of violence make violence a disease" (p. ix-x).

Is addiction similar to other chronic diseases, such as diabetes?

This was Leshner's (1997) assertion. We may ask: is anyone known to have stopped being diabetic of their own free will? The BDMA is forced to tiptoe past the more than ascertained fact that the vast majority of people who, at one point in time, meet criteria for being diagnosed with some addiction, at another point in time simply stop meeting them, without requiring lengthy treatments, drugs or psychotherapy to do so (Heyman, 2013; Klingemann et al., 2010; Lopez-Quintero et al., 2011). By itself, these data should already be enough to abandon a theoretical model that does not respond to reality: instead of a chronic and relapsing disease, it is a process whose most likely evolution is its disappearance, the abandonment of drug use with which the supposed disease was related (MacKillop, 2020).

Proponents of BDMA have insisted on considering that this 'brain disease' is genetically determined, that it can only be controlled (not cured) with medical intervention, that the course of control of consumption is necessarily long and punctuated by constant relapses, and that its impact is destructive in all areas of the addict's life. None of this has any scientific basis. As for the alleged genetic predisposition, despite great efforts to identify it, only a few hundred genes that appear more frequently (but not only) in people who have developed addictive behaviors have been proposed to date, using GWAS techniques, or genome-wide association study (Hancock et al., 2018; Prom-Wormley et al., 2017). Although all studies agree that this is a "promising line of research," the reality is that, today, it is impossible to distinguish between an addicted and a non-addicted person by looking at their genome. It can be argued that at the present time, there is no genomic pattern that can be robustly associated with addictive behaviors and the few findings are not specific to addiction to different substances, but represent common patterns, and are, in many cases, the same as for psychopathological disorders that favor substance use, such as depression (Agrawal et al., 2016; Ducci, & Goldman, 2012; Kreek et al., 2005) and are more responsive to epigenetic factors, that is, they manifest in the presence of environmental triggers (Maldonado et al., 2021). As BDMA advocates themselves acknowledge, all that has been found is a relationship between genetic predisposition to develop certain behavioral manifestations (decision-making, response inhibition, impulsivity, emotional control, sensitivity to stress, etc.) that, under certain circumstances (which necessarily include the environmental availability of drugs), may favour the development of addiction (Volkow et al., 2015). In any case, "*if such a gene were finally identified, it seems unlikely that it would by itself provide a causal explanation of addictive behaviours. Come the genomic utopia, we will still be faced with the complex, troubled human beings whose lives and behaviours have been forged in the same old messy melange of interacting variables –biological, yes, but also sociological, cultural, and psychological– such that at some point in their lives they drink or take drugs too much*" (Reinarman, 2005c). All of which has not represented any obstacle for the defenders of 'dual pathology' to have organized press campaigns, proclaiming truisms such as "nobody chooses to be an addict" and that "he is not an addict who wants to be, but he who can", since one only becomes one when one possesses the genes that favour addiction. Which ones?

Have new drugs useful in addiction been created?

Perhaps we find here the most resounding and bleeding failure of the brain disease model of addiction: a quarter of a century after Leshner's "prophecy" (1987), no new drug has accredited scientific evidence of usefulness in the treatment of substance addiction (nor in behavioral addictions). The pharmacopoeia with evidence of usefulness in this field is limited to what was already available three decades ago: naltrexone, methadone, buprenorphine, disulfiram... and little else. However, their usefulness is only confirmed when they are administered together with psychological therapies. In other words, they are mere adjuvants to psychotherapy and other social interventions.

There has been no shortage of attempts to promote drugs with surprising properties, seeking market niches. For example, varenicline for smoking cessation; some studies find some utility, albeit with minimal effect sizes (Lindson et al., 2019), but this effectiveness only occurs when combined with psychological treatments (Chang et al., 2015). Despite poor scientific evidence, varenicline is funded by the National Health System in Spain as of 2019 (https://www.mscbs.gob.es/gabinete/notasPrensa.do?id=4764). A more surprising case is that of the launch of nalmefene, which was promoted in Europe from 2011, with the unconditional support of 'scientific authorities', as "the first drug to reduce alcohol consumption in patients with dependence"; a drug that was known more than three decades earlier, as an opioid antagonist (Dixon et al., 1987), not marketed because of its side effects, high cost and efficacy not superior to others available. It was soon concluded that its use did not make the slightest progress in alcohol dependence (Inchauspe, 2014; Rösner et al., 2010); in 2014, the British Medical Journal published an article in which, under the title "bad science", all the irregularities committed by the laboratory in its 'accreditation of the drug's properties', which did not exceed what was already known about naltrexone, but quadrupled its price (Spence, 2014), were unveiled. The drug continues to be prescribed and there is no record of rectifications or apologies from its promoters.

