

# CONCURRENT DISORDERS

SUBSTANCE ABUSE IN CANADA | DECEMBER 2009



## TABLE OF CONTENTS

Foreword by Rita Notarandrea, Canadian Centre on Substance Abuse	01
Foreword by Michael Kirby, Mental Health Commission of Canada	02
Précis	03
<b>1</b> Substance Use and Mental Health Disorders — An Introduction to Concurrent Disorders (M. Krausz)	<b>06</b>
<b>2</b> Stress, Trauma and Substance Use Disorders (A. Abizaid, H. Anisman, K. Matheson, Z. Merali)	<b>12</b>
<b>3</b> Anxiety Disorders and Substance Use Disorders (S. Stewart)	<b>20</b>
<b>4</b> Impulsivity and Substance Use Disorders (S. Cox, M. Leyton)	<b>30</b>
<b>5</b> Mood Disorders and Substance Use Disorders (C. Schütz, A. Young)	<b>38</b>
<b>6</b> Psychosis and Substance Use Disorders (T. George, D. Blank)	<b>48</b>
<b>7</b> A Call to Action (F. Vaccarino)	<b>58</b>

This document was published by the Canadian Centre on Substance Abuse (CCSA) and was made possible in part through a financial contribution from Health Canada. The views expressed herein do not necessarily reflect the views of Health Canada.

Suggested citation:  
Canadian Centre  
on Substance Abuse. (2009).  
*Substance abuse in Canada:  
concurrent disorders*.  
Ottawa, ON: Canadian  
Centre on Substance Abuse.

Copyright © 2009 by the  
Canadian Centre on  
Substance Abuse (CCSA).  
All rights reserved.

For additional copies,  
contact CCSA,  
75 Albert St., Suite 500  
Ottawa, ON K1P 5E7  
Tel.: 613-235-4048  
Email: [info@ccsa.ca](mailto:info@ccsa.ca)

This document can also  
be downloaded as a PDF  
at [www.ccsa.ca](http://www.ccsa.ca)

Ce document est également  
disponible en français  
sous le titre : Toxicomanie  
au Canada : Troubles  
concomitants

ISBN 978-1-926705-28-6

## FOREWORD



*Substance Abuse in Canada* is a vital biennial publication—prepared by the Canadian Centre on Substance Abuse in collaboration with researchers and clinical experts—that highlights key alcohol and drug issues in serious need of attention.

The spotlight for this report shines on concurrent disorders—the co-occurrence of mental health and substance use disorders. This version of *Substance Abuse in Canada* aims to ensure concurrent disorders are considered a major priority for several reasons:

- Concurrent disorders are a significant health issue in Canada—more than half of those seeking help for an addiction also have a mental illness. These individuals present some of the most complex and difficult-to-treat cases and consume a significant portion of health care services.
- In Canada, our system of care for concurrent disorders is fragmented and compartmentalized—with varying treatment approaches and programs developed on a paradigm that treats either the addiction or mental health issue exclusively as the primary focus—creating a system that is not well equipped to treat both disorders concurrently and results in poor client outcomes and system inefficiency.
- Increasing evidence suggests that concurrent disorders have a strong developmental trajectory with onset occurring during adolescence—which makes improving our capacity for early detection and intervention all the more imperative.

The report was written and developed by CCSA’s Scientific Advisory Council (SAC)—comprised of prominent Canadian experts in neuroscience, addiction and mental health—that assists CCSA in identifying new emerging research and clinical

advancements that have the potential to improve Canada’s response to alcohol and drug issues. The report summarizes state-of-the-art findings and highlights a number of key areas where advances in our understanding of concurrent disorders have provided a solid platform on which to build treatment, research, and educational efforts to improve care and transform the system supporting care.

I would like to take this opportunity to thank members of SAC and their colleagues—led by Dr. Franco Vaccarino—for generously volunteering countless hours to researching, writing and reviewing this report and for continuing to lend their valuable biomedical, clinical and neuroscience expertise to CCSA. In addition, I would like to thank the Mental Health Commission for its commitment to work alongside CCSA to help mobilize action to ensure greater collaboration and coordination between addiction and mental health services for this group. We believe that by modeling collaboration at the national level and creating sustainable partnerships to maximize our collective efforts on areas identified in the Call to Action, we will see real change within the system and improved outcomes for those individuals and families who are dealing with concurrent disorders.

Rita Notarandrea, Deputy Chief Executive Officer  
Canadian Centre on Substance Abuse

## FOREWORD



Mental illness and addiction are serious health matters that affect the lives of thousands of Canadians and their families. The two share many features and are often closely tied to other issues such as stigma, discrimination, homelessness and poverty. Mental illness and addiction are not problems of moral weakness or personal failings: they are as much ‘real’ illnesses as heart disease, cancer and AIDS.

The Standing Senate Committee on Social Affairs, Science and Technology noted the substantial overlap between mental health and addiction issues—including the large proportion of people living with both mental illness and addiction—in its final report, *Out of the Shadows at Last: Transforming Mental Health, Mental Illness and Addiction Services in Canada*. Research shows that more than half of those seeking help for an addiction also have a mental illness, and 15 to 20% of those seeking help from mental health services are also living with an addiction. Rates are even higher for more vulnerable populations and certain mental health problems.

People seeking help for co-occurring mental health and addiction problems often have difficulty finding appropriate services. Historically, programs have often required that one disorder, either a person’s mental illness or addiction, be identified as the main one rather than recognizing that the two are interconnected. In fact, those seeking mental health services have frequently been excluded from treatment if they admitted to substance use, and those seeking treatment for an addiction have been turned down if they were taking medication for a mental illness. The challenges to integrating mental health and addiction treatment and support for people with concurrent disorders are numerous; many sectors

and jurisdictions are working hard to address these challenges. There is a pressing need for research to build a knowledge base for the development of strong, fact-based prevention, treatment and support services.

This report represents an effort to gather cutting-edge knowledge and state-of-the-art research findings that will help shed light on the complex relationship between addiction and mental illness. The Mental Health Commission of Canada is encouraged by the significant recent developments in this area. New discoveries will lead to more effective supports and services—improving the lives of Canadians and their families as they face the realities of mental illness and substance use.

The Mental Health Commission of Canada and the Canadian Centre on Substance Abuse are committed to working collaboratively to ensure that services and supports for those confronting concurrent mental health and substance use disorders are responsive, effective and better integrated. The Mental Health Commission has recently released a framework for Canada’s first mental health strategy, *Toward Recovery and Well-Being*. Over the next two years, we will be developing a strategy to achieve the vision and goals outlined in the framework. We look forward to working with the Canadian Centre on Substance Abuse and others to ensure the inclusion of the needs of those living with concurrent mental health and substance use problems.

Michael Kirby, Chair  
Mental Health Commission of Canada

## PRÉCIS

*Substance Abuse in Canada* is a biennial publication launched by the Canadian Centre on Substance Abuse in 2005. Its purpose is to draw attention to key contemporary substance abuse issues in this country and highlight areas for action in both policy and practice. Each edition is developed through a review and analysis of the latest research evidence and is targeted primarily at policy makers, program development personnel, researchers, educators and health professionals. Health journalists also make up an important readership of this report as they raise the public profile of the issues and help create the impetus for change.

### THE STORY UNTIL NOW

The first *Substance Abuse in Canada* report, *Current Challenges and Choices*, looked at a range of topics including new directions in preventing alcohol problems, alternative sanctions for cannabis use and possession, drugs and driving, and diversion and abuse of prescription medications. The second edition, *Focus on Youth*, examined the prevalence of substance use and its associated harms in the general youth population and among non-mainstream youth. It reviewed the range of responses available in Canada, explored the underlying neurobiology of substance use in adolescence, and identified a range of gaps in services and areas for action. That edition of the report led in part to the funding of a five-year strategy on youth drug prevention spearheaded by CCSA.

### THIS EDITION OF SUBSTANCE ABUSE IN CANADA

Concurrent disorders—the co-occurrence of mental health and substance abuse problems—are the focus of this 2009 edition. Concurrent disorders are a major health issue in Canada. Research shows that more than half of those seeking help for an addiction also have a mental illness, and 15 to 20% of those seeking help

from mental health services are also living with an addiction. Individuals with concurrent disorders represent the most complex cases and are often the most difficult to care for, with frequent relapses and crises being the norm. It is not surprising then that they consume a significant portion of health care resources and, consequently, represent a large proportion of the costs of care.

Due to independent and compartmentalized mental health and addictions systems, many people with concurrent disorders are treated for their mental health issues or their addictions but not always both, contributing to poor care outcomes. Seeking a more effective treatment approach and the improvement of overall client outcomes, this report assesses the unique features of concurrent disorders and highlights how often addictions and mental health issues are interconnected—and therefore require different approaches.

### A CHAPTER-BY-CHAPTER SUMMARY

#### **Substance Use and Mental Health Disorders — An Introduction to Concurrent Disorders**

This chapter introduces some of the characteristics of individuals with concurrent disorders—a particularly vulnerable group often marginalized in society for their addictions or mental health issues and associated with poverty, homelessness/unstable housing, high rates of HIV, participation in the sex trade and lowered life expectancy. The chapter highlights the need for research into the underlying mental health conditions and patterns of substance use as well as their interactions on different levels. All of this is critical to the development of effective treatments and interventions. Research is also needed to improve understanding of the reasons for increasing rates of concurrent disorders and why some therapies are successful for certain concurrent disorders but not for others.

Finally, the chapter notes the need for new and innovative ways of training and educating professionals in evidence-based specialized and integrated care.

#### **Stress, Trauma and Substance Use Disorders**

This chapter examines the relationship between stressful or traumatic events and substance abuse. Exposure to traumatic events can increase alcohol and drug use, which can lead to new traumatic experiences that, in turn, prompt further substance use—perpetuating the stress-substance use cycle. It is widely recognized that social support is important in successfully dealing with stressful events or situations. However, what matters most is not the quantity of support (or support resources) one has, but rather the quality of that support. Preventative interventions or treatment strategies that teach effective stress appraisal and coping methods may have a significant impact on substance use disorders.

#### **Anxiety Disorders and Substance Use Disorders**

In this chapter, anxiety disorders are defined as more strongly associated with substance dependence—a more severe problem than substance abuse, with panic disorders being most closely associated with alcohol dependence, and generalized anxiety disorders most closely associated with dependence on drugs. People with both an anxiety disorder and a substance use disorder receiving treatment of one problem, without also addressing the other, have poor short-term outcomes and a high risk for relapse. Co-occurring anxiety and substance use disorders need to be addressed at the same time to improve treatment outcomes—preferably through specialized integrated treatment approaches.

#### **Impulsivity and Substance Use Disorders**

Here the report observes that problems with impulse control are the single strongest predictors of future substance abuse—with alcohol abuse particularly common among high “sensation-seeking” people. Impulsive behaviour is also a core problem in several personality and psychiatric disorders, putting those affected at higher risk of substance use problems. For example, individuals with ADHD (attention deficit hyperactivity disorder) are at elevated risk for substance abuse and addiction, especially those who do not receive early treatment. A combination of preventative, early identification and treatment strategies can diminish the most damaging effects of impulsivity and its consequences—including the risk of substance use and addiction.

#### **Mood Disorders and Substance Use Disorders**

Having a mood disorder increases the likelihood that a person will use drugs and alcohol. On the whole, substance dependence is linked with mood disorders to a greater degree than either substance abuse or substance use. The clinical course of both mood and substance use disorders (treatment engagement, thoughts

of suicide, homelessness, increased risk of victimization) and their clinical outcomes (life expectancy, suicide, treatment outcome) is affected when the two conditions co-occur. Changes to the current treatment system are necessary to improve care for people with concurrent substance use and mood disorders. These changes include improved detection and diagnosis, increased awareness and acceptance of the need to treat both disorders at the same time, increased focus on the development of specialized treatments for concurrent disorders, and increased availability of treatment options for these patients.

#### **Psychosis and Substance Use Disorders**

This chapter reveals that psychotic disorders such as schizophrenia co-occur with substance use disorders at the highest rate of any mental health condition. People with schizophrenia are, for example, three times more likely to also have an alcohol problem and six times more likely to have a drug problem than those without a mental disorder. This is a concern because substance abuse can hasten the onset of psychotic disorders, worsen both the symptoms and the course of illness, and lead to higher rates of psychiatric hospitalization and increased health care costs. Changes to the training of mental health and addictions staff and physicians, and reconfiguration of the health care system to better meet the complex needs of clients with both psychosis and substance use disorders, are essential to progress in this area. Ideally, pharmacological and behavioural treatments should be combined for the treatment of co-occurring substance use and psychotic disorders.

#### **A Call to Action**

This chapter draws on the themes explored in the earlier discussions. It reinforces the need for greater collaboration and in some cases an integrated approach to address co-occurring mental health and substance use disorders. Such an approach includes integrated clinical care and practice guidelines, a common education and training platform, collaborative and integrated research projects, and system-level integration of specialized concurrent-disorder services. This chapter also highlights the need to pay special attention to developmental considerations, as many conditions are developmentally sensitive and begin during adolescence. As with any health issue, concurrent disorders are best treated with early intervention and may even be preventable with awareness of sub-clinical indicators and other determinants of vulnerability. That being so, the importance of early detection and intervention represents a theme in and of itself. Finally, the chapter revisits the issue of trauma and stress as an additional risk factor in developing concurrent disorders, and notes there is a sufficient body of knowledge to begin to develop integrated approaches to prevention and treatment.

## TERMINOLOGY NOTES

**Addiction.** The term addiction is generally applied to patterns of heavy use of psychoactive drugs that are taken primarily for their effects on consciousness, mood and perception. In general, addiction has been replaced by the more specifically defined term substance (or drug) dependence. However, “addiction” continues to be used widely and is generally thought of as compulsive use leading to physical symptoms of withdrawal when use is discontinued. For that reason, it is often equated with physical dependence.

Several of the terms used in this document have specific and distinct clinical significance, but to avoid repetition have been used here as equivalents. The definitions below are based on the DSM-IV manual and Chapter 70 “Drug Abuse and Drug Dependence.”

**Substance Use Disorders.** Substance use disorders include disorders related to the taking of a drug of abuse, to the side effects of a medication, and to toxin exposure. In the context of this publication, “substance” refers specifically to a drug of abuse. Substance use disorders can be further subdivided into substance dependence and substance abuse.

**Substance Dependence.** This is also referred to as “drug dependence” and constitutes a cluster of cognitive, behavioural and physiological symptoms

indicating the individual continues his or her substance use despite significant substance-related problems. There is a pattern of repeated self-administration that usually results in tolerance, withdrawal and compulsive drug-taking behaviour.

**Substance Abuse.** This is also known as “drug abuse”; a maladaptive pattern of substance use defined by DSM-IV as resulting in recurrent and significant adverse consequences related to the repeated use of a drug. Substance abuse is not characterized in terms of tolerance and withdrawal;

instead, it includes only the harmful consequences of repeated use, as when that use causes failure to fulfill obligations at work, school or home, becomes physically hazardous, or creates legal, social or interpersonal problems. Popularly, the term “drug abuse” is taken to mean substance use, but this is not approved of. Jaffe (1985) provides the following definition: “Drug abuse refers to the use, usually by self-administration, of any drug in a manner that deviates from the approved medical or social patterns within a given culture.”

## REFERENCES

- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: Author.
- Kalant, H., Grant, D., & Mitchell, J. (Eds.). (2007). Drug abuse and drug dependence. In H. Kalant, D. Grant & J. Mitchell (Eds.), *Principles of Medical Pharmacology* (7th ed.), (Chap. 70) Toronto: Elsevier Canada.



SUBSTANCE USE  
AND MENTAL HEALTH  
DISORDERS

# An introduction to concurrent disorders

**Reinhard Michael Krausz, MD, PhD, FRCPC**  
University of British Columbia

## AUTHOR BIO

**Reinhard Michael Krausz,  
MD, PhD, FRCPC**

Dr. Reinhard Michael Krausz is a Professor of Psychiatry, Epidemiology and Public Health at the University of British Columbia, Medical Director of the Burnaby Centre for Mental Health and Addiction and the regional program for Complex Concurrent Disorders and Founding Fellow of the Institute of Mental Health

at UBC. He serves on several international, national, provincial and city-level Advisory Boards, including the Scientific Advisory Council for CCSA, the Research Advisory Council of the Michael Smith Foundation and Co-Chair of the Collaboration for Change in Vancouver.



# 1

## INTRODUCTION

Substance use disorders occurring together with mental health disorders represent a major health problem in Canada. With high prevalence rates, these concurrent disorders are challenging the system of care (Kessler et al., 2005; McGlynn et al., 2003). To develop effective interventions that include important changes to the treatment system, it is crucial that we better understand the underlying mental health conditions and the patterns of substance use—as well as their interactions on different levels (Rush, 2002).

In established market economies such as Canada and the US, mental health disorders account for 43% of disability and 22% of the total burden of disease (the sum of premature death and years lived with disability). And having more than one disorder—especially the co-occurrence of an anxiety disorder—contributes to greater disability (Andrews, Sanderson & Beard, 1998). The disproportionate disability caused by mental health disorders is a result, in part, of their early age of onset, their chronicity, and the fact that only a minority of individuals ever receive treatment for their conditions (Alegria et al., 2000). Indeed, while rates of professional care for mental health disorders and substance use disorders have increased over the past 30 years, unmet need for care still remains a significant public health concern.

It is recognized that the most complex and difficult-to-treat patients often use a broad range of substances and suffer from coexisting mental health disorders, yet the current treatment paradigm for addiction and concurrent mental health disorders is to treat them as distinct entities (Fairbairn et al., 2007; Fulkerson, 1999). It is clear that from a scientific and clinical perspective, it is necessary to move away from our single substance, single disorder point of view to an approach built upon an understanding of the use of multiple substances and their interaction with co-occurring mental

illness. This has important implications for future research examining the biological basis of addiction and for the development of novel and effective intervention strategies in a variety of treatment settings.

Given that much of the research to date and the existing drug treatment programs have typically focused on only one substance, the use of multiple substances—such as opiates together with stimulants (amphetamines, crack or cocaine)—poses a complicated challenge. For example, neither the biological nor psychological aspects behind the increasing use of crack among patients dependent on opiates are well understood. Nevertheless, current research is telling us that this so-called *poly-substance use* is exceedingly common—perhaps making it the rule and not the exception. Starting with basic research, a broader focus beyond single substance use is needed to explore the factors that influence substance use, including concurrent mental health disorders.

### VULNERABLE POPULATIONS

The entanglement of severe addiction, concurrent mental health conditions and physical illness together with homelessness and marginalization is becoming a major challenge for metropolitan areas across the country. Inner-city populations—particularly

those injecting drugs—are at extremely high risk of drug-related harm including HIV infection, hepatitis C infection, serious bacterial infections and overdose death (Kuyper et al., 2004). The high rates of concurrent mental health disorders and the co-use of other substances in this population continue to challenge the health care and social systems, and therefore necessitate research that addresses these complicated situations (Kamal et al., 2007; O’toole et al., 2007). For example, it is estimated that 130,000 individuals fulfill the criteria for this condition in British Columbia alone (Patterson et al., 2007). Vancouver’s Downtown Eastside (DES) is internationally known for its concentration of individuals who inject drugs, consume crack cocaine, suffer from mental illness and lack housing (Chase-Project-Team, 2005; Wilson-Bates, 2008).

Another group that requires special attention in relation to drug abuse, trauma and concurrent mental health disorders is women. Substance-using mothers and their children are especially vulnerable in inner cities and are in desperate need of customized treatment settings and safer homes.

#### THE NEED FOR RESEARCH AND MODELS

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) is very useful in diagnosing mental health and substance use disorders—but has its limitations. Describing symptoms is a good start, but it’s not enough. We need to understand the reasons behind the increasing rates of concurrent disorders in order to develop better and more effective interventions. And we need to determine why certain therapies are successful in treating some concurrent disorders but not others. The need for further research in these areas is clear.

Descriptive models for concurrent disorders may lead to a better understanding of the use of substances to cope with emotional pain. One such example, known as the “*self-medication hypothesis*”, postulates that substance use in people with mental health disorders is an attempt to self-treat their condition (Khantzian, 1978). This model is discussed in further detail in Chapter 3. *Behaviour*

*pharmacological models* may help improve understanding of the interaction of biology and behavioural experience (such as stress or trauma), enabling interventions to be more effectively targeted.

Unfortunately, patients with concurrent disorders have largely been excluded from mainstream psychiatric or addiction research and scientific trials to avoid “muddying the waters”—if subjects with both substance use and mental health disorders are included in a trial, are the results seen due to the mental health disorder, the substance use disorder, or both? The animal models used in addiction research are often focused on a single condition or substance, making their application to more complex clinical problems—such as concurrent disorders—difficult. Without a solid, focused research base concurrent disorders are not well understood, and the care provided for them may be inappropriate. Future interdisciplinary research incorporating different scientific perspectives is necessary to contribute to a new, more complete understanding of the disorders that would help the system of care to function better in the future.

#### SYSTEMIC ISSUES AND THE NEED FOR INTEGRATION

The present system of care in Canada is not prepared to meet the challenge of concurrent substance use and mental health disorders. The fragmented and compartmentalized system employs differing treatment philosophies and lacks the specialized capacity to treat both disorders simultaneously. People being treated within the addictions system—whether through substitution programs or residential care—are frequently depressed, traumatized or suffering from other mental health issues. Those being treated for mental health disorders often are using drugs and alcohol. Yet these patients are frequently being treated for only one of their co-occurring disorders. In fact, treatment programs often exclude either those with substance use or mental health disorders—despite the disorders being closely connected.

It is time to consider a major reorganization of the delivery of addiction treatment and mental health care in Canada. New and innovative ways of training and educating professionals must be incorporated to achieve an integration of care based on best evidence. Without extensive changes to our current system of care, we will continue to be unable to meet the unique challenge of successfully managing concurrent mental health and substance use disorders.

#### THE ROAD AHEAD

By collaboratively meeting the challenges posed in the following four areas, Canada can begin to successfully address the needs of those with concurrent substance use and mental health disorders.

