Current Addiction Reports (2020) 7:89–98
https://doi.org/10.1007/s40429-019-00282-y

ADOLESCENT / YOUNG ADULT ADDICTION (M HEITZEG, SECTION EDITOR)

Identifying Early Risk Factors for Addiction Later in Life: a Review of Prospective Longitudinal Studies

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Published online: 12 December 2019

Abstract

Purpose of Review To review prospective longitudinal studies that have identified risk factors for the development of substance use disorders in adulthood from individual differences during childhood and adolescence.

Recent Findings Risk factors during childhood and adolescence that have been consistently linked to increased risk for addiction include externalizing and internalizing symptoms, early substance use, and environmental influences, such as parental behavior and exposure to traumatic experiences.

Summary Since the etiology of substance use disorders is complex and likely is attributable to many causal pathways, systematic examination of the associations between risk factors will be necessary to understand the mixed findings in the existing literature, to determine which individuals should be targeted for prevention efforts, and to design interventions that address risk factors that are most likely to improve outcomes.

Keywords Substance use disorders · Predictors · Developmental · Psychiatric · Drug use

Introduction

Substance use disorders are associated with many personal and societal costs. For example, alcohol and tobacco use alone were linked to 568,000 preventable deaths in the US every year from 2006 to 2010 [1, 2], and the financial costs of substance use (e.g., health care, crime) are estimated to be around $740 billion per year [1, 3–7]. Furthermore, treatment for substance use disorders is challenging, with the majority of individuals requiring multiple interventions before achieving stable abstinence [8, 9]. One strategy to reduce the negative consequences associated with substance use is to identify risk factors for the development of substance use disorders that can inform prevention efforts. Prospective longitudinal studies have the potential to provide important information about the complex pathways that lead to the development of substance use disorders; unlike cross-sectional studies, they can use temporal information to disentangle causes from consequences and are less likely to be biased by temporal delay, as is the case in many retrospective studies relying on self-report.

Although many studies have examined factors that predict the quantity of substance use, most people engage in some alcohol and drug use during their lifetime without developing a substance use disorder. For example, it is estimated that 86.4% of Americans drink alcohol in their lifetime, while 68.7% use tobacco products and 46.9% use marijuana [10]. However, 30% of adults in the USA will suffer from an alcohol use disorder in their lifetime [11], and the lifetime prevalence of nicotine and other drug use disorders is 27.9% and 9.9%, respectively [12, 13]. These data suggest that there is considerable heterogeneity in the personal and environmental factors that impact the likelihood of developing addiction. While the negative consequences associated with substance use vary along a continuum, individuals with a substance use disorder, as opposed those who engage in substance use, are likely at highest risk of experiencing negative consequences. Therefore, this article reviews prospective

This article is part of the Topical Collection on *Adolescent/Young Adult Addiction*

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longitudinal studies that assess individual differences in childhood and adolescence (< 18 years old) with the *goal of predicting substance use disorders* later in life (> 18 years old). Since meta-analysis improves the power of small or inconclusive studies, if available, we review meta-analyses of prospective longitudinal studies examining risk factors for substance use disorders instead of detailing individual findings. This review examines the evidence suggesting that personal and environmental factors such as psychopathology, personal substance use, parental and peer influence, socioeconomic status, negative life events, and neurobiology impact the likelihood of developing addiction (see Table 1 for a list of the articles included).

Psychopathology

Psychiatric Diagnoses

Diagnosis of a mental health disorder early in life is one of the most extensively studied predictors of future substance use disorders in adulthood. A recent meta-analytic review found that childhood/adolescent diagnosis of attention-deficit/hyperactivity disorder (ADHD), conduct disorder (CD) or oppositional defiant disorder (ODD), and depression was associated with an increased risk for adult addiction [14••]. In this study, ADHD and CD/ODD were associated with increased risk of alcohol, nicotine, other drug use, and any substance use disorder, while depression was associated with an increased risk for alcohol, nicotine, and any substance use disorder [14••]. While not significant in the meta-analysis by Groenman and colleagues [14••], anxiety disorders in adolescence have also been associated with adult addiction, but findings are limited. One study found that social anxiety disorder in adolescence was associated with alcohol and cannabis dependence in adulthood [15], with a stronger effect in women than men [16]. Below, we review the evidence that externalizing and internalizing symptoms are also risk factors for addiction later in life.

Externalizing Behavior

Using parental and adolescent self-reports, studies have demonstrated that greater levels of externalizing behavior in childhood and adolescence are associated with increased risk for alcohol [17] and cannabis [18, 19•, 20] use disorders, as well as symptoms nicotine use disorder [21] in adulthood. Furthermore, specific symptoms of CD in early adolescence, in the absence of a clinical diagnosis of CD or ODD, predicted alcohol dependence in young adult males [22], while greater ODD symptoms in childhood/early-adolescence predicted nicotine, cannabis, and cocaine abuse and/or dependence in young adulthood [23]. Similarly, in youth without an ADHD diagnosis, two studies have found that greater inattentive symptoms in childhood/early-adolescence predicted alcohol, nicotine, and cannabis abuse/dependence in young adulthood [23, 24].

Several studies have also demonstrated associations with more specific externalizing behaviors and addiction in adulthood. Greater misbehavior at school, greater delinquency, deviant behavior, being sexually active, antisocial behavior, and lower perceived consequences of antisocial behavior are all associated with alcohol abuse and dependence in adulthood [24–27]. Similarly, delinquency and aggression in adolescence also predicted cannabis, nicotine, and other drug abuse/dependence in adulthood [24]. Additionally, novelty seeking in adolescence has also been shown to be predictive of alcohol, nicotine, cannabis, and other illicit substance use disorders in adulthood [28, 29]. Lastly, studies using composite scores that include assessments of externalizing symptoms and cognitive functioning during adolescence have shown that neurobehavioral disinhibition is associated with increased risk for substance use disorders in adulthood [30, 31].

