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The brain disease model of addiction has dominated public and scientific discourse on addiction (termed substance use disorder [SUD] in the DSM-5) over the past 3 decades. The model framed addiction as a chronic and relapsing brain disease caused by structural and functional brain alterations. The purpose of this model was purportedly dual, as both an aetiological 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 conceptualised as a brain disease. In this Personal View, we argue that the absence of an agreed, 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 both narrow and broad views of brain disease coexist and inform addiction research, though often implicitly and inconsistently. The narrow view of brain disease posits that a mental condition qualifies as a brain disease only if it manifests similarly to a paradigmatic brain disease, resulting from either known or unknown structural and functional damage. The broad view of brain disease suggests that brain disease status should be granted automatically to mental disorders, as 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] The brain disease model of addiction (BDMA) has dominated both public and scientific discourse on addiction (termed substance use disorder [SUD] in the DSM-5).[2,3] Endorsement of the BDMA shaped research priorities worldwide, considering that, according to Leshner, NIDA funded over 85% of global addiction research during his tenure as Director.[4,5] The BDMA framed addiction as a chronic and relapsing brain disease caused by structural and functional brain alterations. This view was elaborated and cemented through neuroscientific and genetic advances. An increasingly complex BDMA was purported to lead not only to new treatment avenues for people with SUDs,[6] but also to a 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 15 years, growing criticisms of the BDMA have led to stark disagreement as to whether addiction should be conceptualised as a brain disease.[4,7] Criticism of the BDMA has revolved around two core arguments. First, the dual function of the BDMA as both an aetiological theory and as a tool to reduce stigma has obscured two distinct empirical questions about whether addiction is a brain disease and whether labelling addiction as a brain disease reduces stigma, an important distinction that is rarely acknowledged.[8] These questions are independent, in that addiction might be a brain disease but labelling it as such might not help to reduce stigma, or vice versa. The empirical evidence for addiction as brain disease is weak. Despite many studies finding neurobiological differences between people with SUD and healthy controls, no diagnostic or prognostic biomarkers have been identified,[9] and the BDMA has yet to lead to better or more precisely targeted treatments.[10] Similarly, the use of the BDMA construct has had little effect on reducing stigma associated with SUD.[11] Moreover, there is evidence that the use of the BDMA might have promoted new sources of stigma, related to reduced perceived agency and pessimism about recovery.[11,12] This is unsurprising, given that disease labels can be highly stigmatising, as seen in conditions such as HIV/AIDS.[13] The second argument suggests that, by centring on individual vulnerability, the BDMA could have obscured important factors that have been referred to as the causes of the causes in literature on the development and maintenance of addiction.[14] These social and environmental factors include poverty, unemployment, job insecurity, housing instability, discrimination, low educational attainment, and poor access to health care.[15] This argument relates to general debates in mental health sciences on complex, multifactorial causes and the relative contributions and causal status of biological, psychological, and social factors.[16]

In this Personal View, we propose another key perspective on the role of the BDMA in addiction research. Specifically, we argue that the lack of a clear and consistent definition of what constitutes a brain disease in psychiatry[17–20] and the frequent use of concepts with divergent or shifting meaning has obstructed productive debate. Although the causes and consequences of this conceptual ambiguity are increasingly recognised in the philosophy of psychiatry,[17] 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 these views, which are often used both implicitly and interchangeably in psychiatric research, is to separate the

narrow view from the broad view.[17] 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,[21] for a mental disorder to be classified as a brain disease there should be a unified account of causes and symptoms of brain dysfunction, preceding and independent of mental dysfunction. In contrast, the broad view asserts that brain disease status is granted automatically to mental disorders, because all mental activity is mediated by the brain. It therefore follows that all atypical or pathological mental states are directly derived from atypical or pathological brain states.

