

# Toward a Syndrome Model of Addiction: Multiple Expressions, Common Etiology

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“The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them”

Sir William Bragg (1862–1942)<sup>1</sup>

It is common for clinicians, researchers, and public policymakers to describe certain drugs or objects (e.g., games of chance) as “addictive,” tacitly implying that the cause of addiction resides in the properties of drugs or other objects. Conventional wisdom encourages this view by treating different excessive behaviors, such as alcohol dependence and pathological gambling, as distinct disorders. Evidence supporting a broader conceptualization of addiction is emerging. For example, neurobiological research suggests that addictive disorders might not be independent:<sup>2</sup> each outwardly unique addiction disorder might be a distinctive expression of the same underlying addiction syndrome. Recent research pertaining to excessive eating, gambling, sexual behaviors, and shopping also suggests that the existing focus on addictive substances does not adequately capture the origin, nature, and processes of addiction. The current view of separate addictions is similar to the view espoused during the early days of AIDS diagnosis, when rare diseases were not

yet recognized as opportunistic infections of an underlying immune deficiency syndrome. Our analysis of the extant literature reveals that the specific objects of addiction play a less central role in the development of addiction than previously thought, and it identifies the need for a more comprehensive philosophy of addiction.

In this article, we suggest that evidence of multiple and interacting biopsychosocial antecedents, manifestations, and consequents—within and among behavioral and substance-related patterns of excess—reflects an underlying addiction syndrome. We propose, in particular, that addiction should be understood as a syndrome with multiple opportunistic expressions (e.g., substance use disorders and pathological gambling). Our goals in this column are to (1) describe a new, syndromal model of addiction, (2) review the most recent literature that supports viewing addiction as a syndrome, and (3) indicate how this perspective can advance clinical practice and identify areas in which more research is needed. To accomplish these goals, we review the empirical evidence for this addiction syndrome and organize it into three primary areas: (1) shared neurobiological antecedents, (2) shared psychosocial antecedents, and (3) shared experiences (e.g., manifestations and sequelae).

## MODELING AN ADDICTION SYNDROME

A syndrome is a cluster of symptoms and signs related to an abnormal underlying condition; not all symptoms or signs are present in every expression of the syndrome, and some manifestations of a syndrome have unique signs and symptoms. In addition, syndromes and the expressive signs and symptoms that serve as identifying characteristics of the underlying condition have a distinctive temporal progression.<sup>3</sup> Given the potentially recursive nature of

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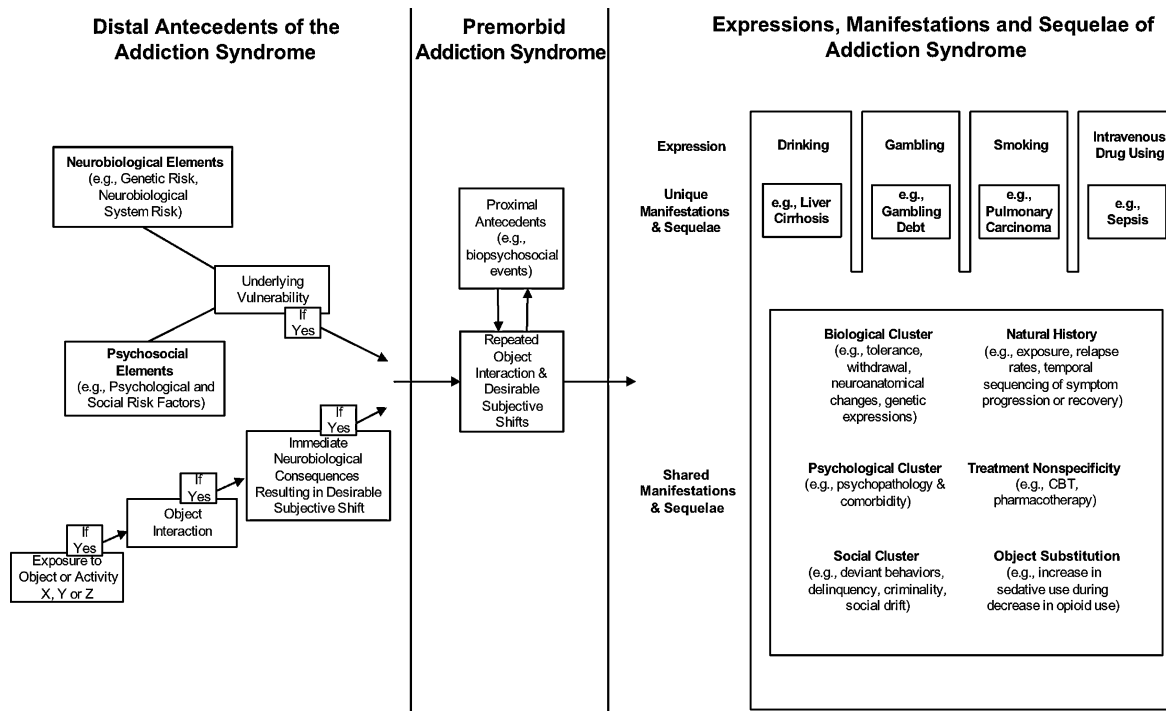