What this brain disease approach has allowed is the indiscriminate use of psychotropic drugs in the treatment of people with addictive behaviors. Based on the concept of dual diagnosis (in Spain and its cultural orbit, the fallacious concept of 'dual pathology') and the supposed comorbidity of addiction with an infinite number of mental disorders, the prescription of pharmacological cocktails has been promoted as a symptomatic treatment: one symptom, one drug (at least). These cocktails usually mix antidepressants, antipsychotics, anticonvulsants, anxiolytics, etc. This is more frequent in cocaine addiction, despite the fact that, as we have known for some time, the only effective treatment is psychological (Pérez de los Cobos, 2008), no other useful drug has been found and neither antidepressants (Pani et al., 2011), nor neuroleptics (Indave et al., 2016), nor anticonvulsants (Minozzi et al., 2015) have reached scientific evidence of usefulness. What is well accredited is the spectrum of side effects, many of them serious, of all these drugs separately, much more if combined, and which in some cases is frightening: the risk of dying prematurely from all causes is increased by 33% in people taking antidepressants (Maslej et al., 2017), blocking of mechanisms necessary for learning alternative behaviors to addiction (Salinsky et al., 2010), and early onset of cognitive impairment and dementia

with prolonged use of antipsychotics (Husa et al, 2017) and antidepressants (Lee et al., 2016; Moraros et al., 2017; Wang et al., 2018). *Primum non nocere*?

An additional problem is the use of medications under off-label conditions, i.e., outside the authorized indication. This practice is common in the psychiatric clinic (Baldwin, & Kosky, 2007; Devulapalli, & Nasrallah, 2009; Kharadi et al., 2015; Vijay et al., 2018) and, in particular, in the field of addiction (Barral et al., 2014), to the point that some authors already consider it the norm rather than the exception (Khanra, & Das, 2018). One study reveals that 88.5% of all DSM-IV-TR classified disorders lack an approved medication for treatment and that atypical antipsychotics have the most extensive off-label use (Devulapalli, & Nasrallah, 2009). This use outside the approved indication is supported by the freedom of prescription enjoyed by physicians, recognized and delimited by collegiate organizations, such as the Spanish Collegiate Medical Organization (1999), whose statement reads:

> "*The physician cannot act according to outdated concepts of clinical freedom based on intuition, anecdotal data or mere empiricism. He must do so in accordance with a current notion of freedom of prescription, a freedom that today consists of the physician's ability to choose, from among the available interventions, the one that best suits his patient, after having weighed its validity and usefulness; after having decided, on the basis of criteria of safety and efficacy, the most suitable and appropriate for the specific clinical circumstances of his patient and after having obtained the necessary consent from the latter. Fortunately, the instruments on which physicians can base their decisions are becoming increasingly abundant, accessible and precise. These are the various forms (large controlled clinical trials, clinical guidelines and protocols, meta-analytical studies, consensus statements) in which what has come to be called "evidence-based medicine" is expressed. Such instruments are not dogmatic, obligatory and permanent formulas, but flexible and temporary, but seriously evaluated clinical guidelines on the recommended ways of acting in certain clinical situations*".

Despite these recommendations, the prescription of psychotropic drugs without an authorized indication is common, even in the absence of a diagnosis with which to know if such an indication exists (Taylor, 2016). The most frequent sources of information for many physicians are the medical representatives of pharmaceutical laboratories, scientific meetings, generally sponsored by the pharmaceutical industry (Moncrieff et al., 2005) and the opinions of colleagues in the same situation; under these conditions, it is common to know possible indications, authorized or not, of the drugs, but serious side effects are unknown (Hickie, 2014; Taylor, 2016). To give an example, it is increasingly common to prescribe antipsychotics to treat insomnia; the aim is to take advantage of the sedative effects of these drugs (Kamphuis et al., 2015). However, several studies find that their efficacy is very low, that the sleep they provide is not physiological, that sedation persists for several hours after awakening, and that they present a toxicity profile that often leads to serious metabolic (e.g., type II diabetes mellitus), cardiovascular complications and increased risk of death (Citrome et al., 2013; Morin, 2014). In the absence of quality scientific information, it is not possible to perform a correct benefit/risk balance and patients are exposed to very serious risks, when less dangerous alternatives are available.