##### More Research

A better understanding of concurrent disorders is crucial to the development of effective interventions. More research and better models are essential for very practical reasons. For example, if trauma is determined to be a significant factor in the development of substance use disorders, addiction treatment could systematically address it. In fact, if this was the case, preventing trauma or effectively managing those who have been exposed to trauma could potentially prevent a significant proportion of substance use disorders—before they even develop. Unfortunately, at this time results from clinical research and indeed the capacity to carry out this type of research are simply not available.

##### Integrated Treatment and Interventions

Prevention and treatment interventions addressing both substance use and mental health disorders need to be developed. In keeping with *A Systems Approach to Substance Use in Canada: Recommendations for a National Treatment Strategy*, the integration of training, services and programs for substance use and mental health disorders within health care, mental health, education, social service, and criminal justice systems would result in improved care. The integration of addiction and mental health planning and services would reflect the reality of concurrent substance use and mental health disorders.

#### PREVALENCE

Research shows that more than 50% of those seeking help for an addiction also have a mental illness, and 15-20% of those seeking help from mental health services are also living with an addiction.

#### DISABILITY/BURDEN OF DISEASE

Mental health disorders account for 43% of disability and 22% of the total burden of disease (the sum of premature death and years lived with disability)—having more than one disorder contributes to even greater disability

#### A SNAPSHOT FROM BC

- An estimated 130,000 individuals meet the criteria for concurrent disorders) in British Columbia alone
- Vancouver Police Department survey in the Downtown Eastside showed that 50% of all emergency calls were found to involve people with mental illness or substance use problem

### **Development of New Therapy Modalities**

The development of new and effective therapies for substance use and concurrent mental health disorders will become possible as our understanding of these disorders and their overlap increases. With improved systems of care, new **medication therapies** will reach those who will benefit most. Pharmacotherapies will, however, become more complex, especially in the backdrop of significant drug interactions and side effects for those who are also being treated for other highly prevalent conditions such as hepatitis C. **Psychosocial treatment** programs such as counselling and therapy (Rawson, 1985) have shown that it is possible to change substance use behaviours even in complex populations. A good example of a successful approach to the treatment of concurrent disorders exists in **milieu therapy**, or so-called “recovery houses”, where appropriate room for change and peer support are the ingredients for success. But these approaches are merely the beginning of more tailored and structured treatment protocols for concurrent substance use and mental health disorders.

### **Recognizing the Challenges**

The unique challenges of vulnerable populations with substance use and mental health disorders cannot be overlooked. Through their limited ability to cope with everyday challenges and the stigma attached to their conditions, these individuals may become homeless, socially marginalized and criminally involved. For example, in a police survey through the Vancouver Police Department in the Downtown Eastside, 50% of all emergency calls were found to involve mentally ill and/or addicted people. Only by addressing these challenges can any approach to concurrent mental health and substance use disorders be successful.

## REFERENCES

- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: Author.
- Boyd, N., Kinney, J. B., McLean, C., Heidt, J., & Otter, I. (2008). *Public Order and Supervised Injection Facilities: Vancouver's SIS*. Presented to the Expert Advisory Committee on Supervised Injection Site Research, Health Canada.
- Chase-Project-Team. (2005). *Community Health And Safety Evaluation (CHASE) Project*. Vancouver Health Authority.
- Cottler, L. B., Price, R. K., Compton, W. M., & Mager, D. E. (1995). Subtypes of adult antisocial behavior among drug abusers. *The Journal of Nervous and Mental Disease, 183*, 154–161.
- Cottler, L. B., Schuckit, M. A., Helzer, J. E., Crowley, T., Woody, G., Nathan, P., & Hughes, J. (1995). The DSM-IV field trial for substance use disorders: major results. *Drug and Alcohol Dependence, 38*, 59–69.
- Fairbairn, N., Kerr, T., Buxton, J. A., Li, K., Montaner, J. S., & Wood, E. (2007). Increasing use and associated harms of crystal methamphetamine injection in a Canadian setting. *Drug and Alcohol Dependence, 88*, 313–316.
- Fulkerson, J. A., Harrison, P. A., & Beebe, T. J. (1999). DSM-IV substance abuse and dependence: Are there really two dimensions of substance use disorders in adolescents? *Addiction, 94*(4), 495–506.
- Health Canada. (2002). *Best practices: Concurrent mental health and substance use disorders*. Ottawa, ON: Author.
- Kamal, F., Flavin, S., Campbell, F., Behan, C., Fagan, J., & Smyth, R. (2007). Factors affecting the outcome of methadone maintenance treatment in opiate dependence. *Irish Medical Journal, 100*, 393–397.
- Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Archives of General Psychiatry, 62*, 593–602.
- Kuyper, L. M., Hogg, R. S., Montaner, J. S., Schechter, M. T., & Wood, E. (2004). The cost of inaction on HIV transmission among injection drug users and the potential for effective interventions. *Journal of Urban Health : Bulletin of the New York Academy of Medicine, 81*, 655–660.
- McGlynn, E. A., Asch, S. M., Adams, J., Keeseey, J., Hicks, J., DeCristofaro, A., et al. (2003). The quality of health care delivered to adults in the united states. *The New England Journal of Medicine, 348*, 2635–2645.
- Network, C. H. A. L. (2005). Injection drug use and HIV/AIDS in Canada: The facts. Canadian HIV/AIDS Legal Network.
- O'Toole, T.P., Pollini, R., Gray, P. Jones, T., Bigelow, G., & Ford, D.E. (2007). Factors identifying high-frequency and low-frequency health service utilization among substance-using adults. *Journal of Substance Abuse Treatment, 33*(1), 51–59.
- Patterson, M., Somers, J.M., McIntosh, K., Shiell, A., & Frankish, C. J. (2008). *Housing and Support for Adults with Severe Addictions and/or Mental Illness in British Columbia*. CARMAH Simon Fraser University.
- Spittal, P., Hogg, R., Li, K., et al. (2006). Drastic elevations in mortality among female injection drug users in a Canadian setting. *AIDS Care, 18*(2), 101–8.
- Wilson-Bates, F. (2008). *Lost in Transition — How a Lack of Capacity in the Mental Health System is Failing Vancouver's Mentally Ill and draining Police Resources*. Vancouver Police Board.
- Wood, E., Kerr, T., Montaner, J. S., Strathdee, S. A., Wodak, A., Hankins, C. A., et al. (2004). Rationale for evaluating North America's first medically supervised safer-injecting facility. *The Lancet Infectious Diseases, 4*, 301–306.
- Wood, E., Tyndall, M. W., Lai, C., Montaner, J. S., & Kerr, T. (2006). Impact of a medically supervised safer injecting facility on drug dealing and other drug-related crime. *Substance Abuse Treatment, Prevention, and Policy, 1*, 13.



# Stress, Trauma

## AND SUBSTANCE USE DISORDERS

**Alfonso Abizaid**  
Carleton University

**Hymie Anisman**  
Carleton University

**Kimberly Matheson**  
Carleton University

**Zul Merali**  
Ottawa Institute of  
Mental Health Research

**Acknowledgements**  
The research of the authors is supported by the Canadian Institutes of Health Research.

### AUTHOR BIOS

**Alfonso Abizaid**

Dr. Alfonso Abizaid is an Assistant Professor at Carleton University's Neuroscience Institute. His work is focused on the effects of metabolic and stress hormones on motivated behaviours including feeding, drinking, sexual and drug-seeking behaviours.

**Hymie Anisman**

Dr. Hymie Anisman, a holder of a Canada Research Chair in Neuroscience, is a Professor within the Institute of Neuroscience at Carleton University. His research,

funded by CIHR and NSERC, has focused on the impact of stressors on various brain neurochemical processes and immune functioning, and how these might come to affect psychological and physical pathologies.

**Kimberly Matheson**

Kimberly Matheson is Acting Vice-President (Research & International) and a Professor in the Department of Psychology at Carleton University. Her research concerns psychosocial factors that influence the stress response, and intervention strategies that might mitigate against the extent to which stress translates into pathological outcomes.

**Zul Merali**

Dr. Zul Merali is the President and CEO of the University of Ottawa Institute of Mental Health Research. He holds academic appointments with the faculties of Social Sciences and Medicine at the University of Ottawa and with Carleton University. His research focuses on how appetitive and aversive events influence brain functioning. He is particularly interested in understanding how various types of stressful experiences precipitate pathological behaviour and/or mental illness.



## ALISA

Alisa is 20 years old and has been using drugs since the age of 11. Stimulants like amphetamines and crack were easy to find on the reserve in Northern BC where she lived with her parents and five other siblings—and numerous other relatives—in the same tiny house. Both of her parents experienced severe problems with alcohol and were largely unavailable to her. In fact, her mother drank heavily while she was pregnant with Alisa. Alisa was only 6 years old when her 12-year-old cousin, who was drunk, forced her to have sex. That was her first experience of violence—but not the last. At 14 years of age, Alisa left the reserve and eventually found herself living on the street in Vancouver. She, like many others, became entrenched in the streets—sleeping in shelters, with

very little support and facing a daily struggle just to survive. It was during this time that she first tried injecting drugs. The opiates helped her by numbing her psychological pain and helping her to forget all that had happened to her. Crack helped her to stay alert—something a person living on the streets needs to be. Now, at age 20, Alisa is living in a Single Room Occupancy (SRO)—a windowless, sparsely furnished room—in Vancouver’s Downtown Eastside. She makes her living in the sex trade, mostly to finance her drug use (survival sex). Abuse and suffering remain as daily occurrences in her life, together with nightmares and flashbacks. And yet, despite all this, she continues to have hope that somehow things might change for the better in her life.

### ISSUE

A real link between stressful or traumatic events and substance use problems exists—and evidence of its existence is supported by research. Indeed, people who experience stressful events such as child abuse, criminal attack, natural disasters, war, or other traumatic events often turn to alcohol or drugs (Cleck & Blendy, 2008; Sinha, 2008). Substance use helps them to deal with the emotional pain, the bad memories, their poor sleep and their guilt, shame, anxiety and terror. Unfortunately, their use of drugs and alcohol can often lead to a self-perpetuating cycle—their original stress or trauma led to substance use, which then resulted in further stress and trauma in their lives which, ultimately, leads to further substance use—and the stress-substance use cycle continues. In fact, their drug use becomes a “stress proliferator”. The distress associated with substance use is not limited to those consuming drugs or alcohol; substance use often creates significant problems for family and friends, as well—the very people who might otherwise help a person to stop drinking or taking drugs if their relationship hadn’t been undermined by the substance use.

Clearly, the relationship between stress or trauma and substance use is complex. Stressful experiences may increase initial drug intake, contribute to ongoing drug consumption, and play a part

in the recurrence or relapse of substance use and addiction. To better appreciate this relationship, it’s helpful to review how people react to and deal with stress in their lives.

### The Stress Response

The human stress response comprises a wide range of behavioural and biological changes—many of which are adaptive to help us meet the demands placed on us. However, each of us responds to stress differently; events or stimuli seen as stressful by one person may not be stressful to another. Even when people find events equally stressful, their responses to that level of stress may be quite different. Thus, the harmful consequences of stress may not be the same for everyone. These individual differences—including the biological factors that contribute to stress-related problems—influence our responses to stress.

When individuals encounter a potentially stressful situation, first they appraise the event (e.g., asking “Is this event a threat?”). A second appraisal then follows, in which they determine if they have the resources available to cope with the stress (Lazarus & Folkman, 1984). How an event is appraised may be influenced by the characteristics of the event or situation—including its perceived severity (Anisman & Matheson, 2005). Based on these appraisals,



coping strategies are then adopted to contend with the situation. Generally, these fall into three broad classes: problem solving, emotional strategies (emotional expression, self- or other-blame, rumination) and avoidant strategies (avoidance/denial, active distraction, wishful thinking, drug consumption). Other strategies include religious coping or the seeking of social support.

A coping strategy, whatever form it may take, may serve different functions. For example, social support-seeking can provide emotional support or a distraction from the stress. It can also yield a source of information or facilitate problem solving, and perhaps even bring forth a financial resource. In fact, the importance of social support resources in coping with stressful events or situations is widely recognized; however, what matters most is not the amount of support but the quality of this support. It's not certain whether *unsupport* (i.e., not receiving support when it is expected, or others' insensitivity to an individual's needs) contributes to drug problems, but it may be a powerful predictor of substance use related to stress and trauma.

People experiencing stress may also use more than one coping strategy—either at the same time or one after the other—and it's often this combination of strategies that determines how well a person copes with a stressful event. With severe stress, a person's ability to think clearly and logically (i.e., their cognitive function-

ing) may be impaired, making appraising the situation difficult and adopting effective coping strategies nearly impossible. In fact, this impaired cognitive functioning can even lead to the adoption of ineffective or counterproductive strategies, including drug use (Anisman & Matheson, 2005). Finally, there are occasions in which it is difficult to know which coping strategies to adopt, simply because the situation is ambiguous (e.g., “Will the biopsy show the tumour to be malignant?”, “Will the economy continue to decline?”).

### The Impact of Stress

The impact of a stressful or traumatic event is also influenced by many factors. Amongst these are the characteristics of the event, previous stressful experiences (including those encountered early in life), individual differences and variables such as gender, age and genetics.

The nature of the stressful event may influence the type of changes that occur in the brain; this in turn may influence whether harmful or unhealthy effects emerge (Merali et al., 2004). More profound behavioural and biological changes have been shown as a result of uncontrollable, unpredictable stress (Maier & Seligman, 1976). Not surprisingly, ambiguous stressors appear to be particularly effective in provoking anxiety, which could contribute to substance use (Matheson & Anisman, 2005). Finally, the chronicity of stress may be especially important in determining unhealthy or negative outcomes. This is significant given that many stressful events or situations are indeed chronic in nature—considering that stress is often followed by worrying and negative thinking. It is believed that responses to chronic, unpredictable stress result in excessive wear and tear on biological systems (McEwen, 2000), leading to behavioural and physiological disturbances that may include substance use.

The experience of previous stress greatly influences the impact of subsequent stressful encounters. Our biological stress responses can be “sensitized” by stress, so that when we are re-exposed to that same stress or to a new stressful event, the stress-related chemical



changes in our brains are exaggerated (Anisman et al., 2003). Such changes can affect the pathways in our brains associated with drug taking and relapse (Koob, 2008). Similarly, negative and stressful events in early life may make the adult response to stress greater (Heim et al., 2008). Thus, although some of the biological changes induced by stress are temporary, they may, in fact, have far-reaching repercussions.

The interrelations between stressful events, their appraisal, adopted coping strategies and elicited biological responses are complex. To add to this complexity, the characteristics of stressful events and the response of individuals to those events are ever-changing. Those who are flexible with a broad range of coping strategies and are either able to switch from one coping strategy to another or employ coping strategies in combination may be more resistant or resilient to the negative impacts of stress (Anisman & Matheson, 2005). But the most profound negative impacts of stress will be felt by those having a restricted range of coping strategies and those who persist in adopting strategies that are ineffective.

#### FURTHER EVIDENCE AND DISCUSSION

Stressful experiences lead to a number of changes in brain chemicals, many of which have been implicated in psychological disorders, including substance use and dependence. Multiple chemical pathways in many areas of the brain are influenced by stress, including those that link the *hypothalamus* to the pituitary and adrenal glands (this pathway and its chemical, *corticotrophin releasing hormone* or CRH, are involved in many of the hormonal responses humans have to stress). In animal models of addiction, CRH has also been associated with increased consumption of drugs of abuse, resistance to stopping drug use, and drug relapse (Stewart, 2000). CRH may also increase activity in brain pathways involved with reward processes—making an individual more vulnerable to the changes caused by alcohol and drugs (Bonci & Borgland, 2009). In fact, blocking CRH has been shown to reduce the self-administration of cocaine, heroin and alcohol as well as blocking stress-induced relapse to these same drugs (Shaham et al., 1997; Stewart, 2000).

Other pathways and areas of the brain affected by stress are those for fear and anxiety (Merali et al., 1998, 2004) and those that contribute to appraisal and motivational processes (Anisman et al., 2008). These too may contribute to increased risk of substance use and addiction. Stress can cause changes in a brain pathway that uses the chemical *dopamine*, and this pathway influences reward-seeking behaviours. This stress-induced change can lead to increased and sustained behavioural responses to drugs—enhancing their reinforcing properties (Saal et al., 2003).

When stress is sufficiently severe and uncontrollable, the brain uses up more of these brain chemicals than it can make. The resulting decline in the amount of these chemicals could affect the brain's ability to transmit messages—and ultimately affect thoughts and behaviour. With chronic stress, it has been shown that the brain can adapt to these lower chemical levels by becoming more sensitive to the amounts present. However, this adaptation can be slow to develop and may not even occur if the stress is intermittent and unpredictable. In this case, behavioural and psychological problems can result—which may include substance use (Anisman et al., 2008).

The various stages of substance use and dependence likely involve different motivations, brain chemicals and pathways. Initial drug consumption may reflect an attempt to simply feel good. Subsequent use of a drug may be in an effort to alleviate the negative feelings that are experienced in the absence of that drug (Heilig & Koob, 2007; Koob & LeMoal, 2008). The implication is that drug craving is fundamental in sustaining an addiction. Both stressful events (e.g., loss of a loved one) and cues associated with a drug (i.e., being in the place where drugs were previously consumed) can lead to further drug use, but may do so in different ways. Drug-related cues leading to drug craving involve reward processes or positive feelings. Craving brought about by stress leads to drug intake to minimize a negative emotional state (Koob & LeMoal, 2008). Evidence of this can be seen with medication used to curb drinking; they are successful in the face of alcohol-related cues but not in stressful situations. Conversely, medications

that block CRH (the brain chemical implicated in stress reactions) can curb drug use related to stress but aren't helpful in preventing use elicited by drug-related cues (Liu & Weiss, 2002). However, the involvement of these various biological processes may vary depending on the stage of substance use and dependence—initiation versus maintenance versus relapse.

Although much of the research into substance use and stress has focused on the brain pathways that involve the brain chemicals CRH and dopamine, new research suggests other possible contributing pathways (Abizaid et al., 2006a; Bonci & Borgland, 2009). These include a pathway related to energy balance that uses the brain chemicals *ghrelin* and *leptin*. The two chemicals stimulate or suppress our food intake and are released depending on whether or not more energy is required. However, they are also secreted in response to stress (Malendowicz et al., 2007; Lutter et al., 2008) and may affect how the body responds to drugs (Fulton et al., 2006; Hommel et al., 2006; Wellman et al., 2007). Further research is also beginning to uncover the role of even more brain chemicals in the relationship between stress and substance use (Ansiman et al., 2008; Koob & LeMoal, 2008; Bonci & Borgland, 2009). Indeed, as research continues, our understanding of the link between stress and substance use will continue to grow.

#### CONCLUSIONS AND IMPLICATIONS FOR CANADA

We know that the risk for addiction is greater for individuals who have encountered stressful experiences early in life. Similarly, adults experiencing stressful events are also vulnerable to substance use and dependence. And it appears that the relationship between addiction and stress is more than a simple co-occurrence; studies show that stress can actually cause or contribute to substance use and dependence. Stress has also been linked to increased drug cravings. In effect, stressful experiences might not only be linked to initiating substance use, but may also influence continued use of and dependence on that substance. Given this complicated relationship between stress and substance use, preventative interventions or treatment strategies that teach effective stress appraisal and coping methods may have a significant impact on substance use disorders. Effective stress management skills, together with high-quality social support resources—which are likely not normally considered part of a drug prevention strategy in Canada—could provide an effective first line of defense against substance use and dependence.

## AT A GLANCE

- The relationship between stressful or traumatic events and substance use problems is complicated but supported by research.
- Exposure to traumatic events can increase alcohol and drug use, which can lead to new traumatic experiences that in turn can lead to further substance use, perpetuating the stress-substance use cycle.
- The human stress response comprises a wide range of behavioural and biological changes to help us meet the demands placed on us—but these changes can lead to unhealthy or negative outcomes in some people.
- Stressful experiences lead to a number of changes in brain chemicals, many of which have been implicated in psychological disorders—including substance use and dependence.
- The impact of a stressful or traumatic event is influenced by many factors, including the specific attributes of the stress, previous stressful experiences (including those encountered early in life), individual differences, and variables such as gender, age, and genetics.
- The importance of social support resources in successfully dealing with stressful events or situations is widely recognized. However, what matters most is not the amount of support (or support resources) one has, but the quality of this support.
- Preventative interventions or treatment strategies that teach effective stress appraisal and coping methods may have a significant impact on substance use disorders.

