Editorial: ‘It’s the environment stupid!’ On epigenetics, programming and plasticity in child mental health

JCPP provides a scholarly interface between the basic science of developmental psychopathology and clinical practice in child and adolescent psychiatry and psychology. Here scientists can set out their data and ideas for both fellow researchers keen to build on, and also for interested clinicians keen to keep abreast of, the latest scientific developments. Aware of the need to speak to this broad constituency, we select manuscripts for publication only if they combine scientific value and clinical relevance. This means that questions typically travel in pairs: the science question comes first, its clinical corollary follows soon after. The scientist asks: What processes drive the development of mental disorder in childhood and adolescence? The clinician naturally follows up with: How can I exploit science to produce more effective ways of working with patients? In JCPP big science themes sit alongside workaday goals to create the translational imperative that is at the heart of our mission. That said, clearly many studies we publish, especially those focusing on causal processes, are not always directly or immediately applicable in practice (although papers reporting high quality trials and practitioner reviews form an important and popular focus of our output). However, when taking the longer and broader view, such studies are of great clinical significance in as much as they address core issues about the nature of disorder.

Take, for instance, the debate over the relative importance of genetic vs. environmental influences on the development of common childhood disorders: a subject of broad but obvious clinical relevance because it has implications about how tractable conditions are to environmental therapies. Unfortunately, this debate has often in the past got bogged down in ideology and politics. Battle lines have been drawn and redrawn and scientist-protagonists have taken extreme positions often well beyond the available data. Thankfully, because of new genetic technologies of immense quantitative power developed over the past 10 to 15 years, and the recent development of sophisticated methods for testing environmental influence on biological processes, we can at last bypass this stale stand-off over nature vs. nurture ‘dogma’. Rather than having to infer genetic and environmental effects on the basis of indirect tests, we can study the role of genes and environments (and the effect they have on each other) directly.

Against the initial expectations of many, approaches employing technologies such as whole-genome association studies have tended not to demonstrate the power of genes alone to determine disorder, but rather have highlighted the complexity and heterogeneity of the causal architecture of common mental disorders and the way that genes and environments work together to shape development. Serious science is now more than ever focused on the power of the environment to shape neurodevelopmental processes and pathways. In a way, the more we have found out about the genetics of common childhood disorders, the more we confirm the importance of environmental factors in the aetiological mix. Now, all but the most dogged of genetic determinists have revised their view of the primacy of genetic factors so as to encompass a central role for the environment in the development of mental disorder. This is the case even for the most heritable conditions. For instance, in my field, attention-deficit hyperactivity disorder (ADHD), despite the remarkable early advances using candidate gene approaches (Turić, Swanston, & Sonuga-Barke, in press), subsequent progress has been slow: we are now using larger and larger samples of patients to demonstrate smaller and smaller molecular genetic main effects. Even the most comprehensive genome-wide scans available, with thousands of patients using hundreds of thousands of genetic markers, such effects appear to account for a relatively small proportion of disorder expression (Neale et al., 2008). At the same time we are seeing fascinating examples of the power of the environment to shape disorder expression and the neurobiological processes presumed to underpin it. Powerful new concepts are being applied to help explain the ways that environments influence gene expression (Mill & Petronis, 2008), program biological systems (Swanson & Wadhwa, 2008) and promote both functional and
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The family, as the crucial organising ‘vector’ mediating the effects of environmental influences on children’s development, is expected to be a key driver of such biological effects. Studies of the way that families influence brain development by shaping the child’s social and physical environment should therefore be a key future focus for collaboration between child psychology and psychiatry on the one hand, and developmental neuroscience on the other.

A number of papers in this issue illustrate the power of environmental influences generally and the role of family-related processes in particular. In the Rodriguez study we see the potential power of maternal lifestyle and behaviour and their physical consequences (in this case obesity) operating even before conception to determine long-term bio-behavioural outcomes. She demonstrates a link between a mother’s pre-pregnancy obesity and the later emergence of inattention and emotionality in her 5-year-old offspring. Given that such an effect could be explained by reference to a range of genotypic and developmental mechanisms, it is especially striking that the findings could not be explained by obvious confounding factors such as maternal ADHD or maternal distress during pregnancy. This result highlights the fascinating possibility that very early prenatal biological programming mechanisms, known for some time to affect the long-term physical development and health of the unborn child, may also influence brain development and mental health.