FIGURE 1. Model of the addiction syndrome.

syndromes and their sequelae, the consequents of the addiction syndrome can influence existing antecedent factors—or become new antecedents—to change the existing risk matrix associated with developing different manifestations of the syndrome.

The extant evidence suggests that (1) many commonalities occur across different expressions of addiction and (2) these commonalities reflect shared etiology: a syndrome. Figure 1 illustrates a hypothetical chain of events leading to the development of an addiction syndrome and its consequences.

As Figure 1 shows, antecedents of the addiction syndrome include individual vulnerability levels, object exposure, and object interaction. More specifically, throughout the course of development, people encounter and accumulate specific combinations of neurobiological and psychosocial elements that can influence their behavior. Some elements increase the likelihood of addiction, whereas other factors are protective and reduce the chance of addiction (e.g., social support networks<sup>4</sup> and dimensions of religiosity).<sup>5</sup> Similarly, during their lifetimes, individuals are exposed to, and have access to, different objects of addiction. Exposure and access to an object of addiction increase an individual's likelihood of interacting with that object. Interacting with an object of addiction can expose at-risk individuals to neurobiological consequences that are both common to all objects of addiction (e.g., activation of reward circuitry) and unique to specific objects of addiction (e.g., psychoactivity).

When (1) individuals engage in repeated interactions with a specific object or objects of addiction, and (2) the neurobiological or social consequences of these interactions produce a desirable (i.e., sought-after) subjective shift that is reliable and robust, the premorbid stage of the addiction syndrome emerges. This sought-after shift in subjective state is requisite for the development of the addiction syndrome. During this stage of the syndrome, people teeter on a delicate balance that can shift them toward either more or less healthy behavior. Although distal antecedents of addiction (see Figure 1) are well documented, the proximal antecedents that influence further development of the syndrome remain poorly identified—though these are likely to be biopsychosocial factors similar to those associated with distal influences.

The addiction syndrome can manifest itself in many different ways; its premorbid characteristics and some sequelae are dependent upon the object with which people interact. To illustrate, if one interacts with cigarettes (e.g., by repeatedly smoking), or if one interacts with a slot machine (e.g., by repeatedly gambling), and the addiction syndrome emerges, then the manifestation of this syndrome and its sequelae will have some characteristics that uniquely reflect each of these objects. In addition, assorted expressions of the addiction syndrome (e.g., substance use disorders and pathological gambling) will share common manifestations and sequelae (e.g., depression, neuroadaptation, and deception). Researchers and clinicians can identify the presence of

the addiction syndrome when at least one of the shared manifestations and sequelae accompany the premorbid characteristics (see Figure 1). Unless this requirement is satisfied, researchers and clinicians should not make a diagnosis of addiction syndrome, because the presence of these central characteristics act as a diagnostic “gate” to identify the presence of a disorder.<sup>6</sup> As we noted earlier, the addiction syndrome can be recursive, and its sequelae can generate an entirely new vulnerability profile (e.g., provoke reward-system malfunction in a previously normal system). The development of the addiction syndrome therefore places people with the syndrome at increased risk for continuing addictive behavior and for developing new addictive behaviors. This chain of events is evident in many ways, but most specifically in the parallel natural histories of different manifestations of addiction, including relapse patterns, addiction hopping, treatment nonspecificity, and addiction comorbidity.

