

# Childhood and Adolescent Pathways to **Substance Use Disorders**



Canadian Centre  
on Substance Abuse  
Centre canadien de lutte  
contre les toxicomanies

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**Prepared for the Canadian Centre on Substance Abuse**

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# Foreword

The Canadian Centre on Substance Abuse (CCSA) is committed to providing national leadership to advance solutions to substance abuse. Part of our leadership involves publishing or promoting cutting-edge research on emerging alcohol- and drug-related issues in Canada and around the world. To this end, CCSA produces a new report in the *Substance Abuse in Canada* series every two years; the latest being a report released in November 2013 on substance use during pregnancy. That report examined the maternal, neonatal and early childhood consequences of abusing substances such as alcohol, tobacco, marijuana, cocaine and heroin. It reinforced the need to address the stigma towards pregnant women with substance use issues and focus on meeting the needs of **both** the women and their children.

Beyond the effects on the mother, the issues raised in the November 2013 SAIC report highlight important questions about the effects of substance abuse and mental health issues on younger children and adolescents. Youth is a time of significant development and change. It is also the period when substance use most commonly begins. Young people are disproportionately more likely than people in other age groups to use substances, engage in risky patterns of use and experience harms from that use. Evidence-informed approaches to drug prevention can have a significant impact on youth substance abuse and contribute to the overall health and well-being of young people. And so CCSA broke with its usual schedule to build on the findings and recommendations of the maternal and neonatal health report by publishing this report as a second installment coupled with it.

The present report focuses on how biological, behavioural and social factors during the early developmental years play a role in later-life substance abuse, as well as in concurrent mental and physical health problems. The report examines how various developmental pathways can lead to substance abuse, with the main goal being to develop more effective prevention, detection and early intervention efforts for young people and their families. Involving the family is important because parents need to know how to support their child and it has been shown that enhancing parental nurturing improves outcomes.

Many factors are at play to make one person more likely to abuse substances than another, including genetics, brain abnormalities, behaviour, personality styles and the environment at home and at school. No one set of experiences or factors directly results in later-life substance abuse because every individual and his or her experiences are unique. A dynamic interplay among genetic, biological, social and environmental experiences and vulnerabilities begins the moment a child is born. This interplay points to the need to ensure that intervention strategies are dynamic and that they target specific developmental ages, key risk and protective factors, and the larger social environment.

This report also suggests that intervention efforts should focus on both children of middle school age and youth during their teenage years. If risk factors, including behaviours and vulnerabilities, can be identified and acted on earlier in life, then interventions might not have to be as significant as those needed by a teenager or young adult who has progressed further into substance abuse. We need further research to help identify and classify these early signs of risk.

As importantly, as a society we need to ensure that those protective factors that have been shown to be most effective in improving outcomes are put into place in the schools and communities in which our youth live so that they have the supports they need to lead a life free of the harms of substance abuse. This integrated view of substance abuse is most effective for identifying risk and putting in place targeted prevention efforts. We must therefore consider both the **presence** of risk factors as well as the **absence** of protective factors in looking at how substance abuse patterns develop. These risk and protective factors all have a role to play in informing health promotion, prevention and early intervention initiatives.

This concept is in line with the findings of a groundbreaking report released by the FrameWorks Institute on how to enhance a common understanding of the developmental causes of addiction (Erard, 2012). The report proposed using the term “brain fault lines” as an analogy with geological fault lines to find more effective ways to talk about how some individuals are



## Acknowledgements



more susceptible to addiction because of complex interactions between genetic and environmental factors. As the real fault lines sometimes result in earthquakes, the metaphorical fault lines sometimes result in addictions. We can help prevent fault lines from developing, we can minimize the chances that they will turn into addictions and we can defend against the damage from happening again.

This latest *Substance Abuse in Canada* report examines how such fault lines could be created and suggests ways in which it might be possible to better manage, reduce or prevent their full expression. These ways include prevention initiatives that look at substance abuse from a developmental perspective, as well as interventions across the spectrum of child, family and community. Most importantly, when we harness opportunities for prevention and intervention at the earliest stages, these investments in our young people can yield long-term improvement in health, socioeconomic, individual and family outcomes.

In simple terms, investing in the well-being of our children — our future leaders — is in everyone's best interests.

It gives me great pleasure to take this opportunity to thank the authors of the report — Dr. Robert Pihl, Malak Abu-Shakra, Dr. Sylvia Cox, Maeve O'Leary-Barrett, Line Brotnow and Dr. Rajita Sinha — for their expertise and superb work in gathering and synthesizing the vast amount of cutting-edge research discussed in this report. Special thanks to the editorial team, Drs. Marco Leyton and Sherry Stewart, for their exceptional editing of and contributions to the entire report, and for integrating the evidence and key messages of the individual authors. Dr. Franco Vaccarino once again played an essential leadership role in developing this report and pulling together all the experts to bring this evidence forward. I am also happy to have the occasion once again to thank members of CCSA's Scientific Advisory Council for their expert advice and assistance with this report and the SAIC series in general. Last but not least, I would like to draw attention to the continued hard work and dedication of CCSA staff, who support our research program and make possible such publications as this.

**Their contributions were invaluable.**

### **Rita Notarandrea**

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# Foreword



The palette of prenatal and postnatal experiences that contribute to a developing individual's normal or abnormal intake of drugs is a rich one. And there is ample evidence that the genetic make-up of the individual provides the canvas on which these experiences are brought to life. The complexities of this interplay are very well laid out and discussed in this fifth installment in the *Substance Abuse in Canada* series. The theme of developmental trajectories is an important one as it provides a timeline that is critical for the assessment of individuals who are at risk for subsequent abuse of drugs and can then inform options for appropriate interventions that would hopefully skew that trajectory toward behaviours that would not harm the individual or society.

The four main chapters take us through an evidence-rich landscape that identifies the many factors that impose risks for developing substance abuse and the two behavioural phenotypes on which these risks are largely played-out. Scientific data are the keys to power and insight, and this is the upbeat theme of this set of chapters. They nicely lay out much of the current work in the field with critical examination and identification of gaps in our knowledge. Four points of note follow.

First, despite the devastating toll that substance abuse can take on an individual, there is much hope that runs throughout this installment of *Substance Abuse in Canada*. Of foremost importance is the understanding that while genes may play a role, there are as yet no confirmed genotypes that ordain substance abuse. Instead, current evidence points to a powerful interplay of genes with environmental factors. This interplay indicates that gene–environment interactions will be key to understanding how environment “gets under our skin” to affect gene expression and brain function. One of the Canadian Institutes of Health Research (CIHR) Signature Initiatives, the Canadian Epigenetics, Environment and Health Research Consortium is designed to support exciting new opportunities to explore the brave new world of epigenetics — essentially how experience modifies the DNA (Health Canada, 2013). While the area is at a nascent stage of scientific inquiry, epigenetic “marks” are thought to be good candidates for biomarkers that might provide warning flags of substance abuse.

Second, a developmental perspective is critical to both understanding and eventually preventing or treating drug abuse, given the compelling argument that the earlier that problems can be detected, the sooner one can intervene, thereby improving the prospects of enjoying a normal life course. The mantra of early detection and early intervention has been the guide for another Canadian initiative called NeuroDevNet, one of the Networks of Centres of Excellence, that studies early brain development and the changes imposed by neurodevelopmental disorders, including substance abuse. NeuroDevNet is developing novel means to assess brain function and tools for early intervention that can enhance forebrain function. These avenues offer agents that can be added to the interventions discussed in Chapter 4, which covers the epochs of child development and identifies age-specific, evidence-based interventions that have been tried and have yielded success.

A third consideration touches on the remarkable advances in the detailed understanding of key brain nuclei and related circuits that constitute the neural substrates of substance abuse. These developments are detailed in Chapters 2 and 3, and they provide the blueprint for how we might use imaging modalities, potentially for diagnostics, and also as sophisticated tools for assessing the success of interventions. The new technologies expected to emerge from the U.S.-sponsored BRAIN initiative (Executive Office of the President of the United States, 2013) and the neuro-informatic tools provided by the European Human Brain Project (European Commission, 2013) will be of inestimable value in this quest.

Fourth, many diverse areas of research are converging on this critical issue in multiple ways. Together, they will offer key insights into the events that create risk or undermine resiliency and how interventions work, and thereby help develop a new generation of approaches that will be age- and phenotype-specific. The current focus on the developmental origins of health and disease, which is largely involved in studies of the role of the prenatal environment, is vitally important in setting the stage. The field of inquiry into how the adversities in postnatal life shape who we are is now an emerging area of study (Centers



for Disease Control and Prevention, 2013). With the availability of numerous longitudinal studies of young children, researchers now have abundant opportunity to examine this critical issue and initial studies are revealing higher amounts of substance abuse in individuals with multiple adverse childhood experiences (Mersky, Topitzes, & Reynolds, 2013).

The most impressive feature of this document is the clear message that a developmental perspective holds the key to changes in understanding, practice and policy that must ensure better protection of our young from the onslaughts of gene–environment interactions that can lead to poor decision making and substance abuse. Canada is well positioned to tackle these challenges and to be a leader in the international effort. National initiatives like the new partnership between CIHR and the Graham Boeckh Foundation to fund a patient-oriented initiative in Transformational Research in Adolescent Mental Health provide optimism for the emergence of more effective research, diagnosis, intervention and policies to stem the problem of substance abuse.

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# Introduction



By **Robert Pihl, Malak Abu-Shakra, Sylvia Cox, Maeve O'Leary-Barrett, Line Brotnow, Rajita Sinha, Sherry Stewart and Marco Leyton**

Launched in 2005, the *Substance Abuse in Canada* series highlights key contemporary issues related to substance abuse along with specific areas for action in both policy and practice. Each *Substance Abuse in Canada* report is intended for a broad audience that includes policy makers, program development personnel, researchers, educators and health professionals. Health journalists also make up an important readership of this report as they can help raise the public profile of the issues and create the impetus for change.

## THE SERIES TO NOW

The first *Substance Abuse in Canada* report, *Current Challenges and Choices*, examined a variety of topics, including the prevention of alcohol problems, alternative sanctions for cannabis use and possession, drug-impaired driving, and the abuse and diversion of prescription medication.

The second report, *Focus on Youth*, looked at the prevalence of substance use and its associated harms among young people, exploring the underlying neurobiology of substance use in adolescence and identifying existing gaps in youth-centric services.

The third edition, *Concurrent Disorders*, focused on the co-occurrence of mental health and substance abuse problems, examining the interconnections between addiction and mental illness, the tremendous costs concurrent disorders places on Canada's healthcare system, and why treating these complex cases requires new and innovative approaches.

The fourth in the series, *Licit and Illicit Drug Use during Pregnancy*, addressed the medical and obstetrical consequences of drug abuse and dependency in pregnant women, as well as the short- and long-term effects prenatal exposure to drugs can have on a child's development.

This fifth *Substance Abuse in Canada* report is a companion to the fourth, which looked at the maternal, neonatal and early childhood consequences of drug use during pregnancy. The current report focuses on influences in childhood and adolescence that can affect substance abuse later in life, as well as the implications an understanding of those influences has for prevention and treatment. After introducing the overarching genetic, neurobiological, environmental and social factors that increase an individual's risk for substance abuse, the report

moves on to discuss the latest research on the impulsive-aggressive (i.e., "externalizing") and anxious-depressive (i.e., "internalizing") developmental pathways that can lead to substance use disorders. Finally, it discusses the practical implications of this research on prevention and intervention during early childhood, school age and adolescence, concluding with a call to action that draws upon the themes explored throughout the earlier chapters.

It should be noted that this report is not meant to be a systematic review of this topic area; instead, it is intended to provide a high-level overview of this important health issue.

## Mapping the developmental pathways that lead to substance abuse

While drug and alcohol use by youth is the norm, not everyone who tries drugs develops a substance use disorder. For most people, this differential susceptibility reflects the outcome of developmental pathways that begin in childhood and continue, in different forms, through adolescence and young adulthood.

Substance use disorders are linked to a large number of childhood and adolescent developmental problems that are shaped by inter-related genetic, behavioural, biological and psychological factors. Given the large number of factors to be considered, this report uses two broad developmental pathways as a general framework for analysis. One pathway is characterized by an enduring tendency toward impulsive risk-taking and aggression (externalizing behaviours); the other pathway is marked by anxiety or depression (internalizing behaviours).

Both tendencies increase the risk not only for substance abuse but also a wide range of potentially co-occurring mental health problems. While the two pathways highlight the multiplicity of factors that can aggravate a person's susceptibility to substance use disorders, our improving ability to identify the relevant developmental processes also provide multiple targets for early prevention and treatment.

As we learn more about the factors that influence these pathways, we may be better positioned to develop trajectory-specific preventative strategies, treatments and interventions.



This growing knowledge of underlying risk factors can also be applied to the treatment of active substance use problems, targeting the factors that have caused the problems in the first place.

This report provides the background for this perspective in more detail, summarizing what has been learned on topics such as heritability, brain circuitry and brain–environment interactions, particularly their potential for pathway-specific prevention and treatment.

### **Youth substance use prevalence and prevention**

The use of psychoactive substances is not new: humans have been using drugs recreationally for millennia. Some geometric cave art, millions of years old, bears a striking resemblance to artwork produced today when certain drugs are ingested, leading anthropologists to surmise such art was created under the influence of intoxicating drugs.

If drug use is part of our nature, attempts to completely curtail it will ultimately prove ineffective. Yet all societies continue to restrict the use of particular drugs, discriminating permissibility on the basis of age, gender or social stature, with prohibitions often determined by religious and traditional practices rather than a drug's objective effects or the physical harm it causes (Nutt, King, & Phillips, 2010). The relative success of restrictive policies seems to vary with the nature of the society, with closed and repressive societies more effective in suppressing drug use.

Not surprisingly, “western” societies have faced considerable difficulties when trying to ban specific drugs or restrict use according to age. Prevention programs such as Drug Abuse Resistance Education (DARE), which preaches abstinence to youth, have generally been ineffective or even increased drug use (Lynam et al., 1999). In contrast, prevention approaches that address the different underlying problems of distinct target populations of higher-risk youth have had more encouraging success (Conrod et al., 2013).

Adolescent drug and alcohol use is exceedingly prevalent — to the point that it can even be considered normal behaviour in our society. Although statistics vary by province, approximately 85 percent of Canadian teenagers have consumed alcohol and 50 percent have consumed illegal drugs (Canadian Alcohol and Drug Use Monitoring Survey, 2011). Rates of illicit drug use and risky drinking are higher in youth under the age of 25 than other age groups; however, the simple use of a drug is a very limited statistic because it treats the one-time experimenter the same as the frequent abuser. Adolescence and the experimental developmental period are often interchangeable terms — meaning it is the potential abuser who deserves the most concern.

### **The costs and consequences of substance abuse**

Excessive alcohol consumption is related to more than 60 disease conditions and, according to the World Health Organization, accounts for four percent of the global burden of health with a greater death toll than HIV/AIDS, violence and tuberculosis combined. One-third of disability-adjusted life years lost is accounted for by alcohol use in individuals between the ages of 15 and 29.

Alcohol's negative ramifications go well beyond health consequences, invading every aspect of the abuser's life. As explained in the previous *Substance Abuse in Canada* report (Finnegan, 2013), prenatal alcohol exposure produces varying syndromes of disability for offspring. Alcohol abuse by caregivers often results in neglect and violence toward the one being cared for, inducing serious decrements in both brain and social development and potentially leading to a self-perpetuating, intergenerational cycle of abuse and neglect. In addition, around half of all violent crimes and suicides occur under the presence of alcohol use, especially alcohol intoxication.

In total, illegal drugs and alcohol cost the Canadian economy an estimated \$40 billion each year (Rehm et al., 2007). Fortunately, there is a growing understanding of which individuals are more likely to develop a substance use problem and under what conditions. Parents, educators, healthcare professionals and government policy makers should focus on this knowledge to reduce substance abuse and its associated costs and harms.



## Chapter-by-chapter summary

### Chapter 1: Understanding the Risk Factors for Substance Abuse

There are multiple developmental pathways to substance use disorders, with the risk factors that can start an individual down one of these pathways ranging from the genetic to the sociocultural. Because these factors tend to cluster and can vary with age, disentangling their unique contributions can be difficult. Consequently, a focus on the stages of development is key. This chapter looks at the latest research on the different risk factors at play during a person's development, including:

- Genetic factors (i.e., the fact that the risk for substance runs in families), which are estimated to contribute 40–60 percent of vulnerability to drug abuse;
- Early brain development, looking particularly at how disruptions in the development of the brain's fear processing and reward cue processing circuitry can predict later behaviour, including substance abuse; and
- The role of the environment in shaping brain functioning, including maltreatment and severe early stress; parental factors such as prenatal exposure to drugs, anti-social behaviour, a non-intact family and maternal depression; the influence of peers, especially among youth with low self-efficacy; and the cultural and social structures that inadvertently channel people toward drug use.

The chapter concludes with a brief look at how these factors contribute to the two major developmental pathways (characterized by external problems such as aggression or internal problems such as anxiety), both of which represent an increased risk for substance use disorders. For example, “externalizers” seem to be more responsive to drug activation of the brain's reward cue system, while “internalizers” appear to use drugs in an attempt to control their hyper-responsive fear-anxiety system.

### Chapter 2: The Externalizing Developmental Pathway to Substance Use Disorders

Almost all young children are impulsive, inattentive and emotionally reactive, and many are aggressive and highly active. In most cases, these behaviours subside as a child matures. In about 25 percent of children, though, these behaviours are unusually elevated and persistent, expressing themselves as an enduring mixture of features that include social gregariousness, risky thrill-seeking, emotionality and irritability.

These externalizing behaviours are predictive of various child- and adolescent-onset disruptive behavioural disorders (DBDs), including oppositional defiant disorder in the preschool years, attention deficit/hyperactivity disorder in the elementary school years, and conduct disorder in middle childhood through adolescence. By adolescence, these DBDs increase the risk for substance use disorders: compared to those without DBDs, individuals with DBDs have double the risk of abusing tobacco, triple the risk of abusing alcohol, and five times the risk of abusing illicit drugs. Indeed, 75 percent of adolescents with a DBD become substance abusers in adulthood and 50 percent of adults with substance use disorders had a history of at least one DBD in childhood or adolescence.

This chapter summarizes the various risk factors that predict the development of DBDs and substance use problems including genetic predispositions, chronic early maltreatment, parental antisocial behaviour and substance abuse, poor inhibitory control, and an early age of onset of drug and alcohol use.

### Chapter 3: The Internalizing Developmental Pathway to Substance Use Disorders

Youth and adults who abuse substances commonly experience co-occurring mental health problems, with mood and anxiety disorders among the most prevalent. Because internalizing personality traits are relatively stable over time and can be detected early in life, behavioural inhibition (i.e., a temperamental factor involving withdrawal, avoidance, over-arousal and fear of the unfamiliar) in infancy can be used to predict internalizing



problems into adulthood. While the rates of depressive disorders in males and females is relatively equal in childhood, this changes dramatically when youth reach adolescence, with females becoming three times more likely to develop mood disorders. Gender differences in anxiety are present from childhood, with females twice as likely as males to experience clinically relevant anxiety in their lifetimes.

In most cases, mood and anxiety problems precede the onset of substance abuse, suggesting individuals self-medicate with alcohol or drugs to temporarily diminish their anxiety. As a corollary, this observation also implies that the shared risk for internalizing behaviours and substance use problems reflects an overlap of pre-existing vulnerabilities. This chapter presents evidence indicating there is indeed an overlap in genetic factors, neurobiological differences that influence personality, responses to drugs and alcohol, and early life experiences such as abuse and neglect.

Once substance use begins, it can lead to worsened mood and more anxiety, further perpetuating the relationship between internalizing problems and substance use. Obtaining a better understanding of the factors that increase risk for substance use in people with anxiety/depression and influence their progress along this pathway is expected to improve our understanding of how addictions develop.

#### **Chapter 4: A developmental approach to prevention and intervention**

The multiple risk factors influencing internalizing and externalizing behaviours are partly a function of the developmental stage of the individual. Each stage presents unique challenges that might increase vulnerability to substance abuse, as well as distinct opportunities for promoting resilience and detecting at-risk individuals.

This chapter outlines the need to consider prevention within this developmental context, summarizing the key risk factors as well as several well-validated preventive interventions for each of the early childhood, school-age and adolescent stages. Such a

framework not only highlights specific developmental pathways and milestones, it also underscores the need to implement personalized prevention strategies in a multidisciplinary manner, working across different social contexts and in developmentally appropriate ways.

For example:

- Exposure to parental substance abuse and psychopathology during early childhood increases the likelihood of poor outcomes later in life. Helping parents improve their ability to care for infants and toddlers can help counteract exposure to these risk factors by improving child–parent attachment and reducing behavioural and emotional dysregulation.
- In school-age children, genetic predispositions, suboptimal parenting and exposure to uncontrollable stressful life events all affect the emergence of internalizing and externalizing behaviours. Multi-level preventive interventions implemented at the individual, family and school levels have proven to be most effective in targeting specific risk patterns while increasing social adaptation and self-efficacy.
- Prevention programs targeted at adolescents are often ineffective, partly because of researchers' inability to distinguish normal features of adolescence (e.g., novelty-seeking, reduced risk aversion, heightened reward salience) from causal mechanisms predicting substance abuse. For instance, internalizing and externalizing symptoms might be associated with specific motivations to use substances that, in turn, could be targeted through personalized interventions to prevent future substance abuse. Reflecting the increased importance of teens' broader social environments, community-based interventions should be implemented alongside individual- and school-based initiatives.



## Chapter 5: A Call to Action

On the basis of the research findings presented in the previous chapters, this final section makes a series of recommendations for prevention research and interventions, and highlights future directions and developments in the field of substance abuse prevention.

Given the inter-relationships between the risk factors for substance abuse and their potentially broad impact on a wide range of negative outcomes, this chapter reinforces the need to take a multidimensional, interdisciplinary approach to future

prevention research and interventions. It also looks at the need to develop a methodology for classifying the early warning signs of risk to help teachers and other childcare professionals identify at-risk youth as soon as possible, as well as the need to codify specific neurobiological and behavioural markers of substance abuse risk so that they can be better matched to specific interventions. Doing so would help streamline early detection efforts and improve the development and implementation of personalized prevention programs.

### TERMINOLOGY NOTES

Several of the terms used in this document have specific and distinct clinical significance, but to avoid repetition have been used as equivalents. Unless otherwise noted, the definitions below are based on those provided in the fourth and fifth editions of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR and DSM-5, respectively) (American Psychiatric Association, 2000, 2013).