## REFERENCES

- Abizaid, A., Gao, Q., & Horvath, T. L. (2006a). Thoughts for food: Brain mechanisms and peripheral energy balance. *Neuron*, *51*, 691–702.
- Anisman, H., Hayley, S., & Merali, Z. (2003). Sensitization associated with stressors and cytokine treatments. *Brain, Behavior, and Immunity*, *17*, 86–93.
- Anisman, H., Merali, Z., & Hayley, S. (2008). Neurotransmitter, peptide and cytokine processes in relation to depressive disorder: Comorbidity between depression and neurodegenerative disorders. *Progress in Neurobiology*, *85*, 1–74.
- Anisman, H., Merali, Z., & Stead, J. D. (2008). Experiential and Genetic Contributions to the Protracted Effects of Stressors: From adaptation to mental diseases. *Neuroscience and Biobehavioral Review*, *32*, 1185–1206.
- Bonci, A., & Borgland, S. (2009). Role of orexin/hypocretin and CRF in the formation of drug-dependent synaptic plasticity in the mesolimbic system. *Neuropharmacology*, *56*(Suppl. 1), 107–111.
- Cleck, J. N., & Blendy, J. A. (2008). Making a bad thing worse: Adverse effects of stress on drug addiction. *Journal of Clinical Investigation*, *118*, 454–461.
- Fulton, S., Woodside, B., & Shizgal, P. (2000). Modulation of brain reward circuitry by leptin. *Science*, *287*, 125–128.
- Heilig, M., & Koob, G. F. (2007). A key role for corticotropin-releasing factor in alcohol dependence. *Trends in Neuroscience*, *30*, 399–406.
- Hommel, J. D., Trinko, R., Sears, R. M., Georgescu, D., Liu, Z. W., Gao, X. B., Thurmon, J. J., Marinelli, M., & DiLeone, R. J. (2006). Leptin receptor signaling in midbrain dopamine neurons regulates feeding. *Neuron*, *51*, 801–810.
- Hyman, S. M., & Sinha, R. (2008). Stress-related factors in cannabis use and misuse: Implications for prevention and treatment. *Journal of Substance Abuse Treatment*, *36*, 400–413.
- Ingram, K. M., Betz, N. E., Mindes, E. J., Schmitt, M. M., & Smith, N. G. (2001). Unsupportive responses from others concerning a stressful life event: Development of the Unsupportive Social Interactions Inventory. *Journal of Social and Clinical Psychology*, *20*, 174–208.
- Ingram, K. M., Jones, D. A., Fass, R. J., Neidig, J. D., & Song, Y. S. (1999). Social support and unsupportive social interactions: Their association with depression among people living with HIV. *AIDS Care*, *11*, 313–329.
- Jentsch, J. D., & Taylor, J. R. (1999). Impulsivity resulting from frontostriatal dysfunction in drug abuse: Implications for the control of behavior by reward-related stimuli. *Psychopharmacology (Berl)*, *146*, 373–390.
- Jorden, S., Matheson, K., & Anisman, H. (2008). Resilience among Somali refugees: Supportive and unsupportive social interactions in relation to cultural adaptation and psychological well-being. *Journal of Cross-Cultural Psychology*, *40*, 853–874.
- Koob, G. F. (2008). A role for brain stress systems in addiction. *Neuron*, *59*, 11–34.
- Koob, G. F., & Le Moal, M. (2008). Addiction and the brain antireward system. *Annual Review of Psychology*, *59*, 29–53.
- Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal, and coping*. New York: Springer.
- Lê, A. D., Quan, B., Juzytch, W., Fletcher, P. J., Joharchi, N., & Shaham, Y. (1998). Reinstatement of alcohol-seeking by priming injections of alcohol and exposure to stress in rats. *Psychopharmacology*, *135*, 169–174.

- Linthorst, A. C. (2005). Interactions between corticotropin-releasing hormone and serotonin: Implications for the aetiology and treatment of anxiety disorders. *Handbook of Experimental Pharmacology*, 169, 181–204.
- Liu, Q. S., Pu, L., & Poo, M. M. (2005). Repeated cocaine exposure in vivo facilitates LTP induction in midbrain dopamine neurons. *Nature*, 437, 1027–1031.
- Liu, X., & Weiss, F. (2003). Stimulus conditioned to foot-shock stress reinstates alcohol-seeking behavior in an animal model of relapse. *Psychopharmacology (Berl)* 168, 184–191.
- Lo, C. C., & Cheng, T. C. (2007). The impact of childhood maltreatment on young adults' substance abuse. *American Journal of Drug and Alcohol Abuse*, 33, 139–146.
- Lutter, M., Sakata, I., Osborne-Lawrence, S., Rovinsky, S. A., Anderson, J. G., Jung, S., Birnbaum, S., Yanagisawa, M., Elmquist, J. K., Nestler, E. J., & Zigman, J. M. (2008). The orexigenic hormone ghrelin defends against depressive symptoms of chronic stress. *Nature Neuroscience*, 11, 752–753.
- Maier, S. F., & Seligman, M. E. P. (1976). Learned helplessness: Theory and Evidence. *Journal of Experimental Psychology: General*, 105, 3–46.
- Maier, S. F., & Watkins, L. R. (2005). Stressor controllability and learned helplessness: The roles of the dorsal raphe nucleus, serotonin, and corticotropin-releasing factor. *Neuroscience and Biobehavioral Review*, 29, 829–841.
- Malendowicz, L. K., Rucinski, M., Belloni, A. S., Ziolkowska, A., & Nussdorfer, G. G. (2007). Leptin and the regulation of the hypothalamic-pituitary-adrenal axis. *International Review of Cytology*, 263, 63–102.
- Markou, A., Weiss, F., Gold, L. H., Caine, S. B., Schulteis, G., & Koob, G. F. (1993). Animal models of drug craving. *Psychopharmacology (Berl)*, 112, 163–182.
- McEwen, B. S. (2000). Allostasis and allostatic load: Implications for neuropsychopharmacology. *Neuropsychopharmacology*, 22, 108–124.
- Merali, Z., Bédard, T., Andrews, N., Davis, B., McKnight, A. T., Gonzalez, M. I., Pritchard, M., Kent, P., & Anisman, H. (2006a). Bombesin receptors as novel anti-anxiety therapeutic target: Non-peptide antagonist PD 176252 reduces anxiety and 5-HT release through BB1 receptor. *Journal of Neuroscience*, 26, 10387–10396.
- Merali, Z., Khan, S., Michaud, D. S., Shippy, S. A., & Anisman, H. (2004). Does amygdaloid corticotropin-releasing hormone (CRH) mediate anxiety-like behaviors? Dissociation of anxiogenic effects and CRH release. *European Journal of Neurosciences*, 20, 229–239.
- Merali, Z., McIntosh, J., Kent, P., Michaud, D., & Anisman, H. (1998). Aversive as well as appetitive events evoke the release of corticotropin releasing hormone and bombesin-like peptides at the central nucleus of the amygdala. *Journal of Neuroscience*, 18, 4758–4766.
- Muller, M. B., Zimmermann, S., Sillaber, I., Hagemeyer, T. P., Deussing, J. M., Timpl, P., Kormann, M. S., Droste, S. K., Kuhn, R., Reul, J. M., Holsboer, F., & Wurst, W. (2003). Limbic corticotropin-releasing hormone receptor 1 mediates anxiety-related behavior and hormonal adaptation to stress. *Nature Neuroscience*, 6, 1100–1107.
- Nestler, E. J. (2001). Molecular basis of long-term plasticity underlying addiction. *National Review of Neuroscience*, 2, 119–128.
- Oswald, L. M., Wong, D. F., Zhou, Y., Kumar, A., Brasic, J., Alexander, M., Ye, W., Kuwabara, H., Hilton, J., & Wand, G. S. (2007). Impulsivity and chronic stress are associated with amphetamine-induced striatal dopamine release. *Neuroimage*, 36, 153–166.

Robinson, T. E., & Berridge, K. C. (2003). Addiction. *Annual Review of Psychology*, 54, 25–53.

Saal, D., Dong, Y., Bonci, A., & Malenka, R. C. (2003). Drugs of abuse and stress trigger a common synaptic adaptation in dopamine neurons. *Neuron*, 37, 577–582.

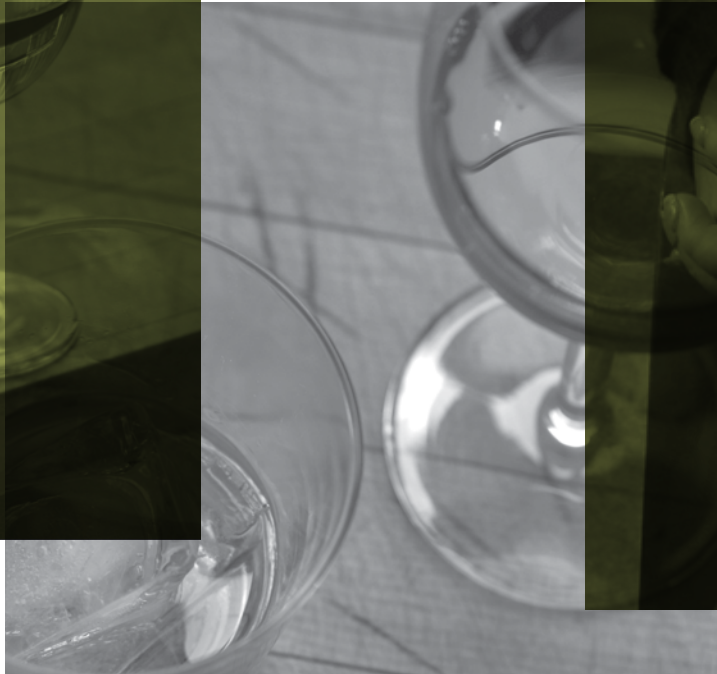
Shaham, Y., Shalev, U., Lu, L., De Wit, H., & Stewart, J. (2003). The reinstatement model of drug relapse: History, methodology and major findings. *Psychopharmacology*, 168, 3–20.

Shimizu, N., Nakane, H., Hori, T., & Hayashi, Y. (1994). CRF receptor antagonist attenuates stress-induced noradrenaline release in the medial prefrontal cortex of rats. *Brain Research*, 654, 145–148.

Sinha, R. (2008). Chronic stress, drug use, and vulnerability to addiction. *Annals of the New York Academy of Sciences*, 1141, 105–130.

Stewart, J. (2000). Pathways to relapse: the neurobiology of drug- and stress-induced relapse to drug-taking. *Journal of Psychiatry and Neuroscience*, 25, 125–136.

Wellman, P. J., Hollas, C. N., & Elliott, A. E. (2007). Systemic ghrelin sensitizes cocaine-induced hyperlocomotion in rats. *Regulatory Peptides*, 146(1-3), 33–37.



# Anxiety Disorders

AND SUBSTANCE USE  
DISORDERS

**Sherry H. Stewart, PhD**  
Dalhousie University

## AUTHOR BIO

### **Sherry H. Stewart, PhD**

Dr. Sherry H. Stewart, PhD, is a Killam Research Professor in the Departments of Psychiatry and Psychology at Dalhousie University. She is also the founding Director of the Centre for Addictions Research at Dalhousie (CARD). Dr. Stewart's research achievements in investigating psychological

aspects of addictions and the co-occurrence of emotional and substance use disorders have received international recognition.

# 3

## JENNA

Jenna, a 25-year-old university student, was sexually assaulted two years ago by a guy she met at a party—a very traumatic experience for her. She’s never told anyone about it and carries a lot of guilt, believing it was her fault, since she’d had a little too much to drink. Since then, Jenna finds that the memories of that night run through her mind over and over again, whether she’s awake or asleep. She is easily startled and has difficulty sleeping. Jenna used to enjoy reading, playing music and going to parties but no longer finds pleasure in those activities. In fact, because of the painful reminders of the assault, she avoids attending parties whenever she can. There is one

thing though, that Jenna finds helpful: alcohol. After a few drinks, she doesn’t feel so keyed up and on edge; she can even sleep. The alcohol helps to block out the memories of that night. It can even make her brave enough to venture out to a party with friends. There is a catch though. Jenna is finding that she needs more and more alcohol to achieve the calm she is seeking. And after a night of drinking, she’s even more edgy and jumpy than usual. Jenna feels like she’s caught in a downward spiral—her anxiety leads her to drink, but the drinking eventually makes her more anxious. The only solution she sees at this point is to simply keep drinking.

### ISSUE

In the previous chapter we explored how stress and trauma are related to substance use disorders. For some, exposure to stress or trauma can also express itself in the form of *anxiety disorders*—a group of mental health conditions that involve fear, worry or dread as well as unpleasant sensations such as sweating or muscle tension. Often individuals with these conditions will extensively avoid the situations that cause the anxiety (Barlow, 2002). And although everyone experiences anxiety from time to time, when that anxiety begins to interfere with a person’s life (e.g., functioning in one’s job or family life) or causes significant discomfort, that’s when an individual is considered to have an anxiety ‘disorder’ (American Psychiatric Association, 2000).

There are a number of anxiety disorders, each with its own characteristics (Barlow, Durand & Stewart, 2009).

“**Specific phobia** involves an excessive fear and avoidance of a particular object or situation. Some common specific phobias involve fears of dogs, heights, flying, and spiders.”

**Social phobia** is characterized by an unrelenting and always-present fear of being evaluated negatively by other people. It is

much more severe than simply being shy; those with social phobia typically avoid social situations such as parties or other social events where they fear they may be the centre of attention.

**Panic disorder** involves repeated intense episodes of anxiety called ‘panic attacks’. These attacks seem to come out of the blue and involve several unpleasant physical sensations including a pounding heart, dizziness, and feeling short of breath. People with panic disorder often report feeling as if they may go crazy or lose control, or worry that they may be dying, when they are experiencing a panic attack. When a person with panic disorder avoids situations where escape would be difficult or where they might be embarrassed if they were to panic, they are said to have the additional problem of agoraphobia.

**Generalized anxiety disorder** involves a more chronic pattern of anxiety that includes tension in the body and constant worry, such as being preoccupied with what might go wrong with one’s finances, health, or work.

**Post-traumatic stress disorder**—the condition Jenna is suffering from—can develop following exposure to an extremely stressful, life-threatening event or ‘trauma’ such as a motor vehicle accident,



military combat, or assault. Post-traumatic stress disorder is characterized by avoidance of reminders of the trauma, emotional numbing such as difficulties experiencing pleasure, excessive arousal such as difficulty sleeping, and re-experiences of the trauma in the form of nightmares or flashbacks.

**Obsessive-compulsive disorder** is characterized by repeated thoughts that the sufferer finds unacceptable. These ‘obsessions’ can involve, for example, thoughts of being contaminated by germs or concerns that one is unsafe. Obsessive thoughts are typically followed by rituals called ‘compulsions’ where the individual attempts to reduce the anxiety caused by the obsession. These rituals might involve hand-washing many times a day until hands are raw, or repeated checking that the stove is turned off.

Anxiety disorders occur together with substance use disorders at alarmingly high rates (Stewart & Conrad, 2008). Surveys of the general population have shown that those with an anxiety disorder are two to five times more likely to have an alcohol or drug use problem than those without an anxiety disorder (Kushner, Krueger, Frye & Peterson, 2008). Although all anxiety disorders are associated with an increased risk for substance dependence, the rates of having both vary across the different anxiety disorders

(Kushner et al., 2008). For example, panic disorder is most closely associated with alcohol dependence, but generalized anxiety disorder is more closely linked with dependence on drugs other than alcohol. The anxiety disorder least strongly associated with alcohol or drug dependence is specific phobia (Kushner et al., 2008).

Also worthy of mention are other patterns that have emerged from surveys of the general population (Kushner et al., 2008). One of these involves the distinction between substance *abuse* and substance *dependence* (American Psychiatric Association, 2000).

**Substance abuse** is the less severe of the two substance use disorders and is diagnosed when a person experiences negative consequences from substance use, such as getting in fights when one has been drinking, or neglecting one’s duties due to drinking or drug taking.

**Substance dependence** is the more severe of the two disorders. It can involve tolerance—needing more and more of the substance to attain the desired effect—and withdrawal symptoms, such as a pounding heart or dizziness, when a person tries to stop or cuts back use of the substance.

Population surveys consistently show that anxiety disorders are more strongly linked to substance dependence than to substance abuse (Kushner et al., 2008). This finding is in line with the theory that links anxious personality traits with a particular style of drinking that is more likely to result in dependence. Other types of personality traits—such as sensation seeking—are said to be linked to a style of drinking more likely to result in abuse (Cloninger, 1987).

Another interesting pattern emerging from population surveys is that anxiety disorders are more strongly associated with problems involving drugs than with alcohol—the reasons for which remain unclear. However, a survey in the US looking at anxiety disorders occurring together with specific substance use disorders (Regier et al., 1990), may offer some clues. For example, this survey



revealed that those with an anxiety disorder were nearly five times more likely to suffer from a substance use disorder involving the misuse of prescription sedative drugs than those with no anxiety disorder. But, perhaps surprisingly, they were also almost three times as likely to suffer from a substance use disorder involving stimulant drugs—like cocaine or amphetamines—than those without an anxiety disorder (Regier et al., 1990).

#### FURTHER EVIDENCE AND DISCUSSION

Why is there such a high overlap of anxiety and substance use disorders? One theory is that anxiety leads to the use of substances. This is often referred to as the *self-medication* theory. It aligns well with the finding discussed in the previous section—that those with an anxiety disorder are more likely to suffer from a substance use disorder involving the misuse of prescription sedative drugs. The theory suggests that individuals with anxiety disorders turn to drugs (including alcohol) that have depressant or calming effects in an attempt to *self-medicate* (or self-treat) their anxiety. Indeed, lab-based research has shown that several problematic drugs for people with anxiety disorders—such as alcohol or prescription drugs like Valium and Xanax—do have effects that can be particularly rewarding for anxious people (MacDonald, Baker, Stewart & Skinner, 2000). Among these desirable effects are sedation (making one sleepy) and the dampening of arousal symptoms like sweating and muscle tension. In addition, a review of epidemiologic, family and lab-based studies has shown that alcohol can actually reduce the chance of a panic attack (Cosci, Schruers, Abrams & Griez, 2007) in those with panic disorder/agoraphobia by reducing fearful expectations and apprehension. This can be a very strong reward, since people with panic disorder are typically extremely frightened of having another attack.

A second theory is that the use of substances leads to the development of anxiety disorders. This is in keeping with the other finding discussed in the section above—that those with anxiety disorders were also almost more likely to suffer from substance use disorders involving stimulant drugs like cocaine or amphetamines. This theory suggests that the misuse of drugs with stimulating effects—

such as cocaine—may perhaps trigger or aggravate anxiety disorders (Kushner, Abrams & Borchardt, 2000). In addition, repeated withdrawal from these substances can lead to worsening of anxiety, which could set the stage for the development of an anxiety disorder (Schuckit & Hesselbrock, 1994). For example, research has shown that tobacco dependence is linked to the development of panic problems (Zvolensky, Bernstein, Yartz, McLeish & Feldner, 2008).

In attempt to determine which of these theories truly explains the co-occurrence of anxiety and substance use disorders, researchers have investigated which disorder appeared first in people affected by both. In a review of these types of studies, it was concluded that in at least three-quarters of those suffering from both disorders, the anxiety disorder developed first (Kushner et al., 2008). This makes the self-medication theory a more likely explanation for the development of the concurrent disorders in the majority of cases.

Another method to distinguish between the two theoretical pathways to concurrent anxiety and substance use disorders has been to examine whether anxiety persists in those individuals who have quit using substances once their symptoms of withdrawal have subsided. This approach was taken in a recent, large-scale survey of the general population in the US (Grant et al., 2004). The results showed that indeed, anxiety did persist in the vast majority of cases, indicating that substance-induced anxiety was actually quite rare.

Support for the two different pathways seems to vary by the different anxiety disorders (Stewart & Conrod, 2008b). For example, generalized anxiety disorder appears to resolve with effective treatment of co-occurring substance misuse, but the same is not true for social phobia and post-traumatic stress disorder (Kushner et al., 2005). This suggests that generalized anxiety disorder occurring together with a substance use disorder is more likely to be caused by the substance. In contrast, social phobia or post-traumatic stress disorder occurring together with a substance use disorder is more likely to represent an attempt at self-medication.

FIGURE 1



#### A VICIOUS CYCLE

Regardless of which pathway is involved in the initial origins of concurrent anxiety and substance use disorders, once an individual has developed both disorders, a vicious cycle may be at play where each disorder maintains—or even exacerbates—the other.

When researchers ask people with anxiety whether they believe they are self-medicating with drugs or alcohol, responses vary across anxiety disorders. One study of this kind (Bolton, Cox, Clara & Sareen, 2006) revealed that self-medication was least likely among those with a form of social phobia where individuals fear speaking in public. In fact, only about 8% of this group reported self-medicating. However, self-medication was much more commonly reported in those with a more complex form of social phobia involving multiple social fears. Over 20% of this group reported self-medicating. The difference is likely due, at least in part, to the greater societal acceptance of the use of alcohol and drugs as a ‘social lubricant’ for parties and events. The same level of acceptance is unlikely for delivering a talk or lecture while under the influence of drugs or alcohol (Kushner et al., 2000).

Whether the co-occurrence of anxiety and substance use disorders is an attempt at self-medication or induced by the substance may depend on the particular substance involved. It has been suggested that drugs with depressant or tranquilizing effects fit best with the self-medication pathway, whereas drugs with stimulant effects align better with the substance-induced anxiety path (Stewart & Conrod, 2008b). But it may not be quite that simple. The boost to a person’s feelings of well-being that can result from

taking stimulant drugs like ecstasy or cocaine could also play a role in self-medication (Kushner et al., 2008).

A third and entirely different explanation for the high overlap of anxiety and substance use disorders must also be considered. Perhaps an individual suffering from both an anxiety and a substance use disorder has a common vulnerability to the two conditions—something about that person makes him or her prone to both (Stewart & Conrod, 2008b). The exact nature of this vulnerability or proneness remains to be firmly identified. However, it could be a common personality trait predisposing an individual to both conditions (Stewart & Conrod, 2008b), or a genetic predisposition passed down through the generations of a family. In fact, twin studies have provided some preliminary evidence to suggest common genetic contributions to the co-occurrence of anxiety and alcohol use (Tambs, Harris & Magnus, 1997). But the evidence isn’t conclusive. For example, a recent family study showed no contribution of alcoholism to either panic disorder or social phobia in families, despite the two anxiety disorders commonly co-occurring with alcohol use disorders (Low, Cui & Merikangas, 2008).

Regardless of which pathway is involved in the initial origins of concurrent anxiety and substance use disorders, once an indi-

vidual has developed both disorders, a vicious cycle may be at play where each disorder maintains—or even exacerbates—the other (see Figure 1) (Stewart & Conrod, 2008, 2008b). The case of Jenna at the beginning of this chapter is a perfect example of just that. The idea of a self-perpetuating cycle suggests that if one were to treat one disorder without simultaneously addressing the second, the risk of relapse would be very high. For example, if we try to address a substance use disorder without helping an individual to manage his or her anxiety, we are likely to see that person quickly revert back to using substances whenever a severe bout of anxiety was experienced. And if we tried to address an anxiety disorder without addressing that person's substance misuse, it's doubtful that the treatment could be very successful (Stewart & O'Connor, 2009), since a person needs to fully confront one's feared situations in order to effectively treat anxiety (Foa & Kozak, 1986). In fact, research does suggest that when people who suffer from both an anxiety and substance use disorder enter treatment for only one of their conditions, the outcome of their treatment is less than desirable. For example, having a concurrent alcohol use disorder has been found to predict poorer anxiety treatment outcomes for those with post-traumatic stress disorder (Forbes, Creamer, Hawthorne, Allen & McHugh, 2003), social phobia (Bruce et al., 2005), generalized anxiety disorder (Bruce et al., 2005), and panic disorder/agoraphobia (Bruce et al., 2005). Most studies of those with a substance use disorder who have received treatment or who are now abstinent suggest that the presence of a co-occurring anxiety disorder increases the likelihood of a relapse to substance misuse (Kushner et al., 2005; Driessen et al., 2001; Book, McNeil & Simpson, 2005). Indeed, one study showed that the relapse rate for alcoholism following treatment was about 30% higher for those with a co-occurring anxiety problem compared to those without such a condition (Driessen et al., 2001). Relapses are costly to the health care system; a recent study has revealed that dramatic health care savings can be realized in the longer term by addressing co-occurring anxiety disorders in those receiving treatment for substance use disorders—even after factoring in the costs of anxiety treatment (Willinger et al., 2002). Together, these findings suggest that the two disorders need to

be addressed simultaneously, both to improve treatment outcomes for people suffering from an anxiety and a substance use disorder and to reduce health care costs associated with these disorders.

