

PREVENTION OF MENTAL ILLNESS: WHY NOT START AT THE BEGINNING?

BY RICHARD E. TREMBLAY, CEECD DIRECTOR

Research on the developmental origins of mental health is on a fast track. It was only four years ago that a committee of the Canadian Senate¹ published a report on mental health, mental illness and addiction that stated: "The pre-school years present two challenges. The first is to identify and provide services to those children who are living with, or who are at risk of developing, mental illness. The second is to manage effectively the transition from early childhood (0-5 years) into the school system." Interestingly, all of the recommendations that followed focused on services to school children and adolescents.

The two challenges highlighted by the report remain and need to be addressed urgently. However there is increasing evidence that the origins of mental health problems diagnosed in later childhood, adolescence and adulthood can be found during pregnancy and very early childhood.

This *Bulletin* highlights two areas of research that are changing our view of the causes of mental health problems. The first is developmental epidemiology of mental health problems with population samples followed from birth onwards. Traditional cross-sectional epidemiological studies of mental health focused on adult mental health while longitudinal studies during the 1970s and 80s studied adolescents and elementary school children. New longitudinal studies initiated during the mid-1990s are providing fascinating data on mental health development during early childhood. One of these "made in Canada" studies is summarized on page 4 and the overview of research

on page 5 refers to another recent study in North America.

Epigenetics (environmental programming of genes) is the second research area changing our views. The genetics revolution in mental health, which started not much more than a decade ago, confirmed that risk of mental health problems could be transmitted from parents to children through genetics. It also showed that negative environmental conditions are generally needed to trigger the onset of the disease. Epigenetics is now suggesting a revolution in itself: the environment, especially during pregnancy and very early childhood, activates and silences good and bad genes that are crucial for mental well-being and social adaptation. These studies also indicate that inadequate perinatal environments are not only silencing or activating a few specific genes, but thousands of genes may be affect-



ed by maternal stress, inadequate nutrition, obesity, diabetes, alcohol and tobacco use. The prenatal factors that eventually lead to obesity, cardiovascular problems and cancer may also lead to serious mental health problems throughout an individual's life.^{2,3,4,5}

Mental health services to school children and youth with mental health problems are key to treating the illness and preventing further negative impacts, but a substantial increase in resources is needed to support pregnant women, preschool children and their families, if we seriously want to prevent mental illness and foster the mental health of the next generation. 🐾

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ON THE ROAD TO POSITIVE MENTAL HEALTH

Research now shows that mental health issues often have their roots in early childhood. Mental disorders include a wide range of conditions, such as depression, anxiety, phobias, substance abuse, schizophrenia, and developmental disorders such as disruptive behaviour, autism, mental retardation and dementia. About 10% of the adult population worldwide will report having some type of mental or behavioural disorder at any point in time.¹ In 2003, 7% of the Canadian adult population was diagnosed with a mental illness, representing nearly 1.9 million people, and 6%, or 1.6 million people, was suffering from a non-diagnosed mental illness.²

The economic impact is huge. In a 2002 report, Health Canada estimated the direct costs related to the use of public health services at \$4.7 billion in 1998, and indirect costs related to the loss of productivity resulting from long- or short-term absences from work or premature deaths at \$3.2 billion.² These stupendous figures are not specific to Canada: of the 10 leading causes of disability worldwide, five are mental disorders: unipolar depression, alcohol use disorder, bipolar affective disorder, schizophrenia and obsessive-compulsive disorder.³

Although many mental health problems were once thought of as “adult” disorders, they often begin in childhood and adolescence. In the last decade, diagnostic tools have been refined to identify mental disorders in very young children. Some disorders may manifest themselves differently in the early years, in keeping with the child’s age and brain development.⁴ Depression and anxiety can be detected in childhood, and symptoms of these conditions tend to increase in frequency over the first five years of life (see page 4 of this *Bulletin*).⁵ Disruptive behaviour problems are another example of mental disorders in children. Depending on the child’s age, these can include aggression, opposition and defiance, rule breaking, stealing and vandalism. *“With age, children learn socially acceptable behaviours from interactions with their environment. A ‘disease’ status is observed when a child uses disruptive behaviours significantly more often than his age group over a long period of*

time,” explains Richard E. Tremblay, Director of the Centre of Excellence for Early Childhood Development.⁶

GENETIC AND ENVIRONMENTAL FACTORS

There is wide consensus that complex disorders such as mental illnesses are based on the interaction of numerous genes and environmental factors.⁶ On the one hand, genes affect complex behaviour through their influence on the development and function of the essential building blocks of the nervous system. Attention Deficit Hyperactivity Disorder (ADHD), for example, appears to be one of the most common heritable mental health disorders of childhood.⁷ One recent study found that inhibitory control deficit is a cognitive marker of genetic risk shared by parents and offspring, and that parents’ inhibitory control ability significantly predicted the ability of their children.⁷