- **Addiction:** Generally applied to patterns of heavy, compulsive use of psychoactive drugs and an inability to stop substance use despite it leading to severe, clinically relevant problems in multiple domains of a person's life (for example, when such use becomes physically hazardous; causes failure to fulfill obligations at work, school or home; or creates legal, social or interpersonal problems). Tolerance and withdrawal commonly occur, but are neither necessary nor sufficient. The term addiction refers not only to substance use disorder — the topic of this report — but also to non-substance-related behavioural addictions like gambling disorder.
- **Substance dependence:** Also referred to as “drug or alcohol dependence,” substance dependence constitutes a cluster of cognitive, behavioural and physiological symptoms indicating continued substance use despite the occurrence of severe substance-related problems. In DSM-5, the diagnosis of substance dependence has been combined with that of substance abuse (see below) and both have been replaced by the single term “substance use disorder.” The elimination of substance dependence in the DSM-5 underscores that a substance use disorder is not synonymous with physical dependence. For example, patients prescribed high dose opiate analgesics would only be considered to have a substance use disorder if they began to use the drug compulsively, taking more than is required for pain control. In the DSM-5, the severity that was previously captured by the diagnostic label of “substance dependence” is now captured by specifying current severity (e.g., “substance use disorder, severe”).
- **Substance abuse:** Also known as “drug or alcohol abuse,” this term refers to a maladaptive pattern of substance use resulting in recurrent and significant adverse consequences. It has also been replaced by the term “substance use disorder,” but is indicative of a disorder of mild severity.



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# 1

# Understanding the Risk Factors for Substance Abuse



*By Robert Pihl*

## Chapter at a Glance

- The two most common developmental pathways to substance abuse disorders are characterized by high levels of impulsive risk-taking and aggression (“externalizing” behaviours) and either anxiety or depression (“internalizing” behaviours).
- The genetic, neurobiological, psychological and environmental factors that influence whether a person begins and remains on one of these pathways are now being identified.

Until recently, much of what was known about risk came from studies of individuals already affected by substance abuse. However, the act of abusing a substance changes a person's biology and psychology, so that studying the abuser might reveal information about the “explosion,” but not necessarily the triggering mechanism. Understanding **why** an individual abuses drugs is essential to developing more effective strategies for prevention and treatment.

While there are multiple pathways to substance use disorders, not everyone who is at risk develops a problem and those who do not can provide important insights into the factors that protect against risk.

The challenge, however, is that these factors range from genetics to sociology. Marrying the diverse literatures — each with their own distinctive language, methodology and

assumptions — can be exceptionally difficult. As a result, important causative factors that interrelate are often viewed in isolation. Diligence is required when considering the risk factors for substance abuse: those factors that appear to be significant might not be causative and treating them as if they were can lead to inappropriate and ineffective policies and interventions.

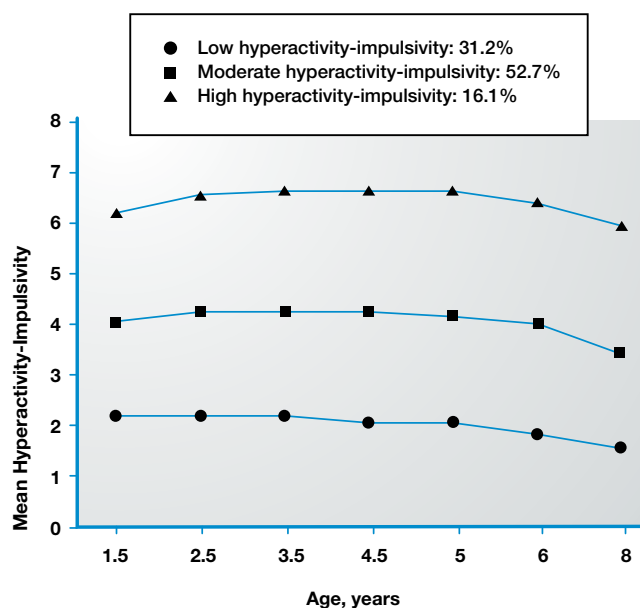
Jaffee and Strait (2012) list three concerns when evaluating studies that observe an association between two things. First, there is always the possibility that the observed association (for example, between genetic family history and risk for substance abuse) is the result of a third factor, such as a chaotic home environment. Second, one can make the error of assuming that a given factor precedes and causes a second factor when the actual order of development might be reversed. This error occurs frequently in the substance abuse field, where the behavioural characteristics of addicts are taken to be the





cause of the problem, but actually reflect the consequences of drug abuse. Finally, the problem of social selection must be considered: for example, drug abusers select like-minded peers to spend time with and yet their affiliation with these peers is suggested to be the cause of their drug abuse.

**Figure 1.** Developmental trajectories of hyperactivity-impulsivity



In general, it is worth noting that because risk factors tend to cluster, disentangling their unique contributions to the development of substance use disorders can be difficult.

Complicating the issue further, risk factors are not static and can vary with age. A focus on stage of development is therefore important. As an example, Figure 1 (Galéra et al., 2011) illustrates the consistency of hyperactivity-impulsivity, an established risk factor for substance abuse, measured at the age of one-and-a-half years and then again each year until age eight.

From this example, one might conclude that a hyperactive-impulsive individual is “doomed” at infancy, likely because of genetic factors. However, this study specifically assessed early environmental risk factors and found that premature birth, low birth weight, prenatal tobacco exposure, non-intact family, young age of mother, maternal depression and paternal antisocial behaviour were all predictors of childhood impulsivity and inattention. Consequently, these findings direct attention to very early childhood and the importance of early intervention.

## 1.1 Genetic risk factors

The fact that risk for substance abuse runs in families has been well established. Early twin and adoption studies, for example, have shown that the sons of male alcoholics are at increased risk of developing the disorder, even if they are raised by a non-alcoholic adoptive family. Smaller but still considerable heritability has since been demonstrated for women as well, while twin studies have also underscored a genetic involvement in risk for the abuse of opiates, tobacco and stimulants.



Representative of this body of work, a follow-up study of nine databases of adoptive children found that risk for drug abuse was doubled when one biological parent was a drug abuser (Kendler et al., 2012). The risk was slightly higher if the biological father was the abuser instead of the mother, indicating the effect was not accounted for by prenatal drug exposure. If both biological parents were drug abusers, the risk tripled. Risk was highest among those with multiple substance-abusing biological relatives and adopted into an adverse family environment.

While most estimates suggest genetic factors contribute 40–60 percent of vulnerability to drug abuse, it still remains unclear which exact genes are responsible. Out of our approximately 25,000 genes, some 400 have been identified as increasing the risk for drug addiction (Li, Mao, & Wei, 2009). However, because the error possibilities in single-association studies can be quite high, such a count will not be viable until there is an understanding of **how** a gene or collection of genes increases risk. On this question, the findings have been generally disappointing, weak or contradictory. The exception can be found in genetic studies of smokers: a genetic alteration that changes a nicotinic receptor is related to the number of cigarettes smoked daily (Saccone et al., 2007), an association replicated in very large samples (Liu et al., 2010) and with implications for more individualized treatments (Bierut, Johnson, & Saccone, 2014).

#### THE ROLE OF GENES

Genes initiate biochemical actions that influence development and susceptibility to how one reacts to environmental events. These effects on behaviour are mostly general rather than specific. For example, the genes affecting the development and function of the nervous system also affect a broad range of behaviours that may include the propensity to abuse drugs. In an adoption study by Kendler and colleagues (2012), not only was an individual's drug abuse predicted by his or her biological parents' drug abuse, but so too were his or her psychiatric and criminal problems.

More generally, even studies of high-risk individuals have failed to be convincing. Wrong ideas about what genes do and how they work are often at fault. For instance, the phrase “turning specific genes on or off” has become increasingly popular. The

state of a gene is not absolute, though: instead of switching on or off, the effect is more like a dimmer that allows for a gradation of expression. This phenomenon is being explored in epigenetics, the field of study that investigates how gene functioning can be modified by environmental factors without altering basic genetic makeup. For example, it has been shown that early childhood physical abuse interacts with certain genes to increase the likelihood of mental disorders such as depression, anxiety and conduct disorder.

In a study of French-Canadian men (Labonté et al., 2012), those with a history of severe childhood abuse displayed alterations to 362 sites that promote gene expression, with the genes that influence “neural plasticity” (i.e., the ability of brain cells to grow and change in response to input) appearing most affected. The study also observed changes to the genes associated with suicide.

Importantly, gene–environment interactions go in both directions. For example, one gene variant has been shown to buffer the effects of childhood physical abuse (Agrawal et al., 2012). These sorts of epigenetic effects might account for the potent gene–environment interaction reported by Kendler and colleagues (2012), where risk for substance abuse was highest in individuals adopted into chaotic home environments whose biological relatives were substance abusers.

## 1.2 Brain development

Compared to other organs, the brain at birth is clearly the most immature. Infant brain volume at birth is about one-fourth to one-third of adult volume. While few if any new neurons develop with age, a massive reorganization occurs where many connections between neurons are pruned and many new ones are formed. Thickening of the insulation (myelin) around parts of nerve cells also occurs and is basic to brain development. These changes are often referred to as “brain plasticity”; the rate and extent of the plastic changes vary with developmental age, contributing to brain growth and efficiency. From three to 13 months of age, infants show change in volume of all brain regions except for the midbrain; growth is particularly striking in areas of the putamen and cerebellum (Choe et al., 2013). Some have suggested that these fastest-growing areas of the brain are most vulnerable to internal and external negative events. Indeed, individual differences in early brain development predict later behaviour.



There is a strong positive relationship between brain volume at the beginning of the second year of life and one's later intelligence; a smaller right amygdala at six months old predicts lower language scores at ages two to five years. Further, experience in early brain development matters as mothers who speak frequently with their infants have children with significantly larger vocabularies at age two than children of relatively non-verbal mothers. Brain volume peaks around age 10–11 for females and 14–15 for males, though connectivity of neurons and integration of brain regions continues into young adulthood. Thus, neither childhood nor adolescence is a period of quiescence.

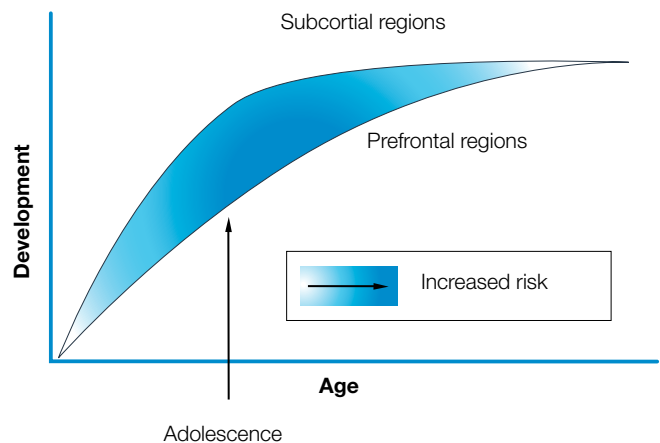
Paralleling research interest in the developing healthy brain, considerable attention has been directed toward children with developmental disorders such as attention deficit hyperactivity disorder (ADHD), conduct disorder, autism and obsessive-compulsive disorder. For example, brain network abnormalities involving the frontal cortex and its connection to the subcortical and cortical regions that are involved in the detection, integration and appraisal of environmental events have been consistently reported among children with ADHD. Some of these brain function deficits have been shown to persist into adulthood (Cubillo, Halari, Smith, Taylor, & Rubia, 2012). In most individuals, there are age-related developmental shifts from “bottom-up” (i.e., limbic to frontal) to “top-down” (i.e., frontal to subcortical) functioning (Rubia, 2012). This shift means that earlier in development, the brain centres influencing emotion regulation are most dominant. As the individual develops, the executive functions of the frontal lobes (i.e., the ability to plan and organize) can exert progressively greater levels of control over the individual's emotions. This transition forms the basis for the cognitive control of behaviour and can be disrupted by psychological trauma and substance abuse.

### 1.2.1 Development of the prefrontal cortex

Totally self-centred, lacking emotional control and overcome by irrational fears, the most violent individuals are two year olds. As developmental theorists have long recognized, the most effective parents, educators and societies are those that teach children inhibition, concern for others, problem-solving skills and the reasons for following rules. These abstract concepts have representation in the developing brain, specifically in the prefrontal cortex, which comprises one-third of the human cortex and is highly interconnected to other brain areas. As

Figure 2 (Somerville, Jones, & Casey, 2010) illustrates, the prefrontal cortex develops later than the subcortical brain regions that support more automatic emotional reactions.

**Figure 2.** Model of development risk according to late maturation of prefrontal brain regions and early maturation of subcortical regions



The late-evolving prefrontal cortex defines us as humans: it allows us to frame events in terms of the past, present and future, and supports our capacity to judge, think abstractly and decide when to act. To obtain control of these functions, the prefrontal cortex develops and differentiates. The focus of this chapter is on the regions that influence impulse control and working memory, particularly the orbital frontal area and dorsal lateral prefrontal cortex, respectively. Yet these brain areas neither contribute to one function alone nor regulate a function in isolation. Moreover, not only can heavy drug consumption result from brain deficits or delayed brain development, substance use can also exacerbate these neurobiological problems. Appropriately, a burgeoning, hopeful new treatment for addiction uses “cognitive control training,” a practise that focuses on the plasticity of the developing brain where specific training procedures are designed to augment the functioning of structures involved in behavioural self-regulation (Wiers, Gladwin, Hofman, Salemink, & Ridderinkhof, 2013).

### 1.2.2 Fear processing

In the simplest terms, life is about survival and reproduction. Our brain mechanisms have evolved to preferentially attend to and react quickly to danger. Seven-month-old infants, for example,



show significantly greater neural activity when presented with fearful facial expressions than happy expressions; they have difficulty disengaging from fearful stimuli that capture and hold their attention (Leppänen & Nelson, 2012). This responsiveness to adult facial expressions appears to generalize to referents in the environment (e.g., if a mother's fearful expression is directed toward a snake). As illustrated in Figure 3 (Feder, Nestler, & Charney, 2009), this development is likely related to growth in the circuitry of the amygdala and orbitofrontal cortex — that is, the brain areas related to the learning of fear.

The amygdala can be seen as serving an “alarm” function, signalling danger in the environment, which can be switched off in an automatic, context-dependent manner by the hippocampus (e.g., “I am at a zoo and the snake is in a cage.”) or with more effort by the prefrontal cortex (e.g., “The snake is three metres away. If I back up slowly, I’ll be fine.”). Inefficient functioning in this circuit can result in an over-reaction to situations perceived as threatening and an excessive release of stress hormones, the latter of which has been demonstrated to further erode the network’s functioning.

Individual differences in fear responses are evident. These differences are important because a frequent rationale for drug abuse is to cope with stress (i.e., to dampen this specific brain network), a view supported in a large study of adult female twins by Littlefield and colleagues (2011). That study found personality traits such as neuroticism (i.e., a tendency to experience negative emotions) were related to symptoms of an alcohol use disorder and a tendency to drink to cope with stress. If susceptibility to negative emotions increases the likelihood one will learn that alcohol can temporarily alleviate these states, it could account for the genetic overlap between neuroticism and alcohol use disorders.

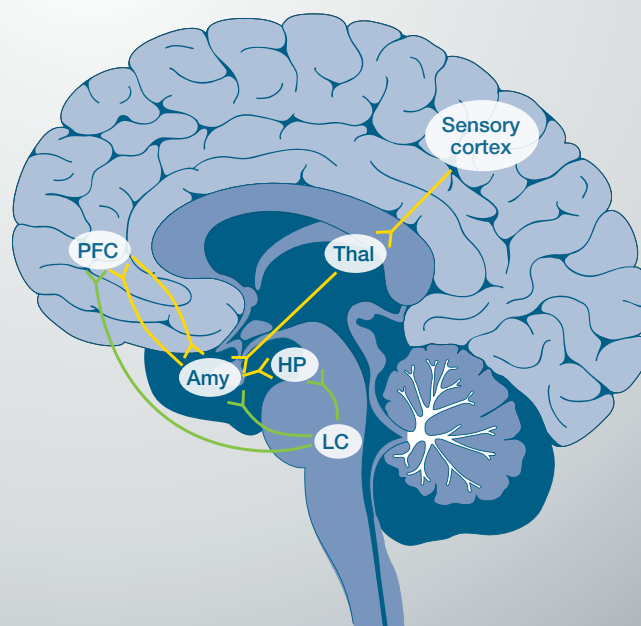
### 1.2.3 Reward cue processing

The fear system does not account for all substance abuse (Doremus-Fitzwater, Varlinskaya, & Spear, 2010). Adolescents are involved in more social interactions than adults and their peers exert considerable influence. Alcohol use increases social interactions, providing a form of social reward that may be particularly valued by young people. Adolescents also display high levels of risk-taking and seek intense stimulation, sometimes achieved by using drugs. During this same

**Figure 3.** Circuits and key regions involved in the brain’s fear system

#### LEGEND

- Thal**  
thalamus
- Amy**  
amygdala
- HP**  
hippocampus
- PFC**  
prefrontal cortex
- LC**  
locus coeruleus





period, the brain's reward circuitry continues its development. As illustrated in Figure 4 (Feder et al., 2009), most research about the reward system has focused on the ascending brain pathways from the ventral tegmental area to the nucleus accumbens and frontal lobes, and the descending pathways that complete the circuit.

The ascending brain pathway uses dopamine, a neurotransmitter that allows communication between brain cells. Stimulation of this brain circuit results mainly from exposure to reward-related cues in the environment, such as seeing a candy bar. Having this reward circuit stimulated results in both the activation and reinforcement of behaviour.

In some animal studies, the stimulation of this reward circuit has been shown to be preferred over eating, even when the animal is starving. The release of dopamine is particularly important for functioning in this brain system and is targeted specifically by most drugs of abuse. Evidence suggests that dopamine influences the ability of reward cues to grab and sustain attention, and to elicit desire and approach. Overt pleasurable effects are more closely related to other neurochemical systems, such as naturally occurring opioids and marijuana-like chemicals that are made and released in the brain.

The brain's reward cue response system continues to develop during adolescence, a period of time in which there is a decrease in excitatory fibres entering the prefrontal cortex, an increase in dopamine fibres and an increase in the enzyme that breaks down dopamine — all factors that, if operating normally, contribute to refining regulatory control. However, dysfunctions in this system, varying from lack of prefrontal control to altered limbic dopamine system responsiveness, appear to greatly increase risk for substance abuse and disinhibited behaviour.

One way to identify the motivational system involved in an individual's substance use is to understand the degree to which each system becomes engaged following drug use (e.g., fear circuitry dampening vs. reward cue circuitry activation; see Pihl, 2010). Drugs that soothe the fear system reduce negative emotional states, which can teach individuals to take the drug when anxious again in future. Certain prescription drugs like Valium and Xanax produce this effect. Activation of the reward cue system, meanwhile, produces a positive state, although not necessarily overt pleasure. This state includes desire (conscious or otherwise) for the reward object and is reinforcing, making the individual more likely to use the drug again in future. While stimulant drugs such as cocaine or amphetamines produce this

**Figure 4.** Circuits and key regions involved in the brain's reward system

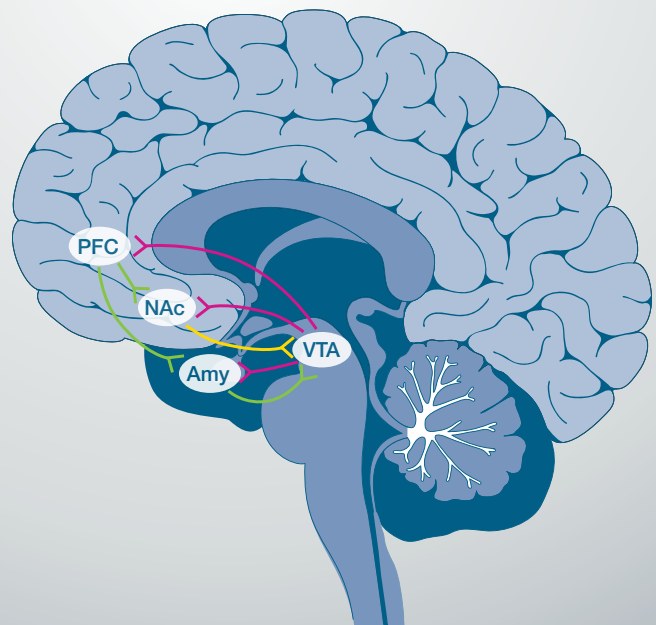
#### LEGEND

**NAc**  
nucleus accumbens

**Amy**  
amygdala

**VTA**  
ventral tegmental area

**PFC**  
prefrontal cortex





effect, the extent to which individuals experience these effects from drugs varies markedly.

Most at-risk individuals experience an unusually strong response in one of these systems, although some individuals display both characteristics. As an example, a longitudinal follow-up study conducted by King and colleagues (2011) found heavy drinkers displayed more of a stimulant effect from drinking alcohol than light drinkers. Two years later, this response predicted binge drinking and a higher likelihood of being diagnosed with an alcohol use disorder.

### 1.3 Environmental risk factors

Although the importance of differential brain development in contributing to risk for substance abuse cannot be emphasized enough, the environment also plays a profound role in shaping brain functioning. As such, it is important to discern the degree to which negative and positive experiences affect brain development.

#### 1.3.1 Maltreatment and early stress

Severe early stress, such as child abuse and maltreatment, can alter gene expression (McEwen, 2012) and brain development, increasing risk for substance abuse as well as a wide range of mental health problems. Unfortunately, the exact percentage of children who are abused or maltreated is not well known: while there were 75,000 police records of violence against children and youth in Canada in 2008, these reports do not include child neglect. In addition, an estimated 90 percent of child abuse cases go unreported. Worse, these problems can be intergenerational, with abused individuals more likely to abuse their own children.

#### 1.3.2 Parenting

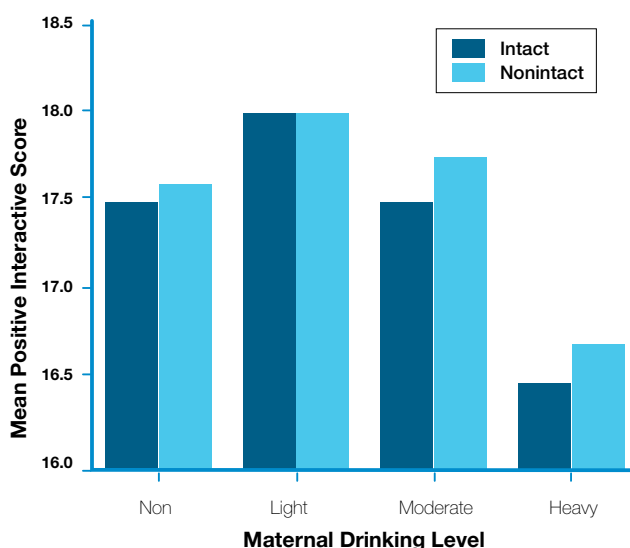
There are many aspects of parenting that are not considered maltreatment, but can still affect a child's risk for drug abuse. Premature birth, low birth weight, prenatal exposure to drugs or alcohol, a non-intact family and the young age of the mother are all associated with risk for drug abuse. However, their individual effects are difficult to determine. In the case of divorce, non-intact families are often occupationally and financially disadvantaged, meaning they are likely to be more dysfunctional than intact families. Also relevant are the ages of the children around the time of the divorce, with adolescents

appearing to be more affected when the divorce occurs before the age of 16.

