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Reevaluating the brain-disease model of addiction

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Abstract

The brain-disease model of addiction (BDMA) has dominated public and scientific discourse on addiction (called substance use disorder/SUD in the DSM-5) over the last three decades. The model framed addiction as a chronic and relapsing brain disease, caused by structural and functional brain alterations. Its function was purportedly dual: an etiological theory and a tool to reduce stigma. Weak empirical support and concerns about the model downplaying fundamental psychosocial causes of SUDs have led to stark disagreement as to whether addiction should be conceptualized as a brain disease at all. In this Personal View, we argue that the lack of an agreed upon, clear, and consistent definition of a brain disease, coupled with frequent recourse to concepts with divergent or shifting meaning have obstructed productive debate and a coherent advance in knowledge and understanding of addiction. Borrowing from the philosophy of psychiatry, we show that a "narrow" and a "broad" definition of brain disease coexist and inform addiction research, though often implicitly and inconsistently. The "narrow" view posits that a mental condition qualifies as a brain disease only if it manifests similarly to a paradigmatic brain disease, resulting from (un)known structural and functional damage. The "broad" view suggests that brain-disease status should be granted automatically to mental disorders because all mental activity resides in

the brain. We examine theoretical assumptions, empirical evidence, and treatment implications for each view and propose ways of moving beyond them.

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Introduction

In 1997, Alan Leshner, then director of the US National Institute on Drug Abuse (NIDA), asserted that "Addiction is a brain disease, and it matters"(1). This paper became one of the most influential in the field's history, cited over 2,500 times. Since then, the brain-disease model of addiction (BDMA) has dominated both public and scientific discourse on addiction (presently called substance use disorder (SUD) in the Diagnostic and Statistical Manual -5 (DSM-5))(2,3) . Endorsement of the model shaped research priorities worldwide, considering that the NIDA funds over 85% of global addiction research(4). The BDMA framed addiction as a chronic and relapsing brain disease, caused by structural and functional brain alterations. This view was further elaborated, and cemented, through neuroscientific and genetic advances. An increasingly complex BDMA was purported to lead not only to new treatment avenues for SUDs(5), but also to the reduction of the stigma associated with SUDs, previously viewed as resulting from moral failure, not brain pathology. The implied utility of the BDMA outweighed its yet to be elucidated construct validity, for which little empirical support had been sought.

Over the past decade, growing criticisms of the BDMA have led to stark disagreement as to whether addiction should be conceptualized as a brain disease(4,6). Criticism of the BDMA has revolved around two core arguments. First, the dual function of the BDMA as both an etiological theory and as a tool to reduce stigma has obscured two distinct empirical questions: whether addiction *is* a brain disease and whether *labelling* addiction as a brain disease reduces stigma, an important distinction rarely acknowledged(7). These questions are independent, in that addiction may be a brain disease but labelling it as such may not help reduce stigma, or vice versa. The empirical evidence for *addiction as brain disease* is weak. Despite a myriad of studies finding neurobiological differences between people with SUD compared to healthy controls, no diagnostic or prognostic biomarkers have been identified(8), and the BDMA has yet to lead to better or more precisely targeted treatments(9). Similarly, the use of the BDMA construct has had a limited impact on reducing stigma associated with SUD(10). Moreover, there is evidence it may have favored new sources of stigma, related to reduced perceived agency and pessimism about

recovery(10,11).This is not surprising, given that disease labels can themselves be highly stigmatizing, as seen in conditions like HIV/AIDS(12). Second, by centering on individual vulnerability, the BDMA may have obscured important social factors, referred to as "the causes of the causes" in the literature on the development and maintenance of addiction(13). These social and environmental factors include poverty, unemployment, job insecurity, housing instability, discrimination, low educational attainment, and poor access to health care, among others(14). This relates to general debates in mental health sciences on complex, multifactorial etiologies and relative contributions and causal status of biological, psychological, and social factors(15).

In this Personal View, we propose another critical angle on the role of BDMA in addiction research. Specifically, we argue that the lack of a clear and consistent definition of what would constitute a brain disease in psychiatry(16–19) and the frequent use of concepts with divergent or shifting meaning has obstructed productive debate. While the causes and consequences of this conceptual ambiguity are increasingly recognized in the philosophy of psychiatry(16), they have not yet permeated empirical addiction research.