Of course, such a generalisation is very plausible (Swanson & Whadwa, 2008). From soon after conception the embryo and developing foetus begin the process of adapting to the intrauterine environment. Epigenetic programmes are laid down that provide the template for long-term biological development.

The next two studies explore the family as mediator and moderator of mental health outcomes. Fiese and colleagues illustrate the power of the family environment to mediate the psychological effects of physical illness. In accordance with previous findings, the authors show that children with asthma-related compromised lung function display increased levels of separation anxiety. They also took part in less involved and well-organised meal-time family interactions. Crucially, they found that these markers of family function carried the effect of compromised lung function on separation anxiety, possibly by increased feeling of isolation and panic. Flouri and colleagues take a very different approach but again their study highlights the power of the family environment in determining children’s psychosocial wellbeing. On the basis of advanced multi-level modelling techniques they concluded that the effects of a child’s neighbourhood on mental health were weak and carried by socioeconomic characteristics of the family and that these were independent of important effects of family life events and functioning.

Establishing the statistical significance of the effects of family factors on mental health outcomes is not the same as understanding the neuro-developmental mechanisms responsible for such effects. The notions of programming and plasticity imply that such effects are mediated directly at the neuro-developmental level: environments change behavioural and mental health outcomes because they alter brain function and associated cognitive processes. In a fascinating study, Legerstee and colleagues provide experimental evidence consistent with such a view. Using data from a randomised controlled trial of stepped-care cognitive behaviour therapy for anxiety (involving a major family-based component), they found that changes in attention to threatening stimuli, a marker of underlying neural response to threat, were linked to treatment-related reduction in anxiety symptoms.

The above papers highlight the power of environmental influences to shape mental health. There is, however, no one-to-one match between exposure to environmental adversity and the development of disorder. Some children appear especially vulnerable to adversity while others appear resilient. Genetic factors play an important role in determining which is the case. In the domain of depression, for instance, a common polymorphism in the serotonin transporter gene seems a strong candidate moderator of the effects of a range of environmental adversity, with the short allele appearing to confer vulnerability. Two papers in the current issue explore this issue further. Benjet et al. found that only those girls who carried two short alleles were at increased risk of depression. Hammen and colleagues found that either one or two short alleles in interaction with stress increased the risk of disorder; interestingly, this affected only girls. These studies add to the growing body of evidence for genetic moderation of environmental effects. Understanding such gene × environment interactions is important in explaining the current apparent mismatch in the high heritability of many childhood disorders and the small percentage of variance in disorder expression accounted for by measured genetic main effects. There are many more examples of published studies reporting gene × environment interactions, investigating different candidate genes and different outcomes. Moving forward from these observations, a crucial next step will be to come to a better understanding of the neurobiological and cellular processes that underlie these interactions. Epigenetic processes that control gene expression, i.e., the translation of genetic
information into functional products, are likely to
be crucial here.

It is a short step in the chain of logic from demon-
strating that neuro-developmental pathways to
mental disorder are established and maintained by
family and social factors, to promoting family-based
therapies for the prevention and treatment of those
disorders. ADHD is an especially interesting case in
point with regard to this. This is because the efficacy
of non-pharmacological treatments (rather than comorbidities) has often been questioned. This
issue’s practitioner review of non-pharmacological
treatments for ADHD by Young and Amarasinghe challenges such a view by showing that family-based
and psychological interventions can be used effect-
ively right across the lifespan. However, effects on
core symptoms are smaller than seen by medica-
tion (e.g., methylphenidate) and there are many
limitations of such approaches. More effective psy-
chological treatments are urgently needed. From a
translational perspective, to achieve this we need (i)
to better understand the way that environments
shape development through mechanisms such as
epigensis, biological programming and brain plas-
ticity and (ii) to harness such an understanding to
drive therapeutic innovation. We are only at the very
start of this process, but by illustrating the power of
the environment to alter outcomes and by illustrat-
ing possible mechanisms, studies such as those
presented in this issue make an important contribu-
tion to this process.

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