Internalizing Symptoms

Similar to externalizing behaviors, internalizing symptoms during adolescence have been linked to a greater likelihood of addiction in adulthood, but perhaps to a lesser extent. Internalizing and more specifically, depressive symptoms in adolescence have been linked to both alcohol dependence and nicotine dependence later in life [33–35]. The associations between depressive symptoms and future substance use disorders may be related to the presence of other risk factors, as depressive symptoms in adolescent males only predicted alcohol dependence in individuals with CD [22]. In contrast, some work suggests that internalizing behavior is inversely associated with cannabis use disorders in adulthood [19•].

Personal Substance Use

Several studies have determined that alcohol and drug use before adulthood is a risk factor for the development of substance use disorders later in life. Research has been conducted to examine whether initiating alcohol use at various age-cutoff points is associated with heightened risk for addiction [36], with one study determining that initiating alcohol use before 11 increased the risk for chronicity of adult alcohol dependence [37]. However, no evidence has been found that later cutoffs are associated with increased risk for alcohol dependence [36, 37]. More recent work suggests that age of the first intoxication is a better predictor of risk for substance use disorder in adulthood, as unlike age of first drink [58]; earlier age of first intoxication is a significant predictor of alcohol use disorder, nicotine, cannabis, and other illicit drug dependence, when controlling for other potential risk factors [38]. Beyond

Table 1 Potential risk factors during childhood and adolescence for substance use disorders in adulthood

Potential risk factor	First author	Year	Sample Size	Relationship between risk factors in childhood or adolescence and adult substance use disorders
Psychopathology				
Psychiatric diagnoses	Groenman [14••]*	2017	22,029	Attention-deficit/hyperactivity disorder ↑ AUD, NUD, other SUD (including cannabis), and any SUD
			434	Oppositional defiant disorder or conduct disorder ↑ AUD, NUD, other SUD (including cannabis), and any SUD
			2451	Major depressive disorder ↑ AUD, NUD, and any substance use disorder (including alcohol, nicotine, and cannabis)
	Buckner [15]	2008	816	Social anxiety disorder ↑ AUD and CUD
	Buckner [16]	2009	1204	Social anxiety disorder ↑ AUD in women
Externalizing behavior	Englund [17]	2008	178	Externalizing ↑ AUD
	Hayatbakhsh [18]	2008	2225	Externalizing ↑ CUD
	Mills [19•]	2017	3778	Externalizing ↑ CUD
	Defoe [20]	2019	364	Conduct problems ↑ CUD
	Fergusson [21]	2007	1265	Conduct problems ↑ cigarette smoking including NUD
	Pardini [22]	2006	506	Conduct disorder symptoms and conduct disorder-by-depression interaction ↑ AUD
	Pingault [23]	2013	1804	Inattention ↑ NUD; opposition ↑ NUD, CUD, and cocaine use disorder
	Hayatbakhsh [24]	2008	2429	Attention problems, delinquency, and aggression ↑ AUD, CUD, NUD, and other SUD
	Guo [25]	2001	808	Misbehavior at school, delinquency, antisocial behavior, being sexually active ↑ AUD
	D'Amico [26]	2005	1986	Deviant behavior ↑ AUD
	Bonomo [27]	2004	1601	Antisocial behavior ↑ AUD
	Foulds [28]	2017	1265	Novelty seeking ↑ AUD, CUD, NUD, and other SUDs
	Palmer [29]	2013	2361	Novelty seeking ↑ AUD, NUD, and other SUDs (including CUD)
	Mezzich [30]	2007	263	Disinhibition ↑ SUD (not specified)
	Tarter [31]	2004	170	Disinhibition ↑ any SUD (excluding nicotine)
	Fergusson [32]	2007	1265	Conduct problems ↑ AUD, NUD, CUD, and other illicit SUD
Internalizing symptoms	Huurre [33]	2010	1471	Depressive symptoms ↑ AUD
	Jester [34]	2019	504	Internalizing ↑ NUD
	Bardone [35]	1998	459	Depressive symptoms ↑ NUD
Personal substance use				
	King [36]	2007	375	Illegal drug use ↑ illicit SUDs
	Guttmannova [37]	2011	808	Alcohol, marijuana, or other illicit drug use ↑ lifetime AUD or chronicity of AUD
	Newton-Howes [38]	2019	1056	Earlier age of first alcoholic intoxication ↑ AUD, NUD, and CUD
	D'Amico [26]	2005	1986	Heaviness of alcohol use ↑ AUD
	Bonomo [27]	2004	1601	Frequent alcohol use ↑ AUD
	Huurre [33]	2010	1471	Drunkenness oriented drinking and cigarette use ↑ AUD
	Guo [39]	2000	808	Earlier and heavier alcohol use ↑ AUD
	Mills [19•]	2017	3778	Alcohol and tobacco use ↑ CUD
	Prince van Leeuwen [40]	2014	1108	Earlier onset and continued tobacco use ↑ CUD
	Swift [41]	2008	1520	Cigarette smoking ↑ CUD
	Brook [42]	2007	475	Early cigarette use ↑ AUD and other SUDs (illicit drugs)
	Strong [43]	2016	1242	Regular cigarette use ↑ SUD (illicit drugs)
	Gil [44]	2004	1273	Experimentation and regular use of substances ↑ any SUD (excluding nicotine)
Environmental influences				
Parental influences	Mezzich [30]	2007	263	Parental SUD ↑ SUD (substances not specified)
	Tarter [31]	2004	170	Parental SUD ↑ any SUD (excluding nicotine)
	King [36]	2007	375	Parental AUD ↑ AUD and other illicit SUD
	Knop [45]	2007	202	Paternal AUD ↑ AUD
	Kosty [46]	2015	719	Parental CUD and other SUD (illicit drugs excluding cannabis) ↑ CUD
	Chassin [47]	1999	454	Parental AUD ↑ AUD and other SUD (substances not specified)