## REVIEWING THE EVIDENCE

### Shared Neurobiological Antecedents

**Neurobiological system nonspecificity.** Both psychoactive drugs (e.g., alcohol, cocaine, and heroin) and behaviors (e.g., gambling) have the capacity to stimulate neurobiological systems, in general, and the brain’s dopamine reward system, in particular.<sup>7–10</sup> Recent functional magnetic resonance imaging (fMRI) studies reveal that the manner in which money and beauty energize the reward system is similar to that associated with the anticipation of cocaine among users.<sup>11,12</sup> Hence, scientists have implicated dopamine as one neurotransmitter that plays a primary role in the development and maintenance of both drug and behavioral addictions. For example, scientists theorize that the “reward deficiency syndrome” is a result of dopamine-system malfunction; this malfunction is complicit in vulnerability to addiction.<sup>13</sup> Neurobiological reward activity represents the most well known evidence that supports an addiction syndrome, but other systems also deserve consideration. As Breiter and Gasic<sup>14</sup> remind us, observations concerning the dopamine reward system should not be taken to eliminate or minimize the potential contribution of learning and memory in the hippocampus, and of emotional regulation in the amygdala, in the development and maintenance of addiction. The findings that disparate objects stimulate similar neurobiological pathways<sup>15</sup> suggest that, regardless of the object of addiction, the neurobiological circuitry of the central nervous system is the ultimate common pathway for addictive behaviors.

**Genetic overlap.** There is evidence suggesting substantial genetic and environmental nonspecificity across addictive behaviors.<sup>8,16,17</sup> For example, genetic studies reveal common

molecular mechanisms for drug addiction and compulsive running behavior.<sup>18–20</sup> Similarly, pathological gambling shares a common genetic vulnerability with alcohol dependence.<sup>21</sup> A recent study of male twins showed that shared genetic and environmental risk factors for psychoactive substance abuse are largely substance nonspecific.<sup>2</sup> Kendler and colleagues<sup>2</sup> note that they “could not find evidence for genetic factors that increase risk for individuals to abuse substance A and not also to abuse substances B, C, and D.”

Other evidence also supports the general genetic-risk hypothesis. For example, Merikangas and colleagues<sup>22</sup> found that similar direct (e.g., exposure to drugs) and indirect (e.g., family discord) factors augment genetic risk for both drug and alcohol abuse. In their study of female twins, Karkowski, Prescott, and Kendler<sup>23</sup> found that (1) genetic and environmental factors significantly influenced substance use in general and (2) there was no evidence of a heritability or familial environmental effect for specific substances. Similarly, except with regard to heroin—which exhibited unique substance-specific genetic risk—investigators of Vietnam-era drug users observed a common vulnerability to using a variety of drug classes.<sup>24</sup> Finally, Bierut and colleagues<sup>25</sup> observed: “Although studies support the familial transmission of alcohol and substance dependence, individuals are frequently dependent on multiple substances, raising the possibility of a general addictive tendency.” These findings provide evidence that the genetic link to addiction does not account for vulnerability to specific objects of addiction; rather, genetics account for a general and increased risk for addiction.

Because genetic risk factors do not distinguish among the many potential objects of addiction, psychosocial factors supplement the underlying neurobiological risk and account for the various ways that individuals express and experience the addiction syndrome. Psychosocial influences are integral to the syndrome model because they account for the considerable heterogeneity across the various expressions of addictive behaviors (e.g., drinking, smoking, gambling, and shopping).

### Shared Psychosocial Antecedents

**Psychological risk factors.** The prevalence of psychopathology is increased among individuals who are dependent on multiple psychoactive substances (e.g., heroin, alcohol, or cocaine)<sup>26–28</sup>—perhaps another indication of a shared vulnerability. Many substance-abuse treatment seekers (e.g., those in treatment for opioid dependence or for driving under the influence of alcohol) have increased rates of anxiety and depressive disorders.<sup>29–32</sup> Likewise, populations with psychopathology (e.g., major depression, generalized anxiety disorder, or posttraumatic stress disorder) often exhibit

increased prevalence of drug use disorders.<sup>33–35</sup> Finally, several studies show that comorbid psychiatric conditions typically precede both alcohol abuse and cocaine use.<sup>3,36,37</sup> More research is needed to determine the extent to which symptom, sign, and disorder patterns for behavioral expressions of addiction resemble or differ from chemical expressions of addiction.

