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FROM GENES TO CHILD CARE: TOP TEN STUDIES ON ECD FOR 2007

BY RAY PETERS, Professor Emeritus of Psychology at Queen's University, Director of Research for the Better Beginnings, Better Futures Longitudinal Study, and CEECD Directing Committee Member

For the seventh consecutive year, the Centre of Excellence for Early Childhood Development (CEECD) has selected the best research studies on early childhood development (ECD) involving at least one researcher from a Canadian institution.

A panel of judges from CEECD committees[1] selected the Top Ten from a larger group of studies on ECD published in the leading scientific journals in 2007. The studies in this year's *Bulletin*, titled "From Genes to Child Care," reflect the broad range of influences on early childhood development.

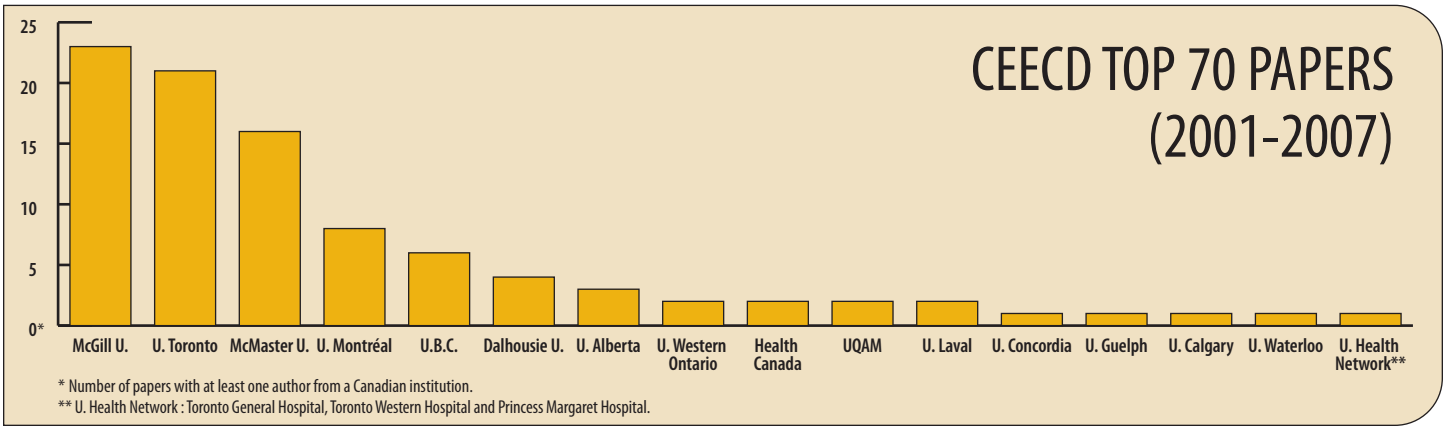
Two of the studies examine genetic structure and development, two examine outcomes associated with low birth weight babies and two involve problems associated with severe developmental delay. It is interesting that two more selected studies reported no effects on some aspects of early childhood development: mother's use of antidepressant medication during pregnancy was not associated with major birth defects, and early breast-feeding was not related to fewer allergies and asthma at age 6. A study of differences in unilingual and bilingual infants' ability to distinguish between spoken English or French, using visual cues, and a study of infant day care complete the Top Ten. It's a virtual tour de force in determining the factors influencing young children's development.

Topping the 2007 list was the study of effects associated with infant day care by the *Université de Montréal*'s Sylvana Côté and a team of colleagues. Results of this 5 year longitudinal study carried out on a large sample of children and their families who live in Quebec can be seen as yielding both good news and bad news. The good news is that use of nonmaternal infant care prior to the age of 9 months was associated with a reduction of later physical aggression in high-risk children, defined as those whose mothers had not completed high school and had a history of behaviour problems and depression in their adolescence. There were no similar effects of infant care for children of mothers with better education. The bad news was that many poorly educated mothers did not use the available infant and day care provided by the Quebec government, as most did not work outside the home.

The Côté study provides an excellent example of how high quality research can influence future research and inform public policy. As an example of the former, *Université Laval* professor George Tarabulsy used Côté's findings to design a study to determine whether active encouragement of infant care use for high risk mothers can be effective. On the political front, the positive effects associated with infant care use have important implications for policy makers in an area that remains highly controversial in Canada.

Over the years, our annual Top Ten has generated a total of 70 scientific papers. The figure at the bottom of the page shows the distribution of authors among Canadian research institutions. McGill University had at least one author on 23 of the 70 articles, the University of Toronto 21, and McMaster University had 16. A sample of 70 over seven years gives a very good idea of where world class excellence in ECD research can be found in Canada.

1. Centre of Excellence for Early Childhood Development. *Bulletin* of the Centre of Excellence for Early Childhood Development. Montréal, Québec: Centre of Excellence for Early Childhood Development; 2001-2007. Available at : http://www.excellence-jeunes enfants.ca/structure.asp?lang=EN. Accessed 09/15/08



STUDYING INFANTS
TO IMPROVE THE LIVES OF FAMILIES

Identifying at-risk children to help them develop beyond dysfunctional family environments has brought Sylvana Côté international recognition. The publication of a paper in the best psychiatry journal last year[1] confirms the importance of her work for the early prevention of mental health problems.

"When low education comes together with family dysfunction and low levels of stimulation in the home, future problems are born."

In the early years of Côté's career, high-profile research about conduct disorder in teens and differences in gender attracted substantial attention, as has her current research about the effect of public day care.

