



## 2001-2008: EIGHT YEARS OF RECOGNIZING THE BEST OF ECD RESEARCH IN CANADA

# A TIME TO PAUSE, REFLECT AND PRAISE

BY MICHEL BOIVIN

This is the eighth edition of our annual *Bulletin* featuring the Top Ten best Early Childhood Development (ECD) research studies in Canada. Over the years, this list has featured a total of 80 scientific papers. The figure below shows the distribution of authors among Canadian research institutions. McGill University (with at least one author on 25 of the 80 articles) and the University of Toronto (24) come in first and second, respectively. McMaster University (16), the Université de Montréal (11) and the University of British Columbia (9) join them in the top five positions. Top-level ECD research is actually being conducted in all regions of Canada: Queen's University, the University of Manitoba, the University of Ottawa and Simon Fraser University have all entered the ranking this year.

This sample of 80 papers over eight years gives a very good idea of Canada's standing in terms of world-class excellence in ECD research. The yearly compilation of Top Ten statistics provides a unique standpoint for analyzing trends in ECD research in Canada. Overall, ECD research is strong, diversified and increasingly characterized by interdisciplinary and international collaborations. Each year brings its unique mix of biomedical, epidemiological and developmental research on population health issues (see article on Page 2). This year is no exception.

Over the years, genetic research has consistently shown a strong presence (see October 2005 *Bulletin*<sup>1</sup>). In this year's edition, one paper highlights the disruption of genomic imprinting as a possible mechanism underlying both autism spectrum disorder and psychotic disorders. Another study shows that adverse

environmental conditions supersede genetic influence on early physiological reaction to novelty.

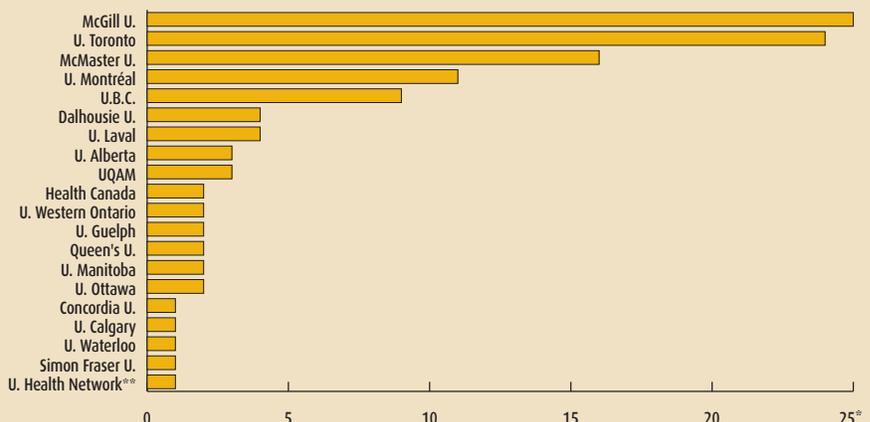
As is often the case, some studies clarify issues of clinical relevance for ECD using more robust scientific methods. Such studies abound in this year's edition. Through sophisticated 3-D scans, one study found an association between asymmetric growth of the face and autism spectrum disorder. Two studies confirmed the benefits of taking medication for controlling asthma and depression during pregnancy. Asthma was also targeted in a study exploring its link with developing a fever very early in life. One study showed that hypother-

mia has no positive effect, and could even have negative consequences, when used to treat severe traumatic brain injury in children. Another international study used a combination of randomized and longitudinal designs to confirm in a large sample that breastfeeding leads to higher cognitive abilities in children. A longitudinal survey was used to describe the early development of peer victimization. Studies may also expand our general knowledge of cognitive capacities in infants, as it has been shown that they intuitively understand statistical math concepts without teaching.

These studies all manifest excellence in various ways: strong designs, large sample sizes, innovative methods, sound theorizing and relevance. They deserve to be celebrated for their scientific breakthroughs. The Strategic Knowledge Cluster on Early Child Development is proud to be associated with this initiative. 🌟

1. Tremblay RE. Canadian ECD research in 2004: Is there a world beyond genetics?. *Bulletin of the Centre of Excellence for Early Childhood Development* 2005;4(2):1. Available at: <http://www.excellence-earlychildhood.ca/documents/BulletinVol4No2Oct05ANG.pdf>. Accessed December 21, 2009.

## 2001-2008 TOP 80 PAPERS



\* Number of papers with at least one author from a Canadian institution.

\*\* U. Health Network : Toronto General Hospital, Toronto Western Hospital and Princess Margaret Hospital.