**Social risk factors.** Subclinical risk factors (e.g., impulsivity, poor parental supervision, and delinquency) also are common across chemical and behavioral expressions of addiction.<sup>38–40</sup> In addition, research shows that individuals who engage in one problem behavior are likely to engage in others.<sup>41–43</sup> Finally, various sociodemographic risk factors (e.g., relating to poverty, geography, family, and peer groups) can influence the onset and course of both drug use and other activities (e.g., gambling) that can similarly affect the likelihood of developing addiction.<sup>44–51</sup>

### Shared Experiences

**Shared manifestations and sequelae.** Different expressions of addiction share various manifestations and sequelae. Accordingly, Zinberg<sup>52</sup> suggested that “the experience of addiction diminishes personality differences and makes all compulsive users seem very much alike.” In addition to reducing preexisting personality differences, various and distinct expressions of addiction stimulate similar biopsychosocial sequelae. Several studies support this notion. Psychosocially, people who engage in substance abuse, pathological gambling, or excessive shopping have recognizable sequelae in common (e.g., deceit, shame, guilt, or dysthymia).<sup>42,53–55</sup>

Chemical and behavioral expressions of addiction also have similar neurobiological consequences, including the emergence of neuroadaptation (e.g., tolerance and withdrawal). Tolerance is evidenced when repeat drug users require increasing doses to achieve the same level of intoxication as before; withdrawal occurs when tolerant users stop using the drug, become stereotypically sick, and are able to alleviate this circumstance by using the drug again. Behavioral excesses also evidence neuroadaptation despite the absence of psychoactive drug ingestion. For example, disordered gamblers often evidence a pattern of increasing bets to achieve the same level of excitement that they previously experienced (i.e., tolerance). When gamblers cut back or stop gambling, they exhibit adverse signs and symptoms that can be alleviated by gambling again (i.e., withdrawal).<sup>56</sup>

Neurobiological and psychosocial sequelae pose important treatment challenges. The recursive nature of some sequelae exacerbate these difficulties: sequelae are concurrently both consequents of the current manifestation of addiction and risk factors that increase the likelihood of developing new or different manifestations of the addic-

tion syndrome. Furthermore, without an independent, objective diagnostic standard (i.e., a gold standard)—free from the problems of impression management that can bias self-report—the manifestations and sequelae of addiction serve as the primary evidence that clinicians use to make diagnostic decisions and inferences about the presence of addiction.

To illustrate, patients experienced with the health care system have learned how to report symptom patterns (e.g., cramps) that influence or “manage” the impressions that health care providers form about their illness (e.g., opioid withdrawal); this social interaction increases the likelihood that these patients will receive the medications or treatment that they want, and decreases health care providers’ confidence in self-reports obtained from patients with addiction.

**Parallel natural histories.** There is a natural history to the course of addiction that begins with risk factors and always includes exposure to potential objects of addiction.<sup>53,57,58</sup> Once addictive behavior patterns emerge, there is a similar natural history across various substances. For example, Hunt<sup>59</sup> presented seminal research, based on 84 studies, demonstrating remarkably similar relapse patterns for alcohol, heroin, and tobacco. Since the same natural history can be observed in the addiction to drugs with important biochemical differences, a reasonable inference is that the object of addiction might be less relevant to the course of addiction than previously thought. These patterns likely reflect the dynamics of a common underlying addiction process and therefore challenge the conventional wisdom that there are various and distinct addictive disorders.<sup>42,58,60–67</sup> Furthermore, although there are few longitudinal studies, investigators have observed a similar natural history for substance and behavioral expressions of addiction. For example, in a prospective study, a large sample of casino employees with intemperate drinking, excessive gambling, or both problems showed almost identical patterns of improvement, relapse, and remission.<sup>42</sup> We cautiously suggest that the natural histories of behavioral expressions of addiction are similar to the histories of many chemical expressions of addictions.

**Object nonspecificity.** Research suggests that addiction is not necessarily inextricably linked to a particular substance or behavior. For example, circumstantial opportunity plays a more influential role in the development of addictive behavior than individuals’ preferences for certain drugs.<sup>68</sup> Further, with or without treatment, it is very common for people recovering from one addiction (e.g., opioids) to “hop” to another (e.g., cocaine, alcohol, gambling, or exercise) before successfully recovering from “all” addictions. Hser and colleagues<sup>69</sup> examined longitudinal patterns of alcohol and narcotic use, and observed a decrease in alcohol consumption at the time that narcotic addiction began; likewise, during periods of decreased narcotics use, alcohol consumption rose.