Since completing a psychology degree at McGill University in 1994, Côté has obtained a master's in clinical psychology from *Université Laval*, a doctorate from the *Université de Montréal*, a postdoctoral fellowship at Carnegie Mellon University in Pittsburgh and the *Belle van Zuylen* chair at Utrecht University in the Netherlands. She is now a professor at the *Université de Montréal*'s Faculty of Medicine and a researcher with CHU Sainte-Justine.

Sylvana Côté's success began when she was a PhD student. She received a McConnell award for Excellence in Public Communication of Research after a presentation at the Canadian legislature on the importance of the early years for children's future social development. Since then, she's received operating and salary awards from the *Fonds québécois de la recherche sur la société et la culture* (FQRSC), the Social Sciences and Humanities Research Council (SSHRC) and the Canadian Psychiatric Research Foundation (CPRF). Her latest grant and award are from the Canadian Institutes for Health Research (CIHR). She leads a team of researchers who follow more than 500 children through day care centres to find out whether the quality of child care settings affects children's social and physical development. This new long-term study represents the achievement of a dream for her. *"I've always been interested in people's life trajectories. They depend so much on how people's personalities and their life situations work together to make what people become. This research is about that. How people develop has a lot to do with their family and their early life experiences. When you study young children, you really are studying their parents."*

According to Côté, her early work in substance abuse and violence led naturally to her current study of day care use and quality. *"I started my career studying the development of children from kindergarten to 16,"* she says. *"But I noticed that at-risk children already had problems by then."*

"With increased evidence, it's clear that among children who exhibit physical aggression in the preschool years there is a group of children who have levels that are atypically high. Not all children who display physical aggression will follow this pattern, but there's a high probability that some will. When low education comes together with family dysfunction and low levels of stimulation in the home, future problems are born."

Côté has become so convinced that the preschool years are the most important developmental stage for children, that she has taken time out to make presentations to legislative committees in Quebec City. *"Child care is not babysitting,"* she says. *"It should be scheduled as a stimulating educational experience. The preschool years are when the brain develops at the highest speed and is malleable. It makes no sense to not invest most of our money in that period as a society. If we invest in our kids at that age, we invest in our future human resources."*

BY TRACEY ARIAL

1. Côté SM, Boivin M, Nagin DS, Japel C, Xu Q, Zoccolillo M, Junger M, Tremblay RE. The role of maternal education and nonmaternal care services in the prevention of children's physical aggression problems. *Archives of General Psychiatry* 2007;64(11):1305-1312.

INFANT DAY CARE
TAKES GOOD CARE OF OUR YOUTH

A 5-year study conducted throughout the province of Quebec clearly showed that nonmaternal care of infants prior to the age of 9 months can help "at-risk" children control physical aggression as they age. Yet parents of at-risk children rarely took advantage of publicly offered day care services, probably because the mothers didn't work outside of the home.

"This study suggests that we have to encourage child care use by high-risk families," says the study's lead author Sylvana Côté. *"People think that if they don't work they don't need child care. That perhaps makes sense in the short term, but it makes no sense in the long run. These kids start school way behind. If we catch them early enough, they can catch up, but 4 years old is too late to do that."*

Côté and her colleagues used data from a study of 1,759 infants selected from Quebec birth registries to provide a representative sampling of the province's babies born in 1997 and 1998. Annual interviews were conducted with the mothers as the children progressed from 5 to 42 months. Information collected about the mothers included age, educational level, job, and incidence of depression or anti-social behaviours in adolescence, such as starting fights or stealing. Each child's sex, race, gestation and birth weight were noted. Family statistics, such as annual income, urban or rural life style, marital status and number of siblings were also recorded. Every year, interviewers asked about changes in family circumstances or the child's general health. They also asked the mothers pointed questions about their child's behaviour, family functioning and parenting perceptions.

After 5 years, researchers had complete data sets for 1,691 children and identified 17% of the children as exhibiting higher-than-usual levels of physical aggression. When they compared these children with the others, they discovered three facts. First, children with mothers who hadn't finished high school were significantly more likely to be among the highly aggressive group unless they had been cared for by someone other than mom before they reached the age of 9 months. Second, for the same children, the benefits of being cared for after 9 months by someone other than a mother who had not finished high school were also significant, though somewhat less so. Third, there were no similar benefits for children of mothers with higher levels of education, but there was no evident harm from nonmaternal care either, as some previous studies had suggested.

"There's an idea out there that if you're growing up in an underprivileged environment, it's better to have some quality day care," says George Tarabulsy, who specializes in infant and adolescent developmental psychology at *Université Laval*. *"This is quite a convincing study."*

"This study suggests that we have to encourage child care use by high-risk families."

In designing an upcoming study on prevention with vulnerable families, Tarabulsy acted on Côté's results and included active encouragement for at-risk parents to use community day care as part of the prevention program. *"It seems to be good advice in two ways. In quality settings, day care provides good stimulation for kids. It also gives parents the time to organize their family life, their schooling and their professional life. Time is one of the resources missing in these families."*

BY TRACEY ARIAL

Ref.: Côté SM, Boivin M, Nagin DS, Japel C, Xu Q, Zoccolillo M, Junger M, Tremblay RE. The role of maternal education and nonmaternal care services in the prevention of children's physical aggression problems. *Archives of General Psychiatry* 2007;64(11):1305-1312.

PROTECTING THE TINIEST BRAINS

When babies are born several weeks before their due date, the focus is usually on keeping them alive. But what about after their survival has been ensured? Can a baby be born extremely early and still lead a healthy, happy life?