Table 1 (continued)

Potential risk factor	First author	Year	Sample Size	Relationship between risk factors in childhood or adolescence and adult substance use disorders
	Newlin [48]	2000	2301	Stepfather AUD ↑ AUD and any other SUD (excluding alcohol or nicotine)
	Yap [49••]*	2017	6456	Parental alcohol use ↑ alcohol misuse (may include AUD)
			5911	Favorable parental attitudes toward alcohol use ↑ alcohol misuse (may include AUD)
			3048	Parental provision of alcohol use ↑ alcohol misuse (may include AUD)
			22,936	Lack of parent-child relationship quality ↑ alcohol misuse (may include AUD)
			19,618	Lack of parental involvement ↑ alcohol misuse (may include AUD)
			15,673	Lack of parental monitoring ↑ alcohol misuse (may include AUD)
			7561	Lack of parental support ↑ alcohol misuse (may include AUD)
Peer influences	Defoe [20]	2019	364	Peer cannabis use ↑ CUD
	Fergusson [21]	2007	1265	Peer smoking ↑ cigarette smoking including NUD
	Guo [25]	2001	808	Best friends who use alcohol and antisocial peers ↑ AUD
	Prince van Leeuwen [40]	2014	1108	Peer cannabis use ↑ CUD
	Gil [50]	2002	643	Peer substance use and approval of substance use ↑ CUD
	Van Ryzin [51]	2014	998	Deviant peers ↑ AUD, NUD, CUD
Socioeconomic status	Poulton [52]	2002	1000	Socioeconomic disadvantage ↑ AUD and NUD
	Ferguesson [21]	2007	1265	Socioeconomic disadvantage ↑ cigarette smoking including NUD
Negative/traumatic events	Abajobir [53]	2017	2526	Any childhood maltreatment (physical and emotional abuse, neglect) ↑ CUD
	Mills [19•]	2017	3778	Childhood maltreatment ↑ CUD
	Newbury [54]	2017	2232	Childhood maltreatment ↑ AUD and CUD
Neurobiology				
	O'Brien [55]	2017	78	Greater ratio of orbitofrontal-to-amygdala volume ↑ survival time to SUD (including alcohol, nicotine, and cannabis)
	Cheetham [56]	2017	107	Smaller orbitofrontal cortex volume ↑ AUD or CUD
	Hill [57]	2009	133	Lower P300 amplitude ↑ SUD (including alcohol, nicotine, and cannabis)

↑ increased risk for

AUD alcohol use disorder, *NUD* nicotine use disorder, *CUD* cannabis use disorder, *SUD* substance use disorder

*Meta-analysis

age of alcohol use initiation, frequency [24] and heaviness [36, 37] of alcohol use during adolescence [25–27, 33, 39] have also been linked to increased risk for alcohol and other substance dependence during adulthood.

Although less well-studied than alcohol, similar effects have been observed with other drugs. For example, earlier onset of tobacco use and continued tobacco use during adolescence were associated with a higher risk of developing cannabis [19•, 40, 41], alcohol [33], and illicit drug use disorders [42, 43] in young adulthood. Furthermore, frequency of marijuana use during adolescence was also associated with higher rates of adult alcohol [37] and cannabis dependence [41]. It has also been demonstrated that youth who experiment with or regularly use alcohol and/or drugs are at higher risk for developing other substance use disorders in young adulthood than those who abstain during this time of life [19•, 44].

Environmental Influences

Parental Substance Use and Behavior

The existing evidence suggests that having parents with a substance use disorder increases the risk for personal addiction in adulthood [30, 31]. More specifically, parental alcoholism during adolescence has been linked to alcohol and drug dependence in offspring in adulthood [36, 45–47]. Similarly, Kosty and colleagues demonstrated that parental history of cannabis and other illicit drug disorder increased the risk of offspring cannabis use disorder. While having a parent that smoked cigarettes during adolescence was associated with greater risk of personal nicotine dependence in young adulthood, after controlling for internalizing and externalizing symptoms, only the association between maternal smoking and amount of personal cigarette use remained significant [34]. Furthermore, parental history of other illicit substance use disorders also increased personal risk for cannabis use disorder, but there was no significant association between the presence of a parental alcohol use disorder and personal risk for cannabis use disorder. These effects are likely attributable to both genetic and environmental risk factors. It is estimated that 40–60% of the variability in risk for developing alcohol, nicotine, or illicit substance use disorders is attributable to genetic factors, and genome-wide association studies have been able to attribute some of that variability to specific genetic loci [59]. However, adoption studies suggest that the association between parental substance use disorders and personal risk for addiction is also attributable to environmental influences. For example, Nwelin and colleagues demonstrated that individuals with adoptive or step-parents with substance use disorders were also more likely to develop a substance abuse/dependence in adulthood [48], suggesting that these familial associations are not entirely genetic in nature.

There is also research suggesting that subclinical parental substance use and behavior can influence personal risk for addiction later in life. A recent meta-analysis of longitudinal studies examined which modifiable parenting factors measured in adolescence were associated with future alcohol misuse (including alcohol use disorders) in their children. The study determined that subclinical levels of parental alcohol use, favorable attitudes toward alcohol use, and parental provision of alcohol use were associated with future alcohol misuse by their children [49••]. Furthermore, lack of parental involvement, monitoring, support, and parent-child relationship quality were associated with increased risk for alcohol misuse later in life.

