What inspired you to study the molecular underpinnings of paediatric behavioural and mental health disorders?

My eureka moment was a conversation with Jim Padbury, MD, a cell biologist and geneticist here at Brown University, about epigenetic changes in placental genes. I was deeply involved in studies of prenatal cocaine exposure at the time, and realised that viewing this drug as a prenatal stressor that induced epigenetic changes, increasing foetal exposure to cortisol and affecting subsequent behavioural development, was a whole new way of thinking about the pathophysiology of cocaine and other prenatal exposures. The jump to broader developmental issues was obvious: understanding the molecular underpinnings of behaviour could be used to study enormously important public health problems, such as mental health disorders. Dr Padbury and I got together with Carmen Marsit, PhD, a card-carrying epigeneticist and epidemiologist also at Brown, and we knew we had a winning team.

What were the outcomes of the first Behavioural Epigenetics conference that you chaired with Ed Tronick, PhD, and Eric Nestler, MD, for the New York Academy of Sciences in 2010 at the University of Massachusetts, Boston?

This was a landmark event: it was the first major conference that brought together scientists doing research on behavioural epigenetics in animals with scientists studying human behavioural epigenetics. It opened up important crosstalk and new lines of communication between scientists, and new doors for collaboration. It enabled us to start piecing together what we could learn from animal studies for human behavioural research, the advantages as well as limitations of both animal and human work and ideas for translational research. In addition, it also helped us to see potential for prevention and treatment. The conference generated a lot of excitement and put human behavioural epigenetics in the spotlight. I don’t think it’s an exaggeration to say that it was at least partially responsible for the spike in research in this area that followed.

Can you outline how environmental factors lead to behavioural disorders?

The emergence of the field of epigenetics has revolutionised biology and our understanding of the role of genetics in explaining behaviour and development. It is pretty clear that the development of many mental health disorders is a product of the interaction between genetic and environmental factors. Environmental differences can change gene expression through epigenetic mechanisms at the cellular level – so epigenetic is, in fact, the quintessential gene-environment...
interaction. By environment we mean both the prenatal and the postnatal environments; epigenetic effects occur both during foetal development and in the broader environment in which the child is raised, and behavioural disorders can arise due to adversity at any of these stages. Needless to say, the ‘double whammy’ of both pre- and postnatal environmental adversity would be the worst case scenario.

Has your work had a tangible impact on policy or treatment options?

Our work (and that of many others) helped establish the knowledge base of the effects of prenatal exposure to drugs such as cocaine, methamphetamine and other substances of abuse on children. It also helped remove some of the stigma associated with women who abuse substances during pregnancy that led to punitive policies. The harmful effect that labelling has on these children was documented. We helped establish the family treatment drug court model as one approach that shows treatment, not punishment, is the better policy.

Our neurobehavioural exam (NICU Network Neurobehavioral Scale or NNNS) is increasingly being used as part of standard care for infants in intensive care.

Furthermore, our research showing improved medical and neurobehavioural outcome in preterm infants cared for in an intensive care unit with single family rooms is helping to establish this as the preferred model of care for these infants.

How do you see your research developing in the future?

I would like to see the research develop along several interconnected lines at the same time; a triangle of normal development, abnormal development/psychopathology and translational (animal and human) studies. The good news is that we know what has to be done, but the bad news is that it’s going to take a lot of resources and the private sector may need to get involved.

With sufficient resources I think it would take about 10 years to make the kinds of advances in epigenetics that would enable us to begin improving the quality of life of our children. This would include treatment for pregnant women to improve foetal and child outcomes; treatment for children with behavioural or mental health problems; and preventive intervention for children at risk for the development of later disorders.

I am 67 years old and have no plans to retire. How interesting that I have spent my career studying development in high risk children, and now we can drill down deeper and see those same kinds of children from a perspective that could reveal the molecular mechanisms of the origins of risk. Imagine a molecular roadmap of the development of human behaviour!
INTRODUCTION

BROWN CENTER FOR THE STUDY OF CHILDREN AT RISK

OBJECTIVE

To nurture, promote and coordinate research, training, education and clinical service in child development and developmental psychopathology.

KEY COLLABORATORS

James F Padbury, MD, Professor of Pediatrics, Warren Alpert Medical School of Brown University, USA • Carmen Marsit, PhD, Associate Professor of Pharmacology & Toxicology, Associate Professor of Community and Family Medicine, Geisel School of Medicine at Dartmouth, USA • Elizabeth Conradt, PhD, Assistant Professor of Psychology, University of Utah, Salt Lake City, Utah, USA

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The Brown Center for the Study of Children at Risk

The Center for Children and Families at Women & Infants Hospital of Rhode Island
http://bit.ly/Center_Children_Families

Clinical services offered by the Center comprise both inpatient and outpatient activities. Staff provide integrated care that spans the disciplines of developmental and clinical psychology, paediatrics, psychiatry, nursing (including psychiatric nursing), social work and substance abuse. The Center also offers occupational therapy services to address specific developmental and feeding concerns.

The Neonatal Intensive Care Unit (NICU) Network Neurobehavioral Scale
http://bit.ly/Neurobehavioiral_Scale

The New York Academy of Sciences Behavioral Epigenetics conference

The Brown Center for the Study of Children at Risk

MISSION:

Stimulating outstanding interdisciplinary research and advancing theories of the developmental pathways from foetal and infancy periods in children in the context of the family environment

Enhancing synergy between research and clinical practice that advances child and family developmental research, treatment programmes for children and their families and social policy

Training scientists and practitioners in interdisciplinary methods from the field of child development in the context of the family environment

EPIGENETIC RESEARCH:

In collaboration with other investigators, research strands at the Center include:

• Development in normal, healthy children
• Children with prenatal methamphetamine exposure
• Infants in withdrawal from opioids
• Children with prenatal toxicant exposure
• Maternal smoking during pregnancy
• Maternal depression during pregnancy and treatment with medications
• Development of infants born very preterm
• Development in children with autism
• Infants of mothers with postnatal depression
• Infants exposed to postnatal adversity
• Translational (mouse-infant) study of medications used to treat maternal depression during pregnancy

Lester anticipates that knowledge of the molecular pathways involved in normal and abnormal development will enable the advancement of preventive interventions for pregnant women to improve foetal and infant outcome, as well as for infants and children who appear to be on their way to developing behavioural or mental health disorders. In Lester’s opinion, epigenetics also has the potential for building resilience in children at risk helping them to adapt and develop coping strategies based on the molecular pathways that drive behaviour. For example, positive parenting may be able to undo, or at least arrest, negative effects on behaviour caused by prenatal and/or postnatal factors, which opens the door to treatment and prevention. Rodent research has shown that epigenetic effects can be reversed and passed down to the next generation, meaning that genes have a memory. “The implications are staggering, suggesting that perhaps we will prevent disorders from appearing altogether in the future,” Lester asserts.