"One of the adverse outcomes of great concern for children who have been preterm is cerebral palsy," says Dr. Charlene Robertson, a pediatric consultant of Glenrose Rehabilitation Hospital in Edmonton. *"The term cerebral palsy (CP) includes a group of permanent disorders of movement and posture that cause activity limitation."* As better care of very preterm infants led to higher survival rates starting in the 1970s, rates of CP also increased.

Robertson and her team looked at the CP rates over the past 30 years among infant survivors born at 20 to 27 weeks, weighing only 500 to 1,249 grams at birth, from a specific catchment area in which a great deal was known about base population, birth rates, prematurity rates, and the nature of care of premature infants. They found that rates of CP peaked in the early 1990s and then steadily dropped off in the last decade. The change is substantial: a child born very preterm in the early 1990s had about a 13% chance of having CP, this probability dropped to under 2% in the early 2000s. Particularly encouraging was a significant drop in rates of severe CP, the type that prevents children from walking. This is indeed heartening news, both for the parents of extremely preterm infants and the professionals who care for them.

The reasons for this change are complex, reflecting changes in overall systems of care. Dr. Peter Rosenbaum, an expert in CP from McMaster University who was not involved in this research, says, *"There have probably been many small but cumulative changes in the care of premature infants that together aggregate to make huge differences to both survival and to intact survival over the period of this report."*

"One of the adverse outcomes of great concern for children who have been preterm is cerebral palsy."

While these findings are undoubtedly positive, Dr. Robertson believes they should not obscure the fact that children born extremely preterm often have special needs and are likely to benefit from early interventions to help maximize their overall potential.

BY ALISON PALKHIVALA

Ref.: Robertson CMT, Watt MJ, Yasui Y. Changes in the prevalence of cerebral palsy for children born very prematurely within a population-based program over 30 years. *Jama-Journal of the American Medical Association* 2007;297(24):2733-2740.

EARLY IDENTIFICATION DIRECTS REHABILITATION CHOICES

Both deafness and blindness are significant disabilities. Imagine what it's like to have both! This is what occurs in a genetic condition known as Usher syndrome.

"In Usher syndrome type I, the hearing loss is congenital and the blindness starts before puberty, while in Usher syndrome type II, the deafness is in early childhood and the blindness starts after puberty," says Dr. Robert K. Koenekoop, of the McGill University Health Centre. Short of a cure, the best thing we can do for these children is identify the condition early so that appropriate rehabilitation can be provided without delay.

The 6 million French Canadians alive today are all descendents of about 8,500 French settlers, making them a relatively homogeneous group, genetically speaking. Dr Koenekoop and his colleagues conducted a genetic analysis of 15 Usher syndrome patients from different parts of Quebec. They found mutations of a gene implicated in Usher syndrome type I, known as USH1C, in 9 of these patients. This mutation has rarely been found outside the Acadian population.

The researchers discovered what's known as a "founder mutation" for both types of Usher syndrome, so now children born either deaf or blind can easily be tested for the presence of the condition, giving them, their families and their physicians an idea of what's in store and how best to manage their disability.

"These findings highlight the need for early screening of deaf infants in Quebec as well as the Acadian population in the Maritime region of Canada," says Dr. James C. MacDougall, an expert on deafblindness who is also at McGill University but was not involved in this study. *"Highly specialized counselling is necessary for the parents of a child who has been identified with Usher syndrome. Parents need genetic counselling concerning the risks for future children they may have and, as well, they need information on the impact of early deafness and progressive hearing loss. Unfortunately, the rehabilitation process for all deaf children remains a controversial topic with one group of professionals favouring an exclusive oral approach while another group favours the addition of some form of sign language to facilitate communication."*

Predicting future disability, however, is crucial to choosing the best rehabilitative option.

BY ALISON PALKHIVALA

Ref.: Ebermann I, Lopez I, Bitner-Glindzicz M, Brown C, Koenekoop RK, Bolz HJ. Deafblindness in French Canadians from Quebec: A predominant founder mutation in the USH1C gene provides the first genetic link with the Acadian population. *Genome Biology* 2007;8(4):R47.

PKU OR HOW TO KEEP YOUNG BRAINS HEALTHY

Children with phenylketonuria, commonly known as PKU, lack the ability to break down the amino acid phenylalanine. They must avoid eating the many foods containing this substance because over time it will build up in their bodies, affecting their nervous system and potentially leading to severe mental retardation.

"Some patients can go off the diet completely, but those are unusual."

Phenylalanine is a building block of protein, and it's in all types of animal products, including meat and dairy. It's also present in wheat. Imagine growing up without ever tasting regular pizza, hamburgers, hot dogs, bread or ice cream. To make matters worse, those with PKU also have to drink a special, not particularly palatable, formula to make sure they receive the nutrients they need.

While young children whose diets are largely controlled by their parents usually stick to safe foods, adolescents with PKU often have a more difficult time. Going off their diet does not make them immediately ill, but it can have a long-term effect on their neurological development, causing problems such as lowered intelligence.

No cure for PKU is available yet, but a international team led by Dr. Harvey Levy at Children's Hospital Boston and involving Canadian researcher Dr. Annette S. Feigenbaum at the Hospital for Sick Children in Toronto, may have found a way to help. They tested a compound known as tetrahydrobiopterin, or BH4, in nearly 90 young people with PKU to see whether taking it could reduce the blood concentration of phenylalanine. BH4 works by boosting the effects of any residual amounts of phenylalanine hydroxylase—the enzyme that breaks down phenylalanine—that might be present in the bodies of those with PKU.