This “hopping” between addiction objects has been demonstrated for illicit drugs and nicotine,<sup>70</sup> for alcohol abuse and bulimia,<sup>71</sup> and for substance abuse and pathological gambling.<sup>72</sup> Finally, clinical research has shown that during early treatment for opioid dependence, as both opioid and cocaine use decreased, sedative use increased.<sup>73</sup>

**Concurrent manifestations of addiction.** The prevalence of polysubstance abuse and dependence is well documented,<sup>74</sup> but the co-occurrence of chemical and behavioral expressions of addiction also is common. For example, intemperate shoppers and gamblers both evidence higher rates of substance use disorders than persons without these patterns of economic excess.<sup>26,43,54,55,75,76</sup> Conversely, compared to those without substance use disorders, individuals who are dependent on psychoactive substances are more likely to be pathological gamblers.<sup>26,43,77</sup> Research demonstrating the frequent co-occurrence of different expressions of addiction suggests the presence of an underlying force responsible for addiction.

**Treatment nonspecificity.** The nonspecificity of pharmacological treatment (i.e., when a drug-specific treatment reduces the immoderate use of another drug or activity) also provides support for reconsidering the current models of addiction. Recently, scientists have identified interesting pharmacological treatment spillover effects. For example, naltrexone, an opioid antagonist used for the treatment of opioid abuse and dependence disorders, has shown efficacy for the treatment of pathological gambling.<sup>78</sup> Treatment programs featuring methadone, an opioid agonist, have shown efficacy in reducing cocaine abuse among opioid-dependent patients.<sup>73</sup> Other research shows that topiramate, an adjunctive treatment for seizure disorders that acts on the brain’s dopamine pathways, has efficacy in treating alcohol-dependence disorders.<sup>16</sup> Similarly, researchers speculate that bupropion, an antidepressant used in smoking-cessation protocols to treat nicotine dependence, might be efficacious because of its dopaminergic and noradrenergic activities, “with the dopaminergic activity affecting areas of the brain having to do with the reinforcement properties of addictive drugs and the noradrenergic activity affecting nicotine withdrawal,” rather than its antidepressant properties.<sup>79</sup> Additional treatment-spillover effects regarding other aspects of the neurobiological reward circuitry (e.g., dopamine or other neurotransmitters) that mediate addictions would provide additional support for a common etiology of addiction. Finally, several nonpharmacological treatments (e.g., cognitive-behavioral therapy, psychodynamic therapy, and behavior therapy) are commonly used interchangeably and effectively to treat both chemical and behavioral expressions of addiction.

The finding that nonspecific treatments can influence seemingly disparate object-specific addictions supports the hypothesis that there are common underlying biopsychosocial causes for these phenotypically complex disorders. A common etiology of behavioral and substance-related addictions encourages the development of an etiology-based, rather than a consensus-based, diagnostic system. And as Hyman and Fenton<sup>80</sup> have commented, “In the absence of objective tests for mental disorders, consensus classification systems [e.g., DSM-IV and ICD-10] were developed of necessity . . . These frameworks for diagnostic classification serve a vital role in facilitating medical communication and clinical care. The strength of these diagnostic manuals, however, lies in their reliability (i.e., different observers arrive at the same diagnosis for the same person), not validity (i.e., defining ‘natural kinds’ of disease).”

#### DISCUSSION: IMPLICATIONS OF THE ADDICTION SYNDROME MODEL FOR RESEARCH AND PRACTICE

Hyman and Fenton<sup>80</sup> have also argued that “major psychiatric syndromes may eventually be understood as families of related disorders that are individually distinguished by specific combinations of genetic and nongenetic susceptibility factors.” Addiction likely will follow this path. Although distinct expressions of addiction have unique elements, these different manifestations also share many neurobiological and psychosocial antecedents and consequences. Coupled with repeated premorbid shifts toward a desirable subjective state, neurobiological and psychosocial characteristics both define and result from the addiction syndrome.