# CANADA'S INTERNATIONAL ECD LEADERS

**Each year for the past eight years, the Centre of Excellence for Early Childhood Development (CEECD) has selected the 10 best international research papers on early childhood development (ECD) by Canadian authors, gathering over the years a valuable overview of Canada's international contribution to the field.**

To be selected, studies had to be published in the journals most frequently cited as sources by researchers around the world. The authors of the 80 papers selected from 2001 to 2008 were primarily from McGill University, followed by University of Toronto, McMaster University and Université de Montréal (see graph on Page 1).

McGill's prevalence is in part due to the two researchers whose papers were the most frequently selected among all Canadian investigators over the last eight years: Michael S. Kramer made the Top Ten with seven papers while Michael J. Meaney had six Top Ten papers. The papers which Dr. Kramer co-authored were based on experimental and epidemiological studies reporting on pregnancy, induction of labour, breastfeeding, use of pacifiers, infant mortality, allergies, asthma, cognitive development and myocardial infarction. Dr. Meaney's co-authored papers reported on experimental research to understand long-term effects of maternal care, in rats and humans, on gene expression, stress reactivity, cognitive development, and dopamine response. Richard E. Tremblay, a Université de Montréal investigator, was the third most frequent researcher profiled, with five Top Ten papers. His co-authored publications reported on early childhood determinants of stress reactivity, development of physical aggression, peer victimization, and gang membership during adolescence.

Seven other prominent Canadian researchers have appeared in the Top Ten *Bulletin* three times each. Four of these published reports on premature babies: Arne Ohlsson (University of Toronto), Robin S. Roberts

(McMaster University), Charlene Robertson (Glenrose Rehabilitation Hospital, Edmonton) and Barbara Schmidt (McMaster University). Three others published studies about genetics, stress, aggression, early peer relation difficulties, and asthma: Cathy L. Barr (University of Toronto), Michel Boivin (Université Laval), and Malcolm R. Sears (McMaster University).

"Canada leads the world in the area of population health of mothers and babies," says Michael S. Kramer, when asked about trends in ECD over the past eight years. He cited a cultural tendency towards globalism as part of the reason. "I grew up in the States, and when I came to Canada in 1978, I noticed a difference. People in the States are usually quite inward-looking. In Canada, there was a lot more in the news about the rest of the world. That gave me an edge."

For his part, Meaney identifies leaders like Fraser Mustard, competition with the United States, a collaborative culture, and universal health care as keys to his success. "The most important advantage is that we operate in a public health system, and that makes it easier to collect data," he says. "There's a shared set of values in Canada that understand that there's a direct link between healthy children, healthy families and a healthy economy."

ECD researchers are starting to understand the importance of multidisciplinary research, says Richard E. Tremblay. "The fields that are studying human development have realized over time that they need each other to tell a better story. This is especially true for those who try to understand the rapid growth between conception and the first few years after birth. We are starting to understand that the

***"Canada leads the world in the area of population health of mothers and babies."***

*environment impacts biological development from the start; that this impact has long term consequence on how we adapt to our environment, and how our environment reacts to our behaviour. Nature and nurture are working together and investigators need to work together to understand how to help when things go wrong."* 🦋

**BY THE CENTRE OF EXCELLENCE FOR EARLY CHILDHOOD DEVELOPMENT,  
INTERVIEWS BY TRACEY ARIAL**

# BREASTFEEDING IMPROVES INTELLECTUAL DEVELOPMENT

**A program that encouraged mothers to breastfeed exclusively for at least four months and to continue breastfeeding, at least partially, for a year resulted in children with higher IQs. Once these children entered school, their teachers reported stronger aptitudes for reading and writing than for their peers.**

Those are the important results that Michael S. Kramer and his colleagues found after seven years of research and another three years of statistical analysis. Their study, known as the "Promotion of Breastfeeding Intervention Trial" (PROBIT), included 17,046 mother and baby pairs from 31 maternity hospitals and clinics in the Republic of Belarus. It is the largest randomized trial about breastfeeding ever conducted.

*"What's important about this study is that we figured out a way to separate the effects of breastfeeding from the different types of women, environments and cultural influences,"* says Kramer. *"It is less likely that children who were breastfed as babies will have intellectual problems."*

The study compared the babies of mothers who took part in a program designed to promote longer exclusive breastfeeding (the experimental group) with the babies of mothers who were not influenced in any way (the control group). All the mothers were of similar age, education and family history and had chosen to breastfeed before the study began.

Almost half (43%) of the women in hospitals that offered the program chose to exclusively breastfeed their babies until they reached three months old. Only 6% of those in hospitals without the program chose similar actions. After a year, almost 20% of the mothers in the experimental group were still breastfeeding, while only 11% of their peers were still doing so.

