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Review article

Biological Contributions to Addictions in Adolescents and Adults: Prevention, Treatment, and Policy Implications

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A B S T R A C T

Purpose: Despite significant advances in our understanding of the biological bases of addictions, these disorders continue to represent a huge public health burden that is associated with substantial personal suffering. Efforts to target addictions require consideration of how the improved biological understanding of addictions may lead to improved prevention, treatment, and policy initiatives.
Method: In this article, we provide a narrative review of current biological models for addictions with a goal of placing existing data and theories within a translational and developmental framework targeting the advancement of prevention, treatment, and policy strategies.
Results: Data regarding individual differences, intermediary phenotypes, and main and interactive influences of genetic and environmental contributions in the setting of developmental trajectories that may be influenced by addictive drugs or behavior indicate complex underpinnings of addictions.
Conclusions: Consideration and further elucidation of the biological etiologies of addictions hold significant potential for making important gains and reducing the public health impact of addictions.

Over the past several decades, substantial research has investigated the biological factors leading to and resulting from addictions [1,2]. The findings emanating from this work are vitally important if we are to continue to make inroads against addictions, particularly with respect to improving prevention and treatment strategies [3]. Despite significant efforts, excessive patterns of alcohol, tobacco, and other drug use have been estimated to cost the United States alone >$400 billion annually [4]. Worldwide, addictions are prevalent, and low- and middle-income countries may not have the resources to adequately address these disorders [5,6]. The impact of addictions typically is widespread, with some estimates indicating seven people being affected for each identified addicted individual, and there often exist substantial social consequences [7]. Addictions may influence employers and families, and the impact may be felt transgenerationally as parents with addictions may neglect children or model unhealthy behaviors [8]. Certain developmental groups, particularly adolescents and young adults, may be particularly vulnerable to developing addictions, as specific brain regions, specifically those involved in exerting behavioral control, typically mature less rapidly than do brain regions involved in promoting motivated behaviors like substance use [9,10]. Consistent with this notion, adolescents and young adults as compared with children and older adults have high rates of addictions [11]. As biological studies identify specific brain pathways and chemicals that may underlie specific aspects of addictions and addiction vulnerability [12], the knowledge gained holds significant potential to advance prevention, treatment, and policy interventions.

Boundaries of Addiction

Before embarking on a discussion of the biological factors contributing to addiction and addiction vulnerability, it is impor-

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tant to consider which disorders are encompassed by the term "addiction." Historically, there has been variation in the application of the word. "Addiction" is derived from the Latin verb addicere meaning "bound to" or "enslaved by," and in its original usage was not associated with substance use behaviors [13]. Dating back several hundred years, the term became linked to excessive patterns of alcohol use and later to excessive patterns of drug use such that by the 1980s, there was apparent consensus among some groups of experts that addiction could be defined as "compulsive drug use" [14]. However, over the past 15 years or so, there has been a debate as to whether excessive participation in nondrug behaviors like gambling, eating, sex, shopping, Internet use, and video gaming, to name several, might be considered addictions [15–17]. All of these domains appear to hold relevance to adolescents, as rates of problem and pathological gambling have been estimated to be two- to fourfold higher in adolescents than adults; problematic gambling, shopping, and Internet use have each been associated with adverse measures of health and functioning in adolescents; and obesity rates have risen dramatically in youth over the past several decades [17–22]. In addition, these behaviors may follow developmental frequencies similar to substance use behaviors, with high rates of use and addiction in adolescence and early adulthood and lower rates in older adulthood [11,23]. Among adolescents, it also appears important to consider levels of engagement that fall short of addiction, as subsyndromal engagement has been associated with immediate and longer-term adverse measures of health and functioning [18,24,25]. The unique characteristics of adolescents as compared with adults (e.g., more likely to have primary emphasis on school as compared with work, more likely to be influenced by parental monitoring, less likely to have head-of-household obligations, less likely to seek treatment for these behaviors, and less likely to have large sums of money to support engagement in addictive behaviors) also warrant consideration and may explain some differences in frequencies (e.g., with respect to compulsive shopping behaviors) in adolescents versus adults [26,27].