After 6 weeks, the BH4 did work, but only partially and only in some patients. Levy estimates that about 40% of those with PKU have some sort of response to BH4 but only about 25% have a meaningful response. *"Some patients can go off the diet completely, but those are unusual,"* he says. *"The majority of patients who respond will be able to increase the amount of protein they can take in their diet and may or may not be able to decrease the amount of formula."*

While this study was conducted primarily in adolescents, what's particularly exciting is the role BH4 might play in younger children—the effects of the buildup of phenylalanine in those with PKU is cumulative, so the sooner it can be halted, the less likely patients are to suffer from long-term neurological and cognitive deficits. Levy says they have already begun testing BH4 in children under the age of 4.

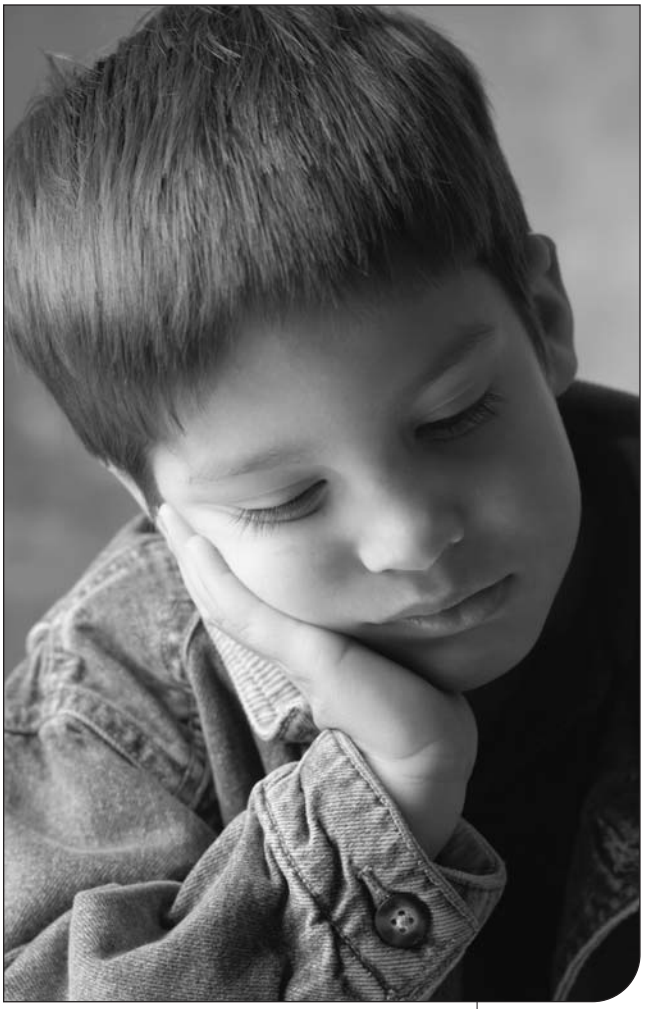
Dr. Grant Mitchell, a PKU expert at CHU Sainte-Justine points out that we've come a long way in the management of PKU. *"Until the mid-20th century,"* he says, *"patients with PKU were common in institutions for the mentally retarded. PKU was the first example of mental retardation with a known chemical cause. Since the 1960s, neonatal PKU screening has been adopted in all developed countries, permitting early diagnosis and treatment. The outcome of PKU has improved immeasurably, and two generations of neonatally-screened, treated patients have normal intelligence."*

These findings, Mitchell says, move PKU treatment forward. *"This article represents a new step from the clinical laboratory towards a normal life for PKU patients but this journey is not ended. The study is also a reminder that biochemical genetic conditions are important considerations in the treatment and prevention of mental retardation."*

BY ALISON PALKHIVALA

Ref.: Levy HL, Milanowski A, Chakrapani A, Cleary M, Lee P, Trefz FK, Whitley CH, Feillet F, Feigenbaum AS, Bedchuk JD, Christ-Schmidt H, Dorenbaum A, Sapropterin Research Group. Efficacy of sapropterin dihydrochloride (tetrahydrobiopterin, 6r-Bh4) for reduction of phenylalanine concentration in patients with phenylketonuria: a phase Iii randomized placebo-controlled study. *Lancet* 2007;370(9586):504-510.

THE GENETICS BEHIND STRESS AND DEPRESSION



We already know that in vulnerable children, certain types of stress, particularly chronic stress, can trigger anxiety and depression. But what makes some children vulnerable and not others?

That question may be too large to answer with one simple study, so an international team of researchers is breaking it down to look at each component separately. The Canadian constituent of the team, led by Dr. Cathy Barr from the Toronto Western Research Institute and the Hospital for Sick Children, is focusing on genetic vulnerability.

Barr and her colleagues examined the genetic make-up of 382 nuclear families in Hungary, in which at least one member was diagnosed with a mood disorder that started before the age of 14. *"This is very early onset,"* says Barr. *"The idea behind that was to get children who are at more risk genetically because when it onsets earlier, it's thought to be more heritable."* They targeted a gene known as AVPR1b because it controls the release of a stress hormone known as vasopressin, which in turn plays a role in the regulation of the hypothalamic-pituitary-adrenal (HPA) axis, a hormonal system, that performs a key function in the stress response. Disturbances in hormonal systems involved in the HPA axis have previously been implicated in mood disorders.