A total of 13,889 of the children were followed up to age six and a half. The children received pediatric exams plus verbal and

performance IQ tests when they were old enough. Once the children started school, their teachers were asked to rate their performance in reading, writing and mathematics. On average, the children in the experimental group had higher verbal IQ scores and higher teacher ratings in reading and writing tests than those in the control group. This follow-up was funded by the Canadian Institutes of Health Research.

*"This article is really important because it's the first randomized study of its type,"* says Suzanne Dionne, a physician in Granby, Quebec, who is frequently asked to assist mothers struggling to breastfeed their infants. *"Those we've been relying on in the past were observational studies, so they weren't as strong. This study will be used in our family program and it should be used in the training of physicians."*

What the study can't tell us, however, is which of the three benefits of breastfeeding have the largest impact on cognitive development: the milk itself, skin-to-skin contact or the verbal contact between the mother and baby. *"One in four women struggles to breastfeed at first,"* explains Dionne. *"A mother who is breastfeeding exclusively at three months can easily continue up to six months, so I use the results of this study to encourage her to do so. For women who are struggling too much and want to stop, I tell*



***"It is less likely that children who were breastfed as babies will have intellectual problems."***

*them: go ahead and switch to formula if you have to; but hold your baby in your arms, next to your bare skin and talk as though you were actually breastfeeding." ❦*

BY TRACEY ARIAL

Ref.: Kramer MS, Aboud F, Mironova E, Vanilovich I, Platt RW, Matush L, Igumnov S, Fombonne E, Bogdanovich N, Ducruet T, Collet JP, Chalmers B, Hodnett E, Davidovszky S, Skugarevsky O, Trofimovich O, Kozlova L, Shapiro S. Breastfeeding and child cognitive development: New evidence from a large randomized trial. *Archives of General Psychiatry* 2008;65(5):578-584.

# IDENTIFYING VICTIMS OF BULLYING BEFORE SCHOOL

**After eight years of follow-up, an international group of researchers found that preschool children who are frequent targets of their peers' aggression tended to display high levels of physical aggression and to experience high levels of harsh parenting as early as 17 months after birth.**

Researchers found that children described as physically aggressive by their mothers when they were 17 months old were likely to be bullied by their peers later on. Harsh reactive parenting and a low family income increased the risk that such victimization would become chronic.

*"We know from looking at other studies that aggressive children tend to be victimized in*

*the early grades," says team leader and author Michel Boivin. "What's new now is that we assessed it early on. The experiences you have with your peers in early childhood can be painful and they predict for similar experiences in the early grades of school."*

To conduct their study, researchers contacted the families of a randomly selected group of children born in Quebec between October 1997 and 1998. Of this group, 1,970 children were assessed at four and a half months of age and then every year thereafter for the next seven years. Mothers were asked whether their children were teased, hit, pushed or called names by other children and whether their children bit, hit, kicked, fought or bullied others. Hyperactive, impulsive and inattentive behaviours were also recorded, as were unhappy, fearful, nervous, worried or upset moods. Mothers were also asked about their parenting

skills and how often they became angry, raised their voices or spanked their children.

After the children started school, teachers and the children themselves were asked similar questions. Children were also asked whether other children at school bullied them, said bad things about them behind their back or left them out of games.

By analyzing the answers to these questions, Boivin and his colleagues identified three clear pathways of peer victimization. Most children (71%) followed a low/increasing trajectory of victimization, while 25% were on a moderate/increasing path and 4% were somewhere along a high/chronic trajectory. By first grade, teachers described children in the moderate and high-risk groups as more highly victimized by their peers, which indicates some continuity in the negative nature of their peer experiences. Children in families with insufficient income or who were raised by a mother using a harsh parenting style were more likely to fall within the high/chronic group. Because of this, researchers recommend that parents be trained not to use these punitive parenting behaviours and to help these at-risk children find positive ways of relating to people while they're young.

Joanne Cummings, the partnership director of PREVNet, a national network of people dedicated to stopping bullying, concurs. *"We already have good parent management training programs, but parents of such young children aren't usually referred for treatment," she says. "This study provides strong evidence that children who exhibit high levels of aggression at an early age are at substantial risk for victimization by their peers. Sadly, the experience of harsh parenting and then peer victimization leads these kids to believe that people will not be good to them."*

Parents can change that cycle, says Cummings. *"For most kids, average parenting skills are good enough. For other kids, parents need extra training in order to enjoy their relationships with their children and decrease aggression."* 🐾

BY TRACEY ARIAL

***"Children who exhibit high levels of aggression at an early age are at substantial risk for victimization by their peers."***



# STRESS RESPONSE IN EARLY CHILDHOOD: WHO'S RESPONSIBLE?

**Early childhood is a vulnerable period when it comes to developing a healthy physiological response to stress. In adverse family situations, environment has been found to play an even greater role in stress response than genetics. These findings have important public policy and societal implications and raise important questions for future research.**

The effect of the environment on gene expression, a process known as epigenetics, "is thought to be both stable and reversible," says lead investigator Isabelle Ouellet-Morin. "This makes it a good target for studying the early influence of adverse environments on development and ... to eventually think of reversing this long-term cost in some children." She conducted the research while a PhD student at the Université Laval. Today she is at King's College London in the United Kingdom.