The study of effective treatments for concurrent anxiety and substance use disorders is in its infancy. Nonetheless, research in this area is growing rapidly (Stewart & Conrod, 2008b). Several promising approaches now exist to treating co-occurring anxiety and substance use disorders through simultaneous treatment. Simultaneous treatments involve either two distinct treatments being provided to a person—called *parallel* treatment—or a single treatment being delivered that is designed to address both disorders and their inter-relations—called *integrated* treatment (Zahradnik & Stewart, 2008). For example, a number of different integrated treatments have been developed and evaluated for co-occurring post-traumatic stress disorder and substance dependence (Brady, Dansky, Back, Foa & Carroll, 2001; Najavits, Weiss, Shaw & Muenz, 1998; Riggs, Rukstalis, Volpicelli, Kalmanson & Foa, 2003; Triffleman, Carroll & Kellogg, 1999; Zlotnick, Najavits, Rohsenow & Johnson, 2003; Riggs & Foa, 2008). Integrated treatments have also been developed for concurrent panic disorder and prescription sedative dependence (Otto, Jones, Craske & Barlow, 2004a), concurrent panic disorder and alcohol dependence (Kushner et al., 2006; Toneatto & Rector, 2008), concurrent panic disorder and tobacco dependence (Zvolensky et al., 2008), and social phobia and alcohol misuse (Stewart & O'Connor, 2009; Tran, 2008). An effective parallel treatment for obsessive-compulsive disorder and substance abuse disorder has been developed as well (Klostermann & Fals-Stewart, 2008).

An example of an effective treatment for co-occurring anxiety and substance use disorders lies in an integrated treatment developed for patients with both panic disorder and dependence on prescription sedative drugs (Otto et al., 2004a). A technique called *interoceptive exposure*, commonly used in the treatment of panic disorder, was extended to the treatment of medication dependence. Interoceptive exposure involves repeated exposure to the sensations that are common during a panic attack—such

as shortness of breath and a racing heartbeat—that are so feared by those with panic disorder (Otto et al., 1993). Tapering sedative medications is known to produce many of these same sensations. Otto and his colleagues expanded the use of this technique to help patients in advance to deal with not only their episodes of panic but also what they are likely to experience while tapering their sedative medications. This treatment program has been shown to be effective both in treating the symptoms of panic disorder and in helping patients discontinue their sedative medications (Stewart & Watt, 2008). This new approach appears to benefit both of the co-occurring disorders (Stewart & O'Connor, 2009).

#### CONCLUSIONS AND IMPLICATIONS FOR CANADA

So, why aren't simultaneous treatments for co-occurring anxiety and substance use disorders being used regularly in practice? First, we are at an early stage in examining their effectiveness. Much more research is needed to identify the best treatment approaches to tackle this complex set of problems (Stewart & O'Connor, 2009). Also, we need to overcome several barriers if we are to develop and implement effective approaches for concurrent anxiety and substance use disorders (Stewart & Conrod, 2008b). A foremost consideration is Canada's continued tendency to separate mental health and addiction services in most health care programs. This separation poses a major obstacle to the delivery of integrated treatments for individuals with concurrent anxiety and substance use disorders, since clinicians in either service are typically not trained to assess or treat the other problem. This would seem to favour a parallel treatment approach accompanied by good communication between addiction and mental health service providers. But this approach presents problems of its own. Parallel treatments can be quite intensive and demanding for people with complex concurrent disorders relative to a single integrated treatment, leading to high drop-out rates or less than desirable treatment outcomes (Conrod & Stewart, 2005; Randall, Book, Carrigan & Thomas, 2008). In addition, those with concurrent anxiety and substance use disorders see their two problems as substantially intertwined (Brown, Stout & Gannon-Rowley, 1998; Stewart, 1996). Thus, the separation of their problem into two separate disorders with two separate treatments can seem artificial and confusing to clients with concurrent disorders. From an economic perspective, however, integrated treatments can be accomplished more efficiently than parallel treatments (Stewart & Conrod, 2008b)—an important consideration in these times of fiscal constraint and health care cutbacks.

## AT A GLANCE

- The risk of having a problem with drugs or alcohol is two to five times greater in people with anxiety disorders.
- Anxiety disorders are more strongly associated with substance dependence—a more severe problem—than substance abuse.
- Anxiety disorders are more strongly associated with drug problems than alcohol problems.
- Panic disorder is the anxiety disorder most closely associated with alcohol dependence, and generalized anxiety disorder is the one most closely associated with dependence on drugs other than alcohol.
- In at least 75% of people with both an anxiety disorder and a substance dependence, the anxiety disorder developed first.
- Anxiety disorders resulting from substance use appear to be relatively rare.
- In people with both an anxiety disorder and a substance use disorder, treating one without also addressing the other leads to poorer short-term outcomes and a high risk for relapse.
- Co-occurring anxiety and substance use disorders need to be addressed at the same time to improve treatment outcomes—preferably through integrated treatment.

## REFERENCES

- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: Author.
- Barlow, D. H. (2002). *Anxiety and its disorders: The nature and treatment of anxiety and panic* (2nd ed.). New York: Guilford.
- Barlow, D. H., Durand, M., & Stewart, S. H. (2009). *Abnormal Psychology: An Integrative Perspective, Second Canadian Edition*. Toronto: Thomson-Nelson.
- Bolton, J., Cox, B. J., Clara, I., & Sareen, J. (2006). Use of alcohol and drugs to self-medicate anxiety disorders in a nationally representative sample. *Journal of Nervous and Mental Disease*, *194*, 818–825.
- Book, S. W., McNeil, R. B., & Simpson, K. N. (2005). Treating alcoholics with a co-occurring anxiety disorder: A Markov model to predict long-term costs. *Journal of Dual Diagnosis*, *1*, 53–62.
- Brady, K. T., Dansky, B. S., Back, S. E., Foa, E. B., & Carroll, K. M. (2001). Exposure therapy in the treatment of PTSD among cocaine-dependent individuals: Preliminary findings. *Journal of Substance Abuse Treatment*, *21*, 47–54.
- Brown, P. J., Stout, R. L., & Gannon-Rowley, J. (1998). Substance use disorder—PTSD co-morbidity: Patients' perceptions of symptom interplay and treatment issues. *Journal of Substance Abuse Treatment*, *21*, 47–54.
- Bruce, S. E., Yonkers, K. A., Otto, M. W., Eisen, J. L., Weisberg, R. B., Pagano, M., et al. (2005). Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: A 12-year prospective study. *American Journal of Psychiatry*, *162*, 1179–1187.
- Cloninger, R. C. (1987). Neurogenetic adaptive mechanisms in alcoholism. *Science*, *236*, 410–416.
- Conrod, P. J., & Stewart, S. H. (2005). A critical look at dual focused cognitive-behavioral treatment for comorbid substance abuse and psychiatric disorders: Strengths, limitations and future directions. *Journal of Cognitive Psychotherapy*, *19*, 265–289.
- Cosci, F., Schruers, K. R., Abrams, K., & Griez, E. J. (2007). Alcohol use disorders and panic disorder: A review of the evidence of a direct relationship. *Journal of Clinical Psychiatry*, *68*, 874–880.
- Driessen, M., Meier, S., Hill, A., Wetterling, T., Lange, W., & Junghanns, K. (2001). The course of anxiety, depression and drinking behaviours after completed detoxification in alcoholics with and without co-morbid anxiety and depressive disorders. *Alcohol and Alcoholism*, *36*, 249–255.
- Foa, E. B., & Kozak, M. J. (1986). Emotional processing of fear: Exposure to corrective information. *Psychological Bulletin*, *99*, 20–35.
- Forbes, D., Creamer, M., Hawthorne, G., Allen, N., & McHugh, T. (2003). Comorbidity as a predictor of symptom change after treatment in combat-related posttraumatic stress disorder. *Journal of Nervous and Mental Disease*, *191*, 93–99.
- Grant, B. F., Stinson, F. S., Dawson, D. A., Chou, P., Dufour, M. C., Compton, W., et al. (2004). Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders. *Archives of General Psychiatry*, *61*, 807–816.
- Klostermann, K. C., & Fals-Stewart, W. (2008). Treatment of co-morbid obsessive-compulsive disorder and substance use disorders. In S. H. Stewart & P. J. Conrod (Eds.), *Anxiety and substance use disorders: The vicious cycle of co-morbidity* (pp. 157–175). New York: Springer.

- Kushner, M. G., Abrams, K., & Borchardt, C. (2000). The relationship between anxiety disorders and alcohol use disorders: A review of major perspectives and findings. *Clinical Psychology Review, 20*, 149–171.
- Kushner, M. G., Abrams, K., Thuras, P., Hanson, K., Brekke, M., & Sletten, S. (2005). Follow up study of anxiety disorder and alcohol dependence in co-morbid patients. *Alcoholism: Clinical and Experimental Research, 29*, 1432–1443.
- Kushner, M. G., Donahue, C., Sletten, S., Thuras, P., Abrams, K., Peterson, J., et al. (2006). Cognitive behavioral treatment of comorbid anxiety disorder in alcoholism treatment patients: Presentation of a prototype program and future directions. *Journal of Mental Health, 15*(6), 697–707.
- Kushner, M. G., Krueger, R., Frye, B., & Peterson, J. (2008). Epidemiological perspectives on co-occurring anxiety disorder and substance use disorder. In S. H. Stewart & P. J. Conrod (Eds.), *Anxiety and substance use disorders: The vicious cycle of co-morbidity* (pp. 3–17). New York: Springer.
- Low, N. C., Cui, L., & Merikangas, K. R. (2008). Specificity of familial transmission of anxiety and comorbid disorders. *Journal of Psychiatric Research, 42*, 596–604.
- MacDonald, A. B., Baker, J. M., Stewart, S. H., & Skinner, M. (2000). Effects of alcohol on the response to hyperventilation of participants high and low in anxiety sensitivity. *Alcoholism: Clinical and Experimental Research, 24*, 1656–1665.
- Najavits, L. M., Weiss, R. D., Shaw, S. T., & Muenz, L. R. (1998). “Seeking Safety”: Outcome of a new cognitive-behavioral psychotherapy for women with posttraumatic stress disorder and substance abuse. *Journal of Traumatic Stress, 11*, 437–456.
- Otto, M. W., Jones, J. C., Craske, M. G., & Barlow, D. H. (2004a). *Stopping anxiety medication: Panic control therapy for benzodiazepine discontinuation*. Oxford, UK: Oxford University Press.
- Otto, M. W., Pollack, M. H., Sachs, G. S., Reiter, S. R., Melzer-Brody, S., & Rosenbaum, J. F. (1993). Discontinuation of benzodiazepine treatment: Efficacy of a cognitive-behavior therapy for patients with panic disorder. *American Journal of Psychiatry, 150*, 1485–1490.
- Randall, C. L., Book, S. W., Carrigan, M. H., & Thomas, S. E. (2008). Treatment of co-occurring alcoholism and social anxiety disorder. In S. H. Stewart & P. J. Conrod (Eds.), *Anxiety and substance use disorders: The vicious cycle of co-morbidity* (pp. 139–155). New York: Springer.
- Regier, D.A., Farmer, M.E., Rae, D.S., Locke, B.Z., Keith, S.J., Judd, L.L., et al. (1990). Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area (ECA) study. *Journal of the American Medical Association, 264*, 2511–2518.
- Riggs, D. S., & Foa, E. B. (2008). Treatment for co-morbid posttraumatic stress disorder and substance use disorders. In S. H. Stewart & P. J. Conrod (Eds.), *Anxiety and substance use disorders: The vicious cycle of co-morbidity* (pp. 119–137). New York: Springer.
- Riggs, D. S., Rukstalis, M., Volpicelli, J. R., Kalmanson, D., & Foa, E. B. (2003). Demographic and social adjustment characteristics of patients with comorbid posttraumatic stress disorder and alcohol dependence: Potential pitfalls of PTSD treatment. *Addictive Behaviors, 28*, 1717–1730.
- Schuckit, M. A., & Hesselbrock, V. (1994). Alcohol dependence and the anxiety disorders: What is the relationship? *American Journal of Psychiatry, 151*, 1723–1733.
- Stewart, S. H. (1996). Alcohol abuse in individuals exposed to trauma: A critical review. *Psychological Bulletin, 120*, 83–112.

- Stewart, S. H., & Conrod, P. J. (2008). *Anxiety and substance use disorders: The vicious cycle of co-morbidity*. New York: Springer.
- Stewart, S. H., & Conrod, P. J. (2008b). Anxiety disorder and substance use disorder comorbidity: Common themes and future directions. In S. H. Stewart & P. J. Conrod (Eds.), *Anxiety and substance use disorder: The vicious cycle of co-morbidity* (pp. 239–257). New York: Springer.
- Stewart, S. H., & O'Connor, R. M. (2009). Treating anxiety disorders in the context of concurrent substance misuse. In D. Sookman & R. Leahy (Eds.), *Treatment Resistant Anxiety Disorders* (pp. 291–323). New York: Routledge.
- Stewart, S. H., & Watt, M. C. (2008). Introduction to the special issue on interoceptive exposure in the treatment of anxiety and mechanisms of action. *Journal of Cognitive Psychotherapy*, 22, 291–302.
- Tambs, K., Harris, J. R., & Magnus, P. (1997). Genetic and environmental contributions to the correlation between alcohol consumption and symptoms of anxiety and depression: Results from a bivariate analysis of Norwegian twin data. *Behaviour Genetics*, 27, 241–249.
- Toneatto, T., & Rector, N. A. (2008). Treating co-morbid panic disorder and substance use disorder. In S. H. Stewart & P. J. Conrod (Eds.), *Anxiety and substance use disorders: The vicious cycle of co-morbidity* (pp. 157–175). New York: Springer.
- Tran, G. Q. (2008). Efficacy of a brief intervention for college hazardous drinkers with social anxiety: A randomized controlled pilot study. *Alcoholism: Clinical and Experimental Research*, 32 (Suppl.), 190A.
- Triffleman, E., Carroll, K., & Kellog, S. (1999). Substance dependence posttraumatic stress disorder therapy: An integrated cognitive-behavioral approach. *Journal of Substance Abuse Treatment*, 17, 3–14.
- Willinger, U., Lenzinger, E., Hornik, K., Fischer, G., Schonbeck, G., Aschauer, H. N., et al. (2002). Anxiety as a predictor of relapse in detoxified alcohol-dependent patients. *Alcohol and Alcoholism*, 37(6), 609–612.
- Zahradnik, M., & Stewart, S. H. (2008). Anxiety disorders and substance use disorder comorbidity: Epidemiology, theories of interrelation, and recent treatment approaches. In M. Antony & M. Stein (Eds.), *Handbook of Anxiety and the Anxiety Disorders* (pp. 565–576). Oxford, UK: Oxford University Press.
- Zlotnick, C., Najavits, L. M., Rohsenow, D. J., & Johnson, D. M. (2003). A cognitive-behavioral treatment for incarcerated women with substance abuse disorder and posttraumatic stress disorder: Findings from a pilot study. *Journal of Substance Abuse Treatment*, 25, 99–105.
- Zvolensky, M. J., Bernstein, A., Yartz, A. R., McLeish, A. C., & Feldner, M. T. (2008). Cognitive-behavioral treatment of co-morbid panic psychopathology and tobacco use and dependence. In S. H. Stewart & P. J. Conrod (Eds.), *Anxiety and substance use disorders: The vicious cycle of co-morbidity* (pp. 177–200). New York: Springer.



# Impulsivity

## AND SUBSTANCE USE DISORDERS

**Marco Leyton, PhD**  
McGill University

**Sylvia M.L. Cox, PhD**  
McGill University

### AUTHOR BIOS

**Marco Leyton, PhD**

Marco Leyton, PhD is President-Elect of the Canadian College of Neuropsychopharmacology (CCNP) and an associate professor in McGill University's Department of Psychiatry, where he holds a William Dawson Research Chair. The focus of his research is the neurobiology of addiction, and addiction-related neuropsychiatric disorders.

**Sylvia M.L. Cox, PhD**

Sylvia Cox, PhD is a research fellow at the Department of Psychiatry at McGill University. She conducted her PhD in Cambridge (UK), where she began her career investigating neural mechanisms of reward-related behaviours. Her current research specializes in cocaine abuse with a particular focus on environmental and neurobiological vulnerabilities in drug-seeking behaviour and the progression to addiction.



# 4

## BRAD

Brad, a 23-year-old who sometimes works in construction, describes himself as a “fun guy who likes to have a good time”. As a child, he was the class clown, always jumping up from his seat and shouting out jokes—and always getting into mischief. Now, his “good times” often involve high-risk activities—his favourite being hanging out of the passenger window of a speeding car to the point that his hair brushes the road below him. He’s fallen out before and hurt himself, but continues to do it because of the great rush it gives him. He describes the experience as “intense and focused”. Besides hanging out of speeding cars, Brad has discovered

something else that gives him the greatest rush: cocaine. He feels that it isn’t a problem for him, since he only does it a couple of times a week when he’s drinking. Not everyone sees Brad as the fun-loving guy he believes himself to be. His girlfriend’s parents do not approve of him. Brad stole a substantial amount of money from them a while back and they’re concerned about what he might do next. Brad didn’t really think about what he was doing at the time he stole the money and he did apologize afterwards. He finds it difficult to understand why they can’t just forgive and forget. Brad doesn’t think his behaviour is any problem—it’s just part of who he is.

### ISSUE

***Impulsivity – the inclination to act without planning, forethought, or restraint.***

Much of our behaviour—the decisions we make, the goals we pursue and the importance that we attach to them—is guided by systems in the brain that are sensitive to rewards and punishments. We need these systems; we would never have survived as a species without them. Reward system activity fosters our interest in food, the opportunity to have sex, and the exploration of those more difficult-to-judge events—the unfamiliar and only potentially positive ones. All of this competes against a punishment avoidance system (Carver et al., 2008; Ernst & Fudge, 2009; Leyton, 2009).

When the reward and punishment systems are in balance, we approach the good and avoid the bad. This balance changes with age; adolescents and teenagers tend to have relatively stronger reward seeking traits, while adulthood and middle age brings proportionately stronger inhibitory ones (Galvan et al., 2006). Regardless of age, though, the sensitivity of these systems seems to vary from person to person. These individual differences help form key features of our personalities—making one person an uninhibited risk-taker, another more cautious and restrained.

For some impulsive individuals, the primary issue is not with the reward-punishment systems but instead with difficulty sustaining attention. These highly distractible individuals are easily sidetracked and hyper-reactive. Their attentional difficulties corrupt decision-making abilities, leading to flash decisions and poorly thought-out plans.

Poorly thought-out plans are also considered the hallmark of another form of impulsivity—those said to have *poor inhibitory control*. These individuals have difficulty holding back a response (such as waiting one’s turn) irrespective of the outcome (de Wit, 2009).

Problems with impulse control are also the single strongest predictor of future substance abuse (Compton, et al., 2007; Perry, 2008). In the absence of other difficulties, impulsive or highly reward-sensitive individuals might be considered outgoing and extraverted, seekers of sensation and novelty, and exist this way without developing problems. However, when other challenges are present (such as childhood abuse or stress coping difficulties), these individuals are more likely to engage in risky behaviours, try addictive drugs and then use them frequently—putting themselves at risk for developing substance use problems. Alcohol abuse seems to be particularly common in this group (Conrod et al., 2000).



In comparison, problems with stimulant and opiate drugs may develop more frequently in individuals whose form of impulsivity is characterized by a relative insensitivity to punishment (Conrod et al., 2000). This may result in a diminished response to social prohibitions and a relative insensitivity to the (often delayed) adverse consequences of the drugs themselves.

At the extremes, personality traits can become personality disorders. Impulsive personality disorders can take various forms, and commonly occur in conjunction with a broad spectrum of co-occurring problems. In addition to having behavioural disinhibition, individuals with impulsive personality disorders frequently experience dramatic mood swings—including sharp spikes of happiness, depression, anger, self-loathing and thoughts of suicide. Their personal relationships tend to be turbulent, alternating between intensely good and bad. Substance use and abuse is common, perhaps as an attempt to soothe their emotional volatility and as a reflection of their difficulty making sensible choices.

In those who are particularly under-sensitive to punishment, antisocial acts are not uncommon. These include such behaviours as lying, disregarding rules, aggressiveness, irresponsibility, showing

little regard for others or remorse for their actions. For such people, the world seems a strange place, ruled by social conventions that, to them, make little sense. To the outsider, such people may often seem cold—even callous and indifferent to the pain of others. Perhaps not unexpectedly, the negative consequences related to drug abuse mean little to them, putting them at particular risk for using substances and developing substance use disorders (Compton et al., 2007).

Impulsive behaviour is also a core problem in several other psychiatric disorders. A relatively common example is *attention deficit hyperactivity disorder* or ADHD. ADHD occurs in 5 to 10% of children, and is characterized by difficulty sustaining attentional focus and in restraining thoughts and behaviours. These features may be associated with emotional or other behavioural problems. In approximately half of affected individuals, many of their ADHD symptoms continue into adulthood. The precise cause of ADHD is unclear, but there is considerable evidence that ADHD involves dysfunctional activity in the same brain pathways that are also implicated in substance abuse and addiction. Indeed, individuals with ADHD are at elevated risk for substance use problems (Molina et al., 2003).