Indeed, the researchers did find a link between minor variations in the AVPR1b gene and the risk for development of mood disorders that begin in childhood, particularly among females. *"What our study shows is that this gene—AVPR1b—is contributing to childhood-onset depression,"* says Dr. Barr.

While the research needs to be repeated in other populations to confirm that these findings are not unique to Hungarians, it does have some intriguing implications. First of all, says Dr. Barr, it contributes to the evidence linking stress with mood disorders in children, thus highlighting the need to teach children, from an early age, how to cope with stress. *"It puts emphasis again on reducing stress and understanding how stress creates risk in children,"* says Barr. *"We already know that the response to stress is important in regulating mood and the risk for depression. It emphasizes that we need to help children modulate their stress response and learn coping behaviour."*

The findings also suggest that the AVPR1b gene may be a good starting point when selecting targets for new antidepressant medications—ones that, unlike many of those on the market today, are safe and effective in children.

Dr. Stan Kutcher, an expert in adolescent mental health from Dalhousie University, who was not involved in this research, says that this study *"takes us a step further to understanding the complexities between the influence of environment and the expression of psychiatric disorders. It has identified a potential mechanism for helping us understand how the stress response might lead to depression in some people but not all."* What remains uncertain, he says, is whether this mechanism functions outside a stress response. That is, will children with variations in the AVPR1b gene that make them vulnerable develop mood disorders even if they are not faced with significant stress? No one knows yet.

Dr. Barr's team is continuing to study families in Hungary affected by early-onset mood disorders. They have now examined about 700 families. *"What we don't know yet is why the gene is different in those with depression,"* says Barr. *"That's the next step in their research, to understand: what's the genetic variation with this gene that causes it to be disregulated in people with depression?"*

"It emphasizes that we need to help children modulate their stress response and learn coping behaviour."

BY ALISON PALKHIVALA

Ref.: Dempster EL, Burcescu I, Wigg K, Kiss E, Baji I, Gadoros J, Tamas Z, Kennedy JL, Vetro A, Kovacs M, Barr CL, International Consortium for Childhood-Onset Mood Disorders. Evidence of an association between the vasopressin V1b receptor gene (AVPR1b) and childhood-onset mood disorders. *Archives of General Psychiatry* 2007;64(10):1189-1195.

MOOD DISORDERS IN PREGNANCY: TO TREAT OR NOT TO TREAT?

Pregnant women suffering from anxiety and depression face a serious dilemma: continue taking medication that effectively controls the condition or stop the medication in case it harms the baby?

In the past few years, research has suggested that taking drugs commonly used to treat anxiety and depression, known as selective serotonin reuptake inhibitors, or SSRIs, during pregnancy may increase the risk of the baby being born with heart abnormalities, lung problems, or temporary signs of withdrawal, including jitteriness and irritability. Many women's instinctive reaction is to protect the baby at all costs, even at the expense of their own health. They are therefore tempted to stop their drug therapy while pregnant, but this may not be best for mother or child.

One research team identifying the benefits and drawbacks of taking SSRIs during pregnancy included Sura Alwan, a PhD candidate at the Medical Genetics Research Unit of Children's and Women's Hospital in Vancouver. *"SSRIs are among the most commonly prescribed drugs in North America,"* says Alwan, *"and their frequency of use has increased dramatically over recent years, especially among women of reproductive age."*

For the National Birth Defects Prevention Study, Alwan and her colleagues collected information on 9,622 infants born with major birth defects and 4,092 infants born without defects in the same geographic areas. They called the infants' mothers to find out whether they had taken SSRIs during their pregnancy and, if so, during what specific periods.

The good news is that no link could be found between the use of SSRIs during pregnancy and the presence of major physical abnormalities among the babies. *"Our findings did not confirm the association with heart defects that was shown before, and we did not find associations with most birth defects we studied,"* says Alwan. *"We did see an association with certain rare birth defects following early pregnancy exposure to SSRIs, but the absolute increase in risk may be small on a population level, compared to the baseline risk of 2% to 3% of birth defects in all pregnancy."*

Dr. Tim Oberlander, of the Child & Family Research Institute and Centre for Community Child Health Research in Vancouver, who was not involved with the Alwan study, calls these findings reassuring. They confirm what some other new research is suggesting—that taking SSRIs during pregnancy does not appear to increase the risk that babies will be born with major structural abnormalities.

But this is far from the end of the story, he cautions. *"I think that the effect of these drugs may not be related to structural abnormalities,"* he says. *"I believe they are more likely to produce microscopic changes or to alter chemical patterns in the brain. These changes may be harder to identify early on but could still have a significant impact on development over several years."* To muddy the waters further, it is still unclear whether abnormalities seen in children whose mothers took SSRIs during pregnancy are a result of the drugs or the condition that is being treated.

Critical research in this area is ongoing. In the meantime, Alwan says, *"It is important that treatment decisions for pregnant women with depression are taken on a case-by-case basis. Decisions should be made in consultation with the patient and her primary care physician or psychiatrist, taking into account all research findings, as well as the woman's specific condition, including the severity of the depression, experience with other methods of treatment (other medications or talk therapy), and other risk factors, such as a family history of birth defects."*

BY ALISON PALKHIVALA

"It is important that treatment decisions for pregnant women with depression are taken on a case-by-case basis."

Ref.: Alwan S, Reefhuis J, Rasmussen SA, Olney RS, Friedman JM, Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. *New England Journal of Medicine* 2007;356(26):2684-2692.

EARLY CAFFEINE THERAPY FOR PREEMIES PROVES BENEFICIAL

Low birth weight babies with respiratory problems who receive caffeine therapy during their first 10 days of life are less likely to be diagnosed with cerebral palsy or other neural-development disabilities at 18 to 21 months of age.