## MEASURING A PHYSIOLOGICAL RESPONSE TO STRESS

Ouellet-Morin and her colleagues measured levels of the stress hormone cortisol in the saliva of 346 19-month-old twins living in Quebec. Some of the twins were fraternal, meaning they shared 50% of their genes, while the others were identical, meaning they shared 100% of their genes. Cortisol measurements were taken both before and after they were presented with an unfamiliar (i.e., stressful) situation. The resulting changes in cortisol are an approximate measurement of the children's physical stress reaction.

The researchers also assessed the degree of family adversity faced by these children and looked at whether their physical reaction to the stress of the unfamiliar situation was affected by the amount of adversity in their family. Family adversity included stresses faced by the children while still in the womb, such as their mothers smoking during pregnancy, as well as stresses they faced after they were born, such as low family income or educational levels and hostile reactions from mothers.



***"Family adversity and multiple stress factors when children are young have an impact that's likely to influence their life course."***

## FAMILY ADVERSITY AFFECTS THE STRESS RESPONSE

The researchers next analyzed their findings to determine the degree to which genetics and/or the environment influenced the children's physical response to stress. They found that among children with a low family adversity background, both environment and genetics played a role. But among those with a high degree of family adversity, environment was the key factor in the stress response.

"The genetic differences tend to pale in comparison to the impact of environment when familial adversity is higher. In other words, stressful environments trump genetic influences," says Janice MacAulay of the Canadian Association of Family Resource Programs. "This means family adversity and multiple stress factors when children are young have an impact

that's likely to influence their life course. This is important in terms of provision of programs and services in this country because every child deserves a good beginning."

"Early adverse environments affect cortisol response to novelty, a change that may remain unnoticeable at the behavioural or cognitive levels for years, but nevertheless could increase the risk for these growing children to suffer from mental and physical pathologies later in life," says Ouellet-Morin. Still, she recommends prudence when it comes to drawing conclusions on the impact of this study, since it does not tell us which specific interventions aimed at helping families with young children will actually have an impact. That's clearly an important question for future research. 🦋

BY ALISON PALKHIVALA

# PREGNANT WOMEN BEING TREATED FOR DEPRESSION CAN HEAVE A COLLECTIVE SIGH OF RELIEF

**If you are pregnant and suffering from depression, take your medication. Recent chilling evidence that taking the antidepressant paroxetine during pregnancy may increase the risk of heart defects appears to be unfounded, according to a newer and better designed study.**

## INITIAL PANIC WITH PAXIL

The panic started when GlaxoSmithKline, the manufacturers of paroxetine under the trade name Paxil, reviewed their databases and found a two-fold increased rate of heart defects among babies whose mothers had been prescribed the drug. But in a prescription database study like that one, it is impossible to tell who actually took their medication. *"Too often women stop their treatment abruptly when they find out they are pregnant, which can lead to a quick relapse of symptoms, possibly leading to adverse effects on the fetus,"* says Alicja D. Fishell, MD, FRCPC, an expert in women's health, psychiatry and pharmacology at the University of Toronto.

## BETTER DESIGNED RESEARCH FINDS FEARS UNFOUNDED

To evaluate this potential risk more rigorously, Adrienne Einarson, RN, of the Motherisk Program at the Hospital for Sick Children in Toronto, and her team obtained health information on 1,174 babies born to mothers around the world who were taking paroxetine during the first trimester of their pregnancy, when the fetus's heart is developing. The outcomes of women taking paroxetine during pregnancy were then compared against the outcomes of an equal number of pregnant women who had not taken paroxetine and were not depressed.

They also evaluated 2,061 published cases of babies whose mothers took paroxetine during pregnancy and obtained more detailed information about the nature of each case.

The rate of heart defects was the same among women who had and had not taken paroxetine: 0.7%. This is on par with the general rate of heart defects in newborns. *"In every pregnancy, about 1 in 100 babies are*

*going to have heart defects,"* says Einarson. *"That's nature."*

## WHY THE DIFFERENCE?

Why the conflicting result? *"Regrettably, studies on first trimester exposure to paroxetine or other antidepressants have a high degree of heterogeneity when it comes to methods used,"* says Fishell. *"This leads to conflicting results, even if some of the studies' designs are similar. This is the largest prospective controlled study [conducted on this topic]."* It is also unique in that it directly confirmed at the time that the women in the paroxetine group were actually taking the drug and that the infants identified as having heart defects really had these defects. Other studies have relied on people's memories of past events.