Factors such as maternal depression, parental substance abuse and parental antisocial behaviour are also of potential predictive value. A mother's depression, whether current or reoccurring, increases risk in her children for numerous adjustment problems, depression, antisocial personality, health problems and substance abuse. Adoption studies and other research methods have indicated that this does not only reflect an inherited genetic predisposition: depressed adoptive mothers also add to risk.

Figure 5 (Pihl, McDuff, Strickler, Assaad, Dubreuil, & Tremblay, 1998) illustrates the effect of a mother's drinking level and the absence of a biological father on her self-rated lack of positive interactions with her 0–23-month-old child. Specifically, heavy drinking mothers showed fewer positive interactions with their infants than the non-, light- and moderate-drinking mothers.

**Figure 5.** Positive maternal interactions as a function of maternal drinking and family status



Data from more than 10,000 families from the Canadian Longitudinal Study of Children and Youth also found that heavy-drinking mothers and mothers from non-intact families had significantly more children rated as anxious, aggressive, hyperactive and with conduct problems between the ages



of two and 11 years (Pihl et al., 1998). These findings are in agreement with other work showing that parental substance abuse, especially alcoholism, increases risk for antisocial behaviour in children. When that effect is controlled, the risk for substance abuse is significantly reduced. Parental antisocial behaviour is, however, a strong predictor of substance abuse in children; this effect appears to occur through both genetic and environmental influences (Jaffee et al., 2012).

Many of these risk factors have been extrapolated from reviews on antisocial behaviour (Jaffee et al., 2012), which is a primary risk factor for substance abuse. This forces focus on the behaviour more likely to represent the underlying predisposing factors. Another example of such a constellation of factors is seen in studies assessing the personality traits of risk-taking, impulsivity and sensation-seeking. The latter, though often seen as an aspect of impulsivity, have also been shown to be separable (Conrod et al., 2000).

It is worth repeating that adolescence is a heightened period of risk-taking, with increased drug use and binge drinking forming part of a larger picture that includes reckless driving, crime, risky sex and other harmful social behaviours. It is commonly believed these behaviours stem from adolescents' lack of knowledge of the risks associated with these activities. For many parents, however, emphasizing the dangers of substance abuse is often the primary way in which they attempt to influence the behaviour of their children. The reality is that adolescents generally do understand the logic of the risks associated with substance abuse, but even with that knowledge, they still do not alter their behaviour. This gap can be explained by the divergence in the timing of the development of logical reasoning, which is well developed by age 15 or 16, and psychosocial maturity, which is not reached until the mid-20s (Steinberg, 2007). This gap also helps explain why information programs describing the dangers of substance abuse often fail or are counterproductive.

### 1.3.3 Peers

Humans are social animals, seeking like-minded others who in turn can influence and reinforce our behaviours. Studies have shown that self-regulation abilities between the ages of 12 and 13 can predict alcohol use problems and peer deviancy at age 15 (Mason et al., 2011), suggesting that young teens with self-regulation problems seek out deviant peers. Notably,

this study does not discount the more general effect of peer influence. A two-way effect is in fact likely, with at-risk children choosing more deviant peers and those peers in turn exerting a strong social influence on the at-risk young person's substance use (Moos, 2006).

Peers potentially influence an individual's beliefs about drugs and as a result can increase the likelihood of substance use. Teens low in self-efficacy (i.e., the belief in one's ability to cope) appear particularly susceptible to peer influences and are at increased risk of problem drinking.

### 1.3.4 Societal factors

Just as there are individuals at risk for drug abuse, the same can be said of cultures, subcultures and social structures that inadvertently channel people toward certain behaviours. One example is the frequent advertising of medications, sending the message that drug use is an acceptable way to solve our problems. Other environments are distinguished by a general absence of rewards, making the choice of drugs seem more understandable. For example, Castello and colleagues (2010) followed Native Americans for a decade after a tribal casino opened. As incomes rose, substance use and antisocial behaviour significantly reduced over time to rates lower than the non-Native controls.

A more surprising example of the effects of social factors is the influence of rules regarding entrance into school. All schools have cut-off age limits for enrolment in kindergarten; children born one month before the cut-off date enter school 11 months earlier than those born the following month. Eight-and-a-half percent of these younger children are diagnosed with ADHD; in comparison, five percent of the children entering school the following year are diagnosed with ADHD. This difference is not trivial, affecting an estimated 900,000 children in the United States (Elder, 2010). An assessment of maturity rather than chronological age for school entrance would help rectify what could be a lifelong adjustment problem associated with a high risk for substance abuse.

## 1.4 Two major pathways of risk

Substance use disorders are linked to numerous child and adolescent developmental problems. Understanding the relevant factors requires a broad understanding of their inter-



relationships. Given the large number of behavioural, biological and psychological factors to be considered, this report uses two broad categories — “externalizing” and “internalizing” — as a framework, based on the notion that some childhood mental health problems manifest outwardly (e.g., aggression), while others manifest inwardly (e.g., anxiety). Statistical analyses of several large databases suggest that many mental health disorders fall into one of these two broad categories (Blanco et al., 2013; Krueger, 1999).

Both internalizing and externalizing problems represent pathways to substance use disorders. Certain internalizing problems, such as mood and anxiety disorders, can double to quadruple the risk for alcohol addiction and significantly increase the risk for other substance use disorders. Kushner and colleagues (2012) showed that it is not individual mood or anxiety disorders that account for this risk, but rather the more general trait of internalization. A similar pattern of results has been found for externalizing mental disorders such as ADHD and conduct disorder (Hicks, Foster, Iacono, & McGue, 2013). The relevant processes differ for these two pathways. Specifically, externalizers seem to be most responsive to drug activation of the reward cue system, while internalizers appear to be attempting to control their hyper-responsive fear-anxiety system.

These internalizing and externalizing disorder clusters are substantially more heritable than any one particular diagnostic category (Nave, Sherman, Funder, Hampson, & Goldberg, 2010). For example, teacher ratings in grades one and two have been shown to predict adult behaviour 40 years later. Children considered impulsive by their grade one and two teachers were later described as being loud, dominating, controlling and ambitious in middle age. Those considered to be self-minimizing as children were seen as adults as insecure, negative about themselves, seeking reassurances, and expressing guilt and victimization.

Our improving ability to identify the relevant developmental processes bodes well for early preventative intervention. Using the underlying risk factors as a strategy for prevention might also contribute to the treatment of active substance use problems by targeting the factors that caused the problems in the first place.



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# 2

## The Externalizing Developmental Pathway to Substance Use Disorders



*By Malak Abu-Shakra and Sylvia Cox*

### Chapter at a Glance

- A common pathway to substance use disorders is the early and sustained expression of temperamental characteristics such as impulsive risk-taking, high sociability and oppositional tendencies.
- High levels of “externalizing” behaviours can lead to oppositional defiant disorder in the preschool years, attention deficit/hyperactivity disorder in the elementary school years and conduct disorder in middle childhood through adolescence.
- Adolescents with impulsive–aggressive tendencies are more likely to try drugs of abuse and develop consequent substance use problems.
- The co-occurrence of behavioural and substance use disorders likely points to a common vulnerability that increases susceptibility for both conditions. This susceptibility is influenced by genetic factors, individual differences in brain development, and environmental conditions and experiences.
- Early diagnosis and intervention can help decrease the frequency of substance use disorders by preventing or reducing the severity of disruptive behavioural disorders.

### 2.1 The link between disruptive behavioural disorders and substance abuse

One of the most common developmental pathways to substance use disorders is characterized by various “externalizing” traits that begin in childhood and continue through adolescence and

into adulthood (Conrod, Pihl, Stewart, & Dongier, 2000; Dick et al., 2013; Hicks, Foster, Iacono, & McGue, 2013; Hicks, Iacono, & McGue, 2013; Kendler, Gardner et al., 2013; Kendler, Sundquist et al., 2012; Moffitt et al., 2011; Pingault et al., 2013; Tarter et al., 2003). These traits include enduring tendencies toward impulsive risk-taking, thrill-seeking, and social boldness





and aggression. Youth following this pathway develop mental health and behavioural problems that manifest outwardly (e.g., as hyperactivity): by the time they reach adolescence, these behaviours greatly increase risk for substance use and abuse.

Hyperactivity can cause problems in the classroom; antisocial behaviours can violate the rights of others. Because externalizing behaviours are typically disruptive to others, these mental health and behavioural problems are commonly referred to as disruptive behavioural disorders (DBDs). Seen in one in five adolescents, DBDs are twice as common in boys as in girls (Merikangas et al., 2010). They are the primary reason youth are referred to mental health services and, while not as common as emotional disorders such as anxiety or depression, are the second most prevalent class of psychiatric conditions among teens between the ages of 13 and 18. Disruptive behavioural **symptoms** are even more common than full-blown clinical disorders.

### **2.1.1 How externalizing disorders affect substance use and abuse**

Disruptive behavioural symptoms and disorders have enormous individual and societal costs, including school maladjustment and dropping out (Tucker-Drob & Harden, 2012), bullying, violence against oneself and others, and serious economic disadvantages in adulthood (Odgers et al., 2008). Compared to those without these behavioural problems, individuals with DBDs have double the risk of abusing tobacco, triple the risk of abusing

alcohol and five times the risk of abusing illicit drugs (Heron et al., 2013; Swendsen et al., 2010). Seventy-five percent of adolescents with DBDs become substance abusers in adulthood and 50 percent of adults with substance use disorders have a history of at least one DBD in childhood or adolescence (Kim-Cohen et al., 2003; Reef, Diamantopoulou, van Meurs, Verhulst, & van der Ende, 2011).

When seeking treatment for substance abuse, individuals with comorbid DBDs suffer worse outcomes than those without these pre-existing, co-occurring problems. They are also less likely to complete treatment and tend to relapse into substance abuse sooner and more frequently (Arcos-Burgos, Velez, Solomon, & Muenke, 2012; White et al., 2004). Among young substance abusers, those with a greater number or more severe co-occurring DBDs tend to have earlier onset of risk and a worse developmental history (Moffitt, 1990). They also have more severe dysfunctions and are less responsive to interventions (Verhulst, Eussen, Berden, Sanders-Woudstra, & van der Ende, 1993; Verhulst & van der Ende, 1993).

### **2.2 How the impulsive–aggressive pathway progresses at various ages**

Almost all young children are impulsive, inattentive and emotionally reactive. In most cases, these behaviours subside as a child matures. In about 25 percent of children, however, these behaviours are unusually elevated and persistent, which is predictive of various child- and adolescent-onset DBDs.



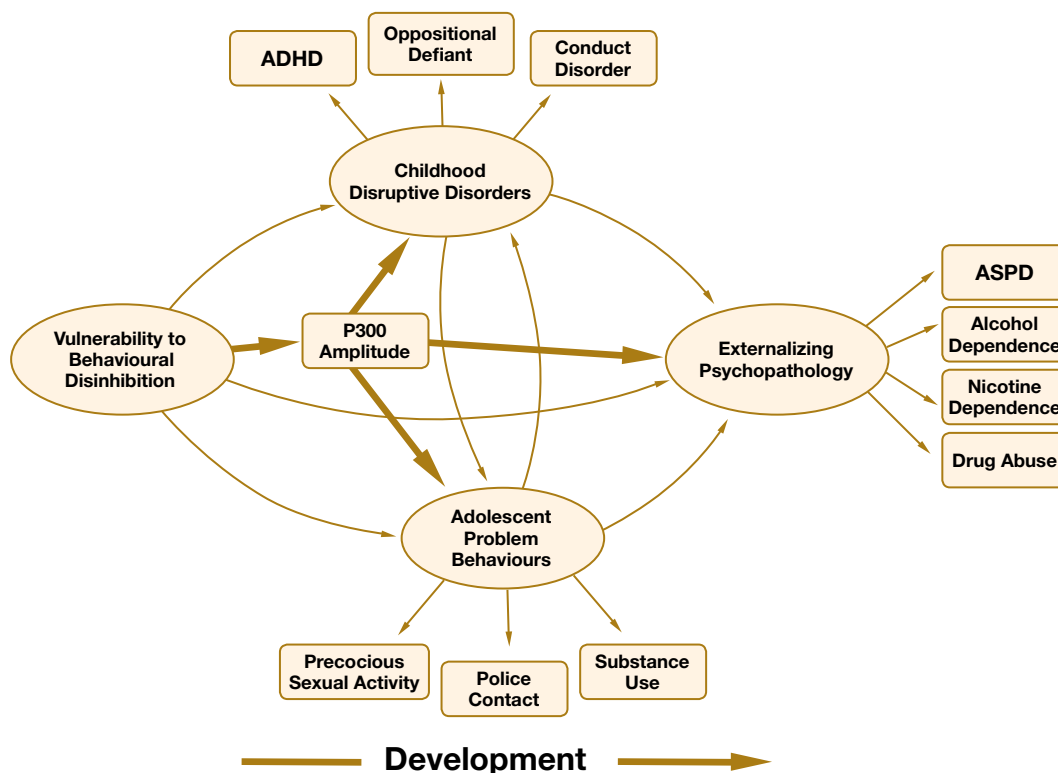
The fourth and fifth editions of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV and DSM-5, respectively) assume oppositional defiant disorder (ODD) in the preschool years leads to conduct disorder in middle childhood and adolescence, which then leads to antisocial personality disorder (ASPD) in adulthood. The existing evidence verifies that assumption: most adults with ASPD previously met criteria for conduct disorder, while most adolescents with conduct disorder previously met criteria for ODD (Moffitt et al., 2008). In general, the earlier children start to show externalizing behaviours, the more negative the consequences they suffer. However, it is important to recognize that not all children who meet the criteria for ODD will transition to conduct disorder and not all adolescents with conduct disorder will transition to ASPD (Moffitt et al., 2008).

Figure 6 (Iacono & Malone, 2011) provides a general overview of the impulsive-aggressive developmental pathway, illustrating how childhood DBDs and adolescent problem behaviours serve as antecedents to externalizing disorders, including substance use disorders, in adulthood.

Much research distinguishes between conduct disorder emerging in childhood from conduct disorder emerging in adolescence (Moffitt et al., 2008; Odgers et al., 2007, 2008). Compared to adolescent-onset conduct disorder, childhood-onset conduct disorder is more often chronic, more common in males, more associated with the presence of other DBDs such as ODD and attention deficit/hyperactivity disorder (ADHD), and more likely to lead to antisocial personality traits and substance use disorders in adulthood. Childhood-onset conduct disorder is typically associated with a history of birth complications, severe maltreatment, parental ASPD, cognitive deficits and lower intelligence, as well as markedly greater academic and social problems.

Adolescence-onset conduct disorder is more common and thought to reflect transient frustrations and modelling of peer behaviour, as opposed to deeply entrenched psychiatric problems. As such, the externalizing behaviours of those with adolescent-onset conduct disorder typically diminish once the individual takes on the roles and responsibilities of adulthood.

**Figure 6.** Impulsive-aggressive developmental pathway to substance use disorders in adulthood





## 2.3 Genetic factors and the heritability of externalizing traits

Both DBDs and substance use disorders run in families and are at least moderately heritable, with conduct disorder and substance use disorders estimated to be 50–60 percent the result of genetic factors (Kendler, Aggen et al., 2011; Kendler, Patrick, Larsson, Gardner, & Lichtenstein, 2013). Much more heritable is the vulnerability for externalizing disorders in general, rather than any specific disorder; accumulating evidence indicates that up to 80 percent of this more general vulnerability is genetic (Wichers, Gillespie, & Kendler, 2013). These findings likely account for why DBDs and substance use disorders substantially co-occur and why, in the children of alcoholic parents, for example, ADHD can be found in one sibling, conduct disorder in another and cocaine addiction in yet another.

### 2.3.1 Shared genes for externalizing disorders and substance abuse

The best evidence for specific genes that contribute to DBDs and substance use disorders comes from the Collaborative Study on the Genetics of Alcoholism, which gives much attention to a gene that affects a receptor for gamma-aminobutyric acid (GABA), an inhibitory transmitter. This particular gene has been correlated with substance use disorders in adulthood (Agrawal et al., 2006), early onset alcoholism (Enoch, 2008), ASPD in adulthood and conduct disorder in childhood and adolescence (Dick et al., 2009). The same gene has also been linked with a brainwave electroencephalography (EEG) marker for behavioural disinhibition (Dick, Aliev, Latendresse, Porjesz, et al., 2013). However, the risk is by no means static — an individual with this genetic profile may have his or her vulnerability to addiction triggered by other factors. For example, genetic risk for externalizing disorders is influenced by factors such as anxiety, parental monitoring and marital status (Dick et al., 2006; Dick, Cho et al., 2013; Dick & Kendler, 2012). In addition, other genes that might play a role in the full spectrum of DBDs and substance use disorders are variations of those related to other neurotransmitters such as endorphin, dopamine and serotonin (Gorwood et al., 2012; Schellekens et al., 2013; Stoltenberg, Christ, & Highland, 2012).

### 2.3.2 Influence of gene–environment interactions on externalizing behaviour

There is evidence that the genes mentioned above do not **encode** for a disease process; instead, they make the individual

more **susceptible** to certain environmental circumstances (Belsky & Pluess, 2009). Specifically, individuals with these genes are especially responsive to the negative effects of low-quality environments, as well as the positive effects of high-quality environments (Cadoret, Yates, Troughton, Woodworth, & Stewart, 1995; Marks, Miller, Schulz, Newcorn, & Halperin, 2007), with environmental events producing long-lasting changes in gene expression (Labonté et al., 2012).

The exact influence of heritable and environmental effects appears to wax and wane across different developmental stages. Social-environmental factors are particularly important as children progress into their teens, when drug and alcohol experimentation typically begins. As adolescents transition into young adulthood, when patterns of heavy consumption are commonly established, genetic effects become steadily more relevant than environmental factors such as parental monitoring (Dick & Kendler, 2012; Palmer et al., 2013). Shifts in relevant influences on behaviour continue into adulthood and the heritable component underlying drinking behaviour during the teenage years appears to differ from the genetic features that influence drinking during adulthood (Edwards & Kendler, 2013). The same dynamic patterns of genetic and environmental effects have also been shown for impulsivity and other externalizing problems and disorders (Arcos-Burgos et al., 2012; Pavlov, Chistiakov, & Chekhonin, 2012; Wichers, Gardner et al., 2013).

## 2.4 Individual factors influencing the impulsive–aggressive pathway

### 2.4.1 Temperament

Because most children are impulsive, identifying abnormally impulsive behaviour at an early age is difficult and the younger the child, the greater the level of impulsivity considered normal (Campbell, Shaw, & Gilliom, 2000). Early impulsivity might be evolutionarily adaptive, fostering exploration of the environment and, with the help of watchful parents, facilitating new learning opportunities without excessive danger (Buchsbaum, Bridgers, Weisberg, & Gopnik, 2012). Before long, however, children are asked to master the ability to suppress inappropriate behaviours and delay gratification. Most are able to do so and their impulsive behaviours steadily decline after the age of two. However, not all children learn to regulate their impulsive tendencies, with behavioural disinhibition persisting or even worsening as they grow older. It is these individuals who are highly vulnerable to DBDs and substance use disorders (Caspi, Henry, McGee,



Moffitt, & Silva, 1995; Caspi, Moffitt, Newman, & Silva, 1996; Mischel et al., 2011; Slutske, Moffitt, Poulton, & Caspi, 2012).

One frequently cited assessment of the ability to delay gratification is the “marshmallow test,” which examines a child’s capacity to reject the immediate receipt of one marshmallow for the later receipt of two (Mischel et al., 2011). Longer waiting times on this test are associated with many positive features later in life, including higher SAT scores and greater academic achievement; better social, cognitive and emotional adjustment in adolescence; higher self-esteem; better coping abilities; and lower drug use and abuse (Mischel et al., 2011).

Comparatively, slow development of inhibitory control in the preschool years increases the risk of using alcohol and drugs by age 17 (Nigg et al., 2006). Preschoolers described as impulsive, fidgety and irritable are also more likely to show disruptive behaviours by age 15 and to develop antisocial personality and alcohol use disorders by age 21 (Caspi et al., 1996; Mischel et al., 2011). When these same traits are used to describe kindergarteners, they robustly predict the use and abuse of tobacco, alcohol and other substances by early to mid-adolescence (Masse & Tremblay, 1997; Pihl & Peterson, 1996), and double the risk of compulsive gambling during adulthood (Slutske et al., 2012). Similarly, impulsivity levels in adolescence reliably predict drinking patterns two years later (Fernie et al., 2013), as well as early onset substance use disorders (Iacono, Malone, & McGue, 2008).

Research suggests the disinhibited personality can be separated into two different components: sensation-seeking (i.e., preference for novel and intense experiences) and impulsivity (i.e., the tendency to act quickly and without forethought when faced with immediate rewards) (Conrod et al., 2000). Each has its own consequences. For example, elevated sensation-seeking traits appear to increase the likelihood of initiating the use of drugs, while the risk of progressing from drug use to abuse seems more related to impulsivity (Ersche, Turton, Muller, Bullmore, & Robbins, 2010).

## 2.4.2 Executive function

Executive function refers to the ability to plan and integrate goal-directed behaviour appropriate to a specific situation (Grace, Floresco, Goto, & Lodge, 2007; Phillips et al., 2003). Problems related to executive function, such as difficulties with attention,

working memory, response inhibition and delaying gratification are frequently seen in youth and adults who are prone to violence (Dery, Toupin, Pauze, Mercier, & Fortin, 1999). Developmental delays in executive function are also seen in those at risk for various DBDs and substance use disorders (Iacono et al., 2008), and are further mirrored by poor motor control, in which executive functions are crucially involved (Cameron et al., 2012; Seitz et al., 2000). For example, infants showing compromised motor tone as early as a few days after birth (resulting in a delayed ability to properly sit and walk) are substantially more likely to become alcoholic (Manzardo et al., 2005). It has also been shown that various deficits in impulse-control, working memory and mental planning are seen not only in individuals addicted to stimulant drugs (e.g., cocaine) but also in their non-addicted siblings — suggesting these deficits reflect a vulnerability that can be inherited (Ersche, Williams, Robbins, & Bullmore 2013; Ersche, Jones, Williams, Turton, Robbins, & Bullmore, 2012; Ersche, Turton et al., 2012).

## 2.4.3 Attention deficit/hyperactivity disorder

ADHD is the most prevalent childhood-onset behavioural disorder. In roughly half of all cases, ADHD symptoms and the associated risk for substance use disorders diminish with age. In other cases, the symptoms can persist into and beyond adolescence, signalling increased risk for adverse academic, social, emotional and cognitive outcomes (Ivanov, Schulz, London, & Newcorn, 2008; Overbey, Snell, & Callis, 2011). Whether ADHD is a **causal** risk factor for substance use disorders, however, is still under debate.