"It's the only neonatal drug that has been convincingly shown to reduce disability," says Barbara Schmidt, the lead author of an international multicentre trial of caffeine therapy for babies. *"Most people predicted that we'd show no difference after 18 months, yet we showed a clear and convincing drop in the incidence of cerebral palsy."*

Although doctors have been treating preemies with caffeine and other nervous system stimulants for more than 30 years now, no clear studies into the practice existed until Schmidt started hers in 1999. In fact, the researcher, who splits her time between McMaster University in Hamilton and the University of Pennsylvania, was horrified at the limited evidence for its use. *"We knew practically nothing,"* she says now. *"That got me thinking and I started talking to colleagues."*

Several colleagues were interested in pursuing a study that would show what effect caffeine had on infant development and whether treatment of low birth weight babies caused harm later. Along with Schmidt's Hamilton hospital, doctors in Australia, Canada, England, Germany, Ireland, Israel, Netherlands, Sweden, Switzerland and the U.S.A. also participated.

They identified 5,292 infants who could be considered for the trial. Of those, 2,006 babies received parental consent and could be randomized so that 1,006 were started on caffeine during their first 10 days of life while the other 1,000 received placebos. In the end, complete data sets were obtained for 937 children in the caffeine group and 932 children in the placebo group.

All the babies were born with a weight of between 500 and 1,250 grams and suffered from respiratory ailments that made the use of caffeine desirable. Some of the babies (62 in the caffeine group and 63 in the placebo group) died before they were 18 months old. Of those that survived, 315 in the caffeine group and 368 in the placebo group suffered from one or more of the following disabilities: cerebral palsy, cognitive delay, hearing loss, and blindness. What was interesting, however, was that 40 children in the caffeine group got cerebral palsy compared to 66 in the placebo group, while 293 babies in the caffeine group suffered cognitive delay compared to 329 in the placebo group.

"The significance of this is that there is a group of premature infants who have trouble breathing and if you give them a dose of caffeine, it appears that there is a drop in their prevalence of cerebral palsy (CP)," says Dr. Nigel Paneth, a paediatrician and professor with the College of Human Medicine at Michigan State University. *"It was a bit of a surprise. I expect that the use of caffeine will increase now. It's been extremely hard in neonatal medicine to show that a pharmaceutical intervention could lower the rate of CP. That's what makes this such an important study. It means that we're moving away from saving lives to saving brains. This is good news."*

"It's the only neonatal drug that has been convincingly shown to reduce disability."

BY TRACEY ARIAL

Note: This study won the inaugural Clinical Trial of the Year award announced by the Society for Clinical Trials (SCT) and Project ImpACT (Important Achievements of Clinical Trials) on May 20th, 2008.

Ref.: Schmidt B, Roberts RS, Davis P, Doyle LW, Barrington KJ, Ohlsson A, Solimano A, Tin W, Caffeine for apnea of prematurity trial group. Longterm effects of caffeine therapy for apnea of prematurity. *New England Journal of Medicine* 2007;357(19):1893-1902.

TROUBLED HEARTS EQUALS TROUBLED BRAINS?

Dramatic advances in cardiac care over the past several years have resulted in a much higher rate of survival among babies born with major heart abnormalities. But as many as half of these infants face neural-development problems, including motor, language, and intellectual impairments.

Until recently, these impairments were believed to be caused by the cardiac surgery the infants underwent to save their lives, but new research suggests that the stage was set for these problems not only before the infants underwent surgery but before they were even born.

In an effort to understand why infants with major congenital heart disease are so neurologically vulnerable, researchers led by Dr. Steven P. Miller from the Division of Neurology at the University of British Columbia, in Vancouver and the University of California, San Francisco, scanned the brains of 41 babies with severe congenital heart abnormalities right after they were born, before they underwent any surgery. These scans are safe and noninvasive technologies that provide a window into brain structure, chemistry and functioning.

The scans revealed a pattern of microstructural and biochemical abnormalities in these infants' brains that are typical of premature babies, even though these babies were born at term. *"This suggested to us that there were changes in how the brains develop in the womb in the babies with heart disease,"* says Miller.

It remains unclear what causes the abnormalities in brain development, but Miller says that animal studies suggest it may be related to impaired delivery of oxygen, in utero, to the brain. *"The next important link we need to make is between these abnormalities in the brain that we see on imaging and the outcomes that we recognize in the clinic,"* he says. *"I also think we need to recognize that brain injury in babies with heart disease is complicated. It's not entirely the result of things that happen during surgery."*

Dr. Annette Majnemer, from the Division of Pediatric Neurology at the McGill University Health Centre, has done extensive research in the area of development among infants with severe congenital heart abnormalities but was not involved in this research. *"These types of studies are very important in helping us to understand the mechanisms and causes of brain injuries so that we can prevent them, or if we can't prevent them then minimize the events that can occur in the immature brain,"* she says.

While standard magnetic resonance imaging (MRI) detects brain injuries well, more sophisticated MRI technology was needed to detect the abnormalities in the brain development of these infants.

