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Neurobiology of Adolescent Substance Use and Addictive Behaviors: Prevention and Treatment Implications

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Abstract

Psychoactive substance and nonsubstance/behavioral addictions are major public health concerns associated with significant societal cost. Adolescence is a period of dynamic biologic, psychological, and behavioral changes. Adolescence is also associated with an increased risk for substance use and addictive disorders. During adolescence, developmental changes in neural circuitry of reward processing, motivation, cognitive control, and stress may contribute to vulnerability for increased levels of engagement in substance use and nonsubstance addictive behaviors. Current biologic models of adolescent vulnerability for addictions incorporate existing data on allostatic changes in function and structure of the midbrain dopaminergic system, stress-associated neuroplasticity, and maturational imbalances between cognitive control and reward reactivity. When characterizing adolescent vulnerability, identifying subgroups of adolescents at high risk for addictive behaviors is a major goal of the addiction field. Genetics, epigenetics, and intermediate phenotypes/endophenotypes may assist in characterizing children and adolescents at risk. Improved understanding of the neurobiology of adolescence and addiction vulnerability has the potential to refine screening, enhance prevention and intervention strategies, and inform public policy.

Keywords

adolescence; neurobiology; addictive behaviors; substance use; development

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Introduction

Adolescence is marked by dramatic biologic, psychological, and behavioral changes, including (1) physical maturation and puberty, (2) identity formation and individuation, (3) increased independence and responsibility, (4) increased salience of social and peer interactions including romantic interests, and (5) increased exploratory behavior.[1] Although adolescence is one of the healthiest periods with regard to acute and chronic diseases, it is also associated with a 2- to 3-fold increase in morbidity and mortality compared to childhood and adulthood.[2] The primary causes of death during adolescence include motor vehicle crashes, suicides, and homicides. All are related to cognitive control and impulsive/risky behaviors that may be exacerbated by substance use.

Recent studies suggest that more than 80% of adolescents experiment with drugs or alcohol before adulthood.[3] Psychoactive drug initiation, progression into more severe use patterns, and dependency rates peak during adolescence and young adulthood, and adolescents have higher rates of substance use and addictive disorders compared to children and older adults.[4] Early use of psychoactive drugs robustly predicts later drug addiction, psychopathology, and deficits in social and occupational functioning.[5, 6] Similar to substance use, other appetitive behaviors are also elevated during adolescence and, in some individuals, may represent nonsubstance/behavioral addictions.[7] Understanding the neurobiologic basis of addiction may facilitate identification of teenagers who are at risk for addiction and its associated health consequences and promote development of effective treatment and prevention strategies. Additionally, understanding the neurobiologic basis of addiction in adolescence may inform policy and public health initiatives relevant to this developmental period.

In this article, we examine the neurobiologic correlates of substance use and addictive behaviors during adolescence and different biologic models of addiction. We discuss biologic risk factors for drug initiation and progression to addiction in adolescence and the neurotoxic effects of specific drugs. Finally, we review implications for treatment, prevention, and policy.

Addictions: Substance and Non-substance/Behavioral

Addiction comes from the Latin *addicere* meaning “enslaved by” or “bound.”[8] Central features of addiction include compulsive engagement in a behavior (eg, drug use), a craving or appetitive urge state immediately preceding engagement in the behavior, diminished control over the behavior, and continued engagement in the behavior despite adverse consequences.[9] Significant debate continues over whether the term *addiction* should be expanded to include nonsubstance appetitive behaviors that are compulsive or excessive in nature. Nonsubstance appetitive behaviors (eg, gambling, eating, sex, shopping, Internet usage, and video gaming) share commonalities in their rewarding properties and propensity for habit formation similar to those of psychoactive substances.[7] Although most people gamble, use the Internet, play video games, and shop adaptively, in a subgroup of people, particularly those with poor impulse control, these activities may constitute behavioral/nonsubstance addictions with associated adverse consequences.[7]

These appetitive behaviors in adolescence may follow parallel developmental trajectories to psychoactive substance use behaviors, with elevated rates of engagement and addiction in adolescence compared to adulthood. Rates of problem and pathologic gambling are 2- to 4-fold higher in adolescents compared to adults, and problematic video gaming, Internet usage, and shopping all have been found to occur in adolescents and are associated with adverse measures of health and functioning.[10–13] Obesity rates among children and adolescents also have risen dramatically over the past several decades, driven in part by overconsumption of palatable foods.[14] Furthermore, the levels of engagement in appetitive behaviors and substance use may be important, especially in adolescence, when subsyndromal levels of engagement that do not meet full threshold for an addiction are still associated with impairments in health and functioning.[15]