Currently, in the absence of a reliable, objective criterion (or set of criteria), diagnosing addiction and many other psychiatric disorders depends upon a tautology: the diagnostic inference of a latent state (i.e., addiction) rests upon the consequences of that very same latent state. The syndrome model encourages an improved understanding of both proximal and distal influences, as well as the development of an objective diagnostic criterion. With such tools in hand, clinicians will be able to advance an etiologically based diagnostic classification that is not dependent upon the self-report of sequelae and that consequently helps to improve primary and secondary prevention programs. Since psychosocial research can identify most shared proximal and distal influences, the development and use of a valid diagnostic criterion will likely emerge from genetics and neuroscience.<sup>80</sup> For example, more objective diagnostic measures (e.g., fMRI and event-related brain potentials) can limit demand characteristics and reduce socially desirable responses; this strategic shift will move the field toward increasingly reliable, valid, and clinically meaningful diagnoses. Unfortunately,

because “the genetic complexity and the early state of the neuroscience of mental disorders means that a satisfactory understanding of the molecular basis for mental disorders is still many years in the future,”<sup>80</sup> an objective diagnostic standard is not close at hand. Nevertheless, the development of more objective diagnostic tests is an important goal that will eventually help limit the use of unnecessary clinical resources and reduce the application of treatments inappropriate for individuals at certain stages of the addiction syndrome.

At this time, the neurobiological and psychosocial antecedent evidence for the syndrome model is strong; however, many important aspects of the model remain undertested. For example, research on hopping between chemical and behavioral addictions, temporal patterns of psychiatric comorbidity (e.g., sign, symptom, and disorder patterns), and treatment nonspecificity is limited. Similarly, there is a paucity of research involving secondary behaviors and object-specific natural history; both of these areas of research are essential to advancing an addiction syndrome model.

Rethinking addiction as a syndrome also holds many direct implications for treatment. About 80 to 90% of individuals entering recovery from addiction will relapse during the first year after treatment.<sup>60,61</sup> This circumstance might be due, in part, to the prevalent use of focused object-specific treatment approaches despite research suggesting that objects of addiction cannot sufficiently account for the dominant underpinnings of addiction. From the syndromal perspective, the most effective addiction treatments are multimodal “cocktail” approaches<sup>81</sup> that include both object-specific and addiction-general treatments. High relapse rates might also be explained by vulnerabilities and neurobiological changes exacerbated by addiction; consequently, new manifestations of the syndrome can appear during the course of the addiction. The syndrome model of addiction encourages clinicians to recognize that patients develop new risk factors during treatment—which can interfere with recovery efforts. This model requires clinicians to develop multidimensional treatment plans that account for the many relationships among the multiple influences and consequences of addiction. Viewing addiction as a syndrome also obligates providers to assess repeatedly the impact of these relationships on relapse, addiction hopping, the course of the illness, and many other treatment-related outcomes.

Finally, with its emphasis on etiology, an addiction syndrome model encourages the use of diagnostic “gates.”<sup>82</sup> Gated diagnosis requires clinicians to identify certain central features of the syndrome (e.g., signs of withdrawal accompanied by premorbid characteristics), without which a diagnosis should not be made. Gates would be applied similarly across both substance and behavioral addictions. This etiologic strategy is different from the current

multidimensional consensus approach that tends to give equal weight to the relevant diagnostic criteria. Instead, a gated diagnostic system attributes unequal and hierarchical value to the diagnostic criteria involved.

Despite the evidence supporting a syndromal view of addiction, the dominant clinical philosophy continues to focus on the “addictive” nature of chemicals, yielding unnecessarily narrow treatment protocols. Since evidence for the efficacy of many pharmacological and psychological non-object-specific treatments for addiction already exists,<sup>82</sup> perhaps our existing treatments are more advanced than our addiction philosophy. This discrepancy between theory and practice might inadvertently contribute to less than optimal treatment outcomes, given that conventional wisdom discourages clinicians from paying sufficient attention to the underlying core of addictive behaviors. Further, because the therapeutic boundaries of various addiction treatments are unknown, clinicians might overlook effective chemical-addiction treatments for behavioral addictions and useful behavioral treatments for chemical addictions. Ultimately, improving treatment outcomes for addiction might be achieved primarily by revising and reordering existing clinical activities and developing new, unobtrusive diagnostic tools. This observation leads to the interesting and promising conclusion that the necessary tools for improving addiction treatment might be already available. All that is required to enhance the use of these devices is a rethinking of addiction.

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