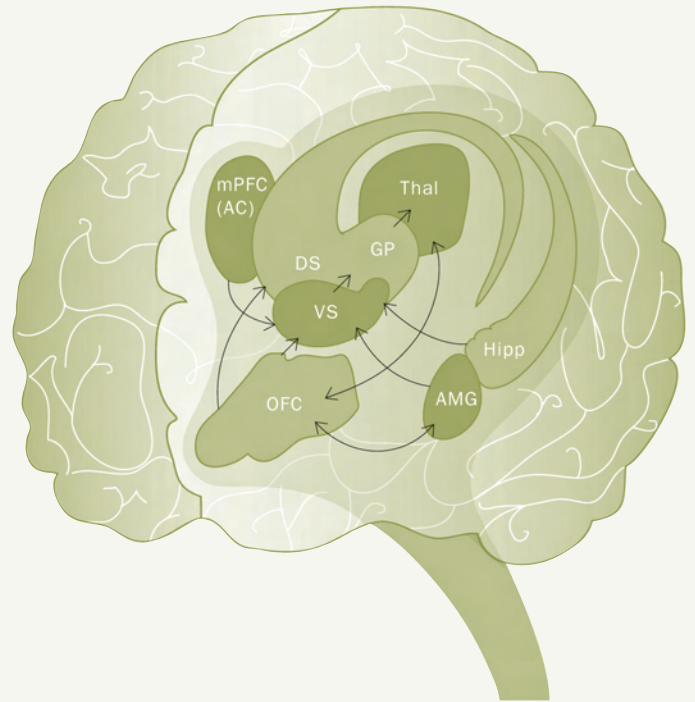
#### FURTHER EVIDENCE AND DISCUSSION

Research has identified regions in the brain that regulate impulsive behaviours, and these regions form integrated loops and networks (Phillips et al., 2003; Everitt & Robbins, 2005; Dalley et al., 2008). Particularly important are evolutionarily old systems of the brain such as the *limbic striatum and amygdala* that influence approach and avoidance behaviours. More recently evolved systems in the brain such as the *frontal and prefrontal cortex* contribute to more complex cognitive planning functions that facilitate focused, selective attention (e.g., the filtering-out of irrelevant information) and the ability to plan behavioural strategies based on previous experience. Together, these systems allow us to make both simple decisions (e.g., eat bananas, not rocks) and more complex ones (e.g., tonight, just two beer instead of seven) (Ernst & Fudge, 2009).

FIGURE 2

## LEGEND

(AC)	<i>anterior cingulate</i>
(AMG)	<i>amygdala</i>
(DS)	<i>dorsal parts of the striatum</i>
(GP)	<i>globus pallidus</i>
(Hipp)	<i>hippocampus</i>
(mPFC)	<i>medial prefrontal cortex</i>
(OFC)	<i>orbitofrontal cortex</i>
(Thal)	<i>thalamus</i>
(VS)	<i>ventral parts of the striatum</i>



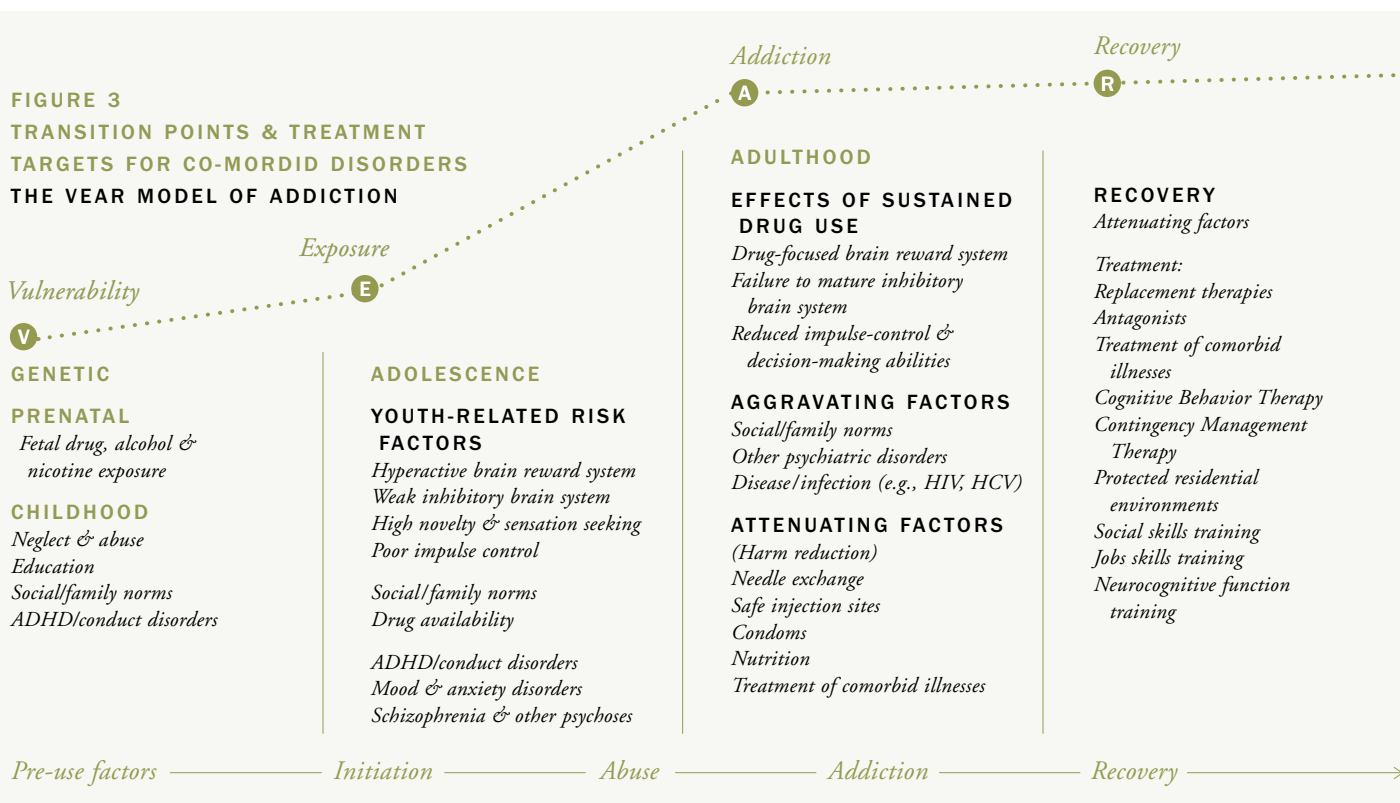
These brain systems are influenced by various factors, including age and drug exposure. For example, recent work suggests that biological changes occurring in adolescence can help explain why the teenage years are peak periods for risk-taking (Galvan et al., 2006). These include (i) a relatively overactive reward system that responds intensely to pleasurable stimuli and events that predict the possibility of pleasure, (ii) an incomplete frontal cortex in the brain, which modulates the approach and avoidance systems, and (iii) a surge in gonadal hormones that brings about optimistic persistence. These three features are thought to account in large part for the increased risk of initiating drug use and various other impulsive behaviours in teens (Chambers et al., 2003).

Aggravating these tendencies further is that many drugs of abuse directly engage the same brain systems involved in impulsivity—turning them on and changing them sometimes in ways that endure for days, months and even years (Robinson & Berridge, 1993; Vezina, 2004; Boileau et al., 2006; Cox et al., 2009; Renthal & Nestler, 2008). These brain changes can interfere with multiple decision-making processes and further increase the tendency to use addictive drugs (Mendrek et al., 1998; Vezina, 2004). The extent of these changes and their persisting effects on behaviours, personality traits and problems may depend on the starting point. For

FIGURE 2

The image depicts inter-connected regions of the brain that are thought to have important roles in the regulation of impulsive behaviours and susceptibility to drug use. This includes the amygdala (AMG) and both ventral and dorsal parts of the striatum (VS & DS). Together, these regions are thought to provide a pre-conscious impetus to approach or avoid cues that signal reward vs. punishment. In comparison, the medial prefrontal cortex (mPFC), anterior cingulate (AC), and orbitofrontal cortex (OFC) are thought to represent subjective responses to rewards and punishments and regulate the planning of actions—sometimes based on prior experience, sometimes when it is unclear what to do. These cortical regions also provide input to the VS, as do the AMG and hippocampus (Hipp). This latter structure, the Hipp, carries contextual memory information. Together, these regions are thought to coordinate flexible, situation-appropriate, goal-directed behaviour. Figure from Everitt & Robbins, 2005. See also Phillips et al., 2003 and Dalley et al., 2008. Frontal parts of the brain are toward the left side of the figure.

**FIGURE 3**  
**TRANSITION POINTS & TREATMENT**  
**TARGETS FOR CO-MORBID DISORDERS**  
**THE VEAR MODEL OF ADDICTION**



**FIGURE 3**  
**VEAR (Vulnerability, Exposure, Addiction, Recovery)**  
 highlights two major points. First, while inherited genetic predispositions are often important, their effects depend on the surrounding environment. Second, all of the listed factors can be influenced, providing multiple opportunities to alter trajectories. A combination of social policies, personality-specific prevention strategies and treatment can change individual, familial and social dynamics, altering the course of an individual's life path.

some vulnerable individuals, the allure of extensive drug use might prove too hard to resist from the beginning. In other cases, a slightly impulsive individual might become more so. For both individuals, repeated substance use might narrow the focus of the reward system toward drugs and drug-related cues, diminishing the ability of other goals to attract and motivate them (Leyton, 2007).

The causes of impulsive traits are still only partially understood. We do know, though, that these traits cluster in families (Cadoret et al., 1986), and recent models suggest that inherited genetic susceptibilities are aggravated by prenatal exposure to drugs (including nicotine and alcohol), childhood traumas, and the influence of parents and peers (Chapman et al., 2007). Whether or not a predisposition to impulsive behaviours leads to substance use problems depends on additional aggravating and protective factors (see Figure 3: VEAR Model of Addiction).

The interactions between these influences can be complex. For example, recent analyses suggest that the behaviour of parents influences which friends their children choose. And, if a child tends to be behaviourally disinhibited, interactions with peers who use drugs will substantially increase the likelihood that they, too, will initiate drug use and progress to addiction (Chapman et al., 2007).

Drug use during adolescence might be particularly problematic. Accumulating studies show that these individuals are at elevated risk for developing severe addiction problems (Chambers et al., 2003). This may be due to their relatively underdeveloped brain structures as well as the long-lasting biological effects of drugs on these still-developing brain systems. Indeed, frequent exposures to addictive drugs can increase impulsive behaviour—in effect multiplying further susceptibilities to substance abuse and addiction.

As our understanding of the different types of impulsive behaviour grows, so too does our ability to effectively target prevention efforts and treatment. For example, of the many treatment options, two particular strategies are promising:

- For high “sensation seekers” **cognitive behaviour therapies** can diminish and delay their risk for alcohol abuse (Conrod et al., 2008).
- For those with ADHD, **medication-based therapies** can help to mitigate the broad spectrum of substance use problems that these individuals are at increased risk for. Since the most common medication treatment for ADHD is the administration of stimulants—a drug class that itself can be abused—there was concern for many years that treatment might aggravate this vulnerability. Fortunately, compelling evidence now exists that treating ADHD-affected children with stimulant drugs does not increase their tendency to abuse drugs—stimulants or otherwise (Wilens et al., 2008).

#### CONCLUSIONS AND IMPLICATIONS FOR CANADA

Impulsive traits can take many forms and lead to many outcomes, depending on circumstances. One “impulsive” person might be exciting and dramatic yet also a fearless leader who draws people near, behaving with courage rather than feckless disregard. In comparison, another individual starting from the same predispositions may become rash and unregulated, overly attracted to mood-altering drugs and insufficiently deterred by dangers. The first may have benefited from a supportive family with reasonable challenges and encouraging opportunities; the second may have suffered childhood abuse and neglect. We cannot yet predict with certainty who will go down which path, but a combination of preventative and treatment strategies can diminish the most damaging effects of the impulsive traits and their consequences, including the risk for substance use and addiction. Strategies such as these benefit us all.

#### AT A GLANCE

- Problems with impulse control are the single strongest predictor of future substance abuse.
- Alcohol abuse seems to be particularly common in “high sensation seeking” people.
- Impulsive behaviour is a core problem in several personality and major psychiatric disorders that put those affected at higher risk for a substance use disorder.
- Individuals with ADHD—an impulsivity-related disorder—are at elevated risk for substance abuse and addiction. This may be particularly true for those who do not receive early treatment.
- The influence of factors such as age and drug use can affect the systems in the brain that regulate impulsive behaviours.
- Evidence suggests that inherited genetic susceptibilities to impulsivity are aggravated by prenatal exposure to drugs (including nicotine and alcohol), childhood traumas, and the influence of parents and peers.
- A combination of preventative and treatment strategies can diminish the most damaging effects of impulsivity and its consequences—including the risk for substance use and addiction.

## REFERENCES

- Boileau, I., Dagher, A., Leyton, M., Gunn, R. N., Baker, G. B., Diksic, M., & Benkelfat, C. (2006). Modeling sensitization to stimulants in humans: A 11Craclopride/PET study in healthy volunteers. *Archives of General Psychiatry*, 63(12), 1386–1395.
- Cadore, R. J., Troughton, E., O’Gorman, T. W., & Heywood, E. (1986). An adoption study of genetic and environmental factors in drug abuse. *Archives of General Psychiatry*, 43(12), 1131–1136.
- Carver, C. S., Johnson, S. L., & Joormann, J. (2008). Serotonergic function, two-mode models of self-regulation, and vulnerability to depression: What depression has in common with impulsive aggression. *Psychological Bulletin*, 134, 912–943.
- Chambers, R. A., Taylor, J. R., & Potenza, M. N. (2003). Developmental neuro-circuitry of motivation in adolescence: A critical period of addiction vulnerability. *American Journal of Psychiatry*, 160(6), 1041–1052.
- Chapman, K., Tarter, R. E., Kirisci, L., & Cornelius, M. D. (2007). Childhood neurobehavior disinhibition amplifies the risk of substance use disorder: Interaction of parental history and prenatal alcohol exposure. *Journal of Developmental and Behavioral Pediatrics*, 28(3), 219–224.
- Compton, W. M., Thomas, Y. F., Stinson, F. S., & Grant, B. F. (2007). Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States: Results from the National Epidemiological Survey on Alcohol and Related Conditions. *Archives of General Psychiatry*, 64(5), 566–576.
- Conrod, P. J., Castellanos, N., & Mackie, C. (2008). Personality-targeted interventions delay the growth of adolescent drinking and binge drinking. *Journal of Child Psychology and Psychiatry*, 49(2), 181–190.
- Conrod, P. J., Pihl, R. O., Stewart, S. H., & Dongier, M. (2000). Validation of a system for classifying female substance abusers on the basis of personality and motivational risk factors for substance abuse. *Psychology of Addictive Disorders*, 14(3), 243–256.
- Cox, S. M. L., Benkelfat, C., Dagher, A., Delaney, J. S., Durand, F., McKenzie, S. A., Kolivakis, T., Casey, K. F., & Leyton, M. (2009). Striatal dopamine responses to intranasal cocaine self-administration in humans. *Biological Psychiatry*, 65(10), 846–850.
- Dalley, J. W., Mar, A. C., Economidou, D., & Robbins, T. W. (2008). Neuro-behavioral mechanisms of impulsivity: Fronto-striatal systems and functional neurochemistry. *Pharmacology, Biochemistry and Behavior*, 90(2), 250–260.
- de Wit, H. (2009). Impulsivity as a determinant and consequence of drug use: A review of underlying processes. *Addiction Biology*, 14(1), 22–31.
- Ernst, M., & Fudge, J. L. (2009). A developmental neurobiological model of motivated behavior: Anatomy, connectivity and ontogeny of the triadic nodes. *Neuroscience and Biobehavioral Reviews*, 33(3), 367–382.
- Everitt, B. J., & Robbins, T. W. (2005). Neural systems of reinforcement for drug addiction: From actions to habits to compulsions. *Nature Neuroscience*, 8(11), 1481–1489.
- Galvan, A., Hare, T. A., Parra, C. E., Penn, J., Voss, H., Glover, G., & Casey, B. J. (2006). Earlier development of the accumbens relative to orbitofrontal cortex might underlie risk-taking behavior in adolescents. *Journal of Neuroscience*, 26, 6885–6892.
- Leyton, M., (2009). The neurobiology of desire: Dopamine and the regulation of mood and motivational states in humans. In M.L. Kringelbach & K.C. Berridge (Eds.), *Pleasures of the Brain* (Chap. 13). New York: Oxford University Press.
- Leyton, M. (2007). Conditioned and sensitized responses to stimulant drugs in humans. *Progress in Neuro-psychopharmacology & Biological Psychiatry*, 31(8), 1601–1613.

- Mendrek, A., Blaha, C., & Phillips, A. G. (1998). Pre-exposure to amphetamine sensitizes rats to its rewarding properties as measured by a progressive ratio schedule. *Psychopharmacology*, *135*, 416–422.
- Molina, B. S. G., & Pelham, W. E. (2003). Childhood predictors of adolescent substance use in a longitudinal study of children with ADHD. *Journal of Abnormal Psychology*, *112*(3), 497–507.
- Perry, J. L., & Carroll, M. E. (2008). The role of impulsive behavior in drug abuse. *Psychopharmacology*, *200*(1), 1–26.
- Phillips, A. G., Ahn, S., & Howland, J. G. (2003). Amygdalar control of the mesocorticolimbic dopamine system: Parallel pathways to motivated behavior. *Neuroscience Biobehavioral Reviews*, *27*, 543–554.
- Renthal, W., & Nestler, E. J. (2008). Epigenetic mechanisms in drug addiction. *Trends in Molecular Medicine*, *14*(8), 341–350.
- Robinson, T. E., & Berridge, K. C. (1993). The neural basis of drug craving: An incentive-sensitization theory of addiction. *Brain Research: Brain Research Reviews*, *18*, 247–291.
- Vezina, P. (2004). Sensitization of mid-brain dopamine neuron reactivity and the self-administration of psychomotor stimulant drugs. *Neuroscience and Biobehavioral Reviews*, *27*, 827–839.
- Weiss, M., Hechtman, L., & Weiss, G. (1999). ADHD in adulthood: A guide to current theory, diagnosis, and treatment. Baltimore MD: John Hopkins University Press.
- Wilens, T. E., Adamson, J., Monueaux, M. C., Faraone, S. V., Schilinger, M., Westerberg, D., & Biederman, J. (2008). Effect of prior stimulant treatment for attention-deficit/hyperactivity disorder on subsequent risk for cigarette smoking and alcohol and drug use disorders in adolescents. *Archives of Pediatrics & Adolescent Medicine*, *162*(10), 916–921.



# Mood Disorders

## AND SUBSTANCE USE DISORDERS

**Christian G. Schütz, MD, PhD, MPH**  
University of British Columbia

**Allan H. Young, MBChB, MPhil, PhD, FRCPsych, FRCPC**  
University of British Columbia

### AUTHOR BIOS

**Christian G. Schütz, MD, PhD, MPH**

Christian G. Schütz holds degrees in Medicine (University of Freiburg), Public Health (Johns Hopkins University) and Chinese Studies (University of Munich). He completed his clinical training in psychiatry, psychotherapy and addiction medicine in Germany and his research training in preclinical and clinical behavioural pharmacology during fellowship at NIDA/NIH. He recently joined the Institute of Mental Health at British Columbia University to study mechanisms of relapse in patients with substance dependence and severe mental disorders.

**Allan H. Young, MBChB, MPhil, PhD, FRCPsych, FRCPC**

Professor Allan Young currently holds the Leading Edge Endowment Fund Endowed Chair in Depression Research in the Department of Psychiatry at the University of British Columbia, Vancouver, Canada, where he is also Director of the Institute of Mental Health. His research interests focus on the cause and treatments for severe psychiatric illnesses, particularly mood disorders.





## CLAUDIA

Claudia, a 39-year-old event manager, has just been hospitalized for the first time after telling friends that she planned to jump off a bridge to “end it all”. After a relatively uneventful childhood, Claudia began experiencing panic attacks as a teen. While in high school, she drank alcohol and smoked some cannabis—but only on weekends. During college she had some difficulty with low moods and lack of motivation, but these eventually resolved on their own. Around this time she started using cannabis more regularly and also used cocaine on the weekends. Once Claudia finished college she took a celebratory trip to Europe. When she arrived there she felt “on top of the world”. She spent all of her money within the

first couple of days and ended up being sent home after getting arrested for “civil disturbance”. It was at this point that Claudia was diagnosed with bipolar disorder. She recovered and opted not to take any medication that would help to prevent future mania (high mood and energy) or depression. However, three years later amidst her daily alcohol and regular cocaine use, she experienced another manic phase. She began taking her medication but still experienced periods of mania (although less severe than before). It was the frequent bouts of depression, however, that caused her to consider ending her life by jumping off the bridge. She simply did not want to live with the depression any longer.

### ISSUE

Mood disorders make up a group of mental health conditions characterized by abnormal changes in mood and affect. These disorders are classified according to signs and symptoms as well as the course of illness. The four most common are *Major Depressive Disorder* (MDD), *Bipolar Disorder* (BD), *Dysthymia* and *Cyclothymia*. The first two are considered major disorders; for either MDD or BD to be diagnosed, the symptoms must be substantial enough to significantly affect a person’s functioning. Both are usually *episodic*, meaning that the people who suffer from them generally recover but may relapse (i.e., have another episode at a later time). Those with MDD or BD experience depression; those with BD also experience periods of *mania*—a state of extremely elevated mood, high energy, unusual thought patterns and even psychosis. Bipolar disorder can be broken down into two different types: BP I (manic and depressive episodes) and BP II (less severe or ‘mild’ mania—called *hypomania*—and depressive episodes).

Dysthymia and Cyclothymia are chronic disorders with less severe symptoms than MDD and BD. Dysthymia is characterized by a persistent depressed mood not severe or extensive enough to fit the diagnosis of MDD. Cyclothymia is characterized by mood shifts both up and down, but not as severe as those seen in BD.