The debate over what behaviors, and the level of engagement in such behaviors, might be considered as addictions has involved consideration of the core components of addiction [23,28]. One proposition is that central features of addiction include continued engagement in a behavior despite adverse consequences, diminished control over participation in the behavior, compulsive participation, and a craving or appetitive urge state immediately preceding engagement in the behavior [23,29]. If one adopts these features as the defining aspects of addiction, then nonsubstance behaviors like gambling might be considered within an addiction's framework. Consistent with this notion, pathological gambling is being proposed for categorization together with substance use disorders in a "Substance Use and Addictive Disorders" category in the *Diagnostic and Statistical Manual of Mental Disorders-5* [30]. Such a definition for addiction and such groupings could substantially increase the estimated costs of addictions to society. For example, if foods and food consumption might be considered addictive [31], the costs to society could increase tremendously given the high prevalence estimates of obesity and the associated health costs related to type 2 diabetes, hypertension, heart disease, and other obesity-related conditions [32]. The consumption of energy drinks and other caffeinated beverages may also be considered within an addiction framework, and this may be particularly relevant to adolescents given their patterns of consumption of these drinks [33].

It should be noted that although many of the common substances of abuse (tobacco, alcohol, and cannabis among the most common, with a recent increase in prescription medication abuse in some countries like the United States) show patterns of initiation and escalation of use during adolescence, food consumption follows a different pattern. That being said, many of the features that might converge to make adolescents vulnerable to addiction (maturation and associated hormonal and other biological changes, greater independence, greater access to addictive substances/materials, emerging nonaddiction psychopathology) may represent factors associated with altered eating behaviors and obesity.

Biological Models of Addiction

Multiple biological models have been proposed to understand addictions and addiction vulnerability, and many of these models are complementary and not mutually exclusive. As an extensive review of each of these models is beyond the scope of this article, interested readers are directed to the references cited for additional aspects of each model. In addition, theories of addiction as related to current neurobiological understandings are reviewed in chapters 2–5 of reference [34].

Early reward-centric models focused on pleasurable aspects of taking drugs and proposed that drugs may "hijack" brain circuits involved in responses to "natural" rewards like sex or food [35,36]. A central component in this circuitry is the nucleus accumbens located in the ventral striatum and receiving dopaminergic innervation from the ventral tegmental area (termed the mesolimbic dopamine system). This nucleus accumbens has at times been termed the brain's "reward center," given that all known drugs with abuse potential, as well as natural rewards, lead to dopamine release in this structure [37,38]. However, a broader range of neurotransmitters (including opioids, cannabinoids, serotonin, norepinephrine, acetylcholine, glutamate, and γ-aminobutyric acid [39–41]) contributes to addiction, and molecular entities (receptors, transporters) for sensing these neurotransmitters are expressed in specific brain regions (e.g., Figure 1 in reference [41]). Recent studies suggest that the functions of the nucleus accumbens and dopamine function therein are more complex and involve learning (particularly reward based) and reward anticipation and valuation, salience attribution (i.e., assigning degrees of relevance to items, decisions, or behaviors), as well as loss processing [1,36]. Consistent with a role for rewarding effects of drugs in addictive processes and a role for dopamine in this process, an incentive salience model of drug addiction proposes that "liking" a drug may be separated from "wanting" [42,43]. Another reward-based model suggests a "reward deficiency syndrome" in which individuals with addictions seek out and engage in addictive behaviors to compensate for hypofunctioning reward signals in the mesolimbic dopamine pathway [44]. In contrast to the incentive salience model, the reward deficiency model may be particularly relevant to self-medication theories of addiction [45,46]. Despite their differences, these two models share some theoretical consistency with other motivational theories like the "IRISA" (impaired response inhibition and salience attribution) and others detailed later in the text that describe behavioral and biological differences in transitions from initial, sporadic to regular, habitual use of drugs [2,47,48]. Specific brain regions or circuits may be particularly