In favour of causality, adults with substance use disorders are more likely to report having childhood ADHD than those without (Ivanov et al., 2008). Moreover, childhood ADHD has been found to increase the risk of subsequent drug use and abuse (Lee, Humphreys, Flory, Liu, & Glass, 2011). The association between ADHD and addictions, particularly to tobacco, sometimes holds up even when controlling for conduct disorder (Elkins, McGue, & Iacono, 2007). In contrast, other evidence suggests the observed association between ADHD and substance use disorders can be attributed to conduct disorder, which is present in one-third to half of adolescents with ADHD (Faraone & Biederman, 2005; Flory & Lynam, 2003). In longitudinal studies, the causal link between ADHD and substance use disorders did not hold after adjusting for concurrent conduct disorder or ODD (August, Winters, Realmuto, Fahnhorst, Botzet, & Lee, 2006; Pingault et al., 2013).



To bridge these contradictory results, some have proposed subtyping ADHD into separate inattention and impulsivity components. After controlling for the impact of co-occurring conduct disorder, only impulsivity has been found to predict the use and abuse of alcohol and tobacco at age 14 and of other substances at age 18 (Elkins et al., 2007).

#### **2.4.4 Early onset substance use**

Individuals who start using drugs earlier are at elevated risk of becoming substance abusers and remaining so throughout much of their lives. This effect can be quite large: as much as a four-fold difference in risk between those who drank to intoxication before age 15 compared to those who started drinking after age 20 (de Girolamo, Dagani, Purcell, Cocchi, & McGorry, 2012). In fact, for every year an adolescent delays using drugs, the risk of becoming addicted shrinks by about five percent (Behrendt, Wittchen, Hoffer, Lieb, & Beesdo, 2009). This reduction might reflect a causal influence of early onset drug use on the later development of substance use disorders, potentially through changes to both social and biological pathways. Early use might promote affiliation with people who model and favour substance use and delinquency, while distancing youth from those who have healthier attitudes and behaviours (DeWit, Adlaf, Offord, & Ogborne, 2000). Early use might also negatively affect cognitive function by disturbing brain development, with impaired cognitive function predicting future substance use disorders (Brown & Tapert, 2004). Early heavy use of alcohol and other drugs can also lead to severe adverse consequences, from sexual victimization (Raghavan, Bogart, Elliott, Vestal, & Schuster, 2004) to drug-related injuries and infections (Hingson, Heeren, Winter, & Wechsler, 2005), all of which can aggravate the risk for substance use disorders.

Another possible explanation does not suppose any causal relation between early onset drug use and later addiction. Instead, early use and abuse might be two sides of the same coin. That is, they may be signatures of a common externalizing tendency that precedes and contributes to both early substance use and later substance abuse (Prescott & Kendler, 1999). Studies have shown that seventh-graders who started drinking before age 13 commit significantly more violence and suicide attempts than those who abstain from drinking at that age (Swahn, Bossarte, & Sullivent, 2008). Further, the early use of alcohol is associated with the later abuse of other drugs along with diverse externalizing behaviours such as early sexual activity

and police contact. These behaviours among others also predict multiple mental health and behavioural problems in adulthood. When alcohol use begins before age 15, ASPD and addiction to tobacco and alcohol develop by age 20 in more than 90 percent of cases, depression in one-third and illicit drug use in virtually all (McGue & Iacono, 2005).

These two proposed models, however, are difficult to disentangle. One possibility is that both are correct: early drug use might represent one particular expression of pre-existing vulnerability and might also aggravate vulnerability to substance use disorders (Krueger et al., 2002). Interventions that delay onset of use could therefore lessen other negative consequences of early drug use.

#### **2.4.5 Poor early socialization**

Social competence includes a child's capacity to maintain positive relationships with peers (Sturaro, van Lier, Cuijpers, & Koot, 2011), which is as stable over development as externalizing symptoms; that is, children who exhibit high levels of social competence early in development will also do so later in life (Burt, Obradovic, Long, & Masten, 2008; Moffitt & Caspi, 2001). Socially incompetent children have few, if any, positive interactions in social contexts and typically struggle with difficulties expressing themselves and understanding others. As a result, they are frequently difficult to understand and respond to. This early psychosocial and emotional maladjustment appears to pave the way for externalizing disorders and later substance abuse (Cicchetti & Schneider-Rosen, 1986).

As an example, four-year-old children who were rated by their mothers and teachers as socially incompetent showed more externalizing problems at age 14 (Bornstein, Hahn, & Haynes, 2010). Similarly, children rejected by their peers show more disruptive behaviours throughout the school-age years (Coie, Lochman, Terry, & Hyman, 1992; Hymel, Rubin, Rowden, & LeMare, 1990). Rejected children are also more likely to affiliate with deviant peers, which further contributes to their conduct problems (Dishion & Patterson, 1999). The converse can also occur with disruptive and delinquent children being less likely to adequately acquire social skills (Masten, 2005; Masten et al., 2005). However, poor early socialization does not seem to directly cause DBDs and substance use disorders. Instead, poorly socialized children frequently suffer from low IQ (Moffitt & Lynam, 1994), which can predict a range of social skills deficits and externalizing problems across childhood (Owens, Shaw, Giovannelli, Garcia, & Yaggi, 1999).



### 2.4.6 Fighting and aggression

Aggression is a multifaceted construct incorporating behaviours ranging from physical and emotional attacks to a lack of empathy (Silver, Arseneault, Langley, Caspi, & Moffitt, 2005). The hypothesized causes of aggression range from the cultural and socioeconomic to the biological and psychological (Siever, 2008).

Like other externalizing features, aggressive behaviours can follow multiple pathways over time, diminishing with maturity in some and continuing as a stable trait in others (Côté, Vaillancourt, & Barker, 2007; Fontaine et al., 2008; Lukkonen, Riala, Hakko, & Räsänen, 2011). The outcomes of aggressive developmental pathways rarely occur in isolation and are most commonly accompanied by other externalizing problems such as conduct disorder in middle childhood to adolescence, substance abuse in adolescence to adulthood (Fontaine et al., 2008; van Lier, Vitaro, Barker, Koot, & Tremblay, 2009), and ASPD in adulthood (de Girolamo et al., 2012).

While the courses of physical and emotional aggression differ over time for males and females, the associations with elevated substance use are the same across gender (van Lier et al., 2009). There is also evidence of bidirectional effects; for example, after controlling for other factors, young adults with at least five symptoms of substance use disorders had double to quadruple the rate of subsequent involvement in physical fights compared to those with no symptoms of substance use disorders (Boden, Fergusson, & Horwood, 2012).

### 2.4.7 Bullying and victimization

Both bullying and victimization reflect difficulty coping with psychosocial challenges. Bullies themselves are often victims (Cook, Williams, Guerra, Kim, & Sadek, 2010), and bullies and victims are both at elevated risk for substance use disorders (Ttofi & Farrington, 2012; Rospenda, Richman, Wolff, & Burke, 2013). There are some differences between bullies and victims, though. For example, drinking among young adult bullies appears to be a direct expression of their aggression and a way to enhance social experiences; drinking by those who are both bully and victim is related to these factors while also serving as a coping strategy. Victims, by comparison, tend to drink less than the other two groups because of fewer social motives and lower alcohol-induced social enhancement (Archimi & Kuntsche, 2014).

## 2.5 Experiential and parental factors influencing the impulsive–aggressive pathway

### 2.5.1 Childhood abuse

Child abuse can take various forms, including physical and emotional abuse, witnessing violence between parents and various forms of neglect such as low parental monitoring or lack of appropriate supervision (Eaves, Prom, & Silberg, 2010). Child abuse can lead to increased aggressive behaviour along with many concomitant behaviours (Jaffee, Caspi, Moffitt, & Taylor, 2004). The effect of child abuse in increasing aggressive behaviours appears to be mediated by disturbances to the child's ability to regulate emotions (Choi & Oh, 2014). Twin studies have found that it is unlikely that physical abuse is triggered by aggression on the part of the child (Jaffee et al., 2004); as with bullying, many abusers were once victims.

The relation between child abuse and substance abuse is commonly noted in clinical practice and well described in the research literature (Afifi, Henrikson, Asmundson, & Sareen, 2012). Twin studies suggest child abuse is a **causative** factor, increasing risk for later substance use problems and combining with the aggravating influence of early drug use (Nelson et al., 2010).

### 2.5.2 Parental substance abuse and psychopathology

Externalizing problems in children can be predicted by the psychiatric disorders seen in their parents, the most extensively studied of which are antisociality, depression and substance use disorders.

#### *The effects of parental antisocial behaviours*

The children of antisocial parents are more likely to develop antisocial behaviours themselves. This tendency reflects a combination of heritable and environmental influences (Cadoret et al., 1995; Jaffee, Strait, & Odgers, 2012). While it is a challenge to disentangle all the various environmental factors that contribute, they likely include modelling, unskilled parenting, abuse and neglect (Blazei, Iacono, & McGue, 2008; Jaffee, Moffitt, Caspi, & Taylor, 2003; Jaffee, Belsky, Harrington, Caspi, & Moffitt, 2006).



## JOHN



John's name has always been synonymous with trouble. In kindergarten, he would fight with those who wanted to play with his toys and never hesitated to roughly take toys from others. Since then, his teachers have consistently described him as out of control: defiant and impulsive, insensitive and inattentive, hyperactive and emotionally reactive.

Now 15, John has been expelled from seven high schools in the past two years. He has shown consistent disregard for the rules, stolen money from peers, kept drugs in his locker and, most recently, had sex with his girlfriend in a school bathroom. He has also been caught stealing his mother's money and jewellery to pay for cocaine and other stimulants, which he has been using on an increasingly regular basis since age 12.

Fed up with his behaviour, his mother dragged John to the general hospital to see a psychologist. The two psychological evaluations performed to date have revealed a lifetime of adversity and trauma: John's parents divorced when he was six years old; his father had severe drug problems and was a drug dealer with a long criminal record; and his mother has a history of depression, including severe postpartum depression. Until the divorce, she was the victim of physical and emotional abuse from John's father, as was John himself. John now lives with his mother in a house where stress and financial struggles are all too frequent. He tells his psychologist that his parents don't love him now — and likely never did.





### **The effects of parental depression**

Maternal depression increases a child's risk for depression and increases risk for drug abuse (Tartter, Hammen, & Brennan, 2014). According to longitudinal and adoption studies, this reflects the effects of being exposed to a depressed mother (Kim-Cohen Moffitt, Taylor, Pawlby, & Caspi, 2005; Tully, Iacono, & McGue, 2008), explained in large part by the development of externalizing behaviours (Tartter et al., 2014). Exposure to maternal depression is associated with increased negative critical interactions between the mother and the child, such as hostile interactions and emotional over-involvement, which in turn contribute to the development of externalizing disorders.

In addition to dysfunctional parenting styles, maternal depression aggravates risk for externalizing disorders through exposure to stressful family environments, and stressors associated with low socio-economic status resulting from the reduced earning potential in depressed parents. Successful treatment of maternal depression has been shown to decrease the child's delinquent behaviours (Weissman et al., 2006). The influence of depression in the father is less understood. Some evidence suggests it can increase the behavioural problems seen in two-year-old children (Pemberton et al., 2010). (Other ways in which parental depression might increase risk for substance abuse, such as the promotion of mood disorders in the child, are discussed in the following chapter.)

### **The effects of parental substance use disorders**

Numerous family studies have established a link between parents with a substance use disorder and later externalizing problems and substance misuse in their children. For example, a parental history of alcoholism puts a 17-year-old adolescent at double to triple the risk of suffering from externalizing and substance use disorders (Marmorstein, Iacono, & McGue, 2009). Like the other factors discussed in this chapter, this association likely reflects the full range of intersecting factors, including a shared genetic vulnerability, poor parenting, modelling, child abuse and neglect (Haber et al., 2010; Jaffee et al., 2012).

### **2.5.3 Peer deviance**

Adolescents are more likely to use and misuse drugs if their friends do (Dick, 2011). In adolescence, peer deviance also predicts conduct problems and risky behaviours (Thornberry & Krohn, 1997). For example, adolescents affiliated with gangs display more conduct problems (Thornberry, Freeman-Gallant, Lizotte,

Krohn, & Smith, 2003) and generally behave more aggressively (Haviland, Nagin, & Rosenbaum, 2007) than those who are not. These associations might indicate **social-influence effects** (e.g., delinquent friends modelling and encouraging conduct behaviours (Dishion, McCord, & Poulin, 1999)) or, alternatively, **social-selection effects** (e.g., those vulnerable to acting antisocially choosing delinquent friends (Kendler, Jacobson, Myers, & Eaves, 2008)).

Both effects might be at play across the course of a youth's development (Thornberry, 1987). A longitudinal twin study assessing peer delinquency between the ages of five and 28 found that as age increased, so did the importance of genetic effects on selecting delinquent friends (Kendler, Jacobson, Gardner et al., 2007). Further, the genetic effects on antisocial behaviour are stronger in the presence of delinquent peers (Button et al. 2007). Essentially, although adolescents who are engaged in antisocial behaviours choose to have deviant friends, doing so aggravates their vulnerability to additional behavioural problems, including drug misuse (Jaffee et al., 2012).

## **2.6 Neurobiological and neurochemical factors influencing the impulsive-aggressive pathway**

Though much remains to be learned about the neurobiology and neurochemistry of the impulsive-aggressive pathway to substance use disorders, a few core features about normal and abnormal brain development have emerged.

### **2.6.1 Prefrontal cortex**

First, because children and adolescents typically act impulsively and disruptively, it has been proposed that they simply have poorly functioning prefrontal cortices. Studies of the developing brain from infancy onward, though, paint a more nuanced picture. Like the rest of the brain, the prefrontal cortex grows rapidly after we are born, reaching 80 percent of its adult size within three years. The three-year old prefrontal cortex has up to twice as many synapses as the adult brain. As such, brain development from early childhood onward appears to be a process of "pruning" as much as growth — eliminating unnecessary connections between neurons and retaining only those that are useful. Whereas pruning of some brain areas is largely complete



by the late teens (Lenroot & Giedd, 2006; Sowell, Thompson, Holmes, Jernigan, & Toga, 1999), other brain maturation processes continue into the 20s and 30s, including changes in the thickness of the cortex, the development of the cortical and subcortical brain regions involved in reward-response processes, and the interconnectivity between these brain regions (Rubia, 2013; Shaw et al., 2006; Somerville, Hare, & Casey, 2011). This sculpting of the brain is thought to be influenced greatly by life experiences (Johnston, Ishida, Matsushita, Nishimura, & Tsuji, 2009; Mangina & Sokolov, 2006; Pascual-Leone, Amedi, Fregni, & Merabet, 2005; Tottenham, 2014).

Second, as illustrated in Figure 7 (Kupfer, Frank, & Phillips, 2012), the prefrontal cortex has multiple sub-regions, some of which function to restrain activity in the subcortical regions that respond to reward and emotional experiences, and others that assist the subcortical regions in the planning of appropriate actions and narrowing our focus to the task at hand. (Of course, this narrowed focus is not always directed toward healthy goals.)

### The role of the prefrontal cortex in regulating and inhibiting behaviour

Because the adolescent brain's cortical wiring and the functional interconnections between brain regions remain immature, it could be assumed that adolescents are unable to regulate their behaviours. However, depending on the social stimuli that are present, adolescents actually perform **better** than adults on some tasks. For example, adolescents can perform better than adults when inhibiting behavioural responses in the presence of neutral faces, but they perform worse in the presence of happy faces. This compromised performance in the presence of happy faces is accompanied by a heightened reactivity of the ventral striatum, a part of the brain that is largely involved in the detection of and learning about novelty and reward (Hare, O'Doherty, Camerer, Schultz, & Rangel, 2008; Somerville, Fani, & McClure-Tone, 2011; Somerville, Hare, et al., 2011).

These findings suggest the brain's ability to exert inhibitory control is not absent in adolescents, but is instead determined by the context. It is the lack of synchrony between the prefrontal cortex

**Figure 7.** Brain circuits involved in the regulation of emotions and processing of rewards

#### LEGEND

##### DLPFC

*dorsolateral prefrontal cortex*

##### VLPFC

*ventrolateral prefrontal cortex*

##### mPFC

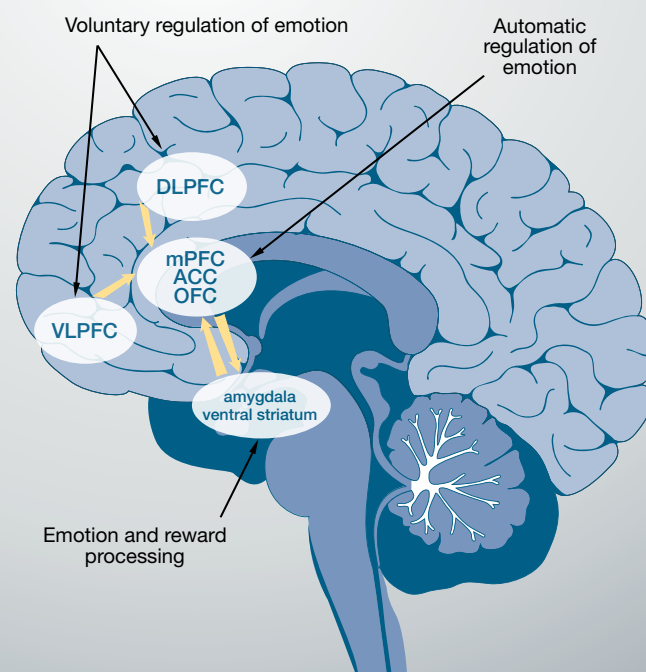
*medial prefrontal cortex*

##### ACC

*anterior cingulate cortex*

##### OFC

*orbitofrontal cortex*





and limbic systems, which is activated by stimuli relevant to an adolescent's motivations, that tips the scales against a calculated rational response in favour of a risky one (Casey & Caudle, 2013). As such, a relatively underdeveloped prefrontal cortex does not entirely account for the rash decisions one makes as an adolescent. Instead, adolescent impulsivity is primarily a battle between two opposing forces — the approach (i.e., "go") and avoidance (i.e., "stop") systems — with the former sometimes overpowering the latter, making adolescents overly sensitive to rewards.

Just as there are individual differences in behaviour, there are also individual differences in the brain. For example, many individuals with substance-abusing parents do not "mature out" of early brain features such as an elevated sensitivity to reward and disinhibited behaviours persist throughout adolescence and into adulthood (Hariri, 2009; Shaw et al., 2009). In addition, impulsive adolescents have a thinner frontal cortex (Schilling et al., 2013), and the non-addicted siblings of cocaine addicts who themselves have high levels of sensation-seeking show disturbances in the cortical-subcortical brain circuits involved in impulsive responding (Ersche, 2013; Ersche, Jones, Williams, Robbins, & Bullmore, 2013; Ersche, Jones, Williams, Smith, Bullmore, & Robbins, 2013; Ersche, Williams, Robbins, & Bullmore, 2013).

Together, these studies indicate that poor cortical-subcortical regulation and poorly regulated inhibitory responses could be familial traits that predate the expression of addictions. Indeed, studies on adolescents have demonstrated that atypical patterns of brain activation during response-inhibition tasks predict subsequent drinking patterns (Norman et al., 2011) and related negative outcomes such as alcohol-induced blackouts (Wetherill, Castro, Squeglia, & Tapert, 2013). These abnormal patterns of brain activation have also been shown to predict the use and misuse of other drugs over the next 18 months (Mahmood et al., 2013).

## 2.6.2 Dopamine and serotonin

Multiple chemical transmitters are involved in the communication between brain cells. Of particular interest for the impulsive-aggressive developmental pathway are cells that communicate

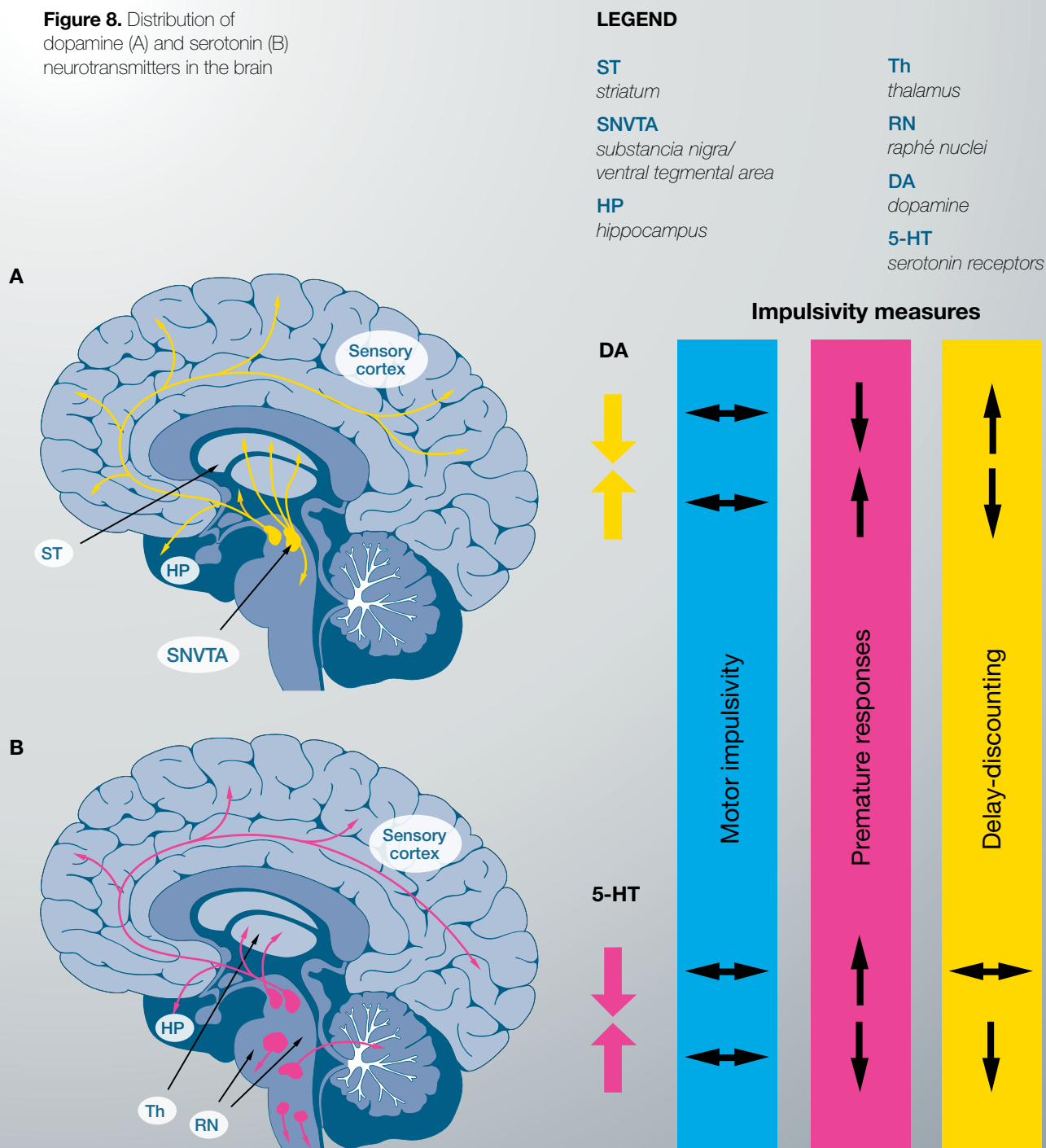
using the neurotransmitters dopamine and serotonin. Both are implicated in approach-avoidance responses to emotionally relevant stimuli, with dopamine being more involved in approach and serotonin more involved in avoidance (Berridge & Robinson, 2003; Depue & Spoont, 1986; Ikemoto & Panksepp, 1999). Figure 8 (Dalley & Roiser, 2012) illustrates the distribution of dopamine and serotonin neurotransmitters in the brain, with the upward and downward arrows denoting increased and decreased impulsivity, respectively. The "stop" and "go" systems are also influenced by gonadal hormones such as testosterone, which surge during the teenage years and promote risky, reward-seeking behaviours (Peper & Dahl, 2013).