Mood disorders make up the single largest group of major psychiatric disorders. Approximately 10 to 25% of women and 5 to 12% of men develop a major depressive disorder at some point, while the lifetime risk for BD is estimated to be around 2%. Men and women are equally likely to develop BD I (mania and depression), but women tend to be diagnosed with BD II (hypomania and depression) more often. Data for the two milder, chronic versions of the mood disorders are less well established. Health Canada estimates the risk of dysthymia over a lifetime is 3 to 6%, and the risk of cyclothymia 0.4 to 1% (Gavel et al., 2005).

As discussed in Chapter 3, the two major substance use disorders are *substance abuse* and *substance dependence*. A number of studies have established that people with mood disorders are more likely to use substances and become dependent than those without mood disorders. Overall, substance use is highest in those diagnosed with BD (Levin & Hennesy, 2004). In fact, recent research shows that even manic symptoms not severe enough to count as “true mania” may still increase the risk of substance use disorders (Marikangas et al., 2008; Marimmani et al., 2007). But that’s not where the relationship ends. People using substances are also more likely to suffer from mood disorders. In general, more severe forms of substance abuse (i.e., dependence) have been



linked to more severe forms of mood disorders, or vice versa. In other words, as one disorder becomes more severe, the likelihood of experiencing the other disorder increases (Merikangas et al., 1998).

A Canadian survey on health (*CCHS on Mental Health and Well Being*) collected information on substance use disorders and MDD. Much like in other countries, the survey found that those who had been diagnosed with MDD within the previous 12 months were more likely to report concurrent harmful alcohol use (12.3% compared to 7% in the general population), alcohol dependence (5.8% compared to 2.6% in the general population), and drug dependence (3.2% compared to 0.8% in the general population). Those experiencing substance use disorders within the previous 12 months were also more likely to report a concurrent MDD (8.8% among alcohol-dependent individuals; 16.1% in individuals dependent on an illegal substance compared to 4.0% in the general population) (Adlaf et al., 2005; Gravel et al., 2005).

Having both a substance use disorder and a mood disorder has an impact on both morbidity (i.e., experiencing illness or harm) and mortality (i.e., dying). Having a mood and a substance use disorder can negatively impact a person's clinical course (i.e., their experience of illness) and their clinical outcome (including

life expectancy and treatment outcomes). For example, studies have shown the negative effects of a substance use disorder on individuals with mood disorders—particularly BD. Alcohol and substance use disorders are linked to high rates of treatment *non-adherence* (i.e., not following a treatment plan including not taking medications as prescribed) and to lower rates of recovery, greater risk of aggression and violence, a higher rate of attempted and completed suicide, and a less favourable response to conventional treatments (Brady & Sonne, 1995; Strakowski, 1995).

Substance use disorders may involve any number of substances—such as nicotine, alcohol, cannabis, cocaine, heroin, amphetamines, MDMA, PCP and others. How frequently the different substances are used can differ greatly, as can the risk of becoming dependent. Given the different ways these substances work, and the various effects they have, it is important to look for specific profiles of substance use in different mood disorders. Although a recent study has suggested that those experiencing mania or hypomania are at increased risk of a substance use disorder involving any substance but those experiencing depression are at increased risk for a substance use disorder involving sedatives only (Merikangas et al., 2007), there really is no clear pattern of specific drugs being associated with particular mood disorders. Further research may help to determine whether or not substances are being used indiscriminately by those with mood disorders or if linkages between certain drugs and mood disorders exist.

#### FURTHER EVIDENCE AND DISCUSSION

The possible causes of concurrent mood and substance use disorders are many, but two theories receive the most attention: *overlapping predisposition* and *disorder inducing disorder*. An overlapping predisposition (as discussed in Chapter 3) encompasses the idea of a common vulnerability to both conditions—something about a person that makes him or her prone to both. This could be due to a genetic predisposition (i.e., being born with genes that make both disorders likely), or common environmental factors that influence both disorders. The theory of disorder inducing disorder postulates that one disorder actually causes the other. With this

theory, either mood disorders would induce substance use disorders, or substance use disorders would induce mood disorders—or perhaps both could be possible.

Research involving family, adoption, and twin studies has shown that genetic factors do play a clear role in mood disorders. Studies that compare identical (monozygotic) and fraternal (dizygotic) twins can help to determine the role of inherited genes in the development of substance use and mood disorders; this concept is referred to as the *heritability* of a condition. The heritability of MDD varies greatly in the research—between 20 and 80%—which is likely due to differences in how the studies were conducted. However, a recent review of many studies concluded that the heritability of MDD is between 31 and 42%. When it comes to BD, the heritability appears to be higher, at around 71% (Edvardsen et al., 2008). As for heritability and substance use disorders, the research findings are consistent and support the major role of genetics in substance use disorders (Agarwal et al., 2008). An overlapping genetic predisposition may increase the risk of concurrent substance use and mood disorders; however, given the difficulty of identifying specific genes for psychiatric disorders (Goldman, 2005; Li & Burmeister, 2009), no specific genes making people vulnerable to both conditions have yet been identified.

A number of environmental factors have also been associated with increased risk for both mood and substance use disorders (i.e., family disruption, poor parental monitoring, and low social class of rearing), supporting the notion of an overlapping environmental predisposition to these disorders (Kendler et al., 2003). Recently, childhood trauma has received attention as a risk factor for post-traumatic stress disorder—but early childhood trauma seems just as likely to lead to substance use and mood disorders (Kilpatrick, 2003). Similarly, low birth weight seems to increase risk for psychiatric disorders including substance use disorders and mood disorders.

The theory that one disorder may cause the other lends itself to the idea of *self-medication* (also discussed in Chapter 3), where

people attempt to treat their mood disorder with drugs or alcohol (Khantzian, 1985). Studies attempting to provide evidence for this have not been very successful. For example, research has shown that substance use disorders often begin before mood disorders. Still, clinical experience indicates that it is possible to identify patients who develop substance use disorders within the context of their mood disorders. Some research has suggested that this may be particularly true for those with manic, hypomanic or mixed states (Marikangas et al., 2008; Marimmani et al., 2006). By contrast, mood disorders caused by substance use disorders are recognized in that they exist as a separate diagnostic entity in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM IV). It is, however, a diagnosis rarely used by clinicians.

Overall, some evidence can be found for each of the possible mechanisms that may lead to concurrent substance use and mood disorders, but none has been shown to explain the majority of cases. Part of the difficulty in explaining how substance use and mood disorders occur together is that the boundaries between different mood disorders and the variety of mood disorders within any given category makes research in this area quite a challenge. The onset of a mood or substance use disorder is also difficult to define. To determine the exact timing and therefore the sequence of the two disorders in an individual is less than straightforward.

Although we currently lack a thorough understanding of the factors that cause concurrent mood and substance use disorders, better animal models and new methods of assessing human brain activity have led to major improvements in our understanding of the brain mechanisms involved in these disorders (Paterson & Markou, 2007; Quello et al., 2005). Brain mechanisms are studied at different levels; at the gross-anatomical or structural level (regions, areas and networks in the brain), regional networks of the brain involved in learning play a role in both mood and substance use disorders. These include the *amygdala-hippocampus-cingulate* network (LaBar & Cabeza, 2006). Changes in other pathways may also have a role. New technologies that directly measure activity in specific brain regions and networks allow for a better appreciation

of the role of brain structures and systems and help improve our understanding of disease processes (see Figure 4). At the inter-cellular level (how specific kinds of cells interact in the brain, e.g., via *neurotransmitters*)—where medications often act—*dopamine*, a chemical in the brain, has been studied heavily in the context of substance abuse and dependence. Other transmitter systems such as the *serotonergic* system and the *noradrenergic* system are also of interest in both substance use and mood disorders. At the intracellular or molecular level (i.e., activity within cells in the brain) the processes are probably the least understood so far, but new knowledge from research is developing at a rapid pace. However, since some medications used to treat BD work at this level, BD research has recently focused at the intracellular level (Bezchlibnyk & Young, 2002; Martinowitch et al., 2009) These medications sometimes work for substance use disorders as well—indicating a possible common intracellular pathway.

So-called *biomarkers* should also be examined. Biomarkers are substances that, when found in the body, indicate a certain disease is present. When they are available, biomarkers can make diagnosing a particular illness more straightforward. The overlap of mood and substance use disorders complicates the search for a biomarker for each disorder. To be useful, biomarkers specific for a disorder such as MDD should not be altered by a substance use disorder such as alcohol use. However, at this point nearly half of the potential markers for MDD are also altered by substance use (Mössner et al., 2007). Given the overlap of mood and substance use disorders, markers for concurrent disorders may be worth considering. These might help refine the diagnosis and treatment for these concurrent disorders.

Given the significant overlap in mechanisms leading to substance use and mood disorders as well as the impact of concurrent substance use and mood disorders on clinical course and outcome, the importance of treating both conditions in an affected individual is obvious. However, our current health care system is struggling to meet this need and provide the best possible care. Because mood disorders are considered mental health conditions best treated by

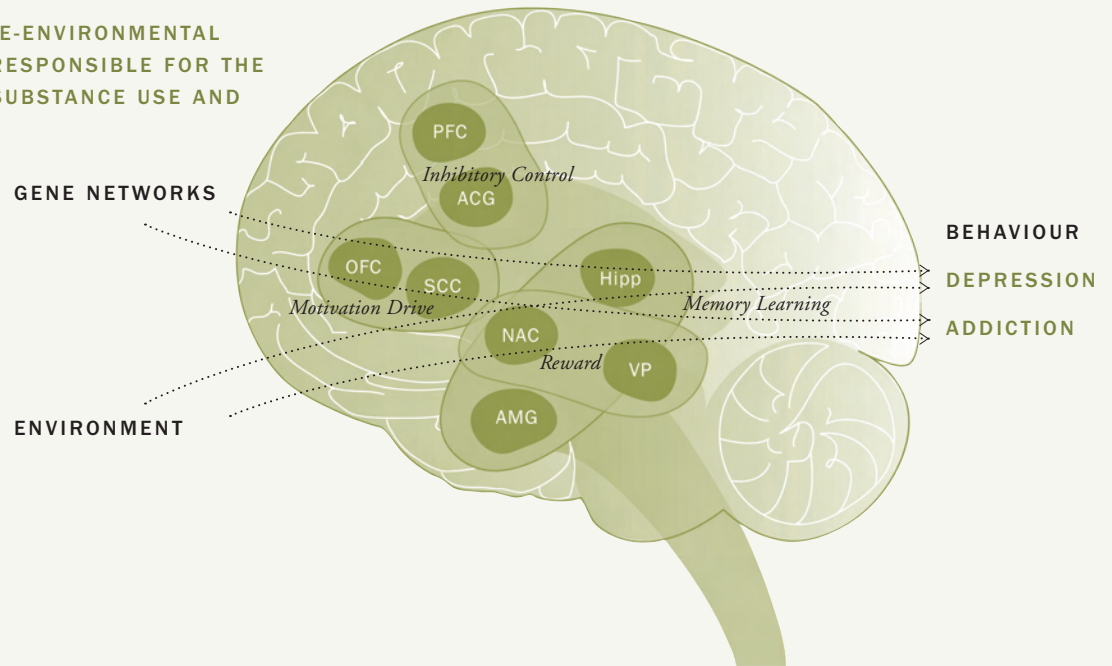
psychiatrists and mental health professionals, and substance use disorders are often not seen as mental health conditions and as such are usually treated by addiction specialists, a number of challenges for patients with both conditions and for the treatment system exist. For example, a patient may not be accepted for treatment of one disorder because the specialist treatment centre does not support patients with the other disorder. Research also tends to focus on patients with one specific disorder—meaning patients with concurrent disorders are not represented in most findings.

This problem has recently received increasing attention, and the need to improve treatment availability for patients with concurrent disorders is becoming better appreciated. To improve care and treatment for such patients, changes to the treatment system are required, including:

- Improved detection and diagnosis of the concurrent disorder
- Increased awareness and acceptance of the need to treat both disorders concurrently
- Increased focus on the development of treatments for concurrent disorders
- Increased availability of treatment options for these patients

To improve detection, diagnosis and treatment of a second disorder in patients already diagnosed with a first disorder, treatment providers need to be aware of concurrent disorders (i.e., build their professional knowledge). Treatment providers also need to appreciate the importance of the second disorder and be aware of available treatment options (a matter of professional attitude and overcoming stigma). One simple way to avoid missing a concurrent disorder is to make sure the right assessment instruments are available. Given professionals' almost universal lack of time, self-assessment instruments may be a feasible option. Up to now, one method of dealing with concurrent disorders has been to defer the treatment of the second disorder until after the first has sufficiently improved. Yet it is considered good practice to treat both disorders at the same time. That said, with treatment providers normally having the expertise to treat one disorder but not necessarily the other, simultaneously treating both can pose a big

**FIGURE 4**  
OVERLAPPING GENE-ENVIRONMENTAL  
FACTORS MAY BE RESPONSIBLE FOR THE  
COMORBIDITY OF SUBSTANCE USE AND  
MOOD DISORDER



**FIGURE 4**  
Shows how genes, the environment and brain  
function interact, and how that interaction likely contributes  
to the behaviour changes that occur in substance abuse  
and in depression. Overlapping environmental, genetic  
or biological factors in the brain could account for the high  
degree of co-occurrence between substance abuse and  
depression (Volkow, 2004).

**LEGEND**  
(ACG)  
*anterior cingulate gyrus*  
(AMG)  
*amygdala*  
(Hipp)  
*hippocampus*  
(NAC)  
*nucleus accumbens*  
(OFC)  
*orbitofrontal cortex*  
(PFC)  
*prefrontal cortex*  
(SCC)  
*subcallosal cortex*  
(VP)  
*ventral pallidum*

challenge. There is a need not only to promote good practice but also to train professionals who are in a position to give treatment for both mood and substance use disorders—at the same level of expertise.

The development of new treatments has tended to focus on single disorders, resulting in a now urgent need to advance the treatment options for concurrent disorders. For example, when the mood stabilizer *Valproate* is used to treat patients with BD, it seems to also decrease heavy drinking when there is concurrent alcohol dependence (Salloum et al., 2005). *Buprenorphin*, a medication for substance use, has been shown to possibly improve the mood of patients with a substance use disorder who also have MDD (Bodkin et al., 1995). Lithium, when used to treat adolescents with BD, has been shown to also be effective in treating their concurrent substance use disorder (Freye & Salloum, 1998). But more studies on the treatment of concurrent disorders are needed (Kosten & Kosten, 2004). To date, a very limited number of studies have been conducted for specific concurrent disorders.

In addition to the development of medications, counselling and psychotherapy specific to patients with concurrent disorders are important (Carroll, 2004). The combination of medication and talk therapy for concurrent mood and substance use disorders needs to be further developed and tested, then put into use outside of the research environment (Weiss et al., 2004). Finally, the effect of specific non-medication-based treatments for mood disorders (like ECT, for example) on substance use disorders needs to be studied.

## AT A GLANCE

- Mood disorders constitute the single largest group of psychiatric disorders and include Major Depressive Disorder, Bipolar Disorder, Dysthymia and Cyclothymia.
- People with mood disorders are more likely to use substances—and people using substances are also more likely to suffer from mood disorders.
- Substance use is highest in those with Bipolar Disorder, but the risk of a substance use disorder is still at least double for those with Major Depressive Disorder.
- In general, substance dependence has been shown to be linked with mood disorders to a greater degree than either substance abuse or substance use.
- Having both a substance use disorder and a mood disorder affects the clinical course of both disorders (treatment engagement, thoughts of suicide, homelessness, increased risk of victimization) and their clinical outcomes (life expectancy, suicide, treatment outcome).
- Mechanisms that might explain the overlap of substance use and mood disorders are an *overlapping predisposition* (a common vulnerability involving genetic and/or environmental factors) and *disorder inducing disorder* (where one disorder causes the other).
- To improve care and treatment for people with concurrent substance use and mood disorders, changes to the current treatment system are required, including:
  - Improved detection and diagnosis of concurrent disorders
  - Increased awareness and acceptance of the need to treat both disorders at the same time
  - Increased focus on the development of treatments for concurrent disorders
  - Increased availability of treatment options for these patients

Increasing the availability of specific treatment options requires establishing new programs within the current treatment system. This need has recently become better appreciated for individuals with both schizophrenia and substance use disorders. However, such programs need to be expanded to reach patients with other concurrent disorders such as mood and substance use disorders—a significantly larger group.

#### CONCLUSIONS AND IMPLICATIONS FOR CANADIANS

The significant overlap between mood and substance use disorders is evident. Clearly, there are a number of gaps in our current knowledge of concurrent mood and substance use disorders; unfortunately, the level of ongoing research into concurrent disorders does not match the public health impact of such disorders. Even so, advancements in the field are being made and significant improvements in the management and treatment of people with these disorders is still possible based on what we know now. The co-occurrence of substance use and mood disorders needs to be a central issue in their effective treatment, and our health care system must adapt to meet the unique challenges they pose.

## REFERENCES

- Adlaf, E. M., Begin, P., & Sawka, E. (Eds.). (2005). Canadian Addiction Survey (CAS): A national survey of Canadians' use of alcohol and other drugs: Prevalence of use and related harms: Detailed report. Ottawa: Canadian Centre on Substance Abuse.
- Agrawal, A., & Lynskey, M. T. (2008). Are there genetic influences on addiction: Evidence from family, adoption and twin studies. *Addiction*, *103*(7), 1069–81.
- Bezchlibnyk, Y., & Young, L. T. (2002). The neurobiology of bipolar disorder: Focus on signal transduction pathways and the regulation of gene expression. *Canadian Journal of Psychiatry*, *47*(2), 135–48.
- Bodkin, J. A., Zornberg, G. L., Lukas, S. E., & Cole, J. O. (1995). Buprenorphine Treatment of Refractory Depression. *Journal of Clinical Psychopharmacology*, *15*(1), 49–57.
- Brady, K. T., & Sonne, S. C. (1995). The relationship between substance abuse and bipolar disorder. *Journal of Clinical Psychiatry*, *56* (Suppl. 3), 19–24.
- Carroll, K. M. (2004). Behavioral therapies for co-occurring substance use and mood disorders. *Biological Psychiatry*, *56*(10), 778–84.
- Conner, K. R., Pinquart, M., & Duberstein, P. R. (2008). Meta-analysis of depression and substance use and impairment among intravenous drug users (IDUs). *Addiction*, *103*(4), 524–34.
- Edvardsen, J., Torgersen, S., Røysamb, E., Lygren, S., Skre, I., Onstad, S., & Oien, P. A. (2008). Heritability of bipolar spectrum disorders. Unity or heterogeneity? *Journal of Affective Disorders*, *106*(3), 229–40.
- Frye, M. A., & Salloum, I. M. (2006). Bipolar disorder and comorbid alcoholism: Prevalence rate and treatment considerations. *Bipolar Disorders*, *8*(6), 677–85.
- Goldman, D., Orozi, G., & Ducci, F. (2005). The genetics of addictions: Uncovering the genes. *Nature Reviews Genetics* (July), *6*, 521–532.
- Gravel, R., & Beland, Y. (2005). Canadian Community Health Survey on Mental Health and Well Being. *Canadian Journal of Psychiatry*, *50*, 573–579.
- Jutkiewicz, E. M. (2006). The antidepressant-like effects of delta-opioid receptor agonists. *Molecular Interventions*, *6*(3), 162–9.
- Kendler, K. S., Prescott, C. A., Myers, J., & Neale, M. C. (2003). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Archives of General Psychiatry*, *60*(9), 929–37.
- Khantzian, E. J. (1985). The self-medication hypothesis of addictive disorders: Focus on heroin and cocaine dependence. *American Journal of Psychiatry*, *142*, 1259–1264.
- Kilpatrick, D. G., Ruggiero, K. J., Acierno, R., Saunders, B. E., Resnick, H. S., & Best, C. L. (2003). Violence and Risk of PTSD, Major Depression, Substance Abuse/Dependence, and Comorbidity: Results From the National Survey of Adolescents. *Journal of Consulting and Clinical Psychology*, *71*(4), 692–700.
- Kosten, T. R., & Kosten, T. A. (2004). New medication strategies for comorbid substance use and bipolar affective disorders. *Biological Psychiatry*, *56*(10), 771–7.
- LaBar, K. S., & Cabeza, R. (2006). Cognitive neuroscience of emotional memory. *Nature Reviews Neuroscience*, *7*, 54–64.
- Levin, F. R., & Hennessy, G. (2004). Bipolar Disorder and substance abuse. *Biological Psychiatry* *56*(10), 738–74.
- Li, M. D., & Burmeister, M. (2009). New insights into the genetics of addiction. *Nature Reviews Genetics* *10*, 225–231.



- Maremmani, I., Perugi, G., Pacini, M., & Akiskal, H. S. (2006). Toward a unitary perspective on the bipolar spectrum and substance abuse: Opiate addiction as a paradigm. *Journal of Affective Disorders* (Jul), 93(1-3), 1-12.
- Martinowich, K., Schloesser, R. J., & Manji, H. K. (2009). Bipolar disorder: From genes to behavior pathways. *Journal of Clinical Investigations*, 119(4), 726-736.
- Merikangas, K. R., Herrell, R., Swendsen, J., Rössler, W., Ajdacic-Gross, V., & Angst, J. (2008). Specificity of Bipolar Spectrum Conditions in the Comorbidity of Mood and Substance Use Disorders: Results From the Zurich Cohort Study. *Archives of General Psychiatry*, 65(1), 47-52.
- Merikangas, K. R., Mehta, R. L., Molnar, B. E., Walters, E. E., Swendsen, J. D., Aguilar-Gaziola, S., Bijl, R., Borges, G., Caraveo-Anduaga, J. J., DeWit, D. J., Kolody, B., Vega, W. A., Wittchen, H. U., & Kessler, R. C. (1998). Comorbidity of substance use disorders with mood and anxiety disorders: Results of the International Consortium in Psychiatric Epidemiology. *Addictive Behaviours*, 23(6), 893-907.
- Mössner, R., Mikova, O., Koutsilieri, E., Saoud, M., Ehlis, A. C., Müller, N., Fallgatter, A. J., & Riederer, P. (2007). Consensus paper of the WFSBP Task Force on Biological Markers: Biological markers in depression. *World Journal of Biological Psychiatry*, 8(3), 141-74.
- Quello, S. B., Brady, K. T., & Sonne, S. C. (2005). Mood disorders and substance use disorder: A complex comorbidity. *Science & Practice Perspectives*, 3(1), 13-21.
- Paterson, N. E., & Markou, A. (2007). Animal models and treatments for addiction and depression comorbidity. *Neurotoxicity Research*, 11(1), 1-32.
- Salloum, I. M., Cornelius, J. R., Daley, D. C., Kirisci, L., Himmelhoch, J. M., & Thase, M. E. (2005). Efficacy of valproate maintenance in patients with bipolar disorder and alcoholism: A double-blind placebo-controlled study. *Archives of General Psychiatry*, 62(1), 37-45.
- Strakowski, S. M., Keck, P. E., McElroy, S. L., Lonczak, H. S., & West, S. A. (1995). Chronology of comorbid and principal syndromes in first-episode psychosis. *Comprehensive Psychiatry*, 36(2), 106-112.
- Volkow, N. D. (2004). The reality of comorbidity: Depression and drug abuse. *Biological Psychiatry*, 56(10), 714-7.
- Weiss, R. D., Jaffee, W. B., de Menil, V. P., & Cogley, C. B. (2004). Group therapy for substance use disorders: What do we know? *Harvard Review of Psychiatry*, 12(6), 339-50.