*"Because of this study's [rigorous] design and the fact that the results are so reassuring, it is a helpful tool in discussions with women and partners who are weighing the risk/benefit of treatment of severe depression or anxiety disorders with paroxetine during pregnancy,"* says Fishell.

That's Einarson's key goal. *"We do this research here at Motherisk so that people can make an evidence-based decision about whether they are going to take these drugs in pregnancy or not. That is the bottom line for us."*

The bottom line for pregnant women? *"There's no evidence to date that taking antidepressants in pregnancy increases the risk for birth defects, including heart defects,"* says Einarson. *"In fact, recently it's being found that being depressed during pregnancy and in the postpartum period may actually have its own adverse effects." ❧*

BY ALISON PALKHIVALA



***"There's no evidence to date that taking antidepressants in pregnancy increases the risk for birth defects."***

Ref.: Einarson A, Pistelli A, Desantis M, Malm H, Paulus WD, Panchaud A, Kennedy D, Einarson TR, Koren G. Evaluation of the risk of congenital cardiovascular defects associated with use of paroxetine during pregnancy. *American Journal of Psychiatry* 2008;165(6):749-752.

# PREGNANT WOMEN NEED TO CONTROL ASTHMA

**Many pregnant women with asthma worry that by taking medication they will harm their babies. They can be informed that the effects of uncontrolled asthma attacks during the first three months of pregnancy are significantly worse. So says a new study by researcher Lucie Blais and her research assistant Amélie Forget, both affiliated with Sacré-Coeur Hospital and the Université de Montréal.**

**"T**here are a few beliefs written in the clinical guidelines saying that it is better to control asthma than to avoid medication, but there was not a lot of scientific evidence to show that that was the case," says Blais. "There is ambivalence about treating pregnant women and knowing that there is a risk of congenital malformation in the child because of the medication, but not having asthma under control is also bad for the fetus."

To find out how bad uncontrolled asthma might be, the researchers decided to compare what happens to asthmatic women in the first trimester of their pregnancies, when their fetuses are growing very fast, with the condition of their babies when born. They wanted to find out whether asthma attacks suffered by a mother at this time would also hurt a baby, and to what extent. They also wondered how such risks compare with the risks of the medications themselves, which have been shown to cause birth defects, such as cleft lips and palates.

Using three Canadian databases of women who gave birth in Quebec between 1990 and 2000, they identified 3,477 pregnant women between 13 and 45 years of age with asthma who delivered during that period. Information about prescriptions, medical visits and diagnoses for the year prior to, during and after each pregnancy provided information about the mothers' health. Hospital and medical services data covering the first year of the babies' lives provided glimpses into the prevalence and severity of birth defects, such as heart and lung damage, circulatory and respiratory system issues, cleft lips and palates, spina bifida and eye, ear, face and neck deformities.

Of the 4,344 babies studied, 398 (9.2%) were diagnosed with at least one birth defect. There were 321 women who had an asthma attack severe enough to require the use of oral steroid hormones, hospitalization, a visit to an emergency department or a combination of all three during the first trimester. Women with such asthma attacks were 48% more likely to have a baby with a birth defect compared to women who did not have an attack during the first trimester.

The risk doubled for women who had an asthma attack and yet took no oral steroid hormones throughout their pregnancies. Researchers also found that women with lower levels of education, multiple pregnancies or epilepsy were more likely to have babies with birth defects than women without such risk factors.

***"Poor control of asthma during pregnancy leading to asthma exacerbations is much more harmful than the medications used for treating asthma."***

*"This paper is particularly important, not only for clinicians who are treating pregnant asthmatic women, but also for pregnant asthmatic women themselves,"* says Catherine Lemière, a respiratory physician at Sacré-Coeur Hospital and a former chairperson of the Canadian Thoracic Society's Asthma Committee. *"Women are often reluctant to take any treatment during their pregnancy for fear of harming the fetus. This paper shows that poor control of asthma during pregnancy leading to asthma exacerbations is much more harmful than the medications used for treating asthma."* 🐾

BY TRACEY ARIAL



## EARLY LIFE EXPERIENCES AND ASTHMA RISK

**The increasing prevalence of asthma in the developed world continues to confound health experts. Many theorize that something about our environment, such as exposure to too few germs due to our overemphasis on hygiene, affects the immune systems of young babies, making them highly sensitive to allergic responses.**



**A** clue into the impact of environment on asthma risk was provided by recent research showing that developing a fever during a specific period very early in life was associated with a reduced risk of developing asthma later on. This finding spurred Anita Kozyrskyj and her colleagues at the University of Manitoba to look at the timing of vaccinations, which can themselves produce a fever as a side effect, on asthma development.