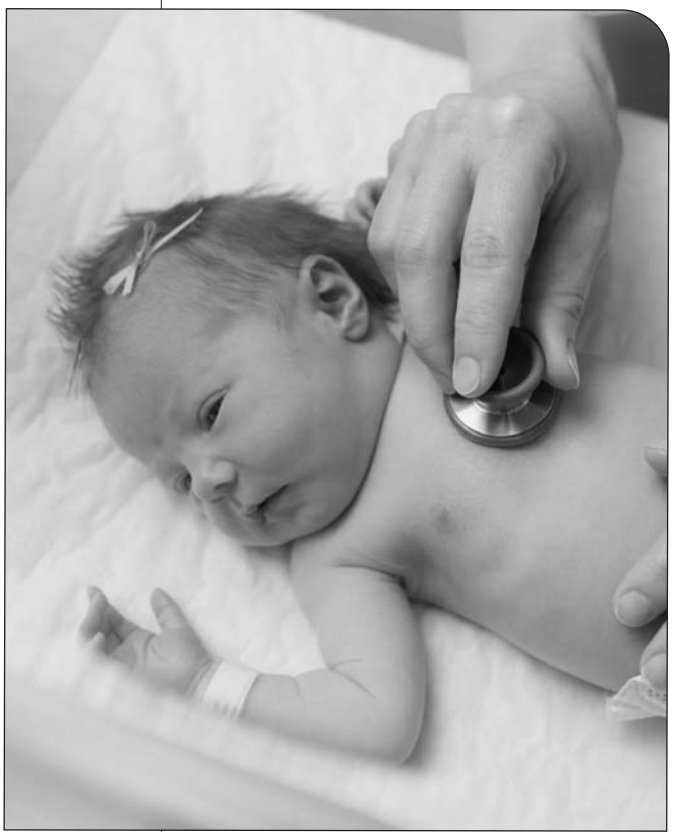
"The study also demonstrated that children born with severe congenital heart abnormalities are a high-risk group, much like premature infants," she says. As a result, they may similarly benefit from years of close follow up and screening for developmental disorders so that problems can be identified and addressed early on. Families of these infants also need support to help them cope with the very stressful situation of having a sick child who may need special care for years to come.

In fact, research conducted by Majnemer's team has already suggested that, by school age, many of the children born with severe congenital heart defects are having trouble. *"Many of the children were not receiving educational and rehabilitation services even though the parents felt they needed it,"* she says.

Another important implication of this research is the need to scan the brain of the babies with congenital heart disease to recognize brain injury and help counsel families.

BY ALISON PALKHIVALA

"This suggested to us that there were changes in how the brains develop in the womb in the babies with heart disease."



Ref.: Miller SP, Mcquillen PS, Hamrick S, Xu D, Glidden DV, Charlton N, Karl T, Azakie A, Ferriero DM, Barkovich J, Vigneron DB. Abnormal brain development in newborns with congenital heart disease. *New England Journal of Medicine* 2007;357(19):1928-1938.

ALLERGY AND ASTHMA EPIDEMIC NOT STEMMED BY BREAST-FEEDING

"Exclusive breast-feeding is important for many reasons but preventing future allergies may not be one of them."

The duration and exclusivity of breast-feeding has no influence on whether children develop allergies or asthma by the time they are 6 1/2 years old.

Michael S. Kramer and his colleagues at the Canadian Institutes of Health Research have always been advocates of long-term exclusive breast-feeding, which lowers the risk of stomach flu, colds, and throat and ear infections. *"With so many benefits to the practice, I wondered whether breast-feeding would also have any effect on the soaring rates of asthma and allergies across the last few generations of children,"* says Kramer.

After almost 7 years of research and another 2 years of statistical analysis, Kramer now says that the answer is an undeniable no. Known as the "Promotion of Breast-Feeding Intervention Trial" (PROBIT), Kramer's study included 17,046 mother and baby pairs from 31 maternity hospitals and clinics in the Republic of Belarus.

All the babies were born at healthy weights in 1996 and 1997 and had mothers who already decided to breast-feed them. Mother and child pairs from half of the selected hospitals participated in a program designed to promote longer exclusive breast-feeding. They became the experimental group. The other mothers were not influenced in any way and, with their babies, became the control group. Both groups contained women of similar ages, education and family history. Some women in each group had allergies, asthma or eczema in the family.

Almost half (43%) of the women in the experimental group exclusively breast-fed their babies until they reached 3 months old, while only 6% of those in the control group did so. Most mothers introduced other foods prior to the babies turning 6 months old. After a year, almost 20% of the experimental mothers were still breast-feeding while 11% of those in the control group were still doing so.

A follow-up took place after the children turned 6 1/2 years old. A total of 13,899 mother-child pairs participated. Symptoms of allergies, asthma, hay fever and eczema were determined by asking the mother to answer an international questionnaire, while allergic reactivity was assessed by administering skin prick allergy tests for house dust mites, cat, birch pollen, mixed northern grasses, and fungus spores. There were no significant differences between the two groups.

Kramer says his research shouldn't influence a mother's decision to breast-feed although she shouldn't expect it to help eliminate allergies.

"It may be that if you breast-feed for a long term and exclusively, it may prevent allergies, but there may be something about introduction of solids during breast-feeding that may influence allergies," says Perle Feldman, an associate professor of family medicine at McGill and the medical director of the Goldfarb Breast-Feeding Program in the Herzl Family Practice Centre of the Jewish General Hospital. *"This study doesn't answer those questions because the exclusive breast-feeding in it wasn't very long."*

Still, Feldman calls Kramer's study *"one of the best studies done on breast-feeding ever, since it is the closest we will ever get to an actual randomized trial on this complex subject,"* and says it may help her to encourage women to do what they need to do without guilt. *"Exclusive breast-feeding is important for many reasons but preventing future allergies may not be one of them."*

BY TRACEY ARIAL

Ref.: Kramer MS, Matush L, Vanilovich I, Platt R, Bogdanovich N, Sevkovskaya Z, Dzikovich I, Shishko G, Mazer B. Effect of prolonged and exclusive breast-feeding on risk of allergy and asthma: Cluster randomised trial. *British Medical Journal* 2007;335(7624):815-820.