On the other hand, it has been well established that parent-child interactions in early life form the foundation for the child’s social and emotional development. Compelling evidence suggests that childhood trauma – abuse, neglect or loss of a parent – is a major risk factor for the development of mood and anxiety disorders.⁸ Conversely, supportive, attentive and sensitive adult care plays a salient role in protecting children from potentially harmful effects of stressors.⁹

The prenatal period is just as important, with maternal behaviour affecting the developing foetus. Maternal prenatal smoking

has been associated with increased risk for ADHD, oppositional behaviour, conduct disorder and substance abuse outcomes in youth.¹⁰ Fetal Alcohol Spectrum Disorder, a permanent birth defect caused by maternal consumption of alcohol during pregnancy, is the leading cause of mental retardation in the Western world. Prenatal exposure to alcohol has also been associated with developmental delays and behavioural problems.¹¹ Psychosocial stress during pregnancy has been linked to increased risk for ADHD, schizophrenia and social abnormalities.¹²

EPIGENETIC EFFECTS

A growing body of research is showing that environmental factors affect development not only via psychosocial mechanisms, but through epigenetics as well. Epigenetics refer to the mechanisms that can change a gene’s function, without changing its sequence.¹³ Epigenetic effects are well known in cancer research, and have recently been shown to possibly play an important role in obesity and in behaviour regulation.⁶ Studies with rats have shown that rat pups that were insufficiently licked by their mothers (i.e. neglected) had chemically-altered expression of genes, affecting the rats’ ability to regulate stress.¹⁴ Subsequent studies suggest that parental care may affect stress regulation in humans as well. (See page 5 of this *Bulletin*.)

Diet may affect gene expression as well. Bart P.F. Rutten, from the School of Mental Health and Neuroscience at the Maastricht

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University Medical Centre in the Netherlands, notes that evidence from two large independent population samples in the Netherlands and China suggests that in utero nutritional deficiency is associated with an increased risk of schizophrenia in adult life. *“Considerable evidence suggests a role for epigenetic changes,”* he states. Folate levels during early development in particular could play a critical role in the risk for major psychotic disorders.¹⁵



INTERVENING AT THE SOURCE

Researchers now have the tools to address much more complex and realistic questions about the development of psychopathy in young children. Some Canadian studies using data from the National Longitudinal Survey of Children and Youth (NLSCY) and the Québec Longitudinal Study of Child Development (QLSCD) have led to the first descriptions of the development of early childhood mental health problems. For example, one study in children 2 to 11 years of age found that those with atypically high physical aggression trajectories were more likely to be boys, from low income families, with mothers who had not completed high school and who reported using hostile or ineffective parenting strategies.¹⁶ Another looked at the early development of hyperactive symptoms in children from 2 to 7 years and found that maternal prenatal smoking, child male gender, maternal depression and hostile parenting were early predictors of high-level hyperactive symptoms.¹⁷ This knowledge can be used to better target prevention and in-

tervention efforts. For example, Sylvana Côté and her colleagues showed that children of mothers with low level education who went to day care before 9 months of age were less likely to have physical aggression problems during early childhood.¹⁸

Given mounting evidence of the importance of environment during the prenatal period and the child’s early years, it becomes imperative to begin interventions as early as possible. *“Risk-disorder associations are already well-established earlier in life than many ‘prevention’ programs begin,”* state Adrian Angold and Helen Link Egger, from the Duke University Medical Centre in Durham, North Carolina. *“If the hope is to prevent the onset of relatively common mental disorders (such as oppositional-defiant disorders or social phobia) in the first place, then we have largely missed the boat by age 2 or 3.”*¹⁴

Richard E. Tremblay notes that most experimental intervention studies target adolescents or pre-adolescents, in part because adolescents create more apparent social disruption than elementary school children or toddlers. However, *“all the early risk factors for disruptive behaviours suggest that early interventions should start as close as possible to conception, and continue supporting the family and the child as long as needed.”*¹⁶ Indeed, in a 2008 report, Canada’s Chief Public Health Officer¹⁹ stated that *“investments in families with children living in poverty and in early child development programs,”* should be a priority area for addressing both physical and mental health issues. 🦋

BY EVE KRAKOW

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SUPPORT TO FAMILIES CAN HELP CHILDREN FIGHT DEPRESSION AND ANXIETY



Even very young children can suffer from depression and anxiety. Identifying those at risk and supporting their mothers and families may go a long way to preventing disorders later in life.

Depressive and anxiety disorders are among the top 10 leading causes of disabilities and can be detected in early childhood. A recent study found that difficult infant temperament at 5 months of age and lifetime maternal depression are the two most important risk factors for atypically high levels of depressive and anxiety symptoms. It also showed that depression and anxiety tend to increase in frequency over the preschool years.

Researchers followed 1,759 children from 5 months to 5 years of age, born in the province of Québec in 1997-1998. The study is the first to map the development of depressive and anxiety symptoms from infancy to school entry (1½ to 5 years) using data from a large

representative population sample. It is also the first to identify risk factors for high levels of depression and anxiety in early childhood.