The research, led by Kozyrskyj's graduate student Kara L. McDonald, was an analysis of 13,980 children born in 1995 in Manitoba for whom complete health care and vaccination information was available through to age seven. Specifically, the investigators looked at the association between the timing of the children's DTP vaccine and the later development of asthma. DTP protects against diphtheria, tetanus and pertussis (also known as whooping cough). It's worth noting that this particular vaccine is no longer used, as cellular pertussis has been replaced by acellular pertussis in the DTaP vaccine.

Among over 11,500 children who received at least four of the five standard doses of the DTP vaccine, *"the likelihood of developing asthma at age seven was reduced by half if the first dose of DTP was delayed more than two*

*"Developing a fever during a specific period very early in life was associated with a reduced risk of developing asthma later on."*

*months,"* says Kozyrskyj. *"The first dose is given at two months of age, usually, so the delayed dose would have been given at more than four months of age."* Delaying later doses may have had an effect too, but the timing of the first dose appeared to have the most impact.

### SHIFTING AWAY FROM AN ALLERGIC IMMUNE RESPONSE

To understand what this might mean for asthma development, it is important to know a little bit about the immune system. It can produce two main types of response, known as TH1 and TH2. TH2 immunity is dominant after birth and is associated with classic allergy symptoms, such as hay fever, itchy skin rashes and asthma. The first year of life is a critical period for balancing out the TH1 and TH2 response, so events during this time period, such as fever induction of TH1 immunity, can affect it. The DTP vaccine may actually reduce the risk of asthma by promoting a shift from a TH2 to a TH1 type of immune response, due to fever caused by the pertussis vaccine or by some other mechanism.

### NO INFORMATION ON WHETHER OR NOT TO VACCINATE

Don't be tempted to overanalyze the findings of this study, however. Fever is a common reason to delay vaccination and may be the reason for the reduced asthma risk, rather than the vaccine itself. Also, the DTaP vaccine currently used is different from the one studied, *"so these findings don't have any direct application to the current immunization protocol,"* says Kozyrskyj. More importantly, this study did not compare children who had been vaccinated with those who had not, so it has nothing to say about whether vaccination versus no vaccination affects asthma rates. Kozyrskyj does point out, however, that the risk of developing potentially deadly diphtheria, tetanus or pertussis is very real among children who are not vaccinated or whose vaccinations are delayed. 🦋

BY ALISON PALKHIVALA

# EXTREME COOLING WORSENS TRAUMATIC BRAIN INJURIES IN CHILDREN

**Using hypothermia for 24 hours to treat severe traumatic brain injury in children doesn't work. It doesn't improve their condition and may even contribute to their death.**

That's the devastating conclusion of a recent study by researchers affiliated with 17 hospitals across Canada, France and the United Kingdom. "That was a big surprise to us and it was discouraging," says study collaborator Jacques Lacroix, a pediatrician who runs the Health Outcomes theme for the CHU Sainte-Justine Research Center in Montreal. "We did this because we truly believed that it would work. We thought that it would be successful."

Compelling animal studies led researchers to believe that cooling a patient's body temperature to a hypothermic level (32.5 degrees Celsius) would work if it were done quickly after the trauma and for a period of 24 hours. So they set up a five-year study of children between one and 17 years old with severe brain injury. They also ensured that all study patients were treated within eight hours of trauma.

Of the 1,441 brain-injured patients who arrived at the participating hospitals between February 1999 and October 2004, a total of 225 children met the study eligibility criteria and received parental consent to participate in time. A centralized telephone system enabled researchers to randomly place the subjects into the experimental or control group. Children in the experimental group were cooled to 32.5 degrees Celsius, while those in the control group were cooled to a normal body temperature of 37 degrees Celsius.

After 24 hours, the body temperatures of the children in the experimental group were raised to normal levels. During this period, several children had to be treated for low blood pressure or because blood circulation through their bodies and brains was less efficient than usual.



The study continued for a period of at least six months after each child's injuries. Unfortunately, 23 children in the experimental group and 14 in the control group died. Nine patients in each group suffered severe disabilities or stayed in vegetative comas. The children who had recovered from their brain injuries and could communicate were psychologically assessed three and 12 months after their accidents. Researchers found that children who had been treated with hypothermia remembered significantly less than those in the control group.

These results, combined with a higher mortality rate and re-warming side effects, led researchers to recommend against 24-hour hypothermia treatment for children with severe traumatic head injury.