Both the narrow and broad views—and perspectives that borrow from both—are used in addiction research, often implicitly and inconsistently. For example, Leshner's early version of the BDMA closely aligns with the narrow view of brain disease, reflecting a more general trend in psychiatry towards biological reductionism.[16] In the early 2000s, addiction was often compared to conditions that were universally accepted as brain diseases, such as Alzheimer's disease and stroke.[1,6] Although comparisons with medical conditions that do not involve the brain were frequently made (eg, asthma,[22] hypertension, and diabetes[23]), the main rationale behind this association was that just as cardiac insufficiency is a disease of the heart, addiction is a disease of the brain and should be treated in the same way as a physical disease.[6] The alignment of the BDMA with the narrow view is also evident in the use of the word disease, which typically refers to conditions with physical causes, as opposed to disorder, which is typically used for combinations of signs and symptoms without a clear cause.[24,25]

Although there are no agreed upon criteria to assess similarity between addiction and brain diseases, the most common criteria for granting (brain) disease status are an underlying (brain) pathology that causes the observable symptoms, which leads to a lack of voluntary control over this pathology.[25,26] Therefore, as addiction was increasingly conceptualised as a chronic and relapsing brain disease, compulsive drug use and associated brain changes moved to the centre of the BDMA.[23,27] The compulsion to use drugs despite negative consequences was thought to result from a genetic susceptibility to the effects of drugs, combined with drug-induced changes in brain regions involved in reward, impulse control, and negative affect, including the basal ganglia, the prefrontal cortex, and the extended amygdala.[6] 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.[28,29] These two constitutive elements of the BDMA—compulsive drug use and associated brain changes—are effectively captured in the hijacked brain metaphor,[30] which states that chronic drug use can alter and redirect the brain's motivational system towards further compulsive drug use.[31]

Since Leshner's publication in 1997, criticisms of the narrow view of addiction as a brain disease have emerged. 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 shown by the effectiveness of contingency management interventions.[32] Unlike paradigmatic brain diseases, addiction is modifiable by an individual's desire to get better.[32] Although SUDs can be chronic and hard to treat, growing evidence suggests that many people with SUDs recover spontaneously without medical intervention, and that many people with SUDs who reach recovery do not experience relapse.[33,34] These findings challenge the presumed chronic and relapsing nature of addiction, thereby refuting a core element of the narrow view.

Furthermore, although countless studies have shown structural and functional brain changes in people with SUDs, it is difficult to establish whether any of these changes are aetiological or pathognomonic.[35] Brain patterns associated with various aspects of SUDs have not proven to be reliable or specific enough to be clinically meaningful,[8,32] probably because of the intrinsically complex nature of the brain changes associated with addiction. However, even if reliable and consistent brain changes were 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 (eg, brain cancer). For addiction, brain alterations could indicate statistical atypicality rather than dysfunction, as brain dysfunction in most psychiatric disorders cannot be established internally by a comparison with normal brain function, but depends on a previous establishment of mental dysfunction.[36] This requirement blurs the line between cause and consequence and often leads to circular explanations and other logical fallacies, such as interpreting brain alterations interchangeably as causes, consequences, and manifestations of the mental disorder.[13,37] Similarly, although the heritability of SUDs is around 38% for opioid use and 50% for alcohol and cannabis use,[38] and despite several genetic loci being associated with SUDs,[39] the complex polygenic nature of SUDs means that genetics are unlikely to predict individual-level outcomes accurately.[40] Heritability merely indicates that genetic variation correlates with a given phenotype, which is a pattern seen across psychological traits and behaviours, such as educational attainment and divorce. Heritability neither explains these behaviours nor implies the existence of a causal genetic mechanism apt for scientific investigation.[41]

In response to growing criticism, Heilig and colleagues attempted to refine the BDMA in a 2021 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 would qualify as a brain disease,[2,42] whereas mild to moderate cases of SUD

were likened to a pre-addiction stage.[43] However, reducing the target of the BDMA from a larger group of people to a smaller one cannot address any of the challenges of the narrow view discussed above. Furthermore, clarifying the boundary between moderate and severe SUD is challenging,[14] and severity is likely on a continuum, rather than in discrete, qualitatively distinct, categories.[43] Second, Heilig and colleagues suggested that compulsive drug use should be seen as a probability shift towards disadvantageous choices, rather than a loss of control.[2] This perspective moved away from a deterministic account of addiction, as the loss of choice was viewed as partial rather than total.[2] Third, Heilig and colleagues acknowledged the absence of a reliable and specific brain pathology associated with compulsive use, although developments in neuroscience are expected to lead to mechanistic insights and personalised treatments for SUDs.[2] However, this argument has been made since the inception of the BDMA, and after decades of investments with disappointing results,[9,44] the optimism seems unwarranted. Based on the evidence, we question whether, instead of circumscribing the application of the BDMA to a shrinking but poorly defined subpopulation, it would be more productive to change the framing of addiction as a brain disease. The final argument put forward by Heilig and colleagues leverages the broad view of brain disease, stating that "viewing addiction as a brain disease simply states that neurobiology is an undeniable component of addiction".[2] This view is logically trivial and beyond disagreement. Acknowledging that all mental activity involves brain activity, without identifying reliable, specific, and targetable brain dysfunctions does not advance the understanding of addiction or lead to improved treatments.