Biological Models of Addiction

Multiple biologic models may explain substance use and addictive disorders and vulnerability to addictions.[9] Most models are not mutually exclusive but rather are complementary; they examine different facets of addictive behaviors, especially as they relate to dopaminergic circuits. The mesolimbic dopaminergic system is a neural circuit involving the nucleus accumbens (located in the ventral striatum), which receives dopaminergic inputs from the ventral tegmental area.[16] This neural circuit is a common neural pathway of reward. Activity with dopamine release in the nucleus accumbens is associated with reward responsiveness to both substance-related rewards (eg, cocaine) and “natural” rewards (eg, sex, video gaming).[17] Reward-centric models of addiction have focused on reward processing and the reinforcing aspect of drug using. One model posits that repeated exposures to a drug or appetitive behavior in susceptible individuals may prime these neurocircuits and shift the hedonic set-point (allostatic loading).[18] Thus, over time addictive behaviors may “hijack” the brain’s natural reward system, in effect making it more responsive to the primary drug of abuse and less responsive to other “natural” reinforcers/rewards.

Dopamine is not the only neurotransmitter of importance, nor is the midbrain dopaminergic system the only brain region of importance to addiction models. Addictive disorders are associated with dysfunction in the expression and function of a broad range of neurotransmitters and neuropeptides, including glutamate, gamma-aminobutyric acid (GABA), serotonin, norepinephrine, and acetylcholine, as well as corticotrophin-releasing factor, opioids, cannabinoids, oxytocin, vasopressin, and neuropeptide Y.[19] Different brain regions also have been linked to different stages of the addiction cycle (see Fig. 1).[9]. Whereas the midbrain dopaminergic system and associated dorsal striatum seem to be relevant to binging and intoxication, stress-related neurocircuitry encompassing the extended amygdala (bed nucleus of the stria terminalis, central nucleus of the amygdala) and the central and peripheral noradrenergic systems seem to be relevant to negative affect and withdrawal states. Prefrontal cortex (PFC) (orbitofrontal, medial prefrontal, anterior cingulate), basolateral amygdalar, insular, and hippocampal contributions are linked to craving states.

Recent studies have sorted psychological components of reward processing into domains of reward anticipation and valuation, reinforcement learning, salience attribution (ie, assigning degree of relevance to stimuli), and loss/punishment processing.[20–22] Berridge and Robinson[20] proposed an incentive salience model of addiction, which suggests that "liking" (the affective response of experiencing pleasure) and "wanting" (stimulus-driven incentive motivation) can be dissociated anatomically and chemically. The "reward deficiency syndrome" is another reward-centric model of addiction vulnerability positing that hyporesponsiveness of the midbrain dopaminergic system may lead individuals at risk for substance dependence and addictive disorders to seek out and engage in addictive behaviors in order to compensate for underarousal.[23] The reward deficiency model is consistent with self-medication theories of addiction.[24] Different biologic models may explain temporally dissociated components of the addiction cycle. For example, preadolescent hypoactive dopamine signaling ("reward deficiency") may lead to earlier onset of drug use, and repeated drug exposures during adolescence may lead to drug-induced "priming" of reward circuitry and progression to dependence. These biologic components contribute to vulnerability at different developmental stages.

Motivation is a process that initiates, guides, and maintains goal-oriented behaviors.[25] Motivation-based models of addiction incorporate elements of motivation, cognitive control, and decision-making. They posit that addictive disorders may represent misdirected motivation in which relatively greater priority is given to appetitive behaviors, such as drug use, and less is given to other behaviors such as work, school, and family care.[26–28] Thus, the motivation to engage in appetitive behaviors "overpowers" other motivational goals. These models incorporate the neuroeconomic concept of temporal discounting: the selecting of smaller immediate rewards over larger delayed rewards. These decisional pathways are associated with discrete brain regions and circuits.[29] Biologically, the choice of smaller immediate rewards seems to be associated with activity in the ventral striatum and ventromedial PFC. In contrast, the choice of larger delayed rewards seems to be associated with dorsal prefrontal regions, although the subjective value of the immediate or delayed reward may influence neural response.[29, 30] Differences in temporal discounting can be found across and within developmental stages, according to severity of addiction. Adolescents are more likely than adults to choose smaller immediate rewards over larger delayed rewards (ie, discount rewards more rapidly).[31] Adults and adolescents with addictive disorders discount rewards more rapidly than do age-matched controls.[29, 32, 33]