The "narrow" and "broad" view of addiction as a brain disease

There are multiple, diverging views on what constitutes a brain disease. One approach to distinguishing views often used implicitly and interchangeably in psychiatric research is to separate a "narrow" from a "broad" view (16). The narrow view posits that a mental condition qualifies as a brain disease only if it manifests similarly to a paradigmatic brain disease, such as neurosyphilis or Alzheimer's Disease. According to the *likeness argument*(20), for a mental disorder to classify as a brain disease there must be a unified account of causes and symptoms of brain dysfunction, preceding and independent of mental dysfunction. In contrast, according to the broad view, brain-disease status is granted automatically to mental disorders, because all mental activity is mediated by the brain. It therefore follows that all abnormal or pathological mental states are directly derived from abnormal or pathological brain states.

Both the "narrow" and "broad" views, as well as perspectives that borrow from both, are employed in addiction research, often implicitly and inconsistently. For instance, Leshner's early version of the BDMA closely aligns with the narrow view of brain disease, reflecting a broader trend in psychiatry toward biological reductionism(15). In the early 2000s addiction was often parallelized with conditions that were universally accepted as brain diseases, such as Alzheimer's

disease and stroke(1,5). Although comparisons with other medical conditions that do not involve the brain were frequently made, including asthma(21), hypertension, and diabetes(22), the main rationale was that just as cardiac insufficiency is a disease of the heart, addiction is a disease of the brain and should be treated like a physical disease(5). The BDMA's alignment with the narrow view is also evident in its use of the word "disease", which typically refers to conditions with (a) physical cause(s), as opposed to "disorder" that is typically used for combinations of signs and symptoms without a clear etiology(23,24).

While there are no agreed-upon criteria to assess similarity between addiction and brain diseases, the most common criteria for granting (brain) disease status are a) an underlying (brain) pathology that causes the observable symptoms which leads to b) a lack of voluntary control over this pathology(24,25). Therefore, as addiction was increasingly conceptualized as a chronic and relapsing brain disease, compulsive drug use and associated brain changes moved to the center of the BDMA(22,26). The compulsion to use drugs despite negative consequences was thought to result from a genetic vulnerability to the effects of drugs, combined with drug-induced changes in brain regions involved in reward, impulse control, and negative affect, including changes in the basal ganglia, the prefrontal cortex, and the extended amygdala(5). These long-lasting brain changes were also viewed as responsible for the high relapse rates observed in people with SUDs and thus identified as key targets for treatment(27,28). These two constitutive elements of the BDMA — compulsive drug use and associated brain changes — are effectively captured in the oft-cited "hijacked brain" metaphor(29), the notion that after chronic drug use, drugs take over the brain's motivational system, making further drug use irresistible(30).

In the decades following Leshner's publication, significant criticisms of the narrow view of addiction as a brain disease have emerged. First, the loss of control associated with compulsive drug use has been questioned, as drug use in people with SUDs was shown to be highly responsive to environmental factors, as for example demonstrated by the effectiveness of contingency management interventions(31). Also, unlike paradigmatic brain diseases, addiction is modifiable by an individual's desire to get better(31). Relatedly, while SUDs can be chronic and hard to treat, there is also growing evidence that many people with SUDs recover spontaneously without medical intervention and many of those who achieve recovery do not experience relapse(32,33).

This challenges the presumed chronic and relapsing nature of addiction, thereby refuting a core element of the narrow view.