On the other hand, off-label prescription is subject in most countries to legal limits, most commonly including the absence of an equally safe and effective licensed alternative, the existence of sufficient scientific evidence to support the use of the drug for the intended indication and having the patient's fully informed consent to be treated outside the indication (in Spain there is Royal Decree 1015/2009, in BOE n. ◦ 174 of July 20, 2009, regulating the availability of medicines in special situations); however, these rules are usually breached: the patient is not informed, consent is not sought, scientific evidence regarding side effects is underestimated, and side effects are not reported, as required by law (Lücke et al., 2018). Consequently, this is a regulated but uncontrolled practice, encouraged by the pharmaceutical industry, in which legal limits are breached, scientific evidence is omitted, and risks are increased for many patients.

In short, the hegemony of the brain disease model of addiction has failed to encourage pharmaceutical research for the treatment of addiction, has failed to discover new useful drugs or potential targets for them; instead, it has favoured an indiscriminate use of psychotropic drugs of dubious usefulness, combined in pharmacological cocktails in which side effects overlap and accumulate, all this outside of legal regulation, scientific evidence, and at the mercy of outside interests.

DISCUSSION

On more than one occasion we have heard high-ranking NIDA officials, in perfect Spanish and off the record, say phrases such as: "it doesn't matter whether it is a disease or not, the problem is that, if it were not, nobody would treat addicts in the United States". In the purest sophist tradition, the truth is not important, as long as the argument is convincing. This sentence sums up the submission of science to political interests, although it can be interpreted as an attempt to benefit people suffering from this problem. However, as Reinarman (2005a; pp. 316-317) pointed out, "*if this disease discourse was only a rhetorical strategy for gaining the right to various services for people who need them, as most proponents of addiction-as-disease claim, then all this might not matter much. But addiction-as-disease has been put to other, arguably less noble uses*" Indeed, two direct consequences of the application of this dogmatic model have been (a) the preeminence of the medical profession and its occupation of the vast majority of decision-making positions and (b) the enthusiasm of the pharmaceutical industry, indiscriminately promoting drugs of very dubious usefulness or proven ineffectiveness, which form part of drug cocktails in which there is a summation of side effects. Because, to paraphrase the NIDA managers, we could ask ourselves: if addiction is not a disease, what role should be reserved for physicians in dealing with it? The answer is obvious: an indispensable role, like that of any other health professional, but not necessarily in running treatment centers, managing programs and holding related political positions. The issue is perfectly stated in the words of Jeffrey Schaler (2000): Smoking cigarettes and drinking alcohol are behaviors that can lead to the diseases we call cancer of the lungs and cirrhosis of the liver. Smoking and drinking are behaviors. Cancer and cirrhosis are diseases. The idea that 'addiction is a treatable disease' is a lie. Addiction is a behavior; drugs can be good or bad: it all depends on how you use them. Anyone can stop or moderate addictive drug use any time they want (in Thorburn, 2005; p. 60).

The biggest problem facing the BDMA and its advocates is the fact that none of its benefits, prophesied by Leshner (1997), have been realized a quarter of a century later. Perhaps the most glaring failure is that of the expected discovery of new drugs useful in the addiction clinic, something difficult to explain considering the complicity of the pharmaceutical industry with the model. Pharmaceutical companies have been reluctant to invest in the development of drugs to treat addiction because they doubt that they are cost-effective, taking into account the limited economic capacity of people with addiction to pay for treatment, as well as the limitations imposed by health insurance [in the United States] for addiction treatments (Hall et al., 2015; Koob et al., 2009).

In the clinic, it has also not been a significant advance. With very few studies to support its effectiveness, what can be stated is that treatments have become more expensive and addicts' accountability has been diminished (Hall et al., 2015), leading to the paradox of asking people to change their behavior from a diseased and incurable brain. In fact, some study finds that the two best predictors of relapse in people in treatment for addiction are: difficulties coping with stress and believing the brain disease model of addiction (Miller et al., 1996). People in treatment who internalize the BDMA tend to reduce their perceived self-efficacy, unlike those who assume a biopsychosocial model (Wiens, & Walker, 2015).