These findings highlight the importance of cognitive control and executive functioning in risk/reward decision-making. Developmentally, the PFCs (the brain regions particularly relevant to exerting "top-down" cognitive control) are among the last brain regions to reach maturation (often not occurring until young adulthood), and this may contribute in part to the specific vulnerability of adolescents to addictions, risk behaviors, and other forms of psychopathology.[1]

Adolescent Brain Development and Addiction Vulnerability

Dynamic shifts in brain morphology, fiber architecture, and biochemistry occur during adolescence. Neurodevelopmental morphology studies indicate that gray matter volume and

cortical thickness follow an inverted parabolic curve across the lifespan, with a peak occurring in early adolescence (ages 12–14 years) followed by a decline.[34–36] Regional brain morphology shows temporal variance. It follows a caudal-to-rostral pattern, with maturation occurring in the occipital and sensorimotor cortices and striatum at an earlier stage of development than the PFC and association cortices, which are among the last to reach adult levels (see Fig. 2).[35, 37, 38] In contrast to gray matter volumes, white matter pathways show more linear growth and fiber tract enhancement across adolescence, and they reach a plateau in adulthood.[39–41] More recently, diffusion tensor imaging (DTI) has permitted in vivo assessments of white matter architecture by relying on diffusion of water molecules through fiber tracts.[42] Fractional anisotropy (FA), a DTI variable that describes the directional variance of motion, provides an index for fiber tract organization and integrity. FA increases during adolescence and young adulthood, with the most robust changes occurring in the tracts of the superior longitudinal fasciculus, superior corona radiate, thalamic radiations, and posterior limb of the internal capsule.[40, 41, 43] Parallel to the temporal lag of gray matter decline, frontotemporal white matter tracts seem to mature at a later stage in development.[44, 45] Multiple biochemical changes that also occur during adolescence include alterations in dopaminergic and GABAergic neurotransmitter systems and pubertal maturation with its associated neuroendocrine changes.[46–49]

Different neurodevelopmental models postulate why adolescents are prone to experimenting with drugs and alcohol and engaging in other risky behaviors. A developmental imbalance between “top-down” cognitive control systems and “bottom-up” incentive-reward systems has been proposed.[26, 50, 51] The ability to resist temptation in favor of long-term goal-oriented behavior is one form of cognitive control.[52] Cognitive control improves in a relatively linear fashion from childhood through adulthood and is associated with maturation of the dorsolateral PFC and anterior cingulate, which are components of a “top-down” executive system.[34] A “bottom-up” subcortical system, including the striatum and midbrain dopaminergic system, is important in reinforcement learning and matures at an earlier stage of development than a “top-down” system.[34, 35, 50] Taken together as a circuit, the imbalance between immature “top-down” cognitive control processes and mature (and possibly hyperactive) “bottom-up” incentive-reward processes during adolescence may allow incentive modulation to supersede cognitive control, leading to increased susceptibility to the motivational properties of psychoactive substances and appetitive behaviors. [50]

A triadic model explains adolescent addiction and risky behavior involving the interface of 3 neurobiologic systems: a control/regulatory system involving the medial and ventral PFCs; a reward (approach) system involving the ventral striatum and midbrain dopaminergic system; and a threat (harm-avoidance) system involving the amygdala.[51] In this model, an inefficient regulatory system, a strong reward system, and a weak harm-avoidance system contribute to increased engagement in substance use and other risky behaviors. [51] Another developmental model of motivation neurocircuitry separates the brain into primary and secondary motivational neurocircuits.[26] The primary neurocircuit involves the PFC, striatum, and thalamus (including cortico-striatal-thalamic-cortical loops) and subserves neural processes of decision-making and the selection of discrete goal-oriented behaviors, including those seen in addictions.[26] This model of appetitive and motivated behavior is applicable to both