"We now know that we don't want to lower the body temperature of our patients to a level of hypothermia," says Claude Mercier, a neurosurgeon at CHU Sainte-Justine. "We are go-

***"We are going back to our traditional way of treating our head trauma patients."***

*ing back to our traditional way of treating our head trauma patients. Before the study, we were never taking account of body temperature in the measurement of the outcome, but we were trying to keep it as normal as possible. We have stopped using hypothermia."*

BY TRACEY ARIAL

# ARE AUTISM AND PSYCHOSIS POLAR OPPOSITES?

**A comprehensive analysis of research in the areas of genetics, physiology, neurology and psychology suggests that autism spectrum disorders and psychotic disorders reflect opposites in the continuum of how individuals function within a social environment. These findings have implications both for treatment and for how these disorders will be viewed and studied in the future.**

## DISRUPTED GENETIC IMPRINTING

Everyone inherits one set of genes from their mother and another from their father. In most cases, both pairs of genes are expressed to produce specific traits, such as the exact shape and size of your nose, but in a few cases, only the mother's or father's gene is active when it is passed onto their offspring. A genetic "tug-of-war" during development helps determine which of the mother's and father's genes are expressed and suppressed. This process is known as genomic imprinting.

A disruption in genomic imprinting and other genetic processes may be at the heart of psychiatric disorders such as autism spectrum disorders and psychosis. Research by Bernard J. Crespi and his team from Simon Fraser University suggests that autism spectrum disorders come about when expression of the father's genes is favoured, while psychotic conditions (including schizophrenia, bipolar disorder and major depression) come about when the mother's genes are favoured. Exactly how this unbalanced expression of genes occurs is still a mystery.

## OPPOSITES IN SOCIAL COGNITION

For these conditions, the key disruption appears to be in the area of social cognition, or the way in which we think and feel about ourselves in relation to the people around us. *"Our research provides broad and deep forms of evidence, from genetics through physiology and morphology to psychology, that autism represents a mental condition that is 'opposite' to psychotic-affective conditions, with normality in*

*the centre,"* says Crespi. *"Thus, in autism, social-cognition traits are under-developed, and in psychotic-affective conditions, social-cognition traits are hyper-developed to dysfunction."*

Examples of these opposite effects, he says, *"include a lack of speech in severe autism vs. auditory hallucination in schizophrenia, and a reduced sense of self in autism vs. megalomania (delusions of grandeur) in schizophrenia."*

## IMPLICATIONS

These findings have important implications for treatment. If a certain drug helps treat psychotic disorders, then a drug with an opposite effect might help those with autism disorders. Research in this area is already ongoing.

Another important component of this research is the way it encourages clinical experts in autism and psychotic disorders to look at these conditions in a new light, says Lisa Goos, an expert on the influence of genomic imprinting on cognition and behaviour at Baycrest

in Toronto. *"This study combines evolutionary theory, novel genetic mechanisms and cognitive psychology in the study of autism and psychosis,"* she says. *"This combined approach is necessary to really understand what is going on in these conditions."*

*"In psychiatric conditions such as autism or psychosis, looking for a single gene or set of genes that always cause the condition will not be successful due to the complexity of the disorder and the wide variety of contributing factors,"* says Goos. *"The lesson of genomic imprinting is that genes from your mother and father aren't equivalent—they don't necessarily function the same when they combine in a new human body. Crespi's study is valuable because it attempts to take this novel process into account, which most people interested in the biological bases (including genetic bases) of disorders often do not do."* 🐾

BY ALISON PALKHIVALA



***"In autism, social-cognition traits are under-developed, and in psychotic-affective conditions, social-cognition traits are hyper-developed to dysfunction."***

# TAKING AUTISM AT FACE VALUE

**Can examining the face provide insight into autism? Perhaps. A consortium of researchers from Canada and the UK are using sophisticated technology to create and analyze detailed 3-D maps of faces of those with and without autism.**

The facial analysis, led by Professor Peter Hammond of the UCL Institute of Child Health in London, offers clues into when the physical processes that lead to autism develop and how the condition might be identified early on. "Because we are interested in heritable genetic factors contributing to autism, we studied families in which several family members had an Autism Spectrum Disorder (ASD)," says Cynthia Forster-Gibson, a collaborator in the research from Queen's University. "In these families, we expect that some family members will have a genetic predisposition that increases their likelihood of having an ASD."

## MORPHOMETRIC ANALYSIS OF THE FACE SHOWS SUBTLE CHANGES IN ASD

The researchers used a special camera to capture 3-D images of the face and a technique called dense surface modelling to compare the face shape of 72 boys with ASD, 128 of their first-degree relatives and 254 unrelated individuals who had not been diagnosed with ASD. "In the boys with autism, we found that there was a very subtle right dominant facial asymmetry, most apparent above the eye and in front of the frontal pole of the underlying brain," says Forster-Gibson. "This was not visible to the naked eye. We think the asymmetric growth of the face could occur in response to the asymmetric growth of the brain underneath, or that the asymmetric growth could occur in parallel. Either situation would be influenced by genetic factors."

