Editorial: Re-imagining the environment in developmental psychopathology: from molecules to effective interventions

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Abstract
The Journal of Child Psychology and Psychiatry's Annual Research Review (ARR) is a must-read special issue of the journal that presents a series of major reviews of key topics in the field. This year the ARR consists of 8 reviews, each accompanied by a commentary from a leading expert in the field, on a diverse range of topics addressing, in complementary ways, the key role of the environment in child psychopathology and in leveraging change in the service of prevention and intervention. Topics include epigenetics, stress physiology, neonatal imaging, inter-parental conflict, bullying, autism treatments and suicide. The papers considered together represent the very best of contemporary child psychology and psychiatry research.

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Welcome to this year's Annual Research Review Special issue, which brings together an outstanding group of leading scientists from around the world to present the cutting edge of research in child psychology and psychiatry. The Annual Research Review has become something of an annual event in the child psychologist or psychiatrist's calendar, giving us all an opportunity to look up from the coal face and be inspired by what we have collectively achieved so far, and what might be possible in the coming years.

It's certainly an exciting time for the field. For example, despite all the challenges, significant strides are being made in psychiatric genetics, which is bringing hope that quantitative genetics and molecular genetics can eventually be brought into alignment. If that happens, we will be much closer to understanding the genetic mechanisms that influence risk for disorder in children and adults. But we're not there yet by any means, and much work remains to be done. Although there are many obstacles ahead, a key one in my view is that we remain a long way from fully understanding the subtleties of gene-environment interplay. We have a comparatively poor understanding of the extent and mechanisms of gene-environment interaction, often relying heavily, at least in the recent past, on candidate genes and cross-sectional designs. Twin and adoption designs are arguably more powerful in this context, but they rarely measure the environment well enough, repeatedly or at high enough temporal resolution to properly capture the dynamics of developmentally-emerging gene-environment interaction. We have also barely scratched the surface of mechanisms of gene-environment correlation (and environmental risk mediation, as articulated byRutter, Silberg, O'Connor, & Simonoff, 1999). A recent paper in Science (Kong et al., 2018) provided a neat twist on that story, by demonstrating that parental alleles that are part of a polygenic score for educational attainment are associated with child achievement even when those alleles were not, by chance, passed on to the