BABIES ALSO LISTEN WITH THEIR EYES

Very young infants who are exposed to a variety of languages can tell the difference between their native languages and other languages, but this ability ceases by the time they reach 8 months old unless they are familiar with the languages tested.

"In auditory studies, they've shown that, at birth, babies can tell apart the sounds from all the world's languages and then over the 1st year of life, they lose sensitivity to sounds that aren't part of their native language," said lead study author Whitney Marie Weikum. *"I wanted to see if it was similar for visual clues."*

Her study clearly showed that it is. She found that babies distinguish between languages visually until they are 6 months old. Bilingual babies are even more capable in that they visually discern their two native languages.

To determine that babies use visual clues, researchers set up silent video clips of three bilingual speakers reciting sentences from *The Little Prince* in French and English. Babies would sit on a parent's lap in front of a 27-inch television screen hooked up to a computer. The parents wore dark sunglasses to prevent them from seeing the screen and influencing their children. Each trial consisted of multiple clips presented to the infant for a maximum of 16 seconds. When the baby looked away, an experimenter watching the baby's face via closed-circuit camera would press a key.

Digital video analysis verified experimenters' response times. It was assumed that if babies looked at a clip for a longer-than-average duration, it was because they noticed the language change. Babies in the control groups would see the same speakers speaking a single language. Babies in the experimental groups saw the same speakers using both languages. Researchers then averaged the test times and compared them with the times babies stared at clips in the control and experimental groups.

They tested 96 infants, 24 of whom were exposed to a second language (French) at least 25% of the time. The others were exposed only to English. Tests were conducted on 3 groups—4-, 6- and 8-month-old babies.

To see if babies could visually distinguish their native English from the rhythmically-different French, the researchers showed the same speakers saying different sentences. They found that at 4 and 6 months of age, the experimental group of infants looked significantly longer at clips when the languages switched. By 8 months of age, however, the babies in monolingual environments no longer noticed the switch, while those in bilingual environments continued to be able to tell the difference. *"It shows that babies' abilities match their language environments,"* says Weikum.

"This study is very important for two reasons," says Dr. Fred Genesee, a specialist in bilingual research and a professor at McGill University. *"It adds scientific evidence that infants have extremely powerful processing capacities that facilitate the challenge of learning language. It is widely believed that dual language exposure is not simply a challenge, but a burden for infants and can slow down and perhaps even impede normal development. This study shows that this perception underestimates infants' learning capacity. The additional stimulation serves to maintain infants' discrimination ability beyond those of monolingual children; this, in turn, lays the foundation for simultaneous bilingual acquisition."*

"It shows that babies' abilities match their language environments."

BY TRACEY ARIAL

Ref.: Weikum WM, Vouloumanos A, Navarra J, Soto-Faraco S, Sebastian-Galles N, Werker JF. Visual language discrimination in infancy. *Science* 2007;316(5828):1159.

NATIONAL NETWORK
LINKS CANADA'S BEST EARLY CHILD DEVELOPMENT RESEARCHERS

In March 2008, 14 of Canada's leading researchers of early child development committed to work closely together for at least the next 7 years.

Known as the Strategic Knowledge Cluster on Early Child Development, the network will make sure that parents, educators, community group leaders, and government policy makers have information about how children develop between pregnancy and the first day of school. This task takes on particular importance given the well-documented links of positive, nurturing experiences early in life with later success, and given the context of the National Children's Agenda (NCA) adopted several years ago by federal and provincial ministers to support the healthy development of children.

The Cluster has received almost $300,000 per year from the Social Sciences and Humanities Research Council (SSHRC) and $100,000 from both *Université Laval* and *Université de Montréal*, along with in-kind contributions from groups within universities located across the country (University of Alberta, University of British Columbia, University of Calgary, McMaster University, University of New Brunswick, University of Ottawa, Queens University, University of Toronto, and University of Western Ontario). Collaboration is also expected from more than 20 nonacademic, private organizations and international and national governmental agencies specialized in the field.

Plans to convey information include an annual conference to bring researchers, students, and partners' organizations to meet face to face. Knowledge mobilization work will also take the form of review papers, policy briefs, and consultations, all under the coleadership of Michel Boivin from *Université Laval* and Richard E. Tremblay from *Université de Montréal*. Both hold Canada Research Chairs in child development and can be counted on to foster collaboration across Canada while nurturing international research associations that will extend the network beyond national borders.

BY TRACEY ARIAL

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The CEECD identifies and summarizes the best scientific work on social and emotional development of young children and makes this information available to service planners, service providers and policy-makers.

The Centre's partners are Université de Montréal, Fondation Lucie et André Chagnon, Alberta Centre for Child, Family and Community Research, CHU Sainte-Justine Research Center , Strategic Knowledge Cluster on Early Child Development, George Brown College, Canadian Association of School Administrators, Canadian Paediatric Society, Montreal Children's Hospital, Canadian Child Care Federation, University of British Colombia, McGill University, Institut national de santé publique du Québec, Dalhousie University, IWK Health Centre, Centre de Psycho-Éducation du Québec, Queen's University, First Nations of Quebec and Labrador Health and Social Services Commission, Invest in Kids, Canadian Association of Principals.

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