Signs of low serotonin function are observed in individuals exhibiting a wide range of impulsive and aggressive behaviours (Leyton et al., 2001; Siever, 2008), including substance use disorders (Berglund, Balldin, Berggren, Gerdner, & Fahlke, 2013; Nishikawa et al., 2009). In addition, evidence suggests low serotonin function is a cause, rather than just a correlate, of these behaviours. For example, in experimental research with both people and lab animals, it has been found that decreasing serotonin transmission can reproduce clinically relevant externalizing behaviours such as aggression (LeMarquand, Pihl, & Benkelfat, 1994a, 1994b; Pihl, Peterson, & Lau, 1993).

Perhaps the most studied neurotransmitter in relation to reward-seeking behaviours and substance abuse is dopamine. Dopamine transmission promotes approach toward rewards and stimuli previously paired with drugs (Robinson & Berridge, 2008; Schultz, 2007a, 2007b; Wise, 2004). Dopamine transmission is also activated by nearly all drugs of abuse (Di Chiara & Imperato, 1988), although its exact role could be less critical for some substances (e.g., opiates) than others (e.g., stimulants) (Badiani et al., 2011). Intriguingly, marked individual differences in the magnitude of the drug-induced activation of the dopamine system are seen, and are positively correlated with the personality traits of novelty-seeking and impulsivity (Boileau et al., 2003; Buckholz et al., 2010; Leyton et al., 2002). Recent evidence indicates increased risk for addictions is associated with altered drug- and drug-cue-induced dopamine responses (Oberlin et al., 2013; Setiawan et al., 2014; Casey et al., 2013).



**Figure 8.** Distribution of dopamine (A) and serotonin (B) neurotransmitters in the brain





## 2.7 Conclusion: Building a framework for treatment and prevention

Although the review of the literature in this chapter was not meant to be exhaustive, it is clear that a broad spectrum of disinhibited behavioural traits increases susceptibility to both disruptive behaviours and substance use problems. When examining the impulsive–aggressive developmental pathway across multiple levels — genetic, neurobiological, psychological, social — three main themes emerge:

1. While most children exhibit some degree of impulsivity and aggression, only some do so with enough severity and persistence to be considered clinically relevant. The most severely affected pass through a developmental pathway that begins with DBDs and ends with substance use disorders.
2. Both DBDs and substance use disorders are influenced at least modestly by a shared heritable risk for externalizing problems. Yet this heritable risk is not inevitable: various social-environmental factors influence how these inherited tendencies are expressed.
3. The neurobiology underlying pre-existing risk traits and behavioural tendencies are beginning to be understood, including the brain systems affecting sensitivity to rewards and punishments, as well as our tendency to be drawn toward positive stimuli and deterred by negative ones. These neurobiological traits can be altered by environmental experiences, learning and drug use itself. While much more needs to be learned, there is now the beginning of a coherent framework for understanding how brain-related disturbances make it difficult for some individuals to restrain substance use and other externalizing behaviours. The hope is that these findings will improve our understanding of the causes of substance use disorders and help identify distinct pathways and treatment needs.

A crucial theme that cuts across all these points is that risk for the impulsive–aggressive pathway to substance use problems is formed in childhood. Thus, interventions targeting children and families at the developmental stage of early childhood could prove most effective in prevention. While the large number of risk factors underscores the complexity of the issue, it also identifies multiple targets for prevention and intervention.



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# 3

## The Internalizing Developmental Pathway to Substance Use Disorders



*By Maeve O'Leary-Barrett*

### Chapter at a Glance

- A tendency toward fear, anxiety and depression (i.e., “internalizing” behaviours) can be detected early in life and could indicate higher risk for substance use problems.
- Females are two to three times more likely than males to experience anxiety and depression, with gender differences in anxiety beginning in childhood and gender differences in depression emerging in adolescence.
- Adolescents with anxious–depressive tendencies are more likely to try drugs of abuse and develop consequent substance use problems. For these individuals, substance use appears to reflect a self-medicating coping style (i.e., an attempt to relieve negative emotions).
- The co-occurrence of internalizing behaviours and substance use disorders likely points to a common vulnerability that increases susceptibility for both. This susceptibility is influenced by genetic factors, individual differences in brain development, child abuse and neglect, and other environmental conditions and experiences.
- Substance use can lead to further anxiety and lowering of mood in the long term, creating an ongoing cycle of internalizing problems and substance misuse.
- Early diagnosis and intervention can help decrease the frequency and severity of substance use disorders by preventing or reducing internalizing symptoms and disorders before the addiction becomes deeply engrained.





### 3.1 The link between mood and anxiety disorders and substance abuse

Mood and anxiety disorders are among the most prevalent mental health problems that co-occur with substance use disorders, having been observed in approximately 40 percent and 30 percent of substance-abusing adults, respectively (Conway, Compton, Stinson, & Grant, 2006). Among youth, 11–32 percent suffer from depression, making it the second-most common mental health problem after conduct problems. Anxiety disorders are also common, occurring in 7–40 percent of youth, with a median estimate of 16–18 percent (O’Neil, Conner, & Kendall, 2011).

After onset, these “internalizing” disorders and behavioural problems are relatively stable across time. For instance, preschoolers who are rated by their parents as having mood or anxiety problems are nearly three times more likely than other children to have similar difficulties at age 10 (Mesman & Koot, 2001). The typical age of onset varies by symptom profile and diagnostic category: separation anxiety and specific phobias usually begin in early to middle childhood, social phobia in early to middle adolescence and panic disorder in early adulthood. An estimated 40–60 percent of anxious children are thought to meet criteria for more than one anxiety disorder and susceptibility to anxiety disorders in general endures longer

than any one specific diagnosis. In comparison, the likelihood of being diagnosed with a mood disorder increases markedly with age, with major depression occurring in approximately one percent of preschool children, two percent of school-age children and five percent of adolescents, with the latter rate being similar to that found in adults.

Internalizing **symptoms** are even more common than full-blown, diagnosed emotional disorders. In young adults, such symptoms are associated with diminished interpersonal functioning, substance misuse, an increased likelihood of major depression and other emotional disorders, and an increased probability of externalizing behaviours and problems.

#### 3.1.1 Challenges in identifying internalizing disorders in early childhood

Research on internalizing disorders in early childhood can be challenging for a variety of reasons. First, mood and anxiety problems are viewed as less problematic by parents and teachers than externalizing problems (Tandon, Cardeli, & Ruby, 2009); a child with internalizing problems is not typically bothering others. In addition, the presence of internalizing disorders in early childhood is considered controversial. They are more difficult to detect, as preschoolers have a limited ability to articulate their internal states, and their existence goes against the social expectation of preschool being a carefree



period. Nevertheless, accumulating evidence indicates that mood and anxiety problems can exist in young children and can be reliably assessed and differentiated from externalizing problems as early as two years of age.

### 3.1.2 How internalizing disorders affect substance use and abuse

In most cases, mood and anxiety problems precede the onset of substance use, with the emotional symptoms first appearing in childhood and substance use starting later. On average, Canadian youth initiate alcohol use at age 15 (Health Canada, 2011), with 10 percent of individuals over the age of 15 reporting symptoms consistent with alcohol or drug dependence (Statistics Canada, 2003). That mood and anxiety problems precede substance use is consistent with the notion that internalizing symptoms are risk factors for the development of substance abuse. There are several explanatory models that can account for this association.

The first is the self-medication model, which holds that individuals use alcohol or drugs to cope with negative emotions such as sadness or anxiety. Although some dislike this term because the long-term effects of the “medication” are negative rather than positive, one of the primary reasons adolescents use alcohol is to relieve stress and forget about problems (Simantov, Schoen, & Klein, 2000). A second model states that there are common causal factors and traits (e.g., personality, genetic, neurobiological, environmental) for both internalizing problems and drug use. A third model says substance misuse can induce or exacerbate subsequent psychological symptoms because of the effect of substances on brain functioning and mood. Lastly, a bidirectional model suggests that psychological symptoms and substance misuse mutually influence one another or even make each other worse over time. These models are not incompatible and support has been found for each of them (Fergusson, Boden, & Horwood, 2011).

The effects of internalizing symptoms on later substance use appear to be more nuanced than those of externalizing symptoms. Notably, while the **concurrent** associations between internalizing symptoms and substance use are clear at the onset of substance use, **prospective** associations are less clear: high levels of internalizing symptoms are reported to predict both greater and lesser involvement with drugs, depending on the presence of additional factors such as the

externalizing behaviours discussed in the previous chapter (Dawson, Goldstein, Moss, Li, & Grant, 2010; Pardini, White, & Stouthamer-Loeber, 2007; Wittchen et al., 2007).

While this chapter focuses on the role mood and anxiety problems play in the development of substance use disorders, it does not assume a dichotomy between internalizing and externalizing problems. These two dimensions of mental health problems can co-exist in the same person and individuals with both types of problems could be at higher risk for substance use disorders than those with symptoms from one dimension alone (Dawson et al., 2010).

## 3.2 Genetic factors and the heritability of internalizing traits

The inheritance patterns of most psychiatric disorders suggest that genetic factors are correlates of general rather than specific risk for mental illness (Kessler et al., 2011). Overall, genetic factors account for 50 percent of the variance in internalizing symptoms and shared environmental factors account for about 30 percent. These figures indicate the substantial influence of family-based factors, both genetic and environmental.

The magnitude of these influences on substance use, however, depends on the stage of development. For example, in those with internalizing traits, genetic influences on alcohol use appear to be lower in adolescents than in adults (Edwards, Larsson, Lichtenstein, & Kendler, 2011). In adolescents, onset of use appears to be more closely related to environmental factors such as availability, peer use and family use. Genetic factors might play a larger role in determining which individuals progress to heavy use, with heritability for addiction estimated at 30–60 percent. Family alcohol problems, stress and the presence of concurrent externalizing mental health problems are the most common factors associated with shared risk for internalizing problems and problem alcohol use in adolescence.

### 3.2.1 Shared genes for internalizing disorders and substance abuse

Although specific risk genes shared between internalizing and substance use disorders have yet to be reliably identified, evidence suggests a modest contribution of several genes that affect dopamine and serotonin, the neurotransmitters that influence approach and avoidance behaviours, respectively. These include the gene that encodes for the serotonin



transporter, which limits the duration of serotonin transmission by taking the transmitter back into the cell; the monoamine oxidase A (MAOA) gene, which influences the breakdown of serotonin and dopamine; and the DRD2 gene, which encodes the dopamine receptor D<sub>2</sub> (Saraceno, Munafo, Heron, Craddock, & Van Den Bree, 2009).

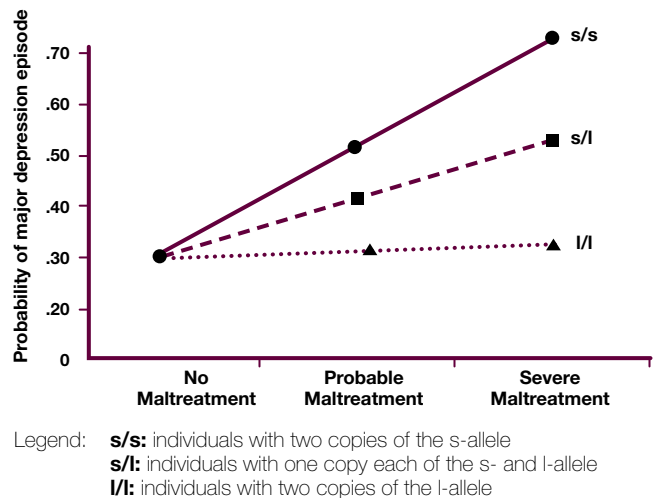
### 3.2.2 Influence of gene–environment interactions on depression

Genetic factors can also interact with an individual's environment to influence the likelihood of experiencing negative outcomes such as depression. The serotonin system has provided a particularly compelling source of candidate genes for mood disorders. For example, a variant in the serotonin transporter gene, SLC6A4, appears to modestly increase the risk for anxiety and depression.

A prospective-longitudinal study by Caspi and colleagues (2003) showed how genetic factors can help explain why stressful life events lead to depression in some people, but not in others. At age 26, individuals with one version of the serotonin transporter gene involving one or two copies of the short (s-) allele showed more depressive symptoms, depressive disorders and suicidality in relation to severely stressful life events (e.g., childhood maltreatment or serious medical conditions) than those with another variant of the gene involving two copies of the long (l-) allele. (An allele is one of two or more alternative forms of a gene that arise by mutation and are found at the same position on a specific chromosome.) Because there were no significant differences between the genetic subgroups in the number of stressful life events experienced, these findings imply that variations in the serotonin transporter gene did not influence exposure to stressful events so much as alter the individual's response to those events.

Figure 9 (Caspi et al., 2003) further illustrates these findings, looking specifically at the association between childhood maltreatment and major depressive episodes during young adulthood. Although not all subsequent studies replicated this association, two recent meta-analyses were supportive, both for depression onset in adults (Karg, Burmeister, Shedden, & Sen, 2011) and adolescents (van Ijzendoorn, Belsky, & Bakermans-Kronenburg, 2012).

**Figure 9.** Likelihood of experiencing a major depressive episode in the past year (ages 18–26 years) following childhood maltreatment (ages 3–11 years), according to variation in the gene that encodes for the serotonin transporter



### 3.2.3 Influence of gene–environment interactions on anxiety

While the majority of studies have focused on the association between the serotonin system and depression, a similar relationship between the serotonin transporter gene and emotional maltreatment during childhood can help explain some of the variability in anxiety sensitivity. Anxiety sensitivity is a personality trait associated with increased susceptibility to anxiety disorders and possibly depressive disorders. The serotonin transporter gene also increases anxiety sensitivity if there had been emotional maltreatment during childhood (Stein, Schork, & Gelernter, 2008). A recent meta-analysis suggests this increase could be related to an attentional bias for negative stimuli (Pergamin-Hight, Bakermans-Kranenburg, van Ijzendoorn, & Bar-Haim, 2012).

### 3.2.4 Influence of gene–environment interactions on substance use

The serotonin transporter s-allele has also been found to increase the risk of early onset alcohol use in maltreated individuals. This increase again suggests some shared genetic vulnerability between depression, anxiety and alcohol abuse (Herman & Balogh, 2012). For example, the serotonin transporter gene has been associated with differences in brain responses to fear-provoking stimuli, including responses by the amygdala, a brain region crucially involved in the processing



of emotional stimuli (Murphy et al., 2013). Overall, it appears that particular genetic variations could confer shared risk for internalizing mental health problems and substance misuse, presumably influencing psychobiological processes that are relevant for both types of problems.

### 3.3 How the anxious–depressive pathway progresses at various ages

Although multiple approaches can be used to disentangle the factors that confer risk for specific disorders as well as mental illness and addiction more generally, perhaps the most informative is to organize risk factors by the problem's age of onset. One such study on depression (Shanahan, Copeland, Costello, & Angold, 2011) found that child- and adult-onset depression are both best explained by the recency of negative events. Put plainly, an event has the strongest impact on depression in the period closely following its occurrence, suggesting the disruptive effects of negative events are time-limited.

Adolescent-onset depression follows a separate risk model and is better accounted for by the biological changes that occur during puberty. This stage of development is associated with physical and hormonal changes that can be disruptive on both the psychological and social levels (e.g., hormonal changes can increase negative emotions; physical changes can increase sensitivity to body image). Pubertal status (i.e., the stage of physical maturation) and its timing relative to peers are also implicated in adolescent depression. In girls, for instance, a more mature pubertal status has been associated with higher rates of depressive symptoms and increased risk for psychosocial distress (Andersen & Teicher, 2009).

For substance use disorders, both pubertal and genetic factors show effects dependent on age. An earlier onset of puberty increases risk for substance use problems, an effect further influenced by sensation-seeking and impulsivity traits (Castellanos-Ryan, Parent, Vitaro, Tremblay, & Séguin, 2013). Similarly, a longitudinal study of same-sex adolescent twins found that both genetic and environmental influences on the frequency of alcohol intoxication are dynamic across adolescence and into early adulthood (Edwards et al., 2011). Specifically, between the ages of 13 and 20, a combination of heritable and environmental factors contributes to early

alcohol use. In mid adolescence, the genetic contribution diminishes and alcohol use becomes more closely related to environmental factors; by late adolescence, as drinking patterns become established, intoxication frequency reflects the genetic influences again as well as the unique experiences of the individual.

Comparing these effects to influences of anxiety and depression indicates that these internalizing symptoms play a large role in early drinking behaviours. However, during later adolescence, high internalizing symptoms actually **decrease** intoxication rates, suggesting additional factors are necessary to convert these traits to further alcohol use problems. The remainder of this chapter looks at some of the individual, environmental and neurobiological risk factors related to internalizing disorders that can direct the anxious–depressive pathway to substance use disorders.

### 3.4 Individual factors influencing the anxious–depressive pathway

#### 3.4.1 Temperament

Neuroticism, the tendency to experience negative emotions, is considered by many to reflect the core of internalizing problems. Some argue neuroticism is the most important factor in behavioural public health, with its economic costs exceeding those associated with other psychiatric disorders (Cuijpers et al., 2010).

Neurotic tendencies can be identified in children at an early age. A series of studies by Kagan and colleagues (Kagan, Reznick, & Snidman, 1987, 1988; Kagan, 1997) indicated that children at two extremes of temperament — inhibited versus impulsive — can be identified at age two using a variety of behavioural and physiological measures (e.g., inhibited children show larger increases in heart rate and skeletal muscle tension in response to stress). These behavioural styles are remarkably stable, remaining constant throughout the school years and into adulthood. In addition, some evidence suggests that, as adults, inhibited individuals show exaggerated brain responses in the amygdala to unfamiliar faces (Schwartz, Wright, Shin, Kagan, & Rauch, 2003), suggesting heightened emotional reactivity to unknown social stimuli. At least some of this variability in the amygdala seems to be related to variability in the serotonin transporter gene discussed earlier (Murphy et al., 2013).



Behavioural inhibition, a temperamental factor involving withdrawal, avoidance, overarousal and fear of the unfamiliar, at age three can predict emotional disorders in adulthood. Inhibited children are much more likely to be diagnosed with depression and to attempt suicide, slightly more likely to experience anxiety and mood disorders, and significantly more likely to develop alcohol use problems by age 21 (Caspi, Moffitt, Newman, & Silva, 1996). When alcohol-dependence data are broken down by gender, the effect of behavioural inhibition appears to be relevant for boys only.

### **How internalizing personality traits affect substance use patterns and behaviour**

Individuals with high levels of internalizing traits report using substances to regulate their negative emotions. Consistent with the self-medication model, individuals with high levels of hopelessness have been shown to cope with depression by drinking (Woicik, Conrod, Stewart, & Pihl, 2009), which can then lead to severe alcohol use problems (Grant, Stewart, & Birch, 2007). Internalizing personality traits can also intensify the association between internalizing symptoms and alcohol use. For example, individuals with high levels of both hopelessness and depressive symptoms, as well as those with high levels of both anxiety sensitivity and anxiety symptoms, show a more rapid increase in alcohol use across adolescence (Mackie, Castellanos-Ryan, & Conrod, 2011).

Although anxiety sensitivity has been consistently associated with substance use to cope with anxiety symptoms as well as increased substance use in adulthood, this personality trait has not been consistently associated with substance use in early and mid adolescence. Anxiety sensitivity might actually protect individuals from risky behaviours during youth, translating to vulnerability to substance misuse only later in development, particularly when combined with other risk factors (Stewart & Kushner, 2001).

Personality traits can also affect a person's substance of choice, with the preferred substance closely matching the self-medicating coping style associated with each trait (Conrod, Pihl, Stewart, & Dongier, 2000; Woicik et al., 2009). For example, women with elevated levels of hopelessness are three times more likely to be dependent on painkillers than those with other personality profiles, whereas women with elevated levels of anxiety sensitivity are three times more likely to be dependent

on anti-anxiety drugs. In addition, women with elevated anxiety sensitivity and hopelessness traits are less likely to be dependent on substances with stimulant properties (e.g., cocaine) than those with high levels of externalizing personality traits.

Personality has also been shown to affect physiological responses to substances, especially to alcohol. Individuals high in anxiety sensitivity are more likely to experience the sedative and anxiety-reduction effects of alcohol, whereas those high in sensation-seeking traits or with a family history of alcohol problems are more sensitive to its stimulant properties (MacDonald, Baker, Stewart, & Skinner, 2000; Brunelle et al., 2004). These studies indicate that subjective experiences of substances and the motivations for using them vary depending on a individual's personality. One implication is that treatment efforts would benefit from selecting different clinical strategies based on the individual's personality traits and motivations.

### **3.4.2 Poor early attachment**

Attachment refers to the tendency to want to be close to emotionally important figures such as, during infancy, parents and caregivers. Parental responses and sensitivity are thought to be particularly important to the development of a secure attachment style; in turn, secure attachment in infancy strongly influences the development of secure relationships and emotional reactions to relationships in later life.

Heritable genetic factors account for 25 percent of a person's style of attachment, with the remainder of the variance attributed to environmental factors unique to the individual (Finkel & Matheny 2000). While rates of attachment disorganization are estimated at 15 percent in normal, non-clinical samples, these figures rise to 80 percent in maltreated samples (Carlson, Cicchetti, Barnett, & Braunwald, 1989). Moreover, the presence and history of attachment figures influences infants' physiological responses to stressful events. For instance, toddlers in secure attachment relationships do not show elevations in cortisol (i.e., the stress hormone) to distress-eliciting events when in the presence of their attachment figure, while toddlers in insecure attachment relationships show marked elevations in cortisol even when their attachment figure is present (Gunnar & Donzella, 2002).