substance and nonsubstance addictions.[26, 53] The primary motivational system influencing motivated decision-making is supported by a secondary motivational neurocircuitry that provides multimodal inputs from other brain circuits (sensory, affective, memory, hormonal/homeostatic).[26] Multiple factors likely influence vulnerability to drug use and addictive behavior; they include internal states (eg, emotional distress) and external influences (eg, peer influence, access, media, parental monitoring).[54] Consistent with this model, the interaction of brain regions that modulate the relationship between the primary reward neurocircuitry and different cognitive processes may be dysfunctional in individuals with addictive disorders and in vulnerable at-risk adolescents. These regions include the amygdala in affective states,[55, 56] hippocampus and temporal cortices in memory,[56] hypothalamus and septum in homeostatic processes (hunger, thirst),[57] and the insula and parietal cortex in sensing physical and somatic states and attention.[58] Because these "bottom-up" secondary motivational systems mature at different temporal rates, their relative influence on the primary motivational systems changes across the lifespan. Thus, during adolescence, when these maturational imbalances are the greatest, adolescents may not be able to regulate motivational or emotional states in the same way as adults, which may explain the onset and elevated rates of both addictive and affective disorders during this developmental period.[26, 50, 51, 59]

Controversy remains as to how reward processing and midbrain dopaminergic functioning contribute to addiction vulnerability and addictive disorders in adolescence and whether hyper- or hypo-activation of dopamine functioning conveys risk.[20, 60–62] Some studies of typically developing adolescents have demonstrated increased reward responses in the striatum,[63, 64] whereas others have shown diminished activation.[65, 66] Similar to adults with addictive disorders, adolescents who meet criteria for substance use and addictive disorders show diminished ventral striatal activation during reward anticipation compared to matched controls.[67–69] Similar patterns of ventral striatal hypo-activation apply to impulsivity and risk-taking in adults and adolescents with addictive disorders.[70] These conflicting results underscore the importance of examining individual differences within adolescents. Whereas adolescents in general may express hyperactivation of ventral striatal circuitry during reward processing, those who demonstrate blunted striatal responses may be more vulnerable with respect to development of addictive disorders.[70]

When considering adolescent vulnerability to addictive disorders, the extent to which findings suggest normal development versus aberrant development or "pathology" currently is unknown. However, behaviors considered developmentally appropriate or normative during adolescence (eg, drug experimentation and risk-taking behaviors) are associated with negative outcomes and real-life measures of adverse functioning.[71, 72] Thus, although considered normative, these behaviors are not without individual, familial, and societal cost. Future research should aim to characterize neural substrates that individually predict why some teens but not others are vulnerable to developing substance use and addictive disorders in order to develop targeted interventions and preventions for specific at-risk subgroups.

Affect of Drug Exposure or Addictive Processes on Brain Structure and Function

Characterizing differences in brain structure and function among adolescents is complicated, especially among those who are using alcohol and other drugs. Biologic changes may represent part of normal development,[34, 73] relate to addictive processes,[26, 74] or reflect neuroadaptation or neurotoxicity related to recent or long-term drug or alcohol exposure that may or may not be central to addictive processes.[75] Further complicating these findings are differences in samples and study design and other confounding variables, such as comorbid psychiatric disorders and polysubstance use, both of which are the norm rather than the exception in adolescents with addictive disorders.[76]

Animal models suggest that the brain is more vulnerable to the effects of psychoactive substances during adolescence.[77] Adolescent alcohol and cannabis use may differentially affect the developing brain, with substance-related differences found in brain morphology, white matter integrity, and activation during cognitive tasks.[78] Among adolescents, differing levels of engagement ranging from alcohol use disorders (AUDs) to binge-pattern drinking for as few as 1 to 2 years have been associated with structural and functional deficits. Alterations have been found in white matter and in regional brain morphology in the hippocampus, PFC, corpus callosum, and cerebellum of adolescents who use alcohol and cannabis compared to those who do not.[79, 80] Hippocampal volumes are smaller among adolescents with heavy alcohol use patterns compared to adolescents with co-occurring alcohol and cannabis use and to nonsubstance-using adolescents.[79, 81–83] Smaller hippocampal volume also has been associated with age at alcohol onset and duration of dependence.[79] PFC volume seems to be smaller among adolescents with AUD compared to nondrinking controls, and the findings vary by gender. Female adolescents with AUDs had significantly smaller PFC volumes compared to female nondrinkers, whereas male adolescents with AUDs had significantly larger PFC volumes compared to male nondrinkers.[80] No differences in PFC volume were observed between adolescent cannabis users and nonusers.[84] Among adolescent cannabis users, the cerebellar vermis was significantly larger than that in matched control subjects.[84] Using DTI techniques, binge-drinking and alcohol-using adolescents demonstrated lower FA than control subjects across multiple white matter pathways, including the corpus callosum, superior longitudinal fasciculus, corona radiata, internal and external capsules, and commissural, limbic, brainstem, and cortical projection fibers.[85–87] Cannabis use among adolescents was associated with lower FA in the superior longitudinal fasciculus, postcentral gyrus, and inferior longitudinal fasciculus compared to control subjects[86, 88] but was associated with increased FA compared to binge-drinking adolescents.[86] Neurocognitive deficits can be found in alcohol- and cannabis-using adolescents across the domains of attentional, visuospatial, and speeded information processing, memory, and executive functioning.[84, 89–91] Using functional magnetic resonance imaging techniques, activation patterns during go/no-go, spatial working memory, and word-pair learning tasks differentiated adolescents who use cannabis and alcohol from those who do not.[92–94] These structural and functional abnormalities seem to occur across brain regions that subserve