Furthermore, though countless studies have evidenced structural and functional brain changes in people with SUDs, it is difficult to establish whether any of these are etiological or even pathognomonic(34). Brain patterns associated with various aspects of the disorder have proven neither reliable nor specific to be clinically meaningful(7,31), likely because of the intrinsically complex nature of the brain changes associated with addiction. However, even if reliable and consistent brain changes were eventually identified, it would be necessary to prove that they precede mental dysfunction and that mental dysfunction is a direct byproduct of these changes, as in paradigmatic brain diseases like brain cancer. For addiction, brain alterations could indicate statistical atypicality rather than dysfunction, as brain dysfunction in most psychiatric disorders cannot be established internally through a comparison to normal brain function, but depends on having established mental dysfunction first(35). This blurs the line between cause and consequence and often leads to circular explanations and other logical fallacies, such as interpreting brain alterations as causes, consequences, and manifestations of the mental disorder interchangeably (12,36). Similarly, while the heritability of SUDs ranges from around 38% for opioid use and 50% for alcohol and cannabis(37), and several genetic loci have been associated with SUDs(38), the disorder's complex polygenic nature makes it unlikely for genetics to accurately predict individual-level outcomes(39). Heritability merely indicates that genetic variation correlates with a given phenotype – a pattern seen across psychological traits and behaviors, including educational attainment and divorce. It neither explains these behaviors nor implies the existence of a genetic mechanism of divorce apt for scientific investigation(40).

In response to growing criticisms, in 2021, several well-known addiction researchers attempted to refine the BDMA in a position paper(2). First, they suggested addiction should be seen as a chronic and relapsing brain disease exclusively for a subpopulation with severe SUD. Thus, only severe SUD qualifies as a brain disease(2,41), whereas mild-to-moderate cases of SUD are likened to a pre-addiction stage(42). But narrowing the target of the BDMA from a larger group of people to a smaller one cannot in principle address any of the challenges of the narrow view discussed above. Furthermore, clarifying the boundary between moderate and severe SUD is challenging(13), and severity is likely on a continuum, rather than in discrete, qualitatively distinct,

categories(42). Second, compulsive drug use is represented as a probability shift towards disadvantageous choices, rather than a loss of control(2). This perspective moves away from a deterministic account of addiction, as the loss of choice is viewed as partial rather than total(2). Third, the lack of a reliable and specific brain pathology associated with compulsive use is acknowledged, though neuroscience is expected to lead to mechanistic insights and eventually personalized treatments for SUDs(2). However, this is the same argument put forward in favor of the BDMA since its inception. After decades of massive investments with disappointing results(8,43), this optimism seems unwarranted. Based on the evidence presented thus far, we question whether instead of further circumscribing the application of the BDMA to a shrinking but not well-defined subpopulation, it would not be more productive to change the framing of addiction as a brain disease itself. The final argument put forward by the expert team that refined the BDMA leverages the broad view of brain disease, "viewing addiction as a brain disease simply states that neurobiology is an undeniable component of addiction"(2)(p1719). Such a view is logically trivial and beyond disagreement. Acknowledging all mental activity involves brain activity, without identifying reliable, specific, and targetable brain dysfunctions, does not advance our understanding of addiction, nor lead to improved treatments.

In sum, the narrow view is untenable because mental disorders are literally diagnosed based on the presence of symptoms, therefore while a person can have brain cancer without having symptoms of cancer, they cannot, by definition, have most mental disorders without having symptoms of these disorders. The broad view is also untenable because it assumes that if neurobiology is the mediator through which a process (i.e., substance use) leads to symptoms, then the process is a brain disease. But the effects of divorce on symptoms of depression are also likely mediated by neurobiology, and no one would argue that divorce should be considered a brain disease.

Furthermore, three arguments challenge both the narrow and the broad views of addiction as a brain disease. First, *multiple realizability* — the fact that a mental state can be realized in multiple ways in the brain(44,45) — implies that observed psychological processes, like craving(46), might not correspond to consistent and specific patterns at the biological level(44,45). Indeed, recent neuroscience findings suggest that psychological processes and brain processes are connected by many-to-one mappings, rather than a one-to-one correspondence(47). Consequently,