During adolescence, poor attachment influences a widening circle of phenomena: it is linked, for example, to substance use by way of its impact on internalizing problems. A consistent



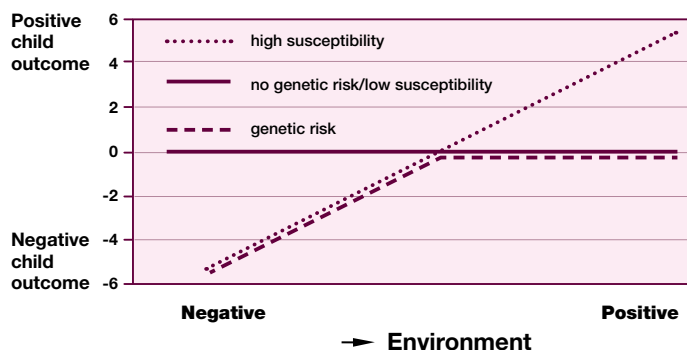
finding is that adolescents in supportive and approving families tend to have fewer depressive symptoms and lower future alcohol consumption (Côté et al., 2009; Nash, McQueen, & Bray, 2005; Sheeber, Davis, Leve, Hops, & Tildesley, 2007). In comparison, the family characteristics most strongly associated with higher levels of depressive symptoms in adolescence are the absence of parental support, attachment and approval; the presence of family conflict, harsh discipline and ineffective problem-solving skills; and an authoritarian parenting style. Limiting these family-based risk factors and promoting positive parenting practices might be an effective way to decrease the risk of internalizing problems in adolescence and, as a result, the risk for later substance abuse.

#### **How poor early attachment can lead to anxiety problems**

The role of attachment in the development of anxiety problems can be understood in combination with child, parent and neurobiological characteristics. Both the serotonin and dopamine systems are implicated in the establishment of social bonds and the regulation of emotions. As with other features, this might start with a gene–environment interaction. For example, a study by Bakermans-Kranenburg and van Ijzendoorn (2007) found that a genetic variant affecting part of the dopamine system — in particular, the dopamine DRD4 7-repeat polymorphism — is associated with disorganized attachment when it is combined with harsh or insensitive parenting and with stronger outcomes when the family environment is positive.

This finding is illustrated further in Figure 10 (Bakermans-Kranenburg & van Ijzendoorn, 2007). Specifically, children without any genetic risk factors (represented by the solid line) do well regardless of environmental conditions, while those carrying a version of the gene that encodes for the dopamine D4 receptors (dotted line) are more influenced by environmental conditions — doing poorly in negative environments and better in positive ones. This effect contrasts with earlier risk models (dashed line), which predicted that a genetic alteration would have effects at only the negative end of the spectrum.

**Figure 10.** Gene–environment interaction affecting child outcome



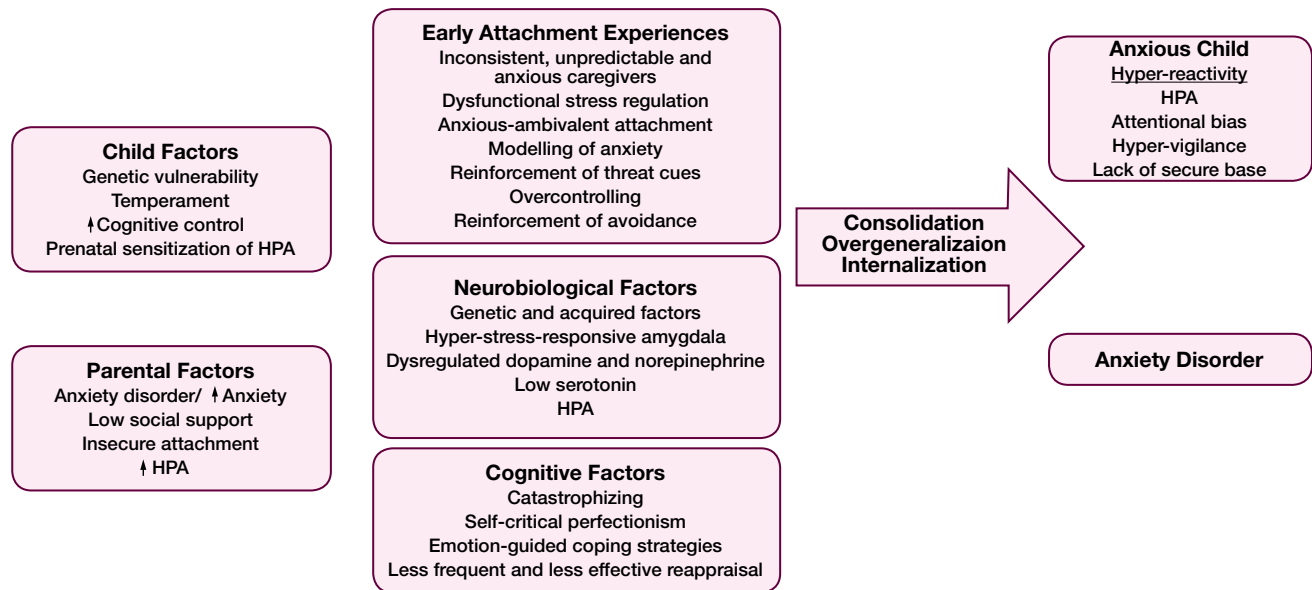
It has also been proposed that attachment plays a pivotal role in the interplay between genetic and environmental influences on the development of anxiety disorders, coping strategies and interpretations of psychosocial challenges. This developmental model of factors contributing to anxiety in children is illustrated in Figure 11 (adapted from Nolte, Guiney, Fonagy, Mayes, & Luyten, 2011). Negative outcomes in this model can also extend to substance use and abuse.

#### **3.4.3 Poor early socialization**

Children face taxing social demands when they first enter school, including making friends and learning new social skills. An inability to successfully adapt to these demands is thought to alter developmental pathways, including the expression of anxiety, depression and behavioural problems in later childhood. For example, preschool teachers' ratings of students' social problems and withdrawn behaviour at ages two and three have been shown to predict preadolescent depression severity eight years later (Mesman & Koot, 2000). This association may be stronger in boys than girls, possibly reflecting that girls learn aspects of social functioning at an earlier age (Mesman & Koot, 2001).

Social difficulties might be a cause or consequence of internalizing problems. Failures in social functioning might foster negative self-perceptions, which are associated with depression. For instance, depressed youth are found to spend more time alone and view themselves as less socially competent (Altmann & Gottlib, 1988). Alternatively, early externalizing problems might lead to rejection by non-aggressive peers, more time spent with peers engaged in risky or antisocial behaviours, and greater susceptibility to diminished self-esteem and other internalizing problems. Each of these factors may foster associations with deviant peers, increasing the likelihood



**Figure 11.** Developmental model of factors contributing to anxiety in children

**Note:** HPA refers to the hypothalamic-pituitary-adrenal axis, the brain's stress response system.

of later substance use and delinquency (Patterson, DeBaryshe, & Ramsey, 1989). Thus, there may be both common (e.g., associations with deviant peers) and unique pathways (e.g., decreased self-esteem leading to self-medication) to substance abuse in children with internalizing problems relative to those with externalizing problems.

### 3.4.4 Bullying and victimization

Children who have difficulties with early socialization can also be victimized by their peers. In particular, bullying is considered to be a form of early trauma and has been associated with internalizing symptoms, externalizing symptoms and the co-occurrence of both (especially when the victimization is severe or frequent). More generally, early stressors, particularly those perceived as uncontrollable (such as victimization), are associated with the severity of mental health problems and substance use, and could trigger or aggravate internalizing symptoms in adolescence.

### 3.4.5 Low self-esteem

Although low self-esteem has been strongly associated with depression in cross-sectional studies, the direction of effect remains unclear. One interpretation is that there are different

effects depending on the stage of development. In children and young adolescents, anxious and depressive symptoms might lead to low self-esteem (Timbremont & Braet, 2006). In young adults, low self-esteem might aggravate susceptibilities to future mood and anxiety problems (Orth, Robins, & Roberts, 2008). The association between low self-esteem and depression appears to be particularly strong in younger populations, suggesting that interventions targeting self-esteem would be pertinent to this age group.

Additional personality features appear to aggravate the effects of low self-esteem. One such trait is self-critical perfectionism, which involves overly critical evaluations of one's behaviour and performance. Once established, self-critical perfectionism appears to be a relatively stable trait that continues into adulthood (Koestner, Zuroff, & Powers, 1991). Longitudinal studies indicate that this trait increases the likelihood of experiencing depressive symptoms over time (Dunkley, Sanislow, Grilo, & McGlashan, 2009). This tendency might be aggravated by negative perceptions of available social support or learned following experiences of poor support, whether real or imagined. For example, self-critical perfectionism has been associated with exposure to negative parenting experiences such as rejection



and excessive restrictiveness. Recent research has also linked self-critical perfectionism not only with depressive symptoms but also with hazardous drinking in young adults (Sherry et al., 2012), further supporting its role in the internalizing pathway to substance misuse.

### 3.4.6 Depression

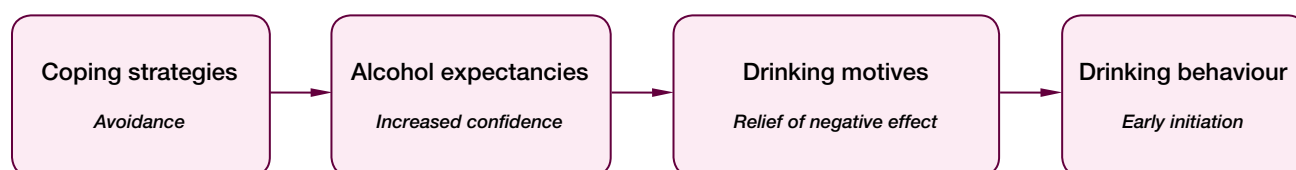
Depressive symptoms are associated with an increased likelihood of drug and alcohol use during adolescence and the later development of substance use disorders. First, depressive problems decrease self-esteem, making individuals more susceptible to the influence of deviant peers and increasing positive expectancies for substance use or the belief that alcohol will help them feel better (Saraceno et al., 2009). As shown in Figure 12 (Hasking, Lyvers, & Carlopio, 2011), these positive expectancies can then influence risky drinking and drug use motives, which are the most immediate predictors of early onset substance use in adolescence. In particular, the desire to cope with depressed mood strongly influences drinking in depression-prone young people and these specific motives are linked with both heavy use and substance-related problems (Grant et al., 2007). Family relationship quality can modulate these processes by altering the choice of peer groups, indirectly protecting against or aggravating the negative effects of depression.

### 3.4.7 Anxiety

Anxiety disorders typically begin much earlier than other types of disorders and predisposing traits such as behavioural inhibition can be reliably identified in early childhood. In contrast with depression, gender differences in anxiety symptoms are present from childhood, with females being twice as likely as males to experience anxiety disorders throughout their lifetime (Lewinsohn, Gotlib, Lewinsohn, Seeley, & Allen, 1998).

Like depression, anxiety also appears to influence alcohol use through the development of the self-medicating coping style. Adults with anxiety disorders tend to prefer substances with sedative and anti-anxiety effects. However, not all childhood anxiety problems affect risk for substance use disorders in the same way. For example, generalized anxiety disorders are associated with increased risk for early onset alcohol use, while separation anxiety disorders reduce the likelihood of alcohol use starting (Kaplow, Curran, Angold, & Costello, 2001). The latter tendency could be owing to the social withdrawal commonly seen in children with separation anxiety, who are often reluctant to go to school or engage in social activities. This reluctance reduces their involvement with peers, through whom most youth are first exposed to alcohol and other drugs.

**Figure 12.** Relationship between coping strategies, expectancies, motives and drinking behaviour in depressed children



Gender is a significant predictor of depression in youth. While the prevalence of depressive disorders is roughly equal for males and females until age 10, it changes dramatically during adolescence, when females become three times more likely to experience depression than males. In addition, while the externalizing and internalizing pathways to substance use disorders are found in both males and females, females have higher mean scores on the internalizing dimension whereas males show higher mean levels on the externalizing dimension. This finding is consistent with the notion that internalizing is a more common developmental pathway to substance abuse for girls.

A longitudinal study of 16–30-year-olds found that social anxiety disorder is a unique risk factor for subsequent onset of cannabis and alcohol dependence, even when controlling for other variables that might contribute, such as other anxiety or alcohol-related problems (Buckner et al., 2008). This association could be explained by the use of cannabis and alcohol for self-medication of anxious reactions to social situations that become more difficult to avoid when individuals reach later adolescence and adulthood. The study's authors suggest other anxiety disorders could be the result of substance use, rather than the precursors to it, as individuals with other types



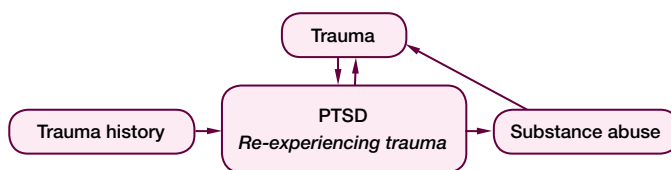
of anxiety disorders such as generalized anxiety might be less inclined to use alcohol and cannabis because of fear of health issues that is characteristic of anxiety problems.

### 3.4.8 Post-traumatic stress disorder

Children who have experienced traumatic events can develop symptoms of post-traumatic stress disorder (PTSD), which is commonly associated with substance abuse as well as with depression and other anxiety disorders (Mueser, Rosenberg, Goodman, & Trumbetta, 2002). The most common forms of trauma leading to PTSD are violent victimization such as rape or assault, natural disasters, witnessing or experiencing bodily harm, and the sudden death of a loved one (Karam et al., 2014). PTSD is associated with physiological sensations of overarousal, repeated intrusive thoughts regarding the trauma experienced and avoidance of reminders of the trauma.

PTSD is linked to alcohol use because it can increase a person's motivations for drinking, either to cope with anxiety and depression or to conform with and be accepted by others (Stappenbeck, Bedard-Gilligan, Lee, & Kaysen, 2013; Stewart, Mitchell, Wright, & Loba, 2004). Individuals with PTSD are also at increased risk of experiencing subsequent trauma (Karam et al., 2014), potentially through increased psychological vulnerability to victimization or indirectly through the adverse consequences of substance abuse, which increase the likelihood of exposure to additional risky situations. This cycle of trauma, PTSD and substance abuse is illustrated in Figure 13 (Mueser et al., 2002).

**Figure 13.** Model of trauma, PTSD and substance abuse



## 3.5 Experiential and parental factors influencing the anxious–depressive pathway

### 3.5.1 Childhood abuse

Adverse early experiences heighten the risk of behavioural and emotional problems in children and adolescents; increase the probability of early onset alcohol use (i.e., before age 14); and

alter stress reactivity, mood, memory and aggression (Anda et al., 2006; Dube et al., 2006). Adolescents remain susceptible to the same forces, with the number of stressful life events occurring during the teenage years predicting risk for drug dependence five to 10 years later (King & Chassin, 2008).

The effects of early adverse experiences can be greater than those produced by later adverse experiences because cognitive schemas about the world are being formed and brain structures are still undergoing development: events that modify these processes can have enduring effects. The most profound effects are seen in those with the largest number of exposures to early life stressors. For example, institutional care such as in an orphanage can, in some cases, represent a form of severe early adversity associated with neglect and abuse. Longer institutional care is associated with greater differences in the structure and function of brain regions that regulate emotional processing (Sheridan, Fox, Zeenah, McLaughlin, & Nelson, 2012; Tottenham et al., 2010).

### 3.5.2 Parental substance abuse and psychopathology

Parental substance use and mental illness are thought to influence child development in a number of ways, including through the transmission of biological or genetic differences that increase the risk of psychiatric and substance use disorders. These problems can also negatively affect the parent-child relationships, including attachment (Duggal, Carlson, Sroufe, & Egeland, 2001). Parental mental health problems have been shown to foster early onset substance use, partly through impaired parental monitoring, which puts children at risk for victimization and increases the likelihood they will associate with deviant peers. Parental substance use has also been associated with a permissive parenting style, in which case it might be the resulting family environment rather than the substance use that constitutes the risk factor.

#### **The effects of parental depression and anxiety**

A parental history of substance use problems and depression, particularly maternal depression, greatly increases the likelihood of internalizing and substance use disorders in children. In addition, the children of two depressed parents have an earlier onset of depression than those with parents who have never had depressive disorders, suggesting a cumulative effect. Parental anxiety also increases risk for internalizing problems in children,



although its impact is less than that of parental depression. There is a stronger association between maternal stress and depression for females than males, indicating that girls could be more susceptible to this particular mode of risk transmission. The effects of depressive and anxious symptoms in a parent also become stronger once a child reaches adolescence.

Parental mental health problems can worsen the effects of other stressors, making it more difficult for the child to cope with negative life events. For instance, youth experiencing high chronic interpersonal stress and a large number of negative life events are more likely to be depressed if their mothers are also depressed. Similarly, poor social functioning is more likely to be associated with depression in the children of depressed mothers.

### **The importance of positive family environments**

Positive parenting practices can buffer the impact of the negative outcomes associated with parental mental health problems. A positive family environment involving parental monitoring and emotional warmth has been shown to reduce the effects of adverse events such as bereavement (Haine, Wolchik, Sandler, Millsap, & Ayers, 2006) and can also reduce the risk of substance abuse through a reduction in associations with deviant peers (Nash et al., 2005). Conversely, parental overprotection or rejection, combined with a behaviourally inhibited temperament in the child, are risk factors for social withdrawal and internalizing problems (Kiff, Lengua, & Zalewski, 2011). Promoting positive parenting practices is an important area of intervention, particularly given growing evidence that parenting behaviour in one generation influences parenting practices in the next (Neppel, Conger, Scaramella, & Ontai, 2009).

### **3.5.3 Peer deviance**

Peer groups can be either protective or risk factors for adolescent development. Affiliation with substance-using, deviant or criminal peers increases the risk for a variety of negative outcomes, including substance use, victimization and externalizing mental health problems. With regard to the anxious–depressive developmental pathway to substance use disorders, affiliation with deviant peers is more likely in youth without close family relationships and in those who have experienced negative life events, a phenomenon described as “hangout coping” (Wills, Sandy, Yaeger, & Shinar, 2001). Thus, children with antisocial peers can have a multitude of vulnerability

factors for emotional and substance-related problems. Peer groups are found to be more immediate predictors of substance use than other factors, as exposure to peer substance use, modelling and social learning can exert direct pressure on youth to use substances. Deviant peer affiliations are also thought to be causally linked to an increase in externalizing behaviours, the negative consequences of which can then lead to depression.

Peer groups can change over time: like adults, youth tend to select peers similar to themselves. A one-year study of youth between the ages of 16 and 17 found that adolescents initiated relationships with peers reporting similar levels of depression and dissolved relationships with those whose levels of depression became dissimilar to theirs over the course of the year (Kiuru, Burk, Laursen, Nurmi, & Salmela-Aro, 2012). Over time, an individual's depression symptoms increasingly converge toward the average level of their peers, not because of a social-influence effect but because of social selection.

High-quality family relationships and parental monitoring have many of the converse effects and can decrease teenagers' associations with deviant peers. Thus, families and parents can indirectly reduce adolescent substance use by reducing their exposure to peers engaged in such activities (Van Ryzin, Fosco, & Dishion, 2012).

## **3.6 Neurobiological and neurochemical factors influencing the anxious–depressive pathway**

Psychosocial risk factors influence emotional functioning and behaviours by influencing neural systems and brain structures. This section provides a summary of the aspects of brain biology relevant to the anxious–depressive developmental pathway to substance use disorders.

### **3.6.1 Ventral medial prefrontal cortex**

The ventral medial prefrontal cortex refers to the location of a number of cortical brain regions that regulate emotional states, the evaluation of motivationally important events and self-referential behaviours and processes. Disruption to this region is implicated in mood disorders, dysregulated impulse control and substance use disorders. (The role of this region in impulse control problems is discussed in Chapter 2.)



## MARTINA



Martina, 15, lives with her mother and older sister. Her parents separated when she was eight, but she remembers many arguments before the divorce, including two occasions when she witnessed her drunken father hitting her mother. Because he was not home very often, Martina never felt close to her father. She misses him now, though, and when they do see each other, Martina tries to seem positive and interesting so he will enjoy spending time with her; she doesn't want him to know that he hurt her.

Nervous around new people and not wanting to be the centre of attention, Martina never felt close to the other kids at school, choosing instead to hang out with her sister and her friends, who are two years older. She started drinking and smoking marijuana with them at age 12. Although she didn't like it at first, she didn't want to be made fun of for refusing to join in. Martina now enjoys drinking alcohol, particularly before parties, as it helps her loosen up and makes it easier to talk to people. Sometimes, when very drunk, she'll "hook up" with guys. While this gives her a self-esteem boost — her sister's friends tell her she's cool — Martina rarely sees the guys again. She wonders if they could tell she wasn't interesting.

When she's feeling down, Martina will have a few beers or smoke marijuana alone in her bedroom. This helps her "switch off" and forget her problems, but the feelings of sadness tend to come back the next day. Martina feels ashamed for being so secretive, but she hasn't told her sister or mother about this habit because she doesn't want to burden them.





In individuals with mood disorders, functional and structural brain imaging studies have shown alterations in the ventral medial prefrontal cortex and connected areas, with increased cerebral blood flow or metabolism suggesting overactivity in this region. These alterations are most consistently found in individuals with family histories of mood disorders, suggesting that a biological predisposition to mood disorders related to emotion regulation might be inherited. While most of these studies have been conducted in adults, the limited results reported in children are consistent with the adult literature.

### 3.6.2 Amygdala

The amygdala is located in the medial temporal lobe and is part of the limbic system. It is centrally involved in the processing of and response to emotionally important stimuli, both positive and negative (Rayport, Sani, & Ferguson, 2006; Tsuchiya, Moradi, Felsen, Yamazaki, & Adolphs, 2009). The size and function of the amygdala differs from the norm in individuals with mood and anxiety disorders, with most studies finding evidence of increased volume and hyper-reactivity, particularly in association with high levels of anxiety and the s-allele of the serotonin transporter gene (Hariri et al., 2002; Murphy et al., 2013).

Some studies suggest early life experiences can alter this brain region. Tottenham and colleagues (2010) have found that the length of a child's orphanage care corresponds to the size and function of the amygdala; the older children were when they were adopted, the greater the volume of their amygdala. A larger amygdala volume might translate into greater risk for anxiety or depression because of increased sensitivity to threat cues or greater engagement of fearful emotions. This possibility indicates that adverse family environments and childhood experiences can perturb the development of the brain's emotion-regulation system. Evidence suggests these differences are initiated quite early in life; for example, greater emotional reactivity in four-month-old infants predicts greater amygdalar reactivity in 18-year-old adolescents (Schwartz et al., 2012).

### 3.6.3 Striatum

Depressed individuals of all ages are shown to have smaller striatal structures. These structures include the gangliothalamic ovoid that encompasses the basal ganglia, which is involved in motivation and motor control, and the thalamus, which processes sensory information and acts as a relay between the cerebral cortex and the basal ganglia and other subcortical

areas. For example, the severity of depression symptoms has been found to negatively correlate with the size of the caudate, one of the three structures of the basal ganglia. These structural differences have been found as early as infancy, where a smaller size of the gangliothalamic ovoid is associated with higher levels of emotional reactivity, anxiety, depression and withdrawn behaviour at 18 and 36 months of age (Herba et al., 2010). Structural differences in these brain regions in infancy might represent risk markers for future internalizing problems, with infants who have the smallest striatal structures at the highest risk for severe internalizing symptoms in the future.