Martha Herbert, an expert in morphometric analysis from Harvard Medical School and Massachusetts General Hospital in Boston, was impressed with this study and the technology involved. She and her team have demonstrated differences in the volume of various parts of

the brain among individuals with and without ASD as well as with developmental language disorders. The current research builds on their findings.

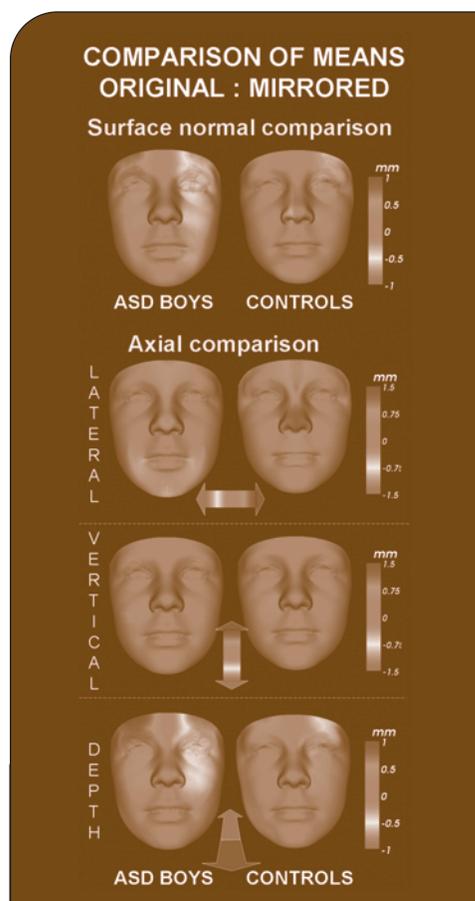
## INSIGHT INTO WHEN TROUBLE STARTS

Forster-Gibson and colleagues conclude that, since facial development occurs during development of the embryo and fetus, their research suggests that the underlying causes of ASD may also occur in that stage. Herbert goes even further. "The literature in autism is showing increases in brain volume that occur rapidly in the first two years after birth, and there does seem to be some relationship between brain volume and the size of the face," she says. So, abnormal brain growth even after birth may also be producing some of the subtle changes picked up by Forster-Gibson's team. In other words, the physiologic mechanisms associated with the development of ASD may occur during fetal development, soon after birth, or both. Teasing this out is important because once it is possible to pinpoint when the problems start to occur, it may be possible to develop interventions that prevent problems from emerging.

## POTENTIAL FOR EARLY DIAGNOSIS

Another exciting implication of these findings is that, with further research, facial scanning could contribute to early diagnosis of autism. "Because we know that many children with ASD benefit from early therapy, we would like to find a way to help to identify children at risk of ASD at the earliest age possible." That is not yet possible with current technology, however. 🐼

BY ALISON PALKHIVALA



*"The physiologic mechanisms associated with the development of ASD may occur during fetal development, soon after birth, or both."*

# MATH COMES EASILY TO BABIES

## Eight-month-old babies intuitively understand statistical math concepts without explicit teaching.

Researchers at the University of British Columbia set up six different experiments to compare the numerical intuition of infants with that of adults. They found that babies share adult abilities to predict information about large populations from small samples, and vice versa.

Such intuitive statistical ability seems to develop in babies at about the age of eight months, says lead researcher Fei Xu. *"When we conducted our experiments on six-month-old*

*babies, they did not perform well. By the time they reached eight months old, most of them were just as capable of rational thinking as the adults were."*

To test the ability of both babies and adults, researchers set up a series of magic shows in which actors manipulated coloured ping pong balls in surprising and predictable ways. In one test, for example, participants were shown the interiors of two boxes. One box contained lots of red balls interspersed with a few white balls, while in the other were white balls interspersed with red. The actor then pulled five ping pong balls out of each of the boxes. Four red balls and one white ball coming from the box containing more red balls would be predictable. The opposite was a surprise.

Sixteen adults rated the predictability of

each case on a scale of one to seven. Then, 20 seven-and-a-half to eight-and-a-half month-old infants watched the show. The length of time they looked at each case was recorded with video cameras. Researchers found that babies' reactions matched parent ratings in that babies looked significantly longer at unexpected situations.

*"Our findings were quite surprising, which is why we kept replicating experiments to make sure that they were robust," says Xu. "We hope these ideas will inform parents about their infants' natural learning abilities. Children are not afraid of math. They like numbers. They like thinking about simple calculations. That's important for our society to know."*

BY TRACEY ARIAL

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## BULLETIN

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