# Psychosis

## AND SUBSTANCE USE DISORDERS

**Tony P. George, MD, FRCPC**  
CAMH and University of Toronto

**Diana Blank, MD**  
University of Toronto

### AUTHOR BIOS

#### **Tony P. George, MD, FRCPC**

Dr. Tony George, MD, FRCPC is Professor of Psychiatry, Psychology and Medical Sciences, and the Chair in Addiction Psychiatry at the University of Toronto, and Clinical Director of the Schizophrenia Program at the Centre for Addiction and Mental Health in Toronto, ON, Canada.

#### **Diana Blank, MD**

Dr. Diana Blank, MD is a PG-4 Resident in Psychiatry at the University of Toronto, Toronto, ON, Canada.

#### **Acknowledgements**

This work was supported in part by grants K02-DA-16611, R01-DA-13672, R01-DA-14039 and R01-DA-15757 from the National Institute on Drug Abuse (NIDA), an Independent Investigator Award from the National Alliance for Research on Schizophrenia and Depression (NARSAD), the Canada Foundation for Innovation (CFI), the Canadian Institutes on Health Research (CIHR) and the Endowed Chair in Addiction Psychiatry from the University of Toronto.



## DEREK

Derek, a 17-year-old who has recently quit school, is afraid that his frequent cannabis use will “fry his brain”. He has tried to quit on numerous occasions but has been unsuccessful. He first tried cannabis at the age of eight, when he found some left-over joints after his sister had a party. By Grade 8, Derek was smoking cannabis daily and now is up to 25 “poppers” each day. A year ago he was hospitalized with psychosis during a period of heavy cannabis use. He’s currently on an antipsychotic medication but continues to experience some psychotic symptoms. It was his

paranoia, in fact, that led him to quit school. He now spends his days in his parents’ basement apartment, smoking cannabis and watching movies. He frequently fantasizes about ending his life and most recently has developed symptoms of depression that add to his hopelessness and lack of self-esteem. Derek wonders if there is any way out of his situation.

### ISSUE

*Psychotic* disorders are a set of severe mental disorders in which contact with reality is highly distorted for those affected. This makes it difficult for a person with psychosis to function in day-to-day life. The most common form of psychosis is schizophrenia, affecting between 1 to 1.5% of the population worldwide (Freedman, 2003). Those with schizophrenia typically experience delusions, hallucinations and disorganized thinking—known collectively as *positive symptoms*, as well as lack of motivation, withdrawal and social isolation—together known as *negative symptoms*. They also experience problems with memory, attention and decision making; these are called *cognitive deficits*.

Studies have shown that prior to the onset of an actual psychotic phase of schizophrenia, changes occur in the brain (Pantelis et al., 2003). This may explain the symptoms often seen before the illness develops (the pre-illness or *prodromal* phase of the disorder). During the early phase, subtle or mild psychotic symptoms together with other manifestations such as reduced concentration and attention, social withdrawal, anxiety, depression and sleep disturbance may occur (Yung & McGorry, 1996). Various degrees of social dysfunction may also be present. The pre-illness or prodrome phase can start as early as five or six years before the first

psychotic episode (Klosterkotter et al., 2001) and usually has a slow onset. The symptoms during this phase typically include things other than psychosis and they tend to wax and wane in severity. Following the onset of these symptoms come unusual behaviours and vague psychotic symptoms that gradually increase and worsen. Often the symptoms are not noticed by others until they become more intense and lead to some degree of social dysfunction (Yung & McGorry, 1996; Heinrichs & Carpenter, 1985). Not everyone who experiences prodromal psychotic symptoms will develop full-blown psychosis; however, these early symptoms together with other risk factors—including substance use (Yung, 2007)—will increase the risk for future psychotic illness.

Substance use disorders, much like psychotic disorders, are chronic, relapsing illnesses. Studies have shown that up to 50% of people with substance use disorders have a co-occurring psychiatric illness (Regier et al., 1990), and substance use disorders are particularly prevalent in those with psychotic disorders such as schizophrenia (Selzer & Lieberman, 1993). In fact, amongst patients with psychotic disorders, the risk of having a substance use disorder is two- to four-fold higher than in the general population (Regier et al., 1990; George & Krystal, 2000; Ziedonis et al., 2005).



A number of factors appear to lead to co-occurring substance use disorders and psychosis—with both genetic and environmental factors playing a role. In cases of first-episode psychosis, the misuse of alcohol and illicit substances may produce a transient, self-limited psychosis or it may lead to a more enduring psychosis (later diagnosed as schizophrenia). If schizophrenia is the diagnosis, it might have been triggered by the drug use (e.g., cannabis smoking) but was likely also promoted by individual biological risk factors (e.g., genetic vulnerability to psychosis).

To complicate the picture further, substance use makes diagnosing the type of psychotic disorder more difficult. For example, studies have shown that over 50% of adolescent patients seen in psychiatric clinics use substances (Green et al., 2007). This underlines the importance of clarifying whether a substance is to blame for any psychotic symptoms, or whether the use of substances may have triggered a functional psychotic illness such as schizophrenia (Boutros & Bowers, 1996). However, it is often not possible in the initial presentation to distinguish between the two. The history of substance use, the types of drugs misused (use of more than one substance is common), and the relationship to the onset of psychosis can help to determine the type of psychosis. Factors associated with periods of drug abstinence or reduction, as well

as circumstances for drug and alcohol relapse are also important. In cases of drug-induced psychosis, it may take several weeks or even months for the psychotic symptoms to fully resolve—and the course of recovery varies greatly. Early treatment with anti-psychotic drugs is crucial to minimize the impact of psychosis on brain function. In fact, it is well-known that early intervention in prodromal and first-episode psychosis improves long-term functional outcomes in these patients (Ricciardi, McAllister & Dazzan, 2008).

Tobacco and cannabis are the most used substances by people with psychotic disorders. The prevalence of cigarette smoking is two- to three-fold higher in patients with schizophrenia (58–88%) compared to that in the general population (Kalman, Morrisette & George, 2005; Morisano, Bacher, Audrain-McGovern & George, 2009). The rate of quitting smoking is much lower than the general population and varies greatly by disorder. The quit rate in those without a substance use or psychiatric condition is 42.5%—compared to only 16.9% in those with an alcohol disorder, 26% in those with bipolar disorder, 26% in those with depression and 0% in persons with psychosis such as schizophrenia (Lasser et al., 2000). Cigarette smoking appears to reduce the side effects of anti-psychotic drugs (e.g., stiffness), and may help with various aspects of cognitive dysfunction (working memory, attention, sensory gating) that are associated with schizophrenia (George, 2007; Sacco, Bannon & George, 2004). Little evidence exists, however, that shows tobacco use worsens symptoms or the course of schizophrenia (Sacco, Bannon & George, 2004).

After tobacco, cannabis is the most used substance by those with co-occurring psychotic disorders. Several studies have examined the role of cannabis in actually triggering psychosis and schizophrenia. In fact, a study from Sweden that followed people for 15 years found that the risk of schizophrenia was six times higher in high users of cannabis (those who used cannabis on more than 50 occasions) than in non-users. Even when other factors such as social background and previous psychiatric illness were taken into account, the link between heavy cannabis use and schizophrenia

remained. This suggests that cannabis is indeed an independent risk factor for developing schizophrenia. A further analysis of the same study population 27 years later (Konings, Henquet, Maharajah, Hutchinson & Van Os, 2008) continued to show a significant risk for schizophrenia—the more cannabis that was used, the higher the risk. The researchers of this study estimated that 13% of schizophrenia cases could actually be averted if cannabis use could be stopped (Zammit et al., 2002).

Since then, several other studies have supported these findings and have even expanded on the results of the Swedish study. Additional findings include:

- Cannabis use decreases the age of onset of first psychotic episode (Gonzalez-Pinto et al., 2008).
- Young adolescents are more vulnerable to the effects of cannabis and at higher risk for developing schizophrenia, which suggests that cannabis may be more harmful during the critical brain developmental periods (Konings et al., 2008).
- Continuing to use cannabis after being diagnosed with schizophrenia or when having psychotic symptoms may cause earlier or more frequent relapses and hospitalizations, and aggravate some symptoms.
- A genetic variation in some people that leads to lower levels of *dopamine* (a brain chemical) in certain areas of the brain has been found to be linked with the diagnosis of early psychosis in those who used cannabis as adolescents. This suggests that, genetically speaking, some people may be more vulnerable to the negative effects of cannabis and at greater risk for developing schizophrenia (Caspi et al., 2005).
- Levels of another brain chemical called *neurotrophins* were higher in schizophrenia patients who used cannabis for more than two years than in either people with schizophrenia who didn't use cannabis and in healthy subjects. This indicates that it's possible that cannabis use in vulnerable people may lead to brain cell damage (Jockers-Scherubl et al., 2004). Regular consumption by these people could hasten the onset of schizophrenia.

- If people with schizophrenia are administered THC (the active ingredient in cannabis), it can temporarily increase positive and negative symptoms of schizophrenia, and further impair cognitive function (D'Souza et al., 2005).

Considered together, these findings suggest that biological risk factors may make some people who are prone to psychosis more vulnerable to the effects of cannabis. In addition, cannabis appears to worsen the symptoms and the course of psychotic disorders.

If alcohol is involved, patients with psychotic disorders more typically have a diagnosis of alcohol abuse rather than dependence, and tend to engage in “binge” drinking instead of regular alcohol use. Reasons for this particular pattern of alcohol consumption are not clear, but it may involve another brain chemical called *glutamate*; both schizophrenia and alcohol are linked to changes in the brain related to glutamate (Heilig & Egli, 2006). Of interest, when people with chronic alcoholism abstain from drinking, they can experience an alcoholic “*hallucinosi*s” in which they have auditory and visual hallucinations and paranoid ideation—common psychotic symptoms.

The use of stimulants (including substances such as cocaine and methamphetamine) is highly prevalent in persons with psychotic disorders. Heavy stimulant use appears to increase the risk of psychotic symptoms possibly through a process known as *drug sensitization*. In patients with schizophrenia, stimulant misuse leads to a worsening of positive symptoms of psychosis (e.g., delusions, hallucinations, thought disorder), but interestingly enough, the negative symptoms of psychotic illness (lack of motivation or meaningful social relationships) appear to be lower in those with psychosis who use stimulants (Talamo et al., 2006).

The class of drugs that includes PCP (phencyclidine) and ketamine is known to produce psychotic symptoms that mimic all the clinical features of schizophrenia—positive, negative and cognitive symptoms. In fact, ketamine administration has been shown to replicate the symptoms of schizophrenia in healthy volunteers

(Krystal et al., 1994), and worsen positive, negative and cognitive symptoms in patients with schizophrenia (Malhotra et al., 1997). The action site of these drugs—receptors in the brain for the chemical *glutamate*—has also been implicated in schizophrenia, suggesting a common neurobiological mechanism.

Substance misuse is associated with an earlier onset of psychosis, greater resistance to treatments that are normally effective, and higher rates of emergency room visits and psychiatric hospitalization (Ziedonis et al., 2005). However, we have few effective treatments for co-occurring psychotic and substance use disorders—and perhaps more profoundly, our treatment systems lack the capacity to manage these highly complex patients.

#### FURTHER EVIDENCE AND DISCUSSION

Much like with anxiety disorders (Chapter 3) and mood disorders (Chapter 5), there are two commonly used theories to explain concurrent psychotic and substance use disorders: the *self-medication* hypothesis and an *addiction vulnerability* hypothesis (Chambers, Krystal & Self, 2001).

The self-medication hypothesis suggests that patients with schizophrenia use drugs to reduce their symptoms or the side effects of their medication. This would infer that their substance use is a consequence of their schizophrenia symptoms and/or its treatment. This hypothesis lacks evidence from research to support it, and as such remains controversial (Khantzian, 1997).

The addiction vulnerability hypothesis suggests that the risk of schizophrenia or psychosis is higher in those who use drugs than those who don't because the two disorders share genes or brain abnormalities. These individuals are vulnerable to both psychosis and substance use. This hypothesis looks at both substance use and schizophrenia as distinct disorders with a shared basis in the brain—specifically, the brain's dopamine systems (Chambers et al., 2001). Unlike the self-medication hypothesis, this theory is supported by experimental evidence (George, 2007).

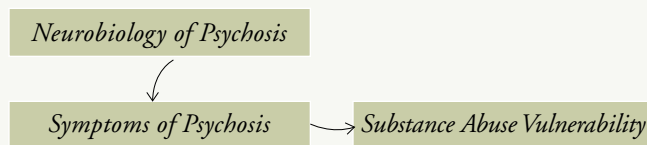
Indeed, evidence of neurobiological mechanisms—relating to the structure and function of the brain—helps explain the co-occurrence of psychosis and substance use disorders. Systems in the brain involving the brain chemical dopamine are thought to be involved in drug use, and may also play a role in the relationship between addictions and psychotic disorders (Green, 2006). In schizophrenia, some parts of the dopamine systems work too much (*hyperfunction*) while others work less than normal (*hypo-function*) (George et al., 2000; George et al., 1995). The resulting imbalance in the level of functioning is thought to lead to increased susceptibility of a person with schizophrenia to substance use disorders—independent of the schizophrenia itself (Yung, 2007). Other dysfunction within the dopamine systems is thought to increase vulnerability to both substance use disorders and psychosis (Sacco, Bannon & George, 2004; Swanson, Van Dorn & Swartz, 2007). For example, some evidence suggests that nicotine may actually improve the cognitive problems and dopamine system abnormalities in the brains of people with psychosis (George, 2007).

In light of the co-occurrence of substance use and psychotic disorders and the possible shared basis for these disorders, treatment options must be carefully considered.

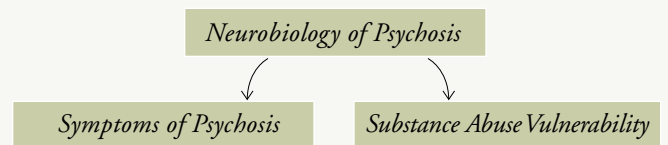
**Pharmacological Approaches:** When treating psychosis with medications, it is critical that even in the presence of active substance use the psychotic symptoms be effectively managed and treated—even if the psychosis is drug-induced. Methods of drug delivery that help to ensure the medication is actually being taken are crucial; these include the use of once-daily dosing regimens and the employment of long-acting, injectable antipsychotic drugs (called *depot* medications) (Green, 2006). Evidence shows that so-called second generation antipsychotic drugs (these include clozapine, olanzapine, and quetiapine) may reduce drug and alcohol craving and misuse (Green, 2006; George et al., 1995; Swanson et al., 2007; Smelson et al., 2006). Medications used to treat addictions may be effective for the treatment of co-occurring substance use disorders in those with schizophrenia (George et al., 2008; Petrakis et al., 2004).

**FIGURE 5**  
**TWO MODELS TO EXPLAIN CO-OCCURRING PSYCHOTIC**  
**AND SUBSTANCE USE DISORDERS**

**SELF-MEDICATION HYPOTHESIS**  
 (negative reinforcement model)



**PRIMARY ADDICTION HYPOTHESIS**  
 (positive reinforcement model)



*Adapted from: Chambers, R. A. et al. (2001)*

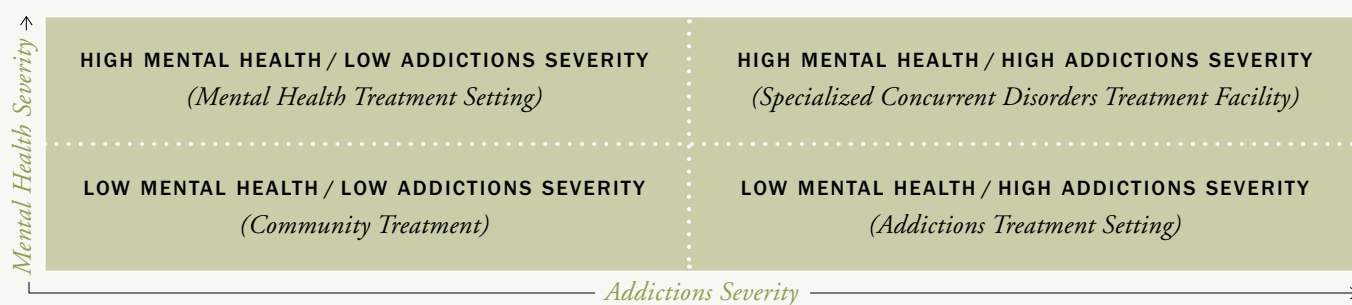
**Behavioural Approaches:** The use of behavioural therapies—and in particular motivational interviewing and cognitive-behavioural therapies—is a necessary component for treating co-occurring psychotic and substance use disorders (Ziedonis et al., 2005). These therapies can also be used to help ensure that patients take their medications as prescribed—called *adherence* to treatment. Ideally, such treatment should take place within a group format, since this is more likely to assist with deficits in social skills and assertiveness commonly seen in those with schizophrenia and other psychotic disorders.

**Integrated “Dual Recovery” Approaches:** Ideally, both pharmacological and behavioural treatments are combined for the treatment of co-occurring substance use and psychotic disorders. Clinical staff should be trained in both initiation of abstinence from drugs and alcohol and in psychosis and crisis stabilization. Unfortunately, this is often not the case with providers.

Once substance use and psychotic symptoms are stabilized, an approach that addresses simultaneous recovery from both disorders is preferred. Using modified cognitive-behavioural (relapse-prevention) approaches for the substance use and psychosis integrated into a single treatment program is ideal (Ziedonis et al., 2005; Weiss et al., 2007).

Given the complexities of treating clients with co-occurring psychosis and substance use disorders, the ideal delivery of these treatment services is at a single centre where providers are trained in both mental health and addictions assessment and interventions (Drake, Mercer-McFadden, Mueser, McHugo & Bond, 1998). This service model (presented in Figure 6) is a version of the *quadrant model* (Ziedonis et al., 2005; Drake et al., 1998), which proposes that clients with the highest mental health (psychosis) and addiction severity should receive services in a highly specialized treatment setting, albeit in a time-limited manner (Minkoff, Zweben, Rosenthal & Ries, 2003). Naturally, given the high costs of such specialized services, the goal would be for rapid stabilization of symptoms and a quick return to more routine levels of care. For example, after such acute stabilization and specialized treatment, clients who have a primary psychotic disorder (e.g., chronic schizophrenia) would then return to a primary mental health treatment setting where a dual recovery approach can be followed. Those clients with a primary substance use disorder (e.g., drug-induced psychosis) would return to an addictions treatment setting. Ultimately, once the patient with complex concurrent psychotic and substance use disorders has achieved long-term psychotic disorder and addictive illness stability, that individual would be placed in community treatment, ideally at a primary care-oriented medical centre.

**FIGURE 6**  
**QUADRANT MODEL FOR TREATMENT**  
**OF CLIENTS WITH COMORBID ADDICTIONS**  
**AND PSYCHOTIC DISORDERS**



**FIGURE 6**  
 This quadrant model proposes that clients with the highest mental health (psychosis) and addiction severity should receive services in a highly specialized concurrent disorders treatment setting, albeit in a time-limited manner. When either mental health or addiction severity diminishes, the patient can be transitioned to specialized addiction or mental health treatment setting. Eventually when both mental health and addiction severity are low, a community treatment setting would be appropriate.



## AT A GLANCE

- Studies have shown that up to 50% of people with substance disorders have a co-occurring psychiatric illness. Of all psychiatric co-occurrences, substance use disorders are particularly prevalent in clients with psychotic disorders such as schizophrenia.
- The rates of substance use disorders in people with psychotic disorders are much higher than those in the general population in Canada.
- People with schizophrenia are almost five times more likely to have substance use disorders than people without mental disorders (three-fold higher for alcohol and six-fold higher for other illicit drugs).
- Substance abuse can hasten the onset of psychotic disorders, worsen both the symptoms and the course of illness, and lead to higher rates of psychiatric hospitalization and increased health care costs.
- Substance misuse makes diagnosing the type of psychotic disorder more difficult. For example, studies have shown that over 50% of adolescent patients seen in psychiatric clinics use substances.
- Tobacco is the most used substance by people with a psychotic disorder, followed by cannabis. The prevalence of cigarette smoking is two- to three-fold higher in patients with schizophrenia (58–88%), compared to that in the general population.
- Studies have found that the risk of schizophrenia in heavy cannabis users is six times higher than in non-users, even when taking into account things such as other psychiatric illnesses and social background.
- If alcohol is involved, patients with psychotic disorders more typically have a diagnosis of alcohol abuse rather than dependence, and tend to engage in “binge” drinking instead of regular alcohol use.
- Evidence suggests that the risk of schizophrenia or psychosis is higher in those who use drugs than those who don’t because of genes or brain abnormalities that are shared by the two disorders.
- Ideally, both pharmacological and behavioural treatments should be combined for the treatment of co-occurring substance use and psychotic disorders.