Summarily, the narrow view is untenable because mental disorders are diagnosed based on the presence of symptoms, and although a person can have brain cancer without having symptoms of cancer, an individual by definition cannot 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 by which a process (ie, substance misuse) leads to symptoms, then the process is a brain disease. However, the effects of divorce on symptoms of depression are also likely mediated by neurobiology, and divorce is indisputably not a brain disease.

Three arguments challenge both the narrow and the broad views of addiction as a brain disease. First, multiple realisability (ie, the fact that a mental state can be realised in multiple ways in the brain)[45,46] implies that observed psychological processes such as craving[47] might not correspond to consistent and specific patterns at the biological level.[45,46] Recent neuroscience research supports this notion; for example, a 2022 paper suggested that psychological processes and brain processes are connected by many-to-one mappings, rather than by one-to-one correspondence.[48] Consequently, individuals with similar mental disorders might not have consistent brain patterns, which could explain the difficulty in identifying reliable diagnostic or prognostic neurobiological markers.[49] Second, it is inherently difficult to distinguish pathological from non-pathological brain function in mental disorders.[50] In most mental disorders, establishing a brain alteration as dysfunctional depends on the corresponding mental dysfunction that this brain alteration realises, rather than on a comparison with typical brain function in the absence of symptoms. Therefore, addiction-related brain changes can be interpreted as brain dysfunctions, in line with the BDMA, or as manifestations of typical learning processes going awry at the behavioural level owing to a lack of alternative reinforcers.[51,52] Third, the same brain processes could 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 the behaviour is harmful for the individual.[53] In psychiatry, dysfunction is typically established by external factors, rather than solely by brain mechanisms, which is why behaviour is usually only dysfunctional in particular contexts. For instance, DSM-5 criteria for SUDs include recurrent substance use resulting in non-compliance with basic duties at work, school, or home. This criterion applies to both alcohol and tobacco use disorder, yet context shapes dysfunction: if one interrupts a work meeting to drink a shot of vodka or smoke a cigarette, only the former is seen as dysfunctional.[54]

Alternative views on the brain disease status of addiction

Overall, the current landscape of addiction research is paradoxical. The narrow view of brain disease is acknowledged as a strategic expedient to facilitate funding into treatment and research, but does not appear to be empirically supported. This view is maintained in the hope that it will eventually lead to the discovery of new treatments and help reduce stigma. However, the novel treatments for SUDs have not yet materialised. Most SUDs, including cannabis, stimulant, benzodiazepine, and inhalant use disorders, are treated with psychosocial interventions, in the absence of approved medications.[42,55] Many of the medications approved by the US Food and Drug Administration for nicotine, alcohol, and opioid use disorders were approved before the neuroscientific and genetics advances associated with the BDMA.[56–58] Efforts to develop new interventions, such as vaccines against drug use[44] or personalised treatments based on brain-derived biomarkers,[9] have shown disappointing results, either due to a lack of efficacy or an absence of substantial evidence to support their use. Neuromodulatory interventions (eg, transcranial magnetic stimulation and direct current stimulation) have shown some promise in the treatment of SUDs,[59] but there are substantial concerns regarding publication bias in these studies.[60] None of these interventions have entered standard clinical practice. In contrast, peer support and mutual aid groups, which have

been widely recognised as some of the most effective interventions for SUDs, have remained largely unchanged.[55] Similarly, the observed decline in tobacco use prevalence over the past decades can be mostly attributed to public health interventions, such as higher tobacco taxes, advertising restrictions, and smoking bans in public places, as opposed to BDMA-related advances.[61] Empirical evidence also does not support the claim that framing addiction as a brain disease helps to reduce stigma.[11]