individuals with similar mental disorders might not exhibit consistent brain patterns, which might explain the difficulty in identifying reliable diagnostic or prognostic neurobiological markers(48). Second, it is inherently difficult to distinguish pathological from non-pathological brain function in mental disorders(49). Establishing a brain alteration as dysfunctional, in most mental disorders, depends on the corresponding mental dysfunction that this brain alteration realizes, rather than on a comparison to normal brain function in the absence of symptoms. Thus, brain changes occurring in addiction can be interpreted as brain dysfunctions, in line with the BDMA, or, alternatively, as manifestations of normal learning processes going awry at the behavioural level due to a lack of alternative reinforcers(50,51). Third, the same brain processes may give rise to behavioural patterns that are considered pathological or not depending on external factors, such as the appropriateness of the behaviour in its environmental context and the extent to which this behaviour is harmful for the individual(52). In other words, in psychiatry, dysfunction is typically established by external factors, rather than solely by brain mechanisms, which is why behaviour is usually only dysfunctional in certain contexts. For instance, DSM-5 criteria for SUDs include recurrent substance use resulting in non-compliance with basic duties at work, school, or home(53). This criterion applies to both alcohol and tobacco use disorder, yet context shapes dysfunction: if one interrupts a work meeting to (A) drink a shot of vodka or (B) smoke a cigarette, only the former is seen as dysfunctional(54).

Alternative views on the brain-disease status of addiction

Overall, the current landscape in addiction research presents a paradox. The narrow brain disease formulation is acknowledged as a strategic expedient to facilitate funding into treatment and research—though it does not appear to be empirically supported. Yet, it is maintained in the hope that it will eventually lead to the discovery of new treatments and help reduce stigma. However, the anticipated breakthroughs in novel treatments for SUDs have not yet materialized. Most of SUDs, including cannabis, stimulant, benzodiazepine, and inhalant use disorders, are currently treated with psychosocial interventions, in the absence of approved medications(41,55). Most of the medications currently approved by the U.S. Food and Drug Administration (FDA) for nicotine, alcohol, and opioid use disorders were approved before the neuroscience and genetics advances associated with the BDMA(56–58). Efforts to develop new interventions, such as vaccines against drug use(43), or personalized treatments based on brain-derived biomarkers(8),

have shown disappointing results. Though neuromodulatory interventions, including transcranial magnetic stimulation and direct current stimulation, have shown some promising results in the treatment of SUDs(59), there are significant concerns regarding publication bias in these studies(60). None of these interventions have penetrated standard clinical practice. In contrast, peer support and mutual aid groups, widely recognized among the most effective interventions for SUDs, have remained largely unchanged during the past decades(55). Likewise, the observed decline in tobacco use prevalence over the past decades can be mostly attributed to public health interventions like higher tobacco taxes, advertising restrictions, and smoking bans in public places, as opposed to BDMA-related advances (61). Similarly, empirical evidence does not support the claim that framing addiction as a brain disease helps to reduce stigma(10).

Several alternatives to the narrow and broad views of brain disorders have been proposed. One proposal is to accept that establishing brain dysfunction in psychiatry must begin by first establishing mental dysfunction(16). However, the concept of mental disorder itself is ambiguous, with fuzzy boundaries(62). As a result, any derivative concept, like brain disorder, will not resolve this ambiguity, but will instead inherit the same challenges. In order to label a mental disorder as a brain disorder too, despite the conceptual challenges considered here, the *sufficiency principle* must be met, i.e. the identified brain dysfunction should then always realize the associated mental dysfunction(16). For example, recent research has shown that brain lesions provoked by stroke led to smoking remission in humans (63). These lesions map to a common brain network, including the insula, the dorsal cingulate, and medial prefrontal cortex, and has been associated with several SUDs in multiple studies(64). Future research should further clarify the reliability and specificity of this network for SUD. Importantly, even if a specific and reliable brain network for addiction is established, the mental disorder status cannot be replaced or reduced to the brain disorder status, as mental dysfunction will remain fundamental in establishing brain dysfunction in the first place.

Another suggestion is to examine whether critical causal pathways leading to the development of a mental disorder occur in the brain(19). For instance, are there genetic risk factors that increase liability to a psychiatric disorder expressed in the brain? If this causal pathway can be proven for a psychiatric disorder, we can claim that brain dysfunction plays a direct causal role in its development. For example, elevated risk variants for schizophrenia have been found in 11 tissues, all of which pertaining to the brain(65). On the contrary, a significant proportion of alcohol

use disorder risk variants are expressed in liver and gastrointestinal tissues, not the brain(66). Other authors argue that brain diseases need to be identified *as diseases at the level of the brain*—a neural (functional or anatomical) correlate of a psychological state is not a brain disease(18). Considering that mental disorders are overwhelmingly multifactorial both in presentation and causes, perhaps the brain disease formulation should be abandoned. Instead, addiction, together with the rest of mental disorders, should be conceptualized as a network of interacting symptoms that lead to emergent global states, without a singular or necessarily common latent cause(18). Empirical research will continue to clarify these issues. However, there is broad agreement that the outdated narrow and broad views, which have long been implicitly accepted in psychiatric research, should be abandoned in favor of more accurate evidence-based concepts.