Another serious problem facing the BDMA is the fact that, despite its pervasiveness and pre-eminence, and the strenuous efforts of advocates, the NIDA dogma is far from being admitted in the general population (Meurk et al., 2014; Pedrero-Perez et al., 2007), in people with addictive behaviors (Wiens, & Walker, 2015), in professionals who design and participate in treatment (Barnett et al., 2017; Barnett et al., 2020; Pedrero Pérez et al., 2007), or in researchers of addiction processes (Heather et al., 2018). Even legal systems have not given credence to this view of the addict as a person acting under the influence of a disease that blurs his or her ethics and responsibility (Morse, 2017). Moreover, the growth of the BDMA has coincided with significant increases in drug use and a reduction in treatment effectiveness and self-recovery rates (Peele, 2016). So why does the model continue to dominate addiction research and the clinical field? In the words of Vrecko (2010), "*as the US government continues both to fund the majority of research into addiction and to prioritize neurobiological styles of thinking about drugs and drug users, the facts of addiction as a disease of the brain will continue to be reproduced, and to challenge other styles of thought and explanations – particularly those that avoid reducing the social to the biological*".

The brain disease model of addiction is today seen as "*useful as a rhetorical tool in debate about public policy; but scientifically, it is both incomplete and premature*" (Bonnie, 2020). At the very least, "*addiction has become an all-purpose meta-metaphor for the often troubling relationships we have with what we love, enjoy, desire, or require, and thus find hard to control*" (Reinarman, 2014). Many years ago, Peele (1980) said the same thing: "*addiction is not caused by a drug or its chemical properties. Addiction has to do with the effect that a drug produces for a given person in a given set of circumstances-a welcome effect that relieves anxiety and (paradoxically) diminishes capacity, so that those things in life that cause anxiety are aggravated. What we are addicted to is the experience that the drug creates for us*".

It is possible that in the future new data will be found that would allow reformulating the BDMA, saving all the findings that have falsified it in recent history, but science does not feed on prophecies, beliefs or promises, but on evidence, and, today, the great evidence is that addiction is a behavior, complex, but subject to all the laws of associative and operant conditioning, even when criteria close to medical concepts are considered (Gifford, & Humphreys, 2007). Other disciplines have also developed models of understanding addictive behaviors as guides to clinical intervention, in which the disease concept is irrelevant (e.g., Helbig, & McKay, 2003). The key is to recognize that people use drugs because they derive great benefits from doing so (e.g., reduced discomfort, increased physical capabilities, coping with stress, role-taking, etc.) and that it is that short-term expected value that leads to choosing repeated use (Pickard, 2020). In other words, people do not take drugs because their brain malfunctions, but because it provides them with benefits that they do not know how to obtain otherwise, and only when the harms outweigh the benefits does the person decide to change behavior, as explained by the theory of behavioral economics (Vuchinich, & Heather, 2003).

The Brain Disease Model of Addiction has had its high point in the post-truth era, when objective data have become less important to the public than the opinions and emotions it arouses. However, science continues to progress and it is time for a paradigm shift to better explain why people continue to take drugs despite the fact that not all of the consequences benefit them. This paradigm shift must confront powerful forces trying to maintain the current status quo, but the force of facts must eventually triumph over largely falsified models. This demand is proclaimed by drug users themselves who, in the Vancouver Declaration in 2006, declared: " *We are people from around the world who use drugs. We are people who have been marginalized and discriminated against; we have been killed, harmed unnecessarily, put in jail, depicted as evil, and stereotyped as dangerous and disposable. Now it is time to raise our voices as citizens, establish our rights and reclaim the right to be our own spokespersons striving for self-representation and self-empowerment*" (INPUD, 2006). Also in the United Nations (2017), there has been a call for a new perspective on mental health problems that circumvents psychiatrization, medicalization and subordination to commercial interests, with respect for people taking precedence (UN, 2017). In this line, other North American state agencies different from NIDA have proposed the lines that treatments should follow, and which are at the opposite pole of those promoted by the BDMA, including the ability of the person with addictive behaviors to participate in the formulation and development of the individualized treatment plan, which should focus on the person and not on his or her "pathology", which should empower rather than annihilate his or her decision-making capacity with psychiatric diagnoses, which should see his or her rights preserved and receive the respect of professionals, and which should favour a climate of hope rather than predictions of chronicity and incurability (SAMHSA, 2006). This is the line along which the paradigm shift should take place in the shortest possible time.

Conflict of interest

The author declares that he has no conflict of interest.

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