In addition to these structural differences, functional abnormalities are also evident, including decreased striatal brain activation to reward in youth with depressive and anxiety disorders. Striatal reactivity is known to evolve during pubertal maturation, reacting less to rewards as pubertal maturation advances (Galvan, Hare, Voss, Glover, & Casey, 2007). Striatal reactivity has been found to correlate positively with positive emotions and negatively with depressive symptoms (Forbes et al., 2010). Thus, individual differences in striatal reactivity might relate to susceptibility to negative emotions and, consequently, mood disorders.

### 3.6.4 Dopamine

The neurotransmitter dopamine potently influences the ability of emotionally salient stimuli to grab and hold attention. This influence has been best demonstrated for positive stimuli, raising the possibility that low dopamine transmission might diminish the influence of reward cues, biasing emotional tone negatively and decreasing the ability to cope with psychological challenges (Leyton et al., 2000). Marked individual differences in dopamine system function have been identified in brain imaging studies, including disturbances related to clinical depression (Moses-Kolko et al., 2012) and vulnerability to substance use disorders (Casey et al., 2013; Oberlin et al., 2013; Setiawan et al., 2014). However, the direction of effect, whether increased or decreased dopamine, is still under debate, as both increases and decreases might occur depending on the testing conditions.

### 3.6.5 Serotonin

Serotonin can influence emotional states, with abnormalities in this system thought to be a marker or correlate of depression and anxiety problems. Severe suicidality has frequently been associated with lower concentrations of 5-hydroxyindoleacetic acid (5-HIAA), a serotonin breakdown product, suggesting



serotonin might be less active in these individuals. Experimentally reducing serotonin system function in the laboratory setting has been shown to transiently reinstate depressive symptoms (Young & Leyton, 2002). Moreover, selective serotonin reuptake inhibitors (SSRIs) are the primary pharmacological choice in treating adolescent mood and anxiety disorders, though for juvenile depression there is a risk that SSRIs can induce manic states (Offidani, Fava, Tomba, & Baldessarini, 2013; Rynn et al., 2011). Despite this caution, evidence suggests the serotonin system likely represents a common biological influence on depression and anxiety, possibly related to a core inability to regulate one's emotions.

Difficulties in emotional self-regulation can lead to attempts to change mood states by other means, such as self-medication with alcohol or drugs. Another possibility is that an emotional regulation problem could underlie risk for both mood disorders and difficulties in regulating behaviour (e.g., substance use). In this way, a serotonergic abnormality and self-regulation deficit could be common factors for both problems.

Functional neuroimaging studies also suggest serotonin plays an important role in mood, anxiety and stress-related disorders, including disturbances to serotonin receptors (Parsey et al., 2010; Sullivan et al., 2013) and in the formation of serotonin (Rosa-Neto et al., 2004). This research has been confined to adults, however, because of restrictions on conducting these kinds of studies in people under the age of 18. Indirect indices of serotonin function can be used in adolescents, though, such as prolactin and cortisol responses to serotonergic drugs as measured in blood. A review of these studies conducted with depressed children and adolescents (Birmaher & Heydl, 2001) found abnormalities after serotonergic stimulation, similar to those found in non-depressed children with a family history of major depression. Together, these studies indicate the serotonin system might be a biological indicator of susceptibility to emotional problems.

### 3.6.6 Stress and gonadal hormones

Following exposure to stressful events, the hypothalamic, pituitary and adrenal glands (HPA axis) release cortisol, prolactin and other hormones into the blood stream. A brief activation of this axis, the brain's stress response system, can be beneficial, helping the individual cope with the stress. More

prolonged or poorly regulated activations, however, can have adverse consequences, diminishing the person's ability to cope (McEwen, 2000; Sapolsky, 1996).

Studies of depressed adults have consistently identified HPA axis dysfunctions. Findings are less consistent in children and adolescents, possibly reflecting the influence of additional factors such as age, sex, maturation, exposure to stress and a family history of mental illness. Nevertheless, HPA axis dysfunction has been found in child and adolescent mood disorders. For instance, these children experience dysregulated growth hormone levels, which appear to be a general marker of vulnerability to internalizing problems. Early life stressors and negative rearing environments (e.g., abuse, family conflict, divorce, death) have a profound impact on HPA axis function, leaving individuals more susceptible to stress. Stressful experiences, in turn, can increase the likelihood of experiencing internalizing and then substance use problems through self-medication and deviant peer influences. As an example, the 10–12-year-old sons of fathers with substance use disorders exhibit disturbed cortisol responses when anticipating stressful events, with individual differences in this response predicting adolescent substance use four years later (Moss, Vanyukov, Yao, & Kirillova, 1999).

Gonadal hormones (i.e., sex hormones such as testosterone, estrogen and androstenedione) can also influence mood, with rapid changes during puberty precipitating mood fluctuations and increased negative emotions. In turn, these mood changes can trigger internalizing problems in those with additional biological, temperamental or psychosocial vulnerabilities. Gonadal hormone levels are also associated with emotional reactivity and can worsen interpersonal conflicts; testosterone reactivity, for example, is associated with family problems.

Lower gonadal hormone reactivity, particularly in combination with heightened HPA axis activity, which can be inherited or shaped by early rearing experiences, might indicate a biological susceptibility to stressful events. The gonadal axis might also be suppressed as a response to HPA overactivity, providing an example of how early adverse experiences can negatively affect biological responses to future stress. Because of these biological factors, some youth could become more susceptible to the influence of environmental stressors than others.



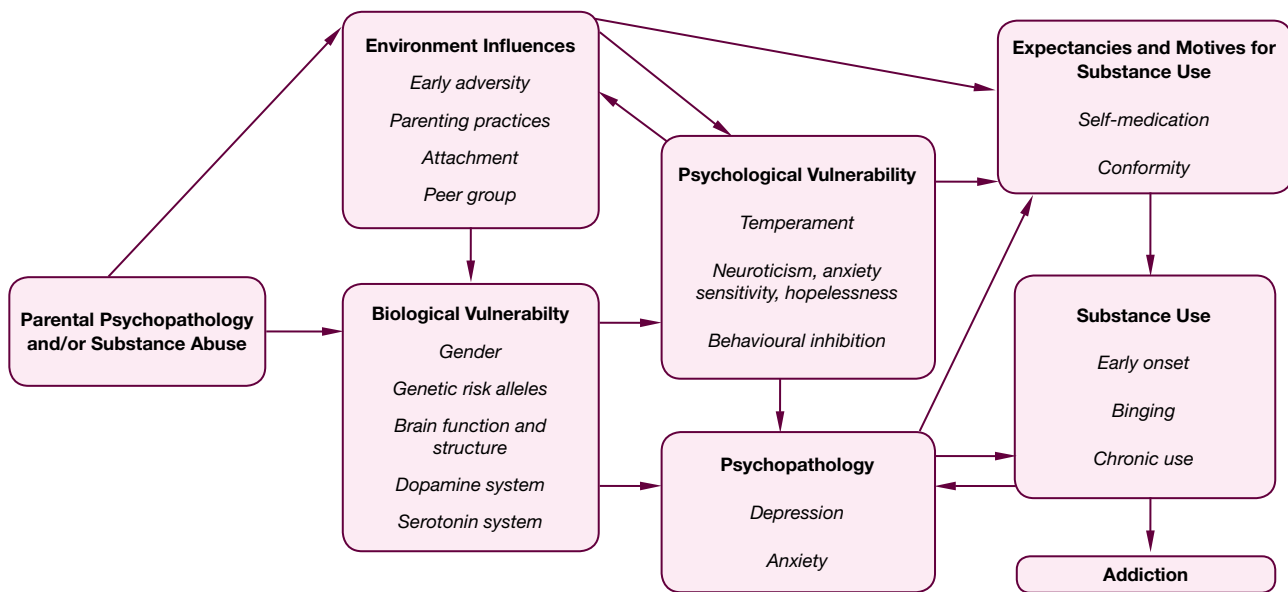
### 3.7 Conclusion: Breaking the cycle of internalizing problems and substance abuse

Alcohol and drugs have marked effects on mood: acutely, of course, but also for extended periods afterward. Substance use in youth who are prone to internalizing problems might aggravate pre-existing symptoms in the longer term. Substance use can also worsen mood and anxiety problems because of withdrawal effects, including anxiety, nervousness, depression and other anxiety-related physical sensations such as rapid heart beat, trembling and sweating. Over the long term, withdrawal can itself lead to an increase in internalizing problems. Once youth learn that taking more drugs can alleviate these withdrawal

symptoms, negative reinforcement processes can motivate further substance use, creating an ongoing cycle of substance use and misuse.

Ultimately, an individual's likelihood of developing internalizing problems and engaging in problematic substance use reflects a complex interaction between biological, environmental and psychological factors (see Figure 14). Obtaining a better understanding of the anxious–depressive pathway to substance use and the factors that influence progression along this pathway could improve our understanding of how addictions develop and help identify pathway-specific targets for early intervention, prevention and treatment.

**Figure 14.** Summary of the developmental model of internalizing problems and addiction





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# 4

## A Developmental Approach to Prevention and Intervention



*By Line Brotnow and Rajita Sinha*

### Chapter at a Glance

- Understanding substance abuse from a developmental perspective — addressing personal and contextual risk factors in relation to the developmental stage when they first become relevant — could allow for earlier detection of at-risk individuals.
- To provide more effective interventions, the causal mechanisms that make people generally vulnerable to substance use must be identified.
- Although adolescence is the primary focus of most prevention research, pre-adolescent interventions could help prevent youth substance use.
- Improved parenting abilities can help counteract exposure to early childhood risk factors associated with parental substance abuse and mental illness, strengthening child–parent attachment and reducing behavioural and emotional dysregulation.
- As school-age children face increasingly taxing academic and social demands, interventions at the individual, family and school levels can target specific risk patterns while increasing social adaptation and self-efficacy.
- Reflecting the increased importance of the broader social environment during adolescence, community-based initiatives should be implemented alongside individual- and school-centred programs.
- At all stages of development, interventions should be personalized, developmentally appropriate and interdisciplinary, and implemented across a range of individual and social contexts.





#### **4.1 Understanding developmental risk and resilience can lead to more effective preventive interventions**

The goal of prevention is to use systematic, well-timed interventions to avoid the developmental pathways that can lead to negative outcomes. Research can inform substance abuse prevention in two main ways: by providing criteria for detecting at-risk individuals and by identifying targets for intervention. Importantly, these two can overlap, meaning the factors identifying at-risk youth can also be those that need to be targeted in prevention.

While this report looks at risk and resilience on many different levels — from the neurobiological and genetic to personality traits and parenting — many of the findings it presents do not translate directly into prevention efforts. For example, despite a rapidly growing literature, genetic, neuroendocrine and neuroimaging techniques are not yet of practical use in identifying at-risk children, nor do they provide direct targets for intervention. In fact, limited access to these tools, coupled with their relatively high cost for large-scale screening, actually **decreases** the value of these techniques in prevention.

That said, findings from the ever-expanding neurobiological sciences have provided incontestable evidence of how early life experiences can change the brain and, in turn, predict behavioural and emotional problems as well as substance use and abuse, making it increasingly important to develop early interventions to target and reverse these changes.

The multiple personal and contextual risk factors influencing internalizing and externalizing behaviours are partly a function of the developmental stage of the individual. A relatively new way to conceptualize substance abuse prevention is to integrate knowledge about how the growing brain and body, and changing social roles interact with risk and resilience factors during development (Sloboda, Glantz, & Tarter, 2012). Each developmental stage presents unique physical growth and maturation challenges, new tasks to be mastered and, consequently, specific difficulties that might increase vulnerability to substance abuse. Over time, these can persist, accumulate and snowball in a variety of ways. Conversely, each stage also offers distinct opportunities for promoting resilience, which underscores the need to think about substance use risk and prevention from multiple perspectives.



This chapter takes a developmental perspective, addressing risk factors according to the developmental stage in which they first become relevant. It outlines how specific risk factors can be used to identify individuals who are likely to benefit from particular prevention programs during early childhood, the elementary and middle school years, and through to adolescence. The chapter also presents the rationale and utility of several well-validated preventive interventions during these key stages of development, encompassing a broad range of intervention settings and types.

## **4.2 Early childhood: When parents and caregivers play a critical role**

During early childhood, survival depends entirely on the care and protection provided by parents and caregivers. A good caregiver is able to compensate for the extreme neurobiological, emotional and physical immaturity of infants and toddlers by limiting their exposure to stressful experiences. Responsive, sensitive interactions between caregiver and child ultimately allow the child to learn to effectively regulate his or her own emotions and behaviours (Gunnar & Fisher, 2006). Conversely, a lack of adequate parental stimulation is one of the most significant stressors during early life (Levine, 2005), with exposure to such stress predictive of both internalizing and externalizing disorders (Rogosch & Cicchetti, 2005; Stevens et al., 2008).

### **4.2.1 Risk factors during early childhood**

The ability to parent is often compromised by substance use and mental health problems, with studies showing a high correlation between these issues and child maltreatment (Mayes & Truman, 2002). Because these frequently co-occurring parental behaviours are predictive of poor child outcomes, they constitute important markers of risk for future substance abuse by the child. However, to intervene effectively, it is necessary to understand the causal mechanisms linking parenting risks and child substance abuse.

Inadequate parenting and early trauma influence the stress system in two main ways. First, early maltreatment can increase responsiveness to threats and reduce a child's ability to self-regulate emotions, both of which are predictive of psychological distress, internalizing problems and substance abuse (McCrory et al., 2011). Maltreatment can also lead to a blunted stress-arousal system that is unable to distinguish threat and challenge from non-challenge or unable to learn goal-directed behaviours

that benefit adaptation and survival. This pattern of risk shows particular sensitivity to developing externalizing problems and substance use disorders (Gunnar & Fisher, 2006).

In addition to the timing, severity and nature of poor parenting (Andersen et al., 2008), genetic factors also have an impact on a child's progression down the internalizing or externalizing developmental pathways. Some children have an additional inherited vulnerability to stress that makes them particularly susceptible to the negative effects of inadequate parenting or early life stress (Caspi et al., 2003; Hariri et al., 2002). Others have a genetic predisposition to difficult behaviour, which can evoke poor caretaking from their parents that, in turn, further aggravates their unregulated behaviour (O'Connor, Deater-Deckard, Fulker, Rutter, & Plomin, 1998).

Having a substance abusing, violent or mentally ill parent might also predispose the child to poor outcomes through direct genetic effects (Gunnar & Fisher, 2006). A developing fetus can be exposed to a number of factors that can jeopardize normal development, including maternal stress, certain bacteria and viruses, chemicals and toxins, and drugs and alcohol (Cornelius & Day, 2009; Glantz & Chambers, 2006; Mayes & Truman, 2002; Mendola, Selewan, Gutter, & Rice, 2002; Wigle et al., 2008; Zhu, Kartiko, & Finnell, 2009). Such exposure might cause the child to be more difficult to parent or to be more in need of structure and support from the parent.

### **4.2.2 Interventions during early childhood**

The immediate family context plays an integral role in early brain and emotional development. It is a source of both risks and resilience for the young child and provides a natural target for intervention.

Some of the risks for poor outcomes, such as substance abuse, mental illness or maltreatment, can be explained by the impact of suboptimal parenting on the child's ability to self-regulate emotions and behaviour (Mayes & Truman, 2002). However, as a prevention strategy, removing children from parents with mental health or substance abuse problems and placing them in foster care has limited effectiveness. Instead, interventions targeting parenting behaviours have been a major focus of efforts to improve both child and family outcomes (Reid & Eddy, 1997).



**Recognizing the importance of child–parent attachment**

Research on parenting in the contexts of maltreatment, substance abuse and mental illness has highlighted the importance of parental sensitivity and responsiveness in promoting children's adaptation. A caregiver's ability to understand and respond appropriately to a child's signals is vital to the development of secure attachment in infants as well as the healthy parenting of older children (Maccoby & Martin, 1983). The absence of this ability is predictive of future mental health problems in the child (Main & Solomon, 1990).

The relationship between parenting style and attachment is well understood. Exposure to frightening or overwhelming parenting behaviours, or behaviours out of step with the child's needs, has been found to increase the risk of disorganized attachment and poor outcomes later in life (Lyons-Ruth, 2003). Evidence also suggests the quality of attachment is predictive of the child's ability to respond to stress and self-regulate behaviour. When compared to children presenting with insecure attachment, securely attached infants do not show elevated cortisol levels during fear-eliciting situations in the presence of their parents (Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996). The quality of attachment has therefore become a target of several intervention studies whose effectiveness can be understood partly in terms of helping children with stress regulation.

**Attachment and Biobehavioral Catch-up program**

The Attachment and Biobehavioral Catch-up (ABC) program is an attachment-based intervention for the caregivers of young children at high risk of being exposed to maltreatment and neglect (Dozier, Peloso, Lewis, Laurenceau, & Levine, 2008). It aims to increase children's ability to self-regulate their emotions and behaviour by increasing parental sensitivity and nurturance, and by decreasing frightening and unpredictable parenting behaviours. Two randomized clinical trials found that caregivers in the ABC program showed increased sensitivity and nurturance compared to those in non-ABC control groups, while the children involved exhibited decreased cortisol levels and higher rates of secure attachment (Bernard et al., 2012; Dozier et al., 2008).

Parental engagement — getting parents to participate in and stick with the intervention — is a key focus of the ABC program. To date, it has been used primarily with families who were recruited through child protective services, where failure

to participate or adhere can result in the loss of custody of the child. In the ABC program, rapport with parents is built through frequent supportive and encouraging feedback, increasing their self-esteem and belief in the possibility of lasting change. The intervention takes place in the home of the child to maximize the likelihood of behavioural change and assure parental engagement.

**Mothers and Toddlers program**

Although randomized clinical trials like those conducted on the ABC program can tell us whether an intervention works, it is more important to identify **how** the intervention works. In an intervention specifically targeting the parenting of substance-abusing mothers, Suchman and colleagues (2010) investigated the particular role of a mother's "reflective functioning" as a means to improve parenting, normalize child behaviour and decrease maternal substance use. Reflective functioning (also known as "mentalizing") involves using the understanding of the mental states of the self and others to regulate one's behaviour, and has been proposed as an underlying core characteristic of adaptive parenting (Fonagy, Gergely, Jurist, & Target, 2002).

In the Mothers and Toddlers program, parents and young children participate in 12 sessions focusing on the quality of their interactions, encouraging the mother to actively consider her own and her child's mental and emotional state when in stressful situations. The improvement in reflective functioning was associated with improvement in caregiving behaviour as well as an overall reduction of maternal substance abuse and depression. This study provides an example of how understanding the specific ways in which inadequate parenting constitutes a risk for poor child outcomes can effectively inform prevention efforts. Further research is needed to establish the efficacy and feasibility of such treatments in community-based or outpatient settings.

### **4.3 Elementary and middle school years: When internalizing and externalizing disorders begin to emerge**

The school-age child is expected to comply with increasingly taxing demands related to academic performance and social interaction. These demands result in cognitive and behavioural coping responses that lead to adaptive or maladaptive



functioning in the child. Examples of adaptive functioning include seeking support from friends and family, and engaging in active positive activities like sports to reduce demand and stress. However, increased school demands and stress at home also increase the likelihood of maladaptive behavioural coping responses that include disruptive externalizing behaviours, as well as harder-to-detect internalizing effects such as fear, withdrawal, anxiety and depression. Such maladaptive coping behaviours reflect a broader set of risks associated with poor outcomes, including substance use. Adaptive functioning in this context depends on the child's ability to develop a sense of independence, self-regulation and self-esteem.

### 4.3.1 Risk factors for school-age children

Internalizing and externalizing disorders and behavioural traits are the most frequent reasons school-age children are referred to specialist services (National Institute of Mental Health, 2011). They are also highly predictive of poor social functioning, including bullying and victimization, and educational outcomes as well as future mental illness and substance abuse (Armstrong & Costello, 2002; Buckner et al., 2008; Chassin, Pitts, DeLucia, & Todd, 1999). What's more, the prevalence of these behavioural patterns is not only high among this age group but is actually **increasing** through childhood, frequently co-occurring in both the general and high-risk populations (Carter et al., 2010). Understanding the origins of these behaviours might shed light on their causes and provide targets for early detection and intervention.

First, heritability estimates for both types of behaviours are high, suggesting that some children are genetically predisposed to developing them. As discussed in the preceding chapters, genetic vulnerability is generally broad and often makes an individual more sensitive to environmental factors such as stressful events or poor parenting. At present, however, genetic analysis is not a readily available or practical tool for identifying at-risk children and youth.

Second, poor parenting and family functioning resulting from parental mental illness and substance abuse remains a risk factor throughout childhood (Mayes & Truman, 2002). Children exposed to maladaptive interactions with caregivers in early childhood are at heightened risk for developing a dysregulated stress-response system and becoming over attentive to potential threats in the environment (McCrory et al., 2011), both

of which are predictive of anxiety, impulsivity and inattention in older children. Related to this, children might learn maladaptive coping strategies and styles of interaction directly from their attachment figures; behaviours such as aggression and social withdrawal are related to early experiences with poor parenting (Rogosch & Cicchetti, 2013).

Finally, the development of internalizing and externalizing behaviours in childhood can result from exposure to uncontrollable stressful life events and major transitions. These behaviours can also appear gradually in response to the greater social and academic requirements placed on children as they mature.

### 4.3.2 Interventions for school-age children

To be effective, prevention programs must target factors that not only are correlated with poor outcomes, but also have a meaningful impact on the causal mechanisms leading to those outcomes. While poor parenting and traumatic experiences often precede abnormal behavioural patterns in children, the opposite is also true: an anxious or aggressive temperament can provoke harsh parenting, put the child at risk of experiencing dangerous situations through novelty-seeking behaviour, or alienate the child from supportive relationships. The relationships among the different risk factors and outcomes at this developmental stage are therefore likely to be multidirectional in nature — a fact that needs to be reflected in any intervention strategy.

Efforts to improve family functioning, prevent or buffer the effects of traumatic experiences, and reduce problem behaviours all represent potential targets for intervention. Given the range of factors that can influence the emergence of externalizing and internalizing disorders in school-age children, preventive interventions implemented in a number of different settings — specifically, the individual, family and school levels — have proven to be most effective.

#### **Individual-level interventions**

There is increasing evidence that personality-centred interventions are effective in delaying the onset of drug and alcohol use (Conrod, Castellanos-Ryan, & Mackie, 2011; Conrod, Stewart, Comeau, & Maclean, 2006). As discussed in the previous chapters, such an approach involves taking into consideration the fact that youth with specific personality characteristics can be at risk for developing substance abuse



or other problem behaviours. Research findings suggest personality traits might moderate treatment efficacy, meaning some prevention programs might be much more effective for certain groups of children than others.