## CONCLUSIONS AND IMPLICATIONS FOR CANADA

Overwhelming evidence reveals the high prevalence of various substance use disorders in persons with psychosis that wreak havoc on their lives. But we now have a better understanding of the risk factors that confer vulnerability to substance use and addictions in people with psychosis, and are developing better medications, behavioural and systems approaches to manage this co-occurrence more effectively. Nonetheless, our current health care system is not well equipped to manage these clients. Changes to our systems for training mental health and addictions staff and physicians, as well as reconfiguring the health care system to better serve the complex needs of these clients, will be crucial if we are to make progress in this area.

## REFERENCES

- Boutros, N. N., & Bowers, M. B., Jr. (1996). Chronic substance-induced psychotic disorders: State of the literature. *Journal of Neuropsychiatry & Clinical Neurosciences*, 8, 262–269.
- Caspi, A., Moffitt, T. E., Cannon, M., McClay, J., Murray, R., Harrington, H., Taylor, A., Arseneault, L., Williams, B., Braithwaite, A., Poulton, R., & Craig, I. W. (2005). Moderation of the effect on adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: Longitudinal evidence of a gene x environment interaction. *Biological Psychiatry*, 57, 1117–1127.
- Chambers, R. A., Krystal, J. H., & Self, D. W. (2001). A neurobiological basis for substance abuse comorbidity in schizophrenia. *Biological Psychiatry*, 50, 71–83.
- Drake, R. E., Mercer-McFadden, C., Mueser, K. T., McHugo, G. J., & Bond, G. R. (1998). Review of integrated mental health and substance abuse treatment for patients with dual disorders. *Schizophrenia Bulletin*, 24, 589–608.
- D'Souza, D. C., Abi-Saab, W. M., Madonick, S., Forselius-Bielen, K., Doersch, A., Braley, G., Guerorguivea, R., Cooper, T. B., & Krystal, J. H. (2005). Delta-9-tetrahydrocannabinol effects in schizophrenia: Implications for cognition, psychosis and addiction. *Biological Psychiatry*, 57, 594–608.
- Freedman, R. (2003). Schizophrenia. *New England Journal of Medicine*, 349, 1738–1749.
- George, T. P. (2007). Neurobiological links between nicotine addiction and schizophrenia. *Journal of Dual Diagnosis*, 3(3/4), 27–42.
- George, T. P., & Krystal, J. H. (2000). Comorbidity of psychiatric and substance abuse disorders. *Current Opinion in Psychiatry*, 13, 327–331.
- George, T. P., Sernyak, M. J., Ziedonis, D. M., & Woods, S. W. (1995). Effects of clozapine on smoking in chronic schizophrenic outpatients. *Journal of Clinical Psychiatry*, 56(8), 344–346.
- George, T. P., Vessicchio, J. C., Sacco, K. A., Dudas, M. M., Allen, T. A., Weinberger, A. H., Feingold, A., & Jatlow, P. I. (2008). A randomized, double-blind, placebo-controlled trial of bupropion SR in combination with transdermal nicotine patch for smoking cessation in schizophrenia. *Biological Psychiatry*, 63, 1092–1096.
- George, T. P., Ziedonis, D. M., Feingold, A., Pepper, W. T., Satterburg, C. A., Winkel, J., Rounsaville, B. J., & Kosten, T. R. (2000). Nicotine transdermal patch and atypical antipsychotic medications for smoking cessation in schizophrenia. *American Journal of Psychiatry*, 157(11), 1835–1842.
- Gonzalez-Pinto, A. V. P., Ibanez, B., Mosquera, F., Barbeito, S., Guiterrez, M., Ruiz de Azua, S., Ruiz, I., & Vieta, E. (2008). Impact of cannabis and other drug use on age of onset of psychosis. *Journal of Clinical Psychiatry*, 69, 1210–1216.
- Grech, A., Van Os, J., Jones, P. B., Lewis, S. W., & Murray, R. M. (2005). Cannabis use and outcome of recent onset psychosis. *European Psychiatry*, 20(4), 349–353.
- Green, A. I., Drake, R. E., Brunette, M. F., & Noordsy, D. L. (2007). Schizophrenia and co-occurring substance use disorder. *American Journal of Psychiatry*, 163, 402–408.
- Green, A. I. (2006). Treatment of schizophrenia and co-morbid substance abuse: Pharmacological approaches. *Journal of Clinical Psychiatry*, 67(Suppl 7), 31–35.
- Heilig, M., & Egli, M. (2006). Pharmacological treatment of alcohol dependence: Target symptoms and target mechanisms. *Pharmacology and Therapeutics*, 111, 855–876.
- Heinrichs, D. W., & Carpenter, W. T. (1985). Prospective study of prodromal symptoms in schizophrenic relapse. *American Journal of Psychiatry*, 142, 371–373.
- Jockers-Scherubl, M. C., Danker-Hopfe, H., Mahlberg, R., Selig, F., Rentzsch, J., Schürer, F., Lang, U. E., & Hellweg, R. (2004). Brain-derived neurotrophic factor serum concentrations in drug-naïve schizophrenic patients with chronic cannabis abuse and multiple substance abuse. *Neuroscience Letters*, 371, 79–83.
- Kalman, D., Morrisette, S. B., & George, T. P. (2005). Co-morbidity of smoking with psychiatric and substance use disorders. *American Journal on Addictions*, 14, 106–123.
- Khantzian, E. J. (1997). The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harvard Review of Psychiatry*, 4, 231–244.
- Klosterkotter, J., Hellmich, M., Steinmeyer, E. M., & Schultze-Lutter, F. (2001). Diagnosing schizophrenia in the initial prodromal phase. *Archives of General Psychiatry*, 58, 158–164.

- Konings, M., Henquet, C., Maharajah, H. D., Hutchison, G., & Van Os, J. (2008). Early exposure to cannabis and risk for psychosis in young adolescents in Trinidad. *Acta Psychiatrica Scandinavica*, *118*, 209–213.
- Krystal, J. H., Karper, L. P., Seibyl, J. P., Freeman, G. K., Delaney, R., Bremner, J. D., et al. (1994). Subanesthetic effects of the non-competitive NMDA antagonist, ketamine in humans: Psychotomimetic, perceptual, cognitive, and neuroendocrine responses. *Archives of General Psychiatry*, *51*, 199–214.
- Lasser, K., Boyd, J. W., Woolhandler, S., Himmelstein, D. U., McCormick, D., & Bor, D. H. (2000). Smoking and mental illness: A population-based prevalence study. *Journal of the American Medical Association*, *284*, 2606–2610.
- Linszen, D. H., Dingemans, P. M., & Lenior, M. E. (1994). Cannabis abuse and the course of recent-onset schizophrenic disorders. *Archives of General Psychiatry*, *51*, 273–279.
- Malhotra, A. K., Pinals, D. A., Adler, C. M., Elman, I., Clifton, A., Pickar, D., & Breier, A. (1997). Ketamine-induced exacerbation of psychotic symptoms and cognitive impairment in neuroleptic-free schizophrenia. *Neuropsychopharmacology*, *17*, 141–150.
- Minkoff, K., Zweben, J., Rosenthal, R., & Ries, R. (2003). Development of service intensity criteria and program categories for individuals with co-occurring disorders. *Journal of Addictive Diseases*, *22S*, 113–129.
- Morisano, D., Bacher, I., Audrain-McGovern, J., & George, T. P. (2009). Mechanisms underlying the co-morbidity of tobacco use in mental health and addictive disorders. *Canadian Journal of Psychiatry*, *54*(6), 356–367.
- Pantelis, C., Velakoulis, D., McGorry, P. D., Wood, S. J., Suckling, J., Phillips, L. J., et al. (2003). Neuroanatomical abnormalities before and after onset of psychosis: A cross-sectional and longitudinal MRI comparison. *Lancet*, *361*(9354), 281–288.
- Petrakis, I. L., O'Malley, S., Rounsaville, B., Poling, J., McHugh-Strong, C., Krystal, J. H., et al. (2004). Naltrexone augmentation of neuroleptic treatment in alcohol abusing patients with schizophrenia. *Psychopharmacology*, *172*(3), 291–297.
- Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., & Goodwin, F. K. (1990). Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area (ECA) Study. *Journal of the American Medical Association*, *264*, 2511–2518.
- Ricciardi, A., McAllister, V., & Dazzan, P. (2008). Is early intervention in psychosis effective? *Epidemiological Psychiatric Society*, *17*, 227–235.
- Rush, B., Urbanoski, K., Bassini, D., Castel, S., Wild, T. C., Strike, C., Kimberley, D., & Somers, J. (2008). Prevalence of co-occurring substance use and other mental disorders in the Canadian population. *Canadian Journal of Psychiatry*, *53*, 800–809.
- Sacco, K. A., Bannon, K. L., & George, T. P. (2004). Nicotinic receptor mechanisms and cognition in normal states and neuropsychiatric disorders. *Journal of Psychopharmacology*, *18*(4), 457–474.
- Selzer, J. A., & Lieberman, J. A. (1993). Schizophrenia and substance abuse. *Psychiatric Clinics of North America*, *16*, 401–412.
- Smelson, D. A., Ziedonis, D., Williams, J., Losonczy, M. F., Williams, J., Steinberg, M. L., & Kaune, M. (2006). The efficacy of olanzapine for decreasing cue-elicited craving in individuals with schizophrenia and cocaine dependence: a preliminary report. *Journal of Clinical Psychopharmacology*, *26*, 9–12.
- Swanson, J., Van Dorn, R. A., & Swartz, M. S. (2007). Effectiveness of atypical antipsychotics for substance use in schizophrenia patients. *Schizophrenia Research*, *94*, 114–118.
- Talamo, A., Centorrino, F., Tondo, L., Dimitri, A., Hennen, J., & Baldessarini, R. J. (2006). Comorbid substance-use in schizophrenia: Relation to positive and negative symptoms. *Schizophrenia Research*, *86*, 251–255.
- Weiss, R. D., Griffin, M. L., Kolodziej, M. E., Greenfield, S. F., Najavits, L. M., Daley, D. C., Doreau, H. R., & Hennen, J. A. (2007). A randomized trial of integrated group therapy versus group drug counseling for patients with bipolar disorder and substance dependence. *American Journal of Psychiatry*, *164*, 100–107.
- Yung, A. R. (2007). Identification and treatment of the prodromal phase of psychotic disorders: Perspectives from the PACE clinic. *Early Interventions in Psychiatry*, *1*, 224–235.
- Yung, A. R., & McGorry, P. D. (1996). The prodromal phase of first-episode psychosis: Past and current conceptualizations. *Schizophrenia Bulletin*, *22*, 353–370.
- Zammit, S., Allebeck, P., Andreasson, S., Lundberg, I., & Lewis, G. (2002). Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: Historical cohort study. *British Medical Journal*, *325*, 1199–1208.
- Ziedonis, D. M., Smelson, D., Rosenthal, R. N., Batki, S. L., Green, A. I., Henry, R. J., Montoya, I., Parks, J., & Weiss, R. D. (2005). Improving the care of individuals with schizophrenia and substance abuse disorders: Consensus recommendations. *Journal of Psychiatric Practice*, *11*(5), 315–339.



# A Call to Action


**Franco J. Vaccarino, PhD**  
University of Toronto

## AUTHOR BIO

### **Franco J. Vaccarino, PhD**

Dr. Franco Vaccarino, PhD, is a full Professor in the Departments of Psychology and Psychiatry, as well as a Vice-President of the University of Toronto and Principal of the University of Toronto Scarborough. His interdisciplinary research accomplishments in the areas of neuroscience, addiction, and mood and

anxiety systems have been recognized internationally. Dr. Vaccarino's prominence in the field was also recognized by the World Health Organization (WHO) in his role as the Principal Editor of its recently published *Neuroscience of Psychoactive Substance Use and Dependence* report.



## AN INTEGRATED APPROACH TO national treatment strategies will go a long way toward developing a unified and coordinated system for addressing concurrent disorders.

The rationale for considering concurrent mental health and substance use disorders a topic of special significance is in many ways self-evident: the two disorders frequently coexist; they affect one another in clinically important ways; they often share common biological, psychological and social roots; and these co-occurring disorders represent a major health challenge. Despite the many good reasons for considering concurrent disorders a subject of high priority, a divide continues to exist. For example, scientific programs aimed at better understanding the processes and mechanisms underlying substance use disorders often exclude mental health disorders, and vice versa. At the community level, a lack of emphasis on the interaction between mental health and substance use disorders can sometimes lead to an underestimation of the effect of one condition on the course of the other. Community addiction programs often deal with substance use and mental health disorders independently, and because treatment programs are ill-equipped to deal with both disorders, those suffering from both a substance use and mental health disorder commonly receive sub-standard care. In fact, a study looking at the degree to which recommended basic care was being followed for a number of different conditions identified that the quality of care varied greatly by condition. It should not be surprising, then, that care for substance use disorders scored the

poorest when it came to following recommended basic standards of care. Concurrent mental health and substance use disorders did not even make the list.

There is no doubt that parallel systems of care for those suffering from only a substance use disorder or a mental health disorder are necessary; however, parallel systems do present a major challenge for those suffering from concurrent disorders. Whether we are talking about hospitals, correctional facilities or community health services, the limited ability of our clinical and community programs to approach concurrent disorders in a coordinated and integrated manner, represents a significant barrier to effectively treating those affected by both. An essential first step to overcoming this barrier is the recognition that the interaction between substance use disorders and mental health disorders is paramount to care and treatment. Today, we are beginning to see the emergence of clinical and community programs that recognize this important interaction, where substance use disorders and mental health disorders are seen as balanced contributors to the overall condition of a client. In publishing the present *Substance Abuse in Canada: Concurrent Disorders*, CCSA's aim is to contribute to the growing efforts to ensure that our approaches to research, education and care in the substance use disorder and mental health fields consider



From these chapters a number of themes arise that demand a call to action.

**CONCURRENT DISORDERS: A NEED FOR INTEGRATION**

**Treatment and Care:** From the information presented in this report it is clear that a major proportion of clients with mental disorders being treated in mental health centres are using drugs of abuse and often have a substance use disorder. Conversely, within addiction care programs, a large number of clients also have significant mental health problems. In these cases, although the client does receive some care, this care is typically not well integrated and under-recognizes the contribution of the co-occurring condition to the course of the primary problem. In other cases, treatment programs often fully exclude either those with substance use disorders or the mentally ill, leaving the client with an unmet serious health need as well as a combined sense of helplessness and urgency.

Institutional accreditation guidelines for clinical care are a good example of the lack of integration. Current accreditation standards allow institutions to choose between addictions or mental health standards, thus perpetuating the separation of addiction and mental health knowledge—and its application to treatment and care. Today, as we better understand the significant unmet need in people suffering from concurrent disorders and now that we have the requisite knowledge base to justify an integrated approach to treatment and care, our present system with its general lack of integration is not easily justifiable.

.....  
**Clinical practice guidelines and standards in the substance use disorder and mental health fields need to be integrated and should reflect a unified national approach for the treatment and care of those suffering from concurrent disorders.**  
.....

**Education and Training:** Not only does this report challenge our system of treatment and care to integrate substance use disorders and mental health disorders, but it also calls for our educational system to do the same. While much remains to be learned, we

concurrent disorders as a major priority. To this end, the present report provides an overview of state-of-the-art findings and highlights a number of key areas where advances in our understanding of concurrent disorders have provided a solid platform on which to build treatment, research and educational efforts to improve care and transform the system supporting care.

In this call to action, we draw on topics explored in earlier chapters and use this foundation as an impetus to explore future priorities in the substance abuse field. We began this report by exploring why the issue of concurrent disorders is so important and why an integrated approach is essential. This led to a more in-depth discussion of the interplay of various mental health problems with substance use disorders. The chapters on anxiety, stress, trauma and impulsivity underline the importance of individual and personality factors as well as environmental and developmental considerations. The chapter on impulsivity further emphasizes the importance of this behavioural dimension; it cuts across mental disorders and is central to substance use disorders. The final two chapters highlight the interplay between substance use disorders and the major mental illnesses: psychosis, depression and bipolar disorder. Together, these conditions represent major contributors to death and disability worldwide and warrant special consideration with respect to the contribution of substance use disorders to their development and clinical courses.

have a sufficient understanding of concurrent disorders to incorporate findings into forward-looking best practices that recognize the integrated nature of substance use disorders and mental health disorders. The best practices that emerge from this new knowledge will be a deviation from past approaches, as they will focus on bridging the knowledge in the substance use disorder and mental health fields towards the development of a common, unified approach. Developing this integrated knowledge of concurrent disorders from existing findings and applying this knowledge to our educational programs—whether in the mental health or the addictions field—is essential and would constitute a major reorganization of our approach to education.

A successful response to concurrent disorders requires trained professionals who have a common understanding of concurrent disorders and who work within a framework shared by other trained professionals in the field.

*A common educational platform with new specialized training programs needs to be created. This would help achieve a common foundation of understanding and would help facilitate the integration of system services.*

A common educational platform would be shared by health professionals from different sectors who share the common purpose of addressing clinical care challenges of clients with concurrent disorders.

**Research:** The present report makes it clear that whether we are speaking of discovery research or more applied research, emerging frameworks for understanding processes underlying substance use disorders and mental disorders continue to highlight the commonalities and interactions between the two. The CIHR recognized this at its inception with the creation of the Institute for Neuroscience, Mental Health and Addiction as a core element of the federal system for funding Canadian health research. It is now time for governments and other sectors that support research to not only recognize the enormous clinical burden represented by

concurrent disorders and the human cost of these disorders to our health care system, but also to prioritize the vast research opportunity represented by this field.

One particular research need is for a focused national approach to clinical research on concurrent disorders with the goal of developing national standards and new best practices for concurrent disorders. This has been successful in other areas, such as AIDS; the success of coordinated national efforts in clinical research within the AIDS field demonstrates the remarkable effectiveness of a national clinical research strategy for developing solutions to trans-disciplinary health challenges.

*The addictions and mental health communities must come together to effectively seize the resources and momentum necessary to address the current gap in research and research funding within the concurrent disorders field.*

Within Canada, the Vancouver East Side is a compelling example of the economic and social costs of not addressing the clinical research needs of substance use disorders, mental health issues and concurrent disorders.

**The System:** Currently, separate national addictions and mental health treatment strategies exist that highlight system needs and priorities. As we move forward, it will be important to integrate national treatment strategies in the mental health and substance use fields.

*An integrated approach to national treatment strategies will go a long way toward developing a unified and coordinated system for addressing concurrent disorders.*

**DEVELOPMENTAL CONSIDERATIONS:  
A CASE FOR FOCUSING ON ADOLESCENCE**

Much of the knowledge presented in this report highlights conditions that are developmentally sensitive. Given that the onset of substance use disorders is common during adolescence, our last *Substance Abuse in Canada* report was dedicated to a focus on youth. It emphasized biological, psychological and social reasons why youth and adolescence deserve special attention. The importance of youth as a target population is further reinforced in the present report for reasons relating to the developmental nature of many mental health disorders.

In recent years, increased efforts have been directed at programs that focus on early detection and intervention of mental health disorders. The prioritization of early detection and intervention in the mental health field speaks to emerging knowledge that indicates many mental health disorders have a strong developmental trajectory with an onset often linked to the adolescent period. Indeed, emerging knowledge in the field supports the notion that, in many cases, mental health disorders can actually be characterized as developmental disorders. Discussions in this report indicate early onset of a variety of mental health disorders including impulse control disorders, anxiety disorders, mood disorders and schizophrenia. Together with last year's report highlighting youth and adolescence as the sensitive developmental period for the onset of substance use disorders, the present report calls for this period to be considered a critical one for the emergence of concurrent disorders.

Not only is integration necessary with respect to research, education and care, but a particular developmental focus on youth and early detection is also called for as we tackle the challenges of concurrent disorders.

**EARLY DETECTION, EARLY INTERVENTION AND  
RAISING AWARENESS**

This report highlights findings that demonstrate the presence of sub-clinical indicators, as well as environmental and genetic determinants of vulnerability to concurrent disorders. These findings represent new tools to help identify individuals and groups at risk for future emergence of a full-blown concurrent disorder. As is the case in other health conditions, concurrent disorders are best treated when intervention is early, and may even be preventable with awareness of sub-clinical indicators and other determinants of vulnerability.

There is a need to ensure that we have practices in place to identify individual and group risk factors early, and to intervene with integrated care programs aimed at preventing concurrent disorders.

**STRESS, TRAUMA AND EXPERIENCE**

This report has also highlighted the importance of stressful life experiences as a risk factor for developing substance use disorders and mental health disorders. While these two effects of stressful life experiences have often been studied independently, the effects of stressors on both conditions—as this report discusses—can be seen as a unified phenomenon that points out the important interplay between substance use disorders and mental disorders. This risk conferred by stressful life events on concurrent disorders can also be seen as both environmentally and developmentally relevant. While stress is a risk factor for substance use disorders throughout the lifespan, it is especially relevant during adolescence, a particularly vulnerable period for the development of substance use and mental health disorders—or both.

Together with discussions concerning the coexistence of anxiety and substance use disorders, the present report underlines the need to attend to risk factors associated with stress and stressful life experiences. While the relationship between stress, trauma, substance use disorders and mental health disorders is complicated, a sufficient body of knowledge exists to begin to develop integrated



approaches to prevention and treatment that are common to the substance use and mental health fields. While the mental health field has made efforts to systematically incorporate biological and psychological knowledge associated with the effects of stressful life events into its educational and treatment programs (e.g., stress appraisal and coping mechanisms, stress management, etc.), the addiction field needs to continue to build on its efforts in this regard. Building on the existing body of knowledge in the area of life stressors and trauma, this field presents a significant opportunity to work towards an integrated and unified approach to prevention and treatment strategies.

#### CONCLUSION

A sustained and serious commitment to concurrent substance use and mental health disorders represents a significant undertaking that will require considerable commitment on the part of policy makers, educators, researchers and health professionals. While the goal of integration of mental health and addiction services may seem daunting, it must be vigorously pursued and promoted. Indeed, this process has already begun as evidenced by the existence of particular institutions and centres both within and outside government that have, in recent years, identified integration of substance use and mental health disorder services as necessary. Moving forward, it will be important to establish a common national framework for understanding the interplay between substance use disorders and mental health disorders and to establish a unified approach to the care and treatment of those affected by concurrent disorders. These efforts will be needed in order to effectively address the challenges faced by those suffering from concurrent disorders and to more effectively coordinate services between the two sectors.