neuropsychological capacities (ie, hippocampus: memory; PFC: executive functions, planning).

Many of these studies are cross-sectional and preclude the ability to draw causality. Longitudinal studies in adolescents with carefully assessed measures of substance use that control for comorbid psychiatric disorders and co-occurring substance use will help to further clarify the extent to which group differences may reflect preexisting characteristics of at-risk youth compared to the sequelae of exposure to specific substances. Recent longitudinal studies suggest that differences in PFC morphology and hypo-activation of PFC during response inhibition in adolescents is associated prospectively with progression to heavier alcohol and drug use.[95–98]

Additionally, possible interactions between developmental stage and drug exposure should be considered. During adolescence, vulnerability windows may exist during which exposure to psychoactive drugs is more likely to affect long-term functioning.[99] Earlier age at onset of alcohol, cannabis, and other drug use has been associated with increased addiction severity and poorer outcomes. Animal models suggest that exposure to psychoactive substances during adolescence increases the risk for addictive behaviors by priming the reward system and making it more responsive.[100] Exposure to psychoactive substances during adolescence also seems to affect pursuit of “natural rewards” and may provide a link between substance and nonsubstance/behavioral addictions.[101]

Genetics, Epigenetics, and Environmental Contributions

The complex interface of genetic predisposition and early environmental exposures that predate the onset of drug use and addictive behaviors may generate brain-behavior relationships in adolescence that can promote subsequent vulnerability or protection.[102–104] Also, gene and environmental influences seem to vary across developmental epochs and stages of addiction.[105, 106] Recent studies suggest that initiation and early patterns of drug use are strongly influenced by family and social factors, whereas progression to heavy and compulsive use is strongly influenced by genetics.[105, 106]

Indeed, genetic contributions to addictive disorders are significant, although few studies in adolescents are available. Twin studies suggest that genetic factors account for 30% to 70% of the variance in substance addictions.[107] Emerging evidence also suggests a role for genetic factors in behavioral addictions, including gambling and Internet use disorders, as well as in childhood- and adolescent-onset obesity.[108–111] Genome-wide association studies have implicated several regions and genes in addictive disorders, but studies in adolescents are lacking.[112] Addictive disorders in adults are associated with genes and genetic loci involving a diverse array of neurobiologic processes, including neurotransmitter/neuropeptide transport and function (serotonin, dopamine, and norepinephrine transporters, dopamine receptor 2, mu-opioid receptor), drug metabolism (cytochrome P450 2A6, dopamine beta-hydroxylase), growth factors (brain-derived neurotropic factor), and secondary messenger signaling.[103, 112] A recent study found evidence that a polymorphism of the mu-opioid receptor encoding gene is associated with adolescent alcohol misuse.[113]

Genetic susceptibility to addictions may be classified according to shared/common versus drug-specific genetic vulnerabilities.[107]

In the past decade, epigenetics and gene-by-environment (GXE) interaction studies have examined how the expression of common gene variants and early childhood environmental conditions may affect development of disease.[114] Understanding GXE interactions and how "nature" and "nurture" interact may have relevance for addictions and other psychiatric disorders. For example, a recent GXE study found an interaction between a variant in the gene coding for the corticotropin-releasing hormone receptor 1 (a receptor that contributes to the biologic response to stress) and stressful life events that influence drinking initiation and progression to heavy alcohol use among adolescents.[115] GXE studies also have been used to characterize the effect of adolescent drug exposure on adult functioning and psychopathology. A functional polymorphism of the gene coding for catechol-O-methyltransferase seems to influence the association between adolescent cannabis exposure and development of psychosis in adulthood, with the valine coding allele conveying increased risk.[116] Studies should clearly define the timing of exposure to environmental factors (eg, childhood trauma) in order to better characterize "vulnerability windows," especially in the context of dynamic brain changes that occur across childhood and adolescent development.[114]