Taking this variable into account can enhance treatment effectiveness across a potentially broad range of interventions. As an example, the Preventure program screens youth using well-established measures for specific traits such as hopelessness, anxiety sensitivity, impulsivity or sensation-seeking (Conrod et al., 2006, 2011). In two 90-minute group sessions, youth are taught skills specific to their identified personality type (e.g., teaching anxiety-sensitive youth to confront feared situations rather than using drugs to cope with their anxiety). Students then work through real-life scenarios depicting potential risk-situations for their personality type. Findings show the expected increase in drinking and other risk behaviours is less steep in the six to 12 months following participation in the Preventure intervention, suggesting a larger effect for short-term interventions when personality features are explicitly considered (Conrod et al., 2011). Research also shows that the preventative benefits on substance misuse last up to two years following the Preventure intervention (Conrod, Castellanos-Ryan, & Strang, 2010).

### **Family-based interventions**

Family characteristics related to internalizing and externalizing behaviours include the absence of parental support and approval, insecure attachment, the presence of conflict, harsh discipline or authoritarian parenting, inefficient problem-solving skills and parental hostility (Mayes & Truman, 2002). In response, a number of parent- and family-based interventions have been developed, emphasizing the importance of family relationships throughout childhood. Stable and supportive family structures buffer the impact of stress and promote resilience in the child. Without that stability and support, the impact of other risk factors can be intensified.

The Strengthening Families Program (SFP) is an example of a well-established family intervention program that targets family communication and parenting skills to reduce risk for a range of negative outcomes including substance abuse. Depending on the specific challenges within a family, certified SFP trainers work with parents and children, individually and together, over

the course of seven to 16 weeks to improve their relationships (e.g., by emphasizing effective communication styles and clear discipline). Changes are achieved through guided exercises and conversation.

Validated for age groups ranging from early childhood through adolescence, SFP has been found to reduce children's internalizing and externalizing behaviours as well as parent and child substance abuse, and to improve family communication and interaction styles (Trudeau, Spoth, Randall, Mason, & Shin, 2012). However, effect sizes associated with these interventions are typically small, suggesting that a wide range of other early risk factors, such as personality, early trauma and brain development, influence the likelihood of benefiting from the treatment. Further research exploring such factors is vital to developing more effective prevention programs.

### **School-based interventions**

Elementary and middle schools are the centre of the childhood universe and have the potential to contribute to early detection and intervention of maladaptive developmental pathways. However, despite dramatic increases in the prevalence of mental health disorders with the onset of puberty, increasingly frequent early experimentation with alcohol and drugs (Substance Abuse and Mental Health Services Administration, 2008), and the understanding that such early exposure might further compromise future adaptation, preventive interventions are given minimal attention in the elementary and middle school settings (Ringwalt, Hecht, & Hopfer, 2010). A lack of knowledge about the risk factors for substance abuse, as well as fear that education might lower thresholds to substance experimentation, might explain this paradox (Donovan, 2007).

Given the state of knowledge about childhood risk-markers for substance abuse, school-based programs that target early school failure and difficulties with social interaction, as well as general efforts to promote supportive relationships and strengthen children's self-efficacy and self-esteem, are most likely to have the greatest impact on substance abuse rates later in development. Schools can deliver these kinds of interventions independently or might choose to detect and refer at-risk children to receive support outside of the school framework.



## 4.4 Adolescence: When the paradox of the dual systems theory comes into play

The developmental context of the adolescent is dominated by the transition to adulthood. Over the span of a few years, teenagers are expected to achieve material and emotional independence from their families and develop a sense of self through stable adult relationships, education and professional life. Physically, puberty represents a dramatic period of transformation, affecting the appearance of the body, reorganizing the brain, and reshaping emotional functioning and thinking processes. However, this process of transformation, like all transitional periods in development, is far from linear.

Although the post-puberty adolescent body matches that of adults in terms of physical strength and ability, some aspects of brain development more closely resemble that of children. The “dual systems” theory of adolescent brain functioning argues that during adolescence, the limbic brain areas (i.e., those involved in emotions) have dominance over the prefrontal cortical brain areas (i.e., those involved in executive functions like planning and organizing). This dominance of the limbic system impairs the ability to self-regulate emotions (Casey, Jones, & Somerset, 2011), with decades of research revealing a tendency for immediate rewards to be more powerful than longer-term negative consequences. These factors cause the average adolescent to take more risks than the average adult despite a similar ability to abstractly estimate the degree of risk involved.

Researchers have also suggested that inhibitory control in this period is contingent on incentives; that is, adolescents are more impulsive in the presence of some cues (e.g., appealing social stimuli), yet perform just as well as adults in the presence of other cues (e.g., emotionally neutral stimuli) (Casey & Caudle, 2013). This phenomenon is accompanied by a heightened sensitivity to novelty, the need for stimulation and an overall lack of life experience. Together, these factors can lower the threshold for initiating risky behaviour. Simply put, during adolescence the “gas pedal” is momentarily more important than the “brake” (Casey et al., 2011).

### 4.4.1 Risks factors during adolescence

When considering the sources of vulnerability that emerge in adolescence, it is crucial to note that these factors rarely operate in isolation and are highly likely to follow from and exacerbate pre-existing risks. For some individuals, adolescence comes out of a childhood already filled with risk factors such as familial dysfunction, major life stressors, and affective and behavioural abnormalities. Considering the developmental past of the individual is therefore critical to detecting people at heightened risk for poor outcomes in adolescence.

The role adolescent substance use plays in the development of addictive behaviours in adulthood has been a primary focus of the substance abuse prevention literature. Recent epidemiological data suggest that upwards of 60 percent of students in grades 7 to 9 have experimented with alcohol (Leatherdale & Ahmed, 2010). These data are of particular interest in the context of this report given that early substance use can predict the presence and severity of adult substance abuse (Behrendt, Wittchen, Hofler, Lieb, & Beesdo, 2009).

Several causal pathways have been proposed to explain the link between adolescent and adult substance abuse. Longitudinal studies assessing adolescents prior to initiating drinking and for several years afterward have found impaired cognitive function relative to a non-drinking control group (Squeglia, Spadoni, Infante, Myers, & Tapert, 2009), with mounting evidence suggesting a heightened sensitivity to the toxic effects of substances in the adolescent brain.

There are also indications that early substance use exacerbates behavioural risk markers for future substance abuse (Newton, O’Leary-Barrett, & Conrod, 2013). For instance, early alcohol use is associated with greater stress-related drinking later in life, suggesting an impact of early alcohol use on systems regulating the stress-response (Blomeyer et al., 2011). Substance abuse in adolescence is also likely to have an impact on the developmental tasks associated with adolescence through its negative effects on learning and adaptation processes. Social interactions and academic performance might be rapidly affected by early substance use, while the risk behaviours that further predispose to adult substance abuse, such as risky sexual behaviour and mental health problems, might follow.



**Rethinking the “gateway” approach to prevention**

Taken together, these findings point to a heightened vulnerability to addiction associated with adolescent substance use, supporting its suggested role as a “gateway” to adult substance abuse (Behrendt et al., 2009). Yet while the conceptualization of early substance use as a gateway has historically served as the foundation for substance abuse prevention in adolescence, not all substance-using adolescents develop addictions. Although correlated, substance use or drinking in adolescence is **not** a highly reliable predictor of adult substance abuse, making it necessary to isolate and explore the interplay of actual causal mechanisms. Rather than thinking of early substance use or deviant peer influence as the cause of subsequent substance abuse, a simpler explanation is that the two result from a common factor and targeting that underlying cause can yield more effective interventions.

In adolescence, sensation-seeking, impulsivity, anxiety sensitivity and hopelessness are associated with early onset substance misuse (Woicik, Stewart, Pihl, & Conrod, 2009). These traits might represent specific motivational pathways to drug use associated with specific patterns of substance use and associated mental health problems (Newton et al., 2013). Hopelessness and anxiety sensitivity are related to self-medicating behaviours, including alcohol use, to numb negative emotions or forget painful memories (Comeau, Stewart, & Loba, 2001; Woicik et al., 2009). Conversely, sensation-seeking and impulsivity are related to a wide range of risk-taking behaviours and are thought to be associated with early substance abuse as socially motivated and thrill-seeking behaviour (Newton et al., 2013).

**4.4.2 Interventions during adolescence**

Because substance use is unlikely to occur before early adolescence (Donovan, 2007), direct prevention efforts are not typically initiated until this developmental stage. As a result, most substance abuse prevention research has focused primarily on adolescents. However, the scientific findings remain largely equivocal, partly because researchers are unable to distinguish normal features of adolescence — novelty-seeking, reduced risk aversion, heightened reward salience and normative experimentation with substance use — from the causal mechanisms that actually predict substance abuse in adolescence and adulthood.

In addition, the toxic effects of substances on the brain, as well as the diverse underlying motivations to use drugs and alcohol, make many interventions ineffective, either because they are the wrong approach for a particular person or because they were introduced too late. As is the case with the earlier stages of development, family well-being, effective stress management and emotional self-regulation remain key components to health during adolescence. The developmental perspective presented in this chapter suggests ways to help formulate targeted interventions that are more effective.

**Focusing on specific personality types and motivations**

The rates of both internalizing and externalizing disorders increase dramatically following the onset of puberty. The understanding that both internalizing and externalizing behaviours are highly correlated with substance use in adolescence and adulthood has the potential to meaningfully shape prevention efforts. For instance, early onset substance use is more reliably predicted by externalizing than internalizing traits (King, Iacono, & McGue, 2004). However, because this pattern has been found to shift with age, internalizing individuals should also be targeted if the end goal is to reduce substance abuse across the entire lifespan.

Interventions can become more efficient when they explicitly address the specific reasons for using substances and how these motivations vary by personality type (Conrod et al., 2011; Stewart, Conrod, Latvala, Wiers, & White, 2013). Currently, several school-based prevention programs targeting specific personality traits have been proposed and the initial results are promising with regard to reducing adolescent alcohol and other drug use (Conrod et al., 2006, 2010, 2013). However, as their effects have been tested only up to two years after treatment, more research is needed to assess the longer-term efficacy of these interventions.

**Recognizing the importance of the broader social environment**

Associated with the push and pull toward independence, peers come to dominate the teenager's social environment. As a complement to individual- and school-centred initiatives, targeting broader social contexts via community-based intervention provides additional opportunities to alter maladaptive developmental pathways and reduce the risks of poor outcome during adolescence.



As an example, the Communities That Care (CTC) program implemented in several U.S. cities over the past decade has been found to significantly reduce substance use and delinquency in youth (Hawkins et al., 2011). Uniquely, the CTC program consists of a long-term, flexible and broad structure within which community members receive the training and support to identify and address specific community-based issues through evidence-based interventions. The goal of this program is to build a broad coalition within the community to carry out any preventive interventions the community itself deems necessary. Interventions are therefore “tailored”: the specific content of a chosen intervention is not dictated by the CTC program and can be targeted to youth and families across multiple settings.

Results from a large-scale, randomized controlled trial involving 24 communities in seven U.S. states suggest that students in CTC communities were 25–33 percent less likely to have health and behaviour problems than those in non-CTC control communities (Hawkins et al., 2011). Although further research is needed to identify how exactly the CTC program works, the choice of evidence-based interventions has been shown to be crucial to the favourable outcome of community interventions (Brown et al., 2013). The success of the CTC program underscores the benefits of applying a multifactorial approach and provides an effective model for community-based substance abuse prevention.

## 4.5 Conclusion: Implications for prevention policy and research

Considering prevention within a developmental context not only highlights developmental pathways and milestones, but also underscores the need to harness opportunities for intervention at early developmental stages. Initiating early interventions at both the parent and child level might decrease risk in later years. Prevention strategies also need to be implemented in a multidisciplinary manner, across contexts and domains (e.g., family, pre-school, parent), and in developmentally appropriate ways:

- In early childhood, the development of effective strategies to regulate behaviour is partly contingent on sensitive, reliable interactions between caregiver and child. Research supports the value of targeting parent–child interactions to reduce risk and improve

resiliency, thereby preventing a range of poor outcomes, including substance abuse. More research is needed to determine how specific interventions work. Is their efficacy a result of social learning, improving parent–child attachment, enhancing a parent’s reflective functioning or some other factor? Although interventions must be developmentally appropriate, the core features of good parenting, such as parental sensitivity and responsiveness, remain relevant across all ages (Bröning et al., 2012) and are therefore of continued interest from a prevention perspective as the child matures.

- The school-age child is expected to comply with increasingly taxing demands related to academic performance and social interaction, with adaptive functioning contingent on developing a sense of independence, self-regulation and self-esteem. At this stage, genetic predispositions, suboptimal parenting and parental psychopathology, and exposure to uncontrollable stressful life events and major transitions are likely to affect the emergence of externalizing and internalizing problems that can lead to the onset of substance use and abuse. In response, preventive interventions implemented at the individual, family and school levels have proven to be most effective when taking into consideration individual patterns of risk and resilience.
- The developmental context of adolescence can both accentuate previously existing risk factors and provide new entries into substance use behaviours. Understanding risks in the context of the developmental history of the individual becomes crucial to detecting and altering maladaptive pathways to substance abuse. Furthermore, unique personality factors and motivations for using drugs and alcohol need to be taken into account to tailor interventions to specific individuals, which can increase the overall effectiveness of prevention programming for youth. The broader social environment also takes on a growing importance during the teenage years. To this end, individual-, school- and community-based programs should be developed and implemented in a flexible manner.



This chapter has presented a number of effective, evidence-based prevention and intervention strategies for each of the key stages of development. Acting to implement these strategies in a flexible and integrated manner will allow for maximum reductions in risk for substance abuse in youth. Nonetheless, even great preventive interventions have non-responders, making it necessary to study non-response to prevention and invest in developing strategies to specifically target non-responders (Gunnar & Fisher, 2006). Developing individualized and personalized prevention approaches that target both general and unique risk factors can be of particular benefit in this regard.



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# 5

## A Call to Action



*By Rajita Sinha and Line Brotnow*

Substance abuse is a large-scale public health concern in Canada. Reducing the concomitant costs to individuals and communities is an explicit public health objective. While many community-, school- and family-based prevention programs have been developed and implemented in the past decades, few have proven particularly effective. More worrisome still, levels of substance use among youth are directly related to higher rates of mental health and addiction problems in adulthood, as well as higher rates of addiction-related chronic diseases that increase the burden on the public health system.

In response, research and intervention efforts are focusing increasingly on prevention. Indeed, early detection of at-risk individuals could divert the cascading chain of events leading to adolescent or adult substance abuse and avoid the direct and indirect negative consequences on mind, brain, behaviour and health.

### 5.1 Key Messages

This report has highlighted scientific advances in the understanding of the two common developmental pathways leading to substance abuse, and has also demonstrated how these advances can be used to inform prevention efforts and policy making. This research can be summarized in five key messages.

- **Substance abuse is a developmental outcome.** Viewing substance abuse as an outcome of the dynamic interplay between genetic and environmental vulnerabilities throughout an individual's development allows for its prediction and intervention. The pathways leading to substance abuse can be traced from inherited vulnerabilities, structural and functional brain abnormalities, and evolving atypical behaviours and personality styles. While identifying patterns of functioning that correlate with the onset of substance abuse is necessary to understanding its development, pinpointing the factors that are truly causal is the ultimate goal of prevention science. Biological, behavioural and social factors interact across many different levels to build risk over the course of an individual's development. Identifying the interactions between these specific risk factors is critical to future substance abuse prevention efforts.
- **Development is non-linear.** Correlational studies tell us that the earlier substance use begins in childhood, the more severe it becomes in adulthood. It seems relatively straightforward to assume that early onset substance use causes more severe substance abuse in adulthood. Ample evidence that early onset drug and alcohol use is associated with altered brain function a few years later lends support to the





assumption (Newton, O'Leary-Barrett, & Conrod, 2013; Squeglia, Spadoni, Infante, Myers, & Tapert, 2009). However, longitudinal studies indicate that both early onset use and altered brain function, while occurring sequentially, might in fact result from a third, underlying factor causing both. Research has shown that interventions targeting exclusively the age of onset of substance use do not always reduce adult substance abuse. Researchers have isolated other variables that reliably predict early onset substance use in youth and severity of substance abuse in adulthood. As a consequence, while age of onset of substance using behaviour can help identify at-risk adolescents, it might not be **causally** related to the subsequent substance abuse. Research to identify effective prevention programs must require specific attention to causal relationships using strong research designs, such as experimental and longitudinal studies.

- **Risks predict non-specific outcomes.** Although many risk factors for substance abuse are heritable, genes seem to confer broad vulnerabilities to negative outcomes as opposed to specific predispositions. Similarly, early biological or behavioural risk factors might not specifically predict later substance abuse; instead, they could index a general risk of poor functioning that, in turn, contributes to high risk for

initiating substance use. The notion of “multi-finality” in developmental terms refers to how similar experiences can produce a variety of outcomes. For example, in response to childhood maltreatment, some individuals might develop aggressiveness and inattention, while others develop anxiety and depression. Combined with the fact that the adult substance abuser is likely to present with a range of co-occurring problems, early intervention targeting specific causal factors could have a broad preventative effect on addiction risk, as well as risks to mental and physical health generally.

- **Risk factors cluster together and have a cumulative impact.** Assessing the likelihood of problematic development must take into account the combined impact of multiple risk factors, in addition to understanding their individual effects. Because the overall risk “load” is most predictive of outcomes, assessment must take into account both the presence of risk factors and the absence of protective factors to fully understand the development of substance abuse. In addition to mechanisms such as the intergenerational transmission of problem behaviours, deeply engrained social structures such as poverty also perpetuate maladaptive behaviours like substance abuse. Multiple risk factors can contribute not only to substance abuse, but also



to other mental and physical health problems. The understanding that sources of vulnerability and resiliency do not operate in isolation should encourage a more integrated view of substance abuse risk and prevention (Sloboda, Glantz, & Tarter, 2012).

- **Predisposition versus predestination.** Human infants are born more immature than any other primate. This immaturity allows the brain to adapt to a wide range of potential living conditions outside of the womb. In other words, experiences are meant to shape the brain. The effects of risk factors and interventions can be understood as consequences of this brain adaptation. Yet the nature of experiences that influence the brain as well as the extent of their impact will vary according to multiple factors contributing to risk. Neither risks nor interventions are “deterministic”: the presence of a risk factor does not inevitably mean a child will develop the associated negative outcome. Still, research findings about isolated risks and average effects can be used to indicate who might be especially in danger of developing problem behaviours. The unique constellation of risks and resilience in each individual must be accommodated by making available a variety of alternative intervention strategies that are targeted to different developmental ages, specific risk factors and larger social contexts.

## 5.2 Recommendations

On the basis of these five key messages, this call to action makes recommendations for prevention research and interventions, and highlights future directions and developments in the field of substance abuse prevention.

### Take a multidimensional approach when identifying and targeting risk factors

Interventions such as the Attachment and Biobehavioral Catch-up program and the Mothers and Toddlers program have demonstrated the value of targeting parent–child interactions to reduce risk and improve resiliency, thereby preventing a wide range of negative outcomes. Although randomized clinical trials can tell us whether these interventions work, more research is needed to determine **how** these interventions work.

As an example, the Strengthening Families Program has been found to reduce problem behaviours as well as parent and child substance abuse by improving family communication and interaction (Trudeau, Spoth, Randall, Mason, & Shin, 2012). However, effect sizes associated with these kinds of interventions are typically small, suggesting that other factors such as personality, early trauma and individual differences in brain development influence the likelihood of a person benefitting from the treatment.

This report has highlighted the general non-specificity of risk factors and their potential broad impact on a variety of negative outcomes. Prevention research needs to choose outcome measures that reflect this broad risk to gauge the true long-term effectiveness of prevention programs. Similarly, to develop more effective prevention programs, future research efforts should be multidimensional in nature, taking an interdisciplinary approach to identifying and targeting markers of risk.

To illustrate, adolescent substance use is associated with elevated rates of other risky behaviours, such as delinquency, sexual promiscuity, school failure and involvement with deviant peers. As a result, there is increasing support in the literature for developing prevention programs that target multiple risks simultaneously. However, little is known about the inter-relationships of these various behaviours, making this a crucial area for research to explore with potentially significant implications for prevention efforts.

### Equip childcare professionals with the skills to detect early signs of risk

Different criteria are used in different settings to identify children who might benefit from early parenting interventions. Contextual characteristics such as child maltreatment or parental substance abuse and mental illness might be reported by medical professionals or social workers, or through the legal justice system. Childcare professionals and preschool or kindergarten teachers might also detect alarming behaviour in individual children, including early externalizing or internalizing behaviours or delayed or abnormal development.

These kinds of professional settings can provide the first line of detection for identifying early warning signs in a young child and early detection is essential for effective preventive interventions.



Researchers need to develop and establish a classification system of specific biological and behavioural early warning signs that goes beyond the simple reporting of abuse, neglect and maltreatment. Such a system could provide a common language that would allow childcare professionals to discuss and address the consequences of adverse family environments with parents and caregivers. Establishing a classification system of risk signs and educating childcare professionals on its use is an implication of these findings.

### **Place greater emphasis on interventions in the school environment**

Teachers are ideally suited to detect early behavioural signs and even to implement evaluations and individualized interventions that address early warning signs and prevent the onset of substance use. However, as discussed elsewhere in this report, while elementary and middle schools have considerable potential to contribute to early detection and prevention, these kinds of interventions are given minimal attention in school settings (Ringwalt, Hecht, & Hopfer, 2010).

School-based interventions that target social and academic difficulties, in combination with more general efforts to strengthen the child's sense of self-efficacy and self-esteem, are likely to reduce substance abuse rates later in life. The literature shows that early intervention can minimize the likelihood of poor outcomes across a wide array of measures. The literature also specifically points to the middle school years as a largely overlooked window of opportunity for prevention efforts.

### **Develop and validate specific neurobiological and biobehavioural risk markers**

Understanding the developmental trajectories leading to substance abuse provides opportunities to detect at-risk individuals and divert the maladaptive chain of events at the earliest possible stage. For example, findings from the neurobiological sciences have demonstrated how early life experiences can change the brain and, in turn, predict poor outcomes. There is a need to develop and validate biobehavioural markers that can reliably indicate such underlying neurobiological risks. More research is needed to identify the multidimensional levels of risk that map onto these specific neurobiological and biobehavioural risk markers. Such research would allow markers to be matched to specific interventions for personalized approaches to prevention.

A methodology for targeting the accumulation of risk should be developed so that early identification of risk signs can support the implementation of low-level interventions with higher payoffs later in life. Identifying specific neurobiological markers and developing a comprehensive codification of behavioural markers are necessary to streamline detection efforts.

When used to identify children who are most susceptible to substance abuse and co-occurring mental and physical health issues, such markers provide the basis for intervention. They could also serve as outcome measures to test and evaluate the effectiveness of prevention programs in real-world settings, as well as in academic research.

## **5.3 Conclusion: A call for continuous, ongoing support**

The research presented in this report reflects a multidimensional, interdisciplinary approach to prevention. Such an approach requires a strong level of support to develop, test and implement the kinds of personalized interventions that will help delay or prevent substance abuse. The prevention of substance abuse and co-occurring mental health and behavioural problems requires long-term investment in broad-based, multilayered prevention, as well as a greater commitment to supporting evidence-based intervention strategies. The results will not be quick — but the payoffs could be dramatic in the long term, leading to significant improvements across multiple health, family and socio-economic outcomes.



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