Peer Influences

Evidence from longitudinal studies suggests that socializing with peers that are engaging in alcohol and other drug use increases the risk for substance disorders later in life [20, 21, 25, 40, 50, 51], but the directionality of the relationships between peer affiliation and personal substance use remain unclear. For example, deviant peer affiliations in adolescence mediated the association between substance use in adolescence and substance dependence in young adulthood [51]. In contrast, another study found that the association between peer affiliations and future cannabis use disorder was mediated by increased cannabis use, but did not find evidence that cannabis use predicted affiliation with peers who used cannabis [20].

Socioeconomic Status

Studies linking economic disadvantage in childhood and adolescence to risk for adult substance use disorders have produced mixed results. While childhood economic disadvantage has been associated with increased risk for alcohol [52] and tobacco [21, 52] dependence in adulthood, one study found that economic disadvantage during childhood was *less likely* to result in harmful drinking in adulthood in female participants [60]. Some studies have also failed to detect a significant association between socioeconomic status during childhood and/or adolescence and adult substance use disorders [22, 33, 40].

Negative or Traumatic Life Events

Most studies examining the association between negative and traumatic life events in childhood and adolescence and risk for developing an addiction in adulthood have relied on retrospective reports [61]. Studies examining prospectively substantiated childhood maltreatment demonstrated that any childhood

maltreatment, physical abuse, emotional abuse, and neglect predicted cannabis dependence in young adulthood [19•, 53]. Given the evidence that retrospective self-reports of childhood maltreatment might be better predictors of substance use disorders than prospective substantiated-reports [54, 62], it is worth noting that longitudinal studies beginning in childhood or adolescence have found associations between retrospective self-report of childhood adversity [61] or physical abuse [63] before the age of 18 and substance use disorders in adulthood.

Neurobiology

Compared with the wealth of literature using neurobiological assessments during adolescence to predict future patterns of substance use [for review, see [64]], there have been few prospective longitudinal studies that investigate neural predictors of risk for substance use disorders. Further, in contrast to the cohort studies described previously, most longitudinal neuroimaging studies to date have sampled across a large age range at baseline and followed subjects for a relatively short time frame. For example, the ratio of orbitofrontal cortex to amygdala volume during adolescence (ages 8–19) has been associated with substance use disorders several years later (ages 12–27) [55], and less orbitofrontal cortex volume at age 12 has been shown to predict diagnosis of a substance use disorder prior to age 18 [56]. Lastly, one study found that the amplitude of the P300 component of the event-related potential and postural sway (a marker of neurodevelopmental delay) during childhood, but not adolescence, predicted substance use disorders in adulthood [57]. Future studies in this domain are needed to isolate neurobiological predictors occurring specifically in childhood and adolescence (< 18 years of age) that can be used to identify a clinical diagnosis of a substance use disorder in adulthood (> 18 years of age).

Examining the Complex Relationships Between Risk Factors for Addiction

Systematic inclusion of risk factors in prospective studies and careful evaluation of the relationships between risk factors is necessary for understanding heterogeneous findings in the existing literature and identifying the optimal targets for intervention. Existing studies suggest that different risk factors explain unique and overlapping variance in the risk for addiction. For example, Fergusson and colleagues determined that conduct and attentional problems during childhood and adolescence predicted alcohol, cannabis, nicotine, and other drug abuse/dependence in young adulthood using univariate models; however, only the effects of conduct problems remained significant when both predictors were modeled concurrently along with childhood adversity, socioeconomic status, family instability and conflict, parental substance use, childhood abuse, anxiety, and cognitive ability [32]. These findings suggest that conduct problems independently predict future substance use disorders; however, the association between inattention and future substance may be best explained by the correlations between inattention and conduct problems or other relevant personal and environmental risk factors. Although this is a single example, this pattern of results is pervasive in the literature, with many studies reporting significant effects in a univariate analysis that are no longer significant when other personal and environmental risk factors are modeled simultaneously [e.g. [33, 34, 36, 38, 40, 58]]. To begin disentangling the complex relationships between variables, Kraemer and colleagues have proposed methodology for determining whether risk factors are working independently, have overlapping influence, or if one variable is only related to the outcome by proxy of another risk factor [65••]. In the existing literature, the examination of many variables at once, the heterogeneity of the variables selected for inclusion, and only reporting the effects associated with variables of interest hamper our understanding of how different variables work together to influence outcomes. Working toward clarifying these relationships is important, because while proxy variables may be useful for identifying individuals who are at risk for addiction, interventions targeted at proxy risk factors are unlikely to improve outcomes.

Another important step in determining how risk factors work together is to test for mediators that provide evidence for hypothesized relationships between chains of risk factors and for moderators that affect the relationship between other variables [65••]. For example, it has been demonstrated that a latent variable of childhood socioeconomic disadvantage was a better predictor of cigarette use in young adulthood (another latent variable combining nicotine dependence and smoking frequency) than 5 observed variables (e.g., parental education, parental income) [21]. This association was mediated by educational achievement, conduct problems, and exposure to parental and peer smoking in adolescence. Given the temporal precedence of risk factors, these findings are consistent with the hypothesis that early economic disadvantage leads to factors in adolescence that promote risk for addiction in adulthood; however, it is important to note that tests of mediation tests do not prove causation. Furthermore, although the meta-analysis by Groenman and colleagues did not find evidence for an association between anxiety disorders in adolescence and adult addiction [14••], one study found this association was moderated by sex, such that social anxiety disorder in adolescence predicted adult alcohol and cannabis dependence in women but not men [16]. Identification of moderators is important because they highlight which interventions might be appropriate for different individuals.