"People tend to be more concerned about aggressive children, because they create greater disturbance in day care," says Sylvana Côté, a researcher in the Department of Social and Preventive Medicine at the Université de Montréal, and one of the study's authors. "The overly anxious or sad child, who may be self-effacing and withdrawn, is not usually disruptive, and so doesn't attract the same attention."

Sylvana Côté notes that a certain level of depression and anxiety is normal. As children mature and become more aware of their environment and demands, they start expressing doubts, fears and sadness. *"But when children become so anxious, sad or fearful that they cannot function, then it is cause for concern."*

High levels of family dysfunction and maternal low sense of self-efficacy were also found to be risk factors. The researchers suggest that depressive and anxiety disorders in adolescence and adulthood may be prevented by helping mothers manage their depression and

"When children become so anxious, sad or fearful that they cannot function, then it is cause for concern."

sense of self-efficacy during pregnancy and early childhood, helping parents manage their infant's difficult temperament, and supporting dysfunctional families in early childhood.

Dr. Jaswant Guzder, Head of Child Psychiatry and Director of Child Day Treatment at the Jewish General Hospital, agrees. This study reinforces what she and her colleagues see in their everyday work. *"Attachment, the early child-parent relationship, is critical: it builds resilience and protective factors. Our dollars need to be spent targeting high-risk families. If environmental factors are at least 50% responsible for child outcomes, then let's look at what we can do to maximize the child's environment."*

She notes that infant visiting programs and prenatal interventions have been shown to have highly protective effects, particularly when they continue for three or four years. *"They put scaffolding in place in high-risk families, to build the infant-mother (or caregiver) relationship. They give the mother a chance to develop competence, skills, and knowledge about child development. Without these interventions, vulnerable infants don't stand a chance."*

Unfortunately, she says there is a huge gap between what practitioners and researchers know and public perception. *"In the preschool years, parents think their child will outgrow the problem. They do not seek services because of the stigma attached. But children do suffer from true disorders, which can be diagnosed and treated early in life,"* Dr. Guzder emphasizes. *"This study underlines that the social cost of not intervening is high."* 🦋

BY EVE KRAKOW

HOW CHILDHOOD ABUSE GETS UNDER THE SKIN

Early life environment can produce chemical changes in the genes that affect brain development, and these changes may help explain why abuse and neglect early in life results in a high risk for suicidal behaviour years later.

The first hint that epigenetics – or the effects of the environment on genes – could help explain mental health problems comes from pivotal animal research led by Michael Meaney and Moshe Szyf from McGill University. This research showed that rat pups who were licking and groomed more by their mothers had more receptors in the hippocampus for an important stress-regulating hormone known as glucocorticoid. The hippocampus is an area of the brain involved in the control of emotion.

FROM RATS TO HUMANS

To find out if similar mechanisms are at play in humans, Drs. Meaney and Szyf teamed up with Dr. Gustavo Turecki, also from McGill University, to examine the brains of suicide victims, comparing them with the brains of those who had died by other means. Individuals who were abused and/or neglected in childhood are at an increased risk for suicide later in life, so the investigators also conducted extensive research into the early life of their subjects, interviewing family and friends as well as studying any relevant police, medical or youth protection files, to see if they had a history of abuse or neglect.

"Individuals who died by suicide and were abused [or neglected] in childhood had decreased levels of expression of [the glucocorticoid receptor, or GR] gene in the hippocampus of their brains as compared to controls," says Dr. Turecki. These findings directly correlate with the animal studies, since the GR gene encodes for glucocorticoid receptor.

ABUSE AND NEGLECT "TURN OFF" THE GR GENE

The suicide victims with a history of abuse were found to have increased chemical changes, known as methylation, in a portion of the GR gene responsible for regulating its activity.



"For the first time in humans we were able to show what molecular mechanisms mediate the effects of early life abuse and neglect."

This methylation essentially "turned-off" the gene.

These results tie in well with other studies demonstrating that suicidal individuals often have a disruption in their hypothalamic-pituitary-adrenal (HPA) system. Glucocorticoid plays a starring role in this hormonal system which is involved in regulating stress.

"For the first time in humans we were able to show what molecular mechanisms mediate the effects of early life abuse and neglect," says Dr. Turecki. Research like this not only highlights the need to intervene early for children in abusive or neglectful environments, it also provides hints as to how to treat suicidal tendencies – perhaps future therapies could somehow reactivate the GR gene or otherwise help balance the HPA system.

According to Martin Alda, an expert in psychiatric genetics at Dalhousie, this research is groundbreaking. *"It is very critical for*

understanding elements of how environmental stressful life events influence brain function and behaviour... It raises a lot of provocative questions," he says, such as, what would happen if abused or neglected children received help early on?

ANIMAL STUDIES OFFER HOPE

Animal studies have shown that transferring rat pups from neglectful mothers to more nurturing foster mothers can undo some of the negative effects of early deprivation. Since the process by which the brain responds to neglect appears to be similar in both humans and rats, it remains an intriguing possibility that abused or neglected children might avoid some of the negative long-term consequences of their deprivation if their environments are improved in time. 🐭

BY ALISON PALKHIVALA

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