Prevention, Treatment, and Policy Implications

Understanding the neurobiology of addiction vulnerability and addictive disorders in adolescents holds significant promise for improved prevention and treatments and for alterations in public policy. For example, such information could aid in the development of novel pharmacotherapies using intelligent drug designs that target specific neurotransmitter systems, neural regions and circuitry, receptor sites, and secondary messenger systems; additional avenues may involve gene therapies and drug vaccines.[117] Dopamine-blocking agents have shown limited efficacy and may exacerbate some nonsubstance addictive behaviors.[117, 118] Instead, agents that modulate dopamine signaling within the reward pathways by way of glutamatergic (N-acetylcysteine, acamprosate) and opioid (naltrexone, buprenorphine) receptor systems have shown promise.[117, 119–122] Few of these agents have been examined in adolescents, so studies are needed to clarify the safety and efficacy in adolescent samples.[119–122] Equally important is the common neurobiology of comorbid psychiatric and addictive disorders and the potential effect of concurrent treatment of co-occurring psychiatric disorders and addictive disorders on addiction severity and psychiatric symptomatology. Preliminary evidence from comorbid substance use disorders (SUDs) and major depressive disorder or attention-deficit/hyperactivity disorder suggests that remission of mood and attentional symptoms is associated with reductions in drug use.[123, 124] Finding common neurobiologic targets for drug development may represent another pathway to new psychopharmacologic treatments.

A major challenge for the field of addiction moving forward is developing biobehavioral markers for early identification of vulnerability to substance use and addictive behaviors. Characterizing the biologic factors related to addiction vulnerability compared to the neurotoxic/neuroadaptive effects of drug exposure is key to developing targeted prevention

programs for at-risk youth. Intermediate phenotypes, including delay discounting,[29] impulsivity,[125] and stress-reactivity/responsiveness,[126, 127] warrant consideration as markers for risk. In vivo neuroimaging "challenge" studies involving behavioral challenges that require cognitive control in the presence of appetitive cues or affective stimuli may be useful assays for determining those adolescents who have elevated cognitive control to reward activity imbalance or elevated affective reactivity that potentially conveys enhanced risk for addictive behaviors.[64, 128, 129]

Prevention and interventional strategies should take into account the specific biologic vulnerabilities and strengths of adolescents. Because adolescents are biologically more responsive to rewards and are less responsive to aversive stimuli/losses compared to adults, programs that utilize positive reinforcement rather than punishment or negative reinforcement may be more effective. Rather than trying to eliminate "stimulating" risky behaviors, providing access to exciting activities under controlled settings may help replace or limit harmful risk-taking opportunities.[50] Incorporating contingency management with positive reinforcers (ie, rewards) for prosocial behavior, engagement, and reduction in drug use (ie, negative urine drug tests) has been successfully utilized in treatment of adolescents with SUDs.[130] Alternatively, attempting to enhance cognitive control by cognitive training or cognitive behavioral therapy has been effective for addictive disorders in adolescents.[131–134] Preliminary evidence suggests that the effect of cognitive therapies is related to changes in function/activity in neural circuitry of motivation and cognitive control.[133–134] Recent epidemiologic and phenomenologic data also suggest that adolescent females have different protective factors and risk profiles and may be more likely to abuse illicit substances compared with adolescent males.[135, 136] Thus, clarifying the role of gender in treatment response and development of gender-informed interventions may improve outcomes in adolescents.

Public policy and legislation also should be neurodevelopmentally informed. Tax strategies targeting tobacco products have been an effective deterrent to both adult and adolescent smoking behaviors, and taxation of "hyperpalatable" calorie-dense foods such as sugared sodas warrants exploration.[137, 138] Additionally, limiting sugared sodas and unhealthy food choices in school cafeterias and vending machines may influence obesity rates. Adolescents are arguably "hyperconsumers" of media, and a better understanding of the influence of advertising/marketing of appetitive/hedonic products (eg, alcohol, tobacco, palatable foods) on adolescent addictions is warranted, especially in the realm of nonsubstance appetitive behaviors.[139–141]

Conclusion

Addictive disorders, including both substance and behavioral addictions, remain among the most costly diseases in society, and adolescence is a critical developmental period for protecting the next generation and curbing future social costs. Emerging evidence on the neurobiology of addictive disorders and addiction vulnerability has the potential to advance the field by enhancing prevention and treatment and influencing public policy.