An alternative technique for examining the complicated relationships between risk factors involves the use of more data-driven statistical machine learning methods approaches that can use a large number of predictor variables and include higher order interactions between predictors in statistical models (e.g., random forest, support vector machine learning). Although, to our knowledge, statistical machine learning has not been utilized to predict *substance use disorders* in adulthood from childhood and adolescent risk factors, these approaches have been used to predict binge drinking [66] and moderate/heavy alcohol use during adolescence [67]. In both studies, a variety of demographic, behavior, personality, cognitive, and neurobiological factors predicted alcohol use. Although these findings suggest that more complex models may improve our ability to predict addiction in adulthood, translating these findings into policy and preventions may prove to be challenging due to the highly dimensional nature of the results.

Developing indices of risk for substance use disorder which are easy to calculate and rely on a limited number of features may facilitate the translation of findings from prospective longitudinal studies for use in public health initiatives. For example, Meier and colleagues created a cumulative risk index by summing the presence of 9 childhood and adolescent risk factors: being male, lower family socioeconomic status, family history of substance use disorders, childhood conduct disorder and depression, early exposure to substances, and adolescent frequent alcohol, tobacco, and cannabis use [68]. The composite score predicted persistent substance use disorder in adulthood with 80% accuracy. They determined that 3% of adolescents without risk factors, 27% of adolescents with 3 risk factors, and 74% of adolescents with 6+ risk factors had persistent substance use disorder as adults. Similar work predicted cannabis use disorder in young adulthood using two composite scores thought to reflect transmissible and nontransmissible risk factors for substance use disorders derived from assessments obtained in boys during childhood [69]. Although promising due to their ease of use, careful examination of the variables included in composite scores is helpful for ensuring that important relationships between variables are not being obscured by aggregation of risk factors into composite scores. Lastly, across all approaches employed, replication in independent datasets is necessary to validate the veracity of findings.

Conclusions and Future Directions

Although progress has been made in identifying risk factors for addiction, the complicated relationships between risk factors are less well-understood and may hamper accurate identification of those at greatest risk and the creation of interventions targeted at the risk factors that have the greatest impact on risk for substance use disorders. This review highlights several risk factors that have been most consistently linked to a higher risk for addiction, such as the presence of externalizing and internalizing symptoms, early substance use, and environmental influences including different aspects of the parent-child relationship and exposure to trauma. Further research to identify how these variables interact and to identify novel risk factors will be important for understanding the complexity of the various mechanisms that lead to the development of substance use disorders.

Since rates of illicit substance use are relatively lower, prospective longitudinal studies have predominately focused on predicting variable patterns alcohol, nicotine, and/or marijuana use. To the extent that some risk factors for addiction are drug specific, larger longitudinal studies or recruitment of samples at higher risk for illicit drug use would aid in determining the factors that predict illicit substance use disorders. For example, a recent study determined that adolescents who experienced chronic pain were more likely to misuse opioids than adolescents without chronic pain [70]. With rates of opioid overdoses increasing 12.9-fold from 2007 to 2017 [71], more research is needed to determine which individuals are at greatest risk for opioid misuse and addiction.