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 should begin by establishing mental dysfunction.[17] However, the concept of mental disorder is ambiguous, with unclear boundaries.[62] Any derivative concept (eg, brain disorder) will not resolve this ambiguity, but will inherit the same challenges. For a mental disorder to be labelled as a brain disorder despite the discussed conceptual challenges, the sufficiency principle should be met—the identified brain dysfunction should always realise the associated mental dysfunction.[17] For example, a 2022 study by Joutsa and colleagues has shown that brain lesions provoked by stroke led to smoking remission in humans.[63] These lesions map to a common brain network that includes the insula, the dorsal cingulate, and medial prefrontal cortex, and have been associated with several SUDs in multiple studies.[64] Future research should clarify the reliability and specificity of this network for SUD. However, even if a specific and reliable brain network for addiction is established, a mental disorder status cannot be replaced or reduced to a brain disorder status, as mental dysfunction will remain fundamental in initially establishing brain dysfunction.

Another suggestion is to examine whether key causal pathways that lead to the development of a mental disorder occur in the brain.[20] For instance, are genetic risk factors that increase liability to a psychiatric disorder expressed in the brain? If such a causal pathway were proven for a psychiatric disorder, brain dysfunction could be claimed to play a direct causal role in its development. For example, genetic risk variants associated with a higher risk for schizophrenia have been found exclusively in brain tissue.[65] Conversely, many risk variants associated with alcohol use disorder 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.[19] Considering that mental disorders are multifactorial in both presentation and causes, perhaps the brain disease formulation should be abandoned. Instead, addiction, together with other mental disorders, should be conceptualised as a network of interacting symptoms that lead to emergent global states, without a singular or common latent cause.[19] 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 favour of more accurate and evidence-based concepts.

Future research

Moving beyond the narrow and broad view of addiction starts by acknowledging points of convergence among both proponents and critics of the BDMA. There is agreement in rejecting moralist views on addiction and on the importance of combating stigma. Additionally, there is consensus that both neurobiological and psychosocial factors play key 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 or the ability to make decisions freely.[53] The main point of contention is whether addiction should be primarily labelled as a brain disease, which carries implications for peoples' self-perception and identity and has far-reaching consequences for resource allocation, treatment, and public policy.

A first step for future research is to use large longitudinal studies to explore the risk factors for severe SUD, such as the NIDA Adolescent Brain Cognitive Development study.[67] For instance, the transition from moderate to severe SUD could be related to socioeconomic deprivation and high-stigma environments.[67] Studies are also needed to ascertain whether addressing these risk factors prevents severe SUD or affects treatment outcomes.[68]

Mental health professionals and researchers should espouse epistemic humility, acknowledging the limitations of the current understanding of addiction, both in clinical encounters and in public. Scientific pluralism in addiction research and psychiatry would entail moving away from narratives that seek grand unifying explanations of mental disorders, and instead embracing a plurality of perspectives and levels of analysis that are equally valid.

Ways to reduce stigma surrounding SUDs should be investigated by engaging with different stakeholders, especially people with SUDs, to understand their perspectives and frame research questions and theoretical models accordingly. Evidence suggests that although most people with SUDs 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]

Acknowledging that the focus on discovering novel and innovative treatments for addiction should not obscure existent beneficial interventions that are currently under-implemented is essential. Possible interventions could instead focus on the lack of alternative reinforcers, such as meaningful social, educational, and employment opportunities, which are recognised as major drivers of addiction.[70] Moreover, substantial evidence supports the

efficacy of measures such as 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] These measures are poorly implemented, however, 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 (eg, poverty, systemic racism, and social inequality) are not adequately addressed.[74] For instance, the driving forces of the current opioid use disorder epidemic in the USA—the SUD that most closely aligns with the BDMA due to its severity, chronicity, and need for medical intervention—are largely social and systemic rather than biological and individual, and include aggressive marketing for prescription opioids, deindustrialisation, 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 pioneering cures for addiction that often result in a small advantage for a 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 conceptualised 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. All authors reviewed the final manuscript and made the decision to submit for publication.

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