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Abbreviations

SUD substance use disorder

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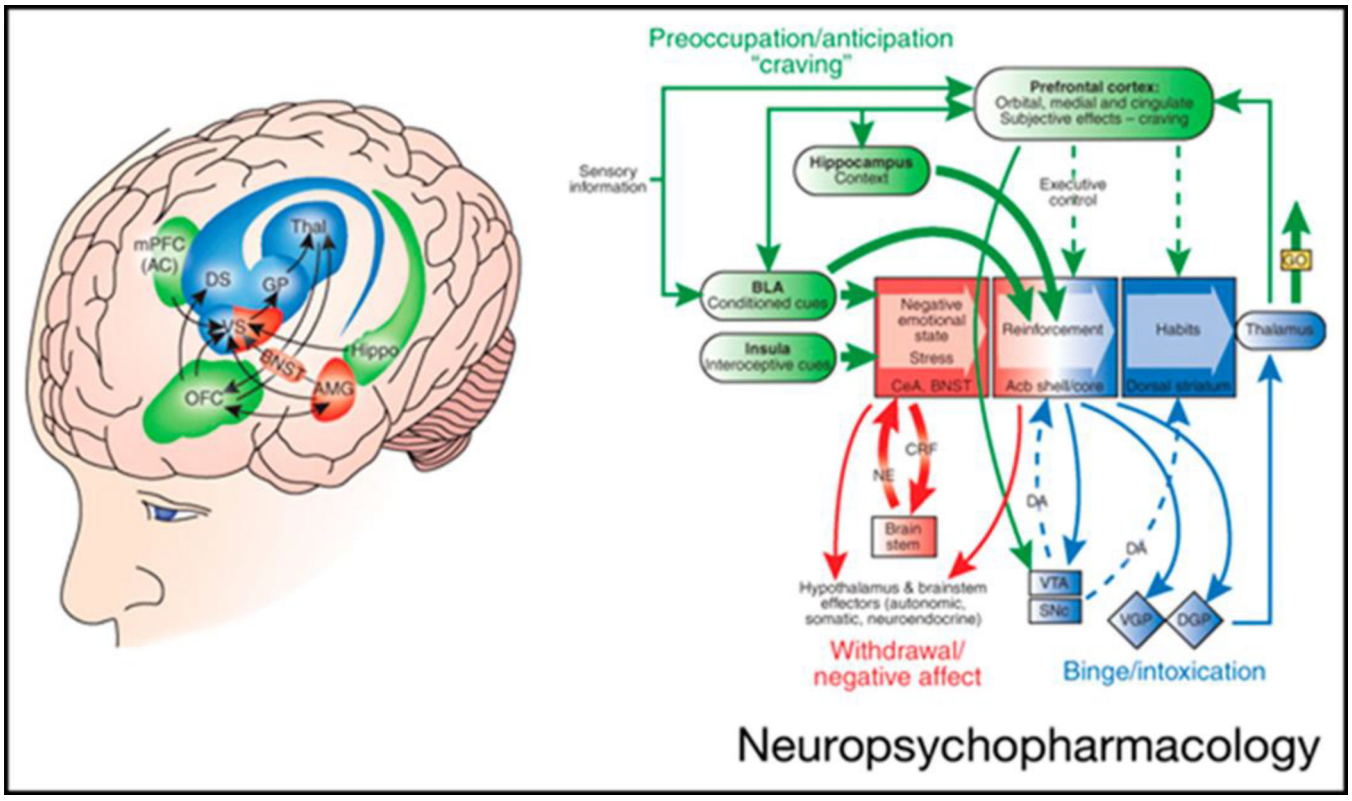

Figure 1.

Neurocircuitry schematic illustrating the combination of neuroadaptations in the brain circuitry for the three stages of the addiction cycle: 1) binge/intoxication; 2) withdrawal/ negative affect; 3) preoccupation/anticipation 'craving'. Figure reproduced with permission from Koob GF,Volkow ND. Neurocircuitry of Addiction. Neuropsychopharmacology (2010), 35, 217–238. Copyrighted ©2013, American College of Neuropsychopharmacology.