While several large cohort studies exist for examining environmental and neurocognitive predictors of adult addiction, studies using neurobiological predictors have been limited. Large-scale prospective longitudinal studies, such as the Adolescent Brain Cognitive Development Study (ABCD), will provide an unprecedented opportunity to examine how cognitive, behavioral, and environmental risk factors for addiction are related to neurobiology and risk for addiction. For example, based on a review of the existing literature, it has been hypothesized that the relationship between internalizing symptoms and substance use is partially attributable to individual differences in the development of frontostriatal circuitry that predict the onset and escalation of depression, anxiety, and substance use [72]. Studies, like ABCD, should have an adequate sample size to examine this and many other hypotheses about the development of psychopathology, including addiction. Identifying biomarkers that predict increased risk of developing a substance use disorder could inform interventions that target and strengthen relevant circuitry.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. U.S. Department of Health and Human Services. The health consequences of smoking-50 years of progress. A report of the surgeon general. In: U.S. Department of Health and Human Services CfDCaP, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, editor. Atlanta; 2014.
2. Centers for Disease Control and Prevention. Alcohol-attributable deaths and years of potential life lost — 11 states, 2006–2010. In: CDC, editor. Atlanta, GA; 2014.
3. Xu X, Bishop EE, Kennedy SM, Simpson SA, Pechacek TF. Annual healthcare spending attributable to cigarette smoking: an update. Am J Prev Med. 2015;48(3):326–33. https://doi.org/10.1016/j.amepre.2014.10.012.
4. Centers for Disease Control and Prevention. Excessive drinking is draining the US economy. 2016.
5. National Drug Intelligence Center. National Drug Threat Assessment. In: Justice Do, editor. Washington, DC: United States; 2011.
6. Birnbaum HG, White AG, Schiller M, Waldman T, Cleveland JM, Roland CL. Societal costs of prescription opioid abuse, dependence, and misuse in the United States. Pain Med. 2011;12(4):657–67. https://doi.org/10.1111/j.1526-4637.2011.01075.x.
7. Florence CS, Zhou C, Luo F, Xu L. The economic burden of prescription opioid overdose, abuse, and dependence in the United States, 2013. Med Care. 2016;54(10):901–6. https://doi.org/10.1097/MLR.0000000000000625.
8. Dennis ML, Scott CK, Funk R, Foss MA. The duration and correlates of addiction and treatment careers. J Subst Abus Treat. 2005;28(Suppl 1):S51–62. https://doi.org/10.1016/j.jsat.2004.10.013.
9. De Soto CB, O'Donnell WE, De Soto JL. Long-term recovery in alcoholics. Alcohol Clin Exp Res. 1989;13(5):693–7.
10. Center for Behavioral Health Statistics and Quality. 2015 National Survey on Drug Use and Health. 2015.
11. Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, et al. Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry. 2015;72(8):757–66. https://doi.org/10.1001/jamapsychiatry.2015.0584.
12. Grant BF, Saha TD, Ruan WJ, Goldstein RB, Chou SP, Jung J, et al. Epidemiology of DSM-5 drug use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. JAMA Psychiatry. 2016;73(1):39–47. https://doi.org/10.1001/jamapsychiatry.2015.2132.
13. Chou SP, Goldstein RB, Smith SM, Huang B, Ruan WJ, Zhang H, et al. The epidemiology of DSM-5 nicotine use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. J Clin Psychiatry. 2016;77(10):1404–12. https://doi.org/10.4088/JCP.15m10114.
14.•• Groenman AP, Janssen TW, Oosterlaan J. Childhood psychiatric disorders as risk factor for subsequent substance abuse: a meta-analysis. J Am Acad Child Adolesc Psychiatry. 2017;56(7):556–69. **A meta-analysis that examines the evidence that childhood/adolescent psychiatric disorders are risk factors for adult substance use disorders.**
15. Buckner JD, Schmidt NB, Lang AR, Small JW, Schlauch RC, Lewinsohn PM. Specificity of social anxiety disorder as a risk factor for alcohol and cannabis dependence. J Psychiatr Res. 2008;42(3):230–9. https://doi.org/10.1016/j.jpsychires.2007.01.002.
16. Buckner JD, Turner RJ. Social anxiety disorder as a risk factor for alcohol use disorders: a prospective examination of parental and peer influences. Drug Alcohol Depend. 2009;100(1–2):128–37. https://doi.org/10.1016/j.drugalcdep.2008.09.018.
17. Englund MM, Egeland B, Oliva EM, Collins WA. Childhood and adolescent predictors of heavy drinking and alcohol use disorders in early adulthood: a longitudinal developmental analysis. Addiction. 2008;103:23–35.
18. Hayatbakhsh MR, McGee TR, Bor W, Najman JM, Jamrozik K, Mamun AA. Child and adolescent externalizing behavior and cannabis use disorders in early adulthood: an Australian prospective birth cohort study. Addict Behav. 2008;33(3):422–38. https://doi.org/10.1016/j.addbeh.2007.10.004.
19.• Mills R, Kisely S, Alati R, Strathearn L, Najman JM. Child maltreatment and cannabis use in young adulthood: a birth cohort study. Addiction. 2017;112(3):494–501. https://doi.org/10.1111/add.13634. **Although the focus of this study is on childhood maltreatment, statistical analyses control for potential confounds and report the significance of especially important additional covariates (e.g., externalizing behavior and personal substance use).**
20. Defoe IN, Khurana A, Betancourt LM, Hurt H, Romer D. Disentangling longitudinal relations between youth cannabis use, peer cannabis use, and conduct problems: developmental cascading links to cannabis use disorder. Addiction. 2019;114(3):485–93. https://doi.org/10.1111/add.14456.
21. Fergusson DM, Horwood LJ, Boden JM, Jenkin G. Childhood social disadvantage and smoking in adulthood: results of a 25-year longitudinal study. Addiction. 2007;102(3):475–82. https://doi.org/10.1111/j.1360-0443.2006.01729.x.
22. Pardini D, White HR, Stouthamer-Loeber M. Early adolescent psychopathology as a predictor of alcohol use disorders by young adulthood. Drug Alcohol Depend. 2007;88(Suppl 1):S38–49. https://doi.org/10.1016/j.drugalcdep.2006.12.014.
23. Pingault JB, Cote SM, Galera C, Genolini C, Falissard B, Vitaro F, et al. Childhood trajectories of inattention, hyperactivity and oppositional behaviors and prediction of substance abuse/dependence: a 15-year longitudinal population-based study. Mol Psychiatry. 2013;18(7):806–12. https://doi.org/10.1038/mp.2012.87.
24. Hayatbakhsh MR, Najman JM, Jamrozik K, Al Mamun A, Bor W, Alati R. Adolescent problem behaviours predicting DSM-IV diagnoses of multiple substance use disorder. Findings of a prospective birth cohort study. Soc Psychiatry Psychiatr Epidemiol. 2008;43(5):356–63. https://doi.org/10.1007/s00127-008-0325-1.
25. Guo J, Hawkins JD, Hill KG, Abbott RD. Childhood and adolescent predictors of alcohol abuse and dependence in young adulthood. J Stud Alcohol. 2001;62(6):754–62.
26. D'Amico EJ, Ellickson PL, Collins RL, Martino S, Klein DJ. Processes linking adolescent problems to substance-use problems in late young adulthood. J Stud Alcohol. 2005;66(6):766–75.
27. Bonomo YA, Bowes G, Coffey C, Carlin JB, Patton GC. Teenage drinking and the onset of alcohol dependence: a cohort study over seven years. Addiction. 2004;99(12):1520–8. https://doi.org/10.1111/j.1360-0443.2004.00846.x.
28. Foulds JA, Boden JM, Newton-Howes GM, Mulder RT, Horwood LJ. The role of novelty seeking as a predictor of substance use disorder outcomes in early adulthood. Addiction. 2017;112(9):1629–37. https://doi.org/10.1111/add.13838.
29. Palmer RH, Knopik VS, Rhee SH, Hopfer CJ, Corley RC, Young SE, et al. Prospective effects of adolescent indicators of behavioral disinhibition on DSM-IV alcohol, tobacco, and illicit drug dependence in young adulthood. Addict Behav. 2013;38(9):2415–21. https://doi.org/10.1016/j.addbeh.2013.03.021.