Moving forward

Moving beyond the narrow and broad view of addiction starts by acknowledging points of convergence among both proponents and critics of the BDMA. First, there is agreement in rejecting moralist views on addiction and on the critical importance of combating stigma. Additionally, there is consensus that both neurobiological and psychosocial factors play significant roles in the development and maintenance of addiction. Furthermore, it is accepted that chronic and relapsing cases of addiction exist at the severe end of the SUD spectrum, which are accompanied by brain changes that are related to a pathologically narrowed space of choice(52). Thus, the primary point of contention is whether addiction should be primarily labeled as a brain disease, which carries significant implications for individuals' self-perception and identity and has far-reaching consequences for resource allocation, treatment, and public policy.

To further advance the debate, a first step for future research is to employ large longitudinal studies to explore the risk factors for severe SUD, such as the NIDA Adolescent Brain Cognitive Development (ABCD® study)(67). For instance, the transition from moderate to severe SUD might be related to socioeconomic deprivation and high-stigma environments (67). Relatedly and crucially, studies are needed to ascertain whether addressing these risk factors prevents severe SUD or significantly impacts treatment outcomes(68). Second, mental health professionals and researchers should espouse epistemic humility, acknowledging the limitations of our current understanding of addiction, both in clinical encounters and in public. The case for labeling addiction as a brain disease is presently weak from an empirical standpoint, offers limited benefits,

and might even have harms. Scientific pluralism in addiction research and psychiatry generally would entail moving away from paradigm shift narratives that seek grand unifying explanations of mental disorders and instead embracing a plurality of perspectives and levels of analysis that are equally valid. Third, we should further investigate ways to reduce stigma surrounding SUDs. To this end, it is crucial to engage with different stakeholders, especially people with SUD, to understand their perspectives and frame research questions and theoretical models accordingly. For example, there is evidence that while most people with SUD do not endorse an oversimplified brain-disease formulation of addiction, more nuanced biological explanations can serve as valuable hermeneutical tools, especially when presented alongside other perspectives(69).

Finally, it is essential to acknowledge that the focus on discovering novel, innovative treatments for addiction should not obscure existent beneficial interventions that are currently under-implemented. For instance, interventions could focus on the lack of alternative reinforcers, such as meaningful social, educational, and employment opportunities, known to be major drivers of addiction(70). Moreover, substantial evidence supports the efficacy of measures like free and unconditional access to medical and psychological treatment, harm reduction interventions, access to stable housing, and enhanced community support to combat loneliness(71,72). Yet, these measures are poorly implemented, as access to mental health care remains inadequate due to an undersized workforce and insufficient resource allocation(73). Similarly, systemic issues that are well-known drivers of addiction—such as poverty, systemic racism, and social inequality—are not adequately addressed(74). For instance, the major forces that drove the current opioid use disorder epidemic in the US - the SUD most closely aligning to the BDMA due to its severity, chronicity, and need for medical intervention - are largely social rather than biological and systemic rather than individual, including aggressive marketing for prescription opioids, deindustrialization, and poverty(75). By framing addiction primarily as an individual problem, the BDMA has contributed to obscuring the broader societal and systemic factors at play. Beyond finding cutting-edge cures for addiction that often result in a small advantage for a limited subgroup of patients, the real challenge lies in confronting and dismantling the systemic barriers that prevent us from effectively leveraging existing knowledge to address patients' living situations, including material conditions, families, social networks, and all other factors that give meaning to people's lives(72).

Contributors

CB, EIF and IAC conceptualized the manuscript. CB wrote the first draft of the manuscript. EIF, EA, MF and IAC contributed to information relevant to a specific topic and critically revised and edited the manuscript.

Declaration of interests

We declare no competing interests

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