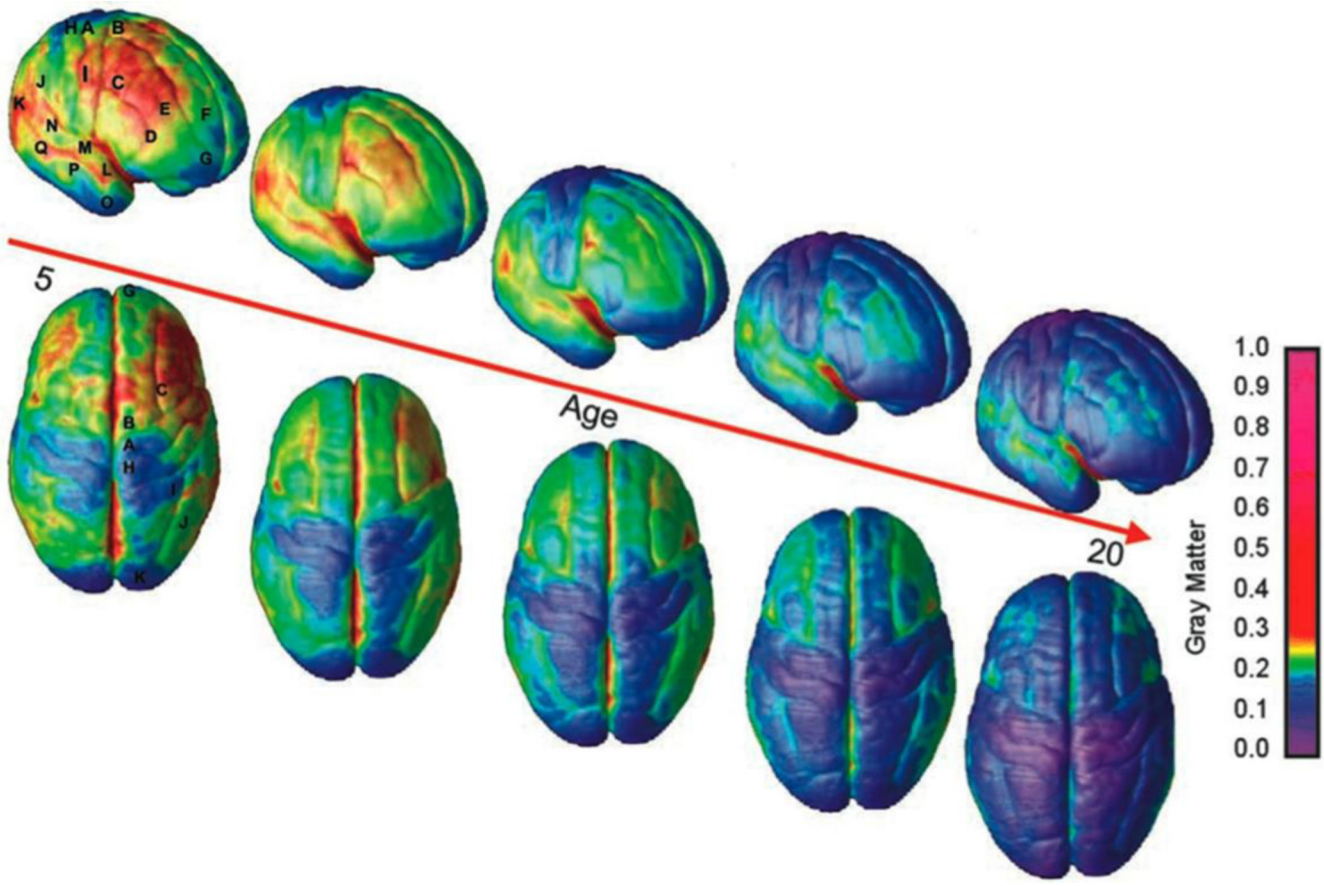

Figure 2.

Dynamic sequence of Cortical Gray Matter (GM) Maturation from childhood through early adulthood from right lateral and top views. The sidebar shows a color representation in units of GM volume. Figure reproduced with permission from Gotay N et al. Dynamic mapping of human cortical development during childhood through early adulthood. Proceedings of the National Academy of Sciences (2004), 101(21), 8174–8179. Copyrighted © 2004, The National Academy of Sciences of the USA.