30. Mezzich AC, Tarter RE, Kirisci L, Feske U, Day BS, Gao Z. Reciprocal influence of parent discipline and child's behavior on risk for substance use disorder: a nine-year prospective study. Am J Drug Alcohol Abuse. 2007;33(6):851–67. https://doi.org/10.1080/00952990701653842.
31. Tarter RE, Kirisci L, Habeych M, Reynolds M, Vanyukov M. Neurobehavior disinhibition in childhood predisposes boys to substance use disorder by young adulthood: direct and mediated etiologic pathways. Drug Alcohol Depend. 2004;73(2):121–32.
32. Fergusson DM, Horwood LJ, Ridder EM. Conduct and attentional problems in childhood and adolescence and later substance use, abuse and dependence: results of a 25-year longitudinal study. Drug Alcohol Depend. 2007;88(Suppl 1):S14–26. https://doi.org/10.1016/j.drugalcdep.2006.12.011.
33. Huurre T, Lintonen T, Kaprio J, Pelkonen M, Marttunen M, Aro H. Adolescent risk factors for excessive alcohol use at age 32 years. A 16-year prospective follow-up study. Soc Psychiatry Psychiatr Epidemiol. 2010;45(1):125–34. https://doi.org/10.1007/s00127-009-0048-y.
34. Jester JM, Glass JM, Bohnert KM, Nigg JT, Wong MM, Zucker RA. Child and adolescent predictors of smoking involvement in emerging adulthood. Health Psychol. 2019;38(2):133–42. https://doi.org/10.1037/hea0000703.
35. Bardone AM, Moffitt TE, Caspi A, Dickson N, Stanton WR, Silva PA. Adult physical health outcomes of adolescent girls with conduct disorder, depression, and anxiety. J Am Acad Child Adolesc Psychiatry. 1998;37(6):594–601. https://doi.org/10.1097/00004583-199806000-00009.
36. Newton-Howes G, Boden JM. Relation between age of first drinking and mental health and alcohol and drug disorders in adulthood: evidence from a 35-year cohort study. Addiction. 2016;111(4):637–44. https://doi.org/10.1111/add.13230.
37. King KM, Chassin L. A prospective study of the effects of age of initiation of alcohol and drug use on young adult substance dependence. J Stud Alcohol Drugs. 2007;68(2):256–65.
38. Newton-Howes G, Cook S, Martin G, Foulds JA, Boden JM. Comparison of age of first drink and age of first intoxication as predictors of substance use and mental health problems in adulthood. Drug Alcohol Depend. 2019;194:238–43. https://doi.org/10.1016/j.drugalcdep.2018.10.012.
39. Guo J, Collins LM, Hill KG, Hawkins JD. Developmental pathways to alcohol abuse and dependence in young adulthood. J Stud Alcohol. 2000;61(6):799–808.
40. Prince van Leeuwen A, Creemers HE, Verhulst FC, Vollebergh WA, Ormel J, van Oort F, et al. Legal substance use and the development of a DSM-IV cannabis use disorder during adolescence: the TRAILS study. Addiction. 2014;109(2):303–11. https://doi.org/10.1111/add.12346.
41. Swift W, Coffey C, Carlin JB, Degenhardt L, Patton GC. Adolescent cannabis users at 24 years: trajectories to regular weekly use and dependence in young adulthood. Addiction. 2008;103(8):1361–70. https://doi.org/10.1111/j.1360-0443.2008.02246.x.
42. Brook JS, Balka EB, Ning Y, Brook DW. Trajectories of cigarette smoking among African Americans and Puerto Ricans from adolescence to young adulthood: associations with dependence on alcohol and illegal drugs. Am J Addict. 2007;16(3):195–201. https://doi.org/10.1080/10550490701375244.
43. Strong C, Juon HS, Ensminger ME. Effect of adolescent cigarette smoking on adulthood substance use and abuse: the mediating role of educational attainment. Subst Use Misuse. 2016;51(2):141–54. https://doi.org/10.3109/10826084.2015.1073323.
44. Gil AG, Wagner EF, Tubman JG. Associations between early-adolescent substance use and subsequent young-adult substance use disorders and psychiatric disorders among a multiethnic male sample in South Florida. Am J Public Health. 2004;94(9):1603–9.
45. Knop J, Penick EC, Nickel EJ, Mednick SA, Jensen P, Manzardo AM, et al. Paternal alcoholism predicts the occurrence but not the remission of alcoholic drinking: a 40-year follow-up. Acta Psychiatr Scand. 2007;116(5):386–93. https://doi.org/10.1111/j.1600-0447.2007.01015.x.
46. Kosty DB, Farmer RF, Seeley JR, Gau JM, Duncan SC, Lewinsohn PM. Parental transmission of risk for cannabis use disorders to offspring. Addiction. 2015;110(7):1110–7. https://doi.org/10.1111/add.12914.
47. Chassin L, Pitts SC, DeLucia C, Todd M. A longitudinal study of children of alcoholics: predicting young adult substance use disorders, anxiety, and depression. J Abnorm Psychol. 1999;108(1):106–19.
48. Newlin DB, Miles DR, van den Bree MB, Gupman AE, Pickens RW. Environmental transmission of DSM-IV substance use disorders in adoptive and step families. Alcohol Clin Exp Res. 2000;24(12):1785–94.
49.•• Yap MBH, Cheong TWK, Zaravinos-Tsakos F, Lubman DI, Jorm AF. Modifiable parenting factors associated with adolescent alcohol misuse: a systematic review and meta-analysis of longitudinal studies. Addiction. 2017;112(7):1142–62. https://doi.org/10.1111/add.13785. **This meta-analysis aggregates findings from studies examining how parenting behaviors influence alcohol-related problems in adulthood.**
50. Gil AG, Vega WA, Turner RJ. Early and mid-adolescence risk factors for later substance abuse by African Americans and European Americans. Public Health Rep. 2002;117(Suppl 1):S15–29.
51. Van Ryzin MJ, Dishion TJ. Adolescent deviant peer clustering as an amplifying mechanism underlying the progression from early substance use to late adolescent dependence. J Child Psychol Psychiatry. 2014;55(10):1153–61. https://doi.org/10.1111/jcpp.12211.
52. Poulton R, Caspi A, Milne BJ, Thomson WM, Taylor A, Sears MR, et al. Association between children's experience of socioeconomic disadvantage and adult health: a life-course study. Lancet. 2002;360(9346):1640–5. https://doi.org/10.1016/S0140-6736(02)11602-3.
53. Abajobir AA, Najman JM, Williams G, Strathearn L, Clavarino A, Kisely S. Substantiated childhood maltreatment and young adulthood cannabis use disorders: a pre-birth cohort study. Psychiatry Res. 2017;256:21–31. https://doi.org/10.1016/j.psychres.2017.06.017.
54. Newbury JB, Arseneault L, Moffitt TE, Caspi A, Danese A, Baldwin JR, et al. Measuring childhood maltreatment to predict early-adult psychopathology: comparison of prospective informant-reports and retrospective self-reports. J Psychiatr Res. 2018;96:57–64. https://doi.org/10.1016/j.jpsychires.2017.09.020.
55. O'Brien JW, Hill SY. Neural predictors of substance use disorders in Young adulthood. Psychiatry Res Neuroimaging. 2017;268:22–6. https://doi.org/10.1016/j.pscychresns.2017.08.006.
56. Cheetham A, Allen NB, Whittle S, Simmons J, Yucel M, Lubman DI. Orbitofrontal cortex volume and effortful control as prospective risk factors for substance use disorder in adolescence. Eur Addict Res. 2017;23(1):37–44. https://doi.org/10.1159/000452159.
57. Hill SY, Steinhauer SR, Locke-Wellman J, Ulrich R. Childhood risk factors for young adult substance dependence outcome in offspring from multiplex alcohol dependence families: a prospective study. Biol Psychiatry. 2009;66(8):750–7. https://doi.org/10.1016/j.biopsych.2009.05.030.
58. Guttmannova K, Bailey JA, Hill KG, Lee JO, Hawkins JD, Woods ML, et al. Sensitive periods for adolescent alcohol use initiation: predicting the lifetime occurrence and chronicity of alcohol problems in adulthood. J Stud Alcohol Drugs. 2011;72(2):221–31.
59. Hancock DB, Markunas CA, Bierut LJ, Johnson EO. Human genetics of addiction: new insights and future directions. Curr

Psychiatry Rep. 2018;20(2):8. https://doi.org/10.1007/s11920-018-0873-3.

60. Maggs JL, Patrick ME, Feinstein L. Childhood and adolescent predictors of alcohol use and problems in adolescence and adulthood in the National Child Development Study. Addiction. 2008;103(Suppl 1):7–22. https://doi.org/10.1111/j.1360-0443.2008.02173.x.
61. LeTendre ML, Reed MB. The effect of adverse childhood experience on clinical diagnosis of a substance use disorder: results of a nationally representative study. Subst Use Misuse. 2017;52(6):689–97. https://doi.org/10.1080/10826084.2016.1253746.
62. Widom CS, Weiler BL, Cottler LB. Childhood victimization and drug abuse: a comparison of prospective and retrospective findings. J Consult Clin Psychol. 1999;67(6):867–80.
63. Silverman AB, Reinherz HZ, Giaconia RM. The long-term sequelae of child and adolescent abuse: a longitudinal community study. Child Abuse Negl. 1996;20(8):709–23.
64. Squeglia LM, Gray KM. Alcohol and drug use and the developing brain. Curr Psychiatry Rep. 2016;18(5):46. https://doi.org/10.1007/s11920-016-0689-y.
65.•• Kraemer HC, Stice E, Kazdin A, Offord D, Kupfer D. How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. Am J Psychiatry. 2001;158(6):848–56. https://doi.org/10.1176/appi.ajp.158.6.848. **This paper proposes a method for systematically evaluating relationships between risk factors and classifying them into different categories to help identify individuals at high-risk for developing psychiatric disorders and in need of preventative interventions.**
66. Whelan R, Watts R, Orr CA, Althoff RR, Artiges E, Banaschewski T, et al. Neuropsychosocial profiles of current and future adolescent alcohol misusers. Nature. 2014;512(7513):185–9. https://doi.org/10.1038/nature13402.
67. Squeglia LM, Ball TM, Jacobus J, Brumback T, McKenna BS, Nguyen-Louie TT, et al. Neural predictors of initiating alcohol use during adolescence. Am J Psychiatry. 2017;174(2):172–85. https://doi.org/10.1176/appi.ajp.2016.15121587.
68. Meier MH, Hall W, Caspi A, Belsky DW, Cerda M, Harrington HL, et al. Which adolescents develop persistent substance dependence in adulthood? Using population-representative longitudinal data to inform universal risk assessment. Psychol Med. 2016;46(4):877–89. https://doi.org/10.1017/S0033291715002482.
69. Kirisci L, Tarter R, Mezzich A, Ridenour T, Reynolds M, Vanyukov M. Prediction of cannabis use disorder between boyhood and young adulthood: clarifying the phenotype and environtype. Am J Addict. 2009;18(1):36–47. https://doi.org/10.1080/10550490802408829.
70. Groenewald CB, Law EF, Fisher E, Beals-Erickson SE, Palermo TM. Associations between adolescent chronic pain and prescription opioid misuse in adulthood. J Pain. 2019;20(1):28–37. https://doi.org/10.1016/j.jpain.2018.07.007.
71. Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple causes of death 1999-2017 on CDC WONDER online database.
72. Jones SA, Morales AM, Lavine JB, Nagel BJ. Convergent neurobiological predictors of emergent psychopathology during adolescence. Birth Defects Res. 2017;109(20):1613–22. https://doi.org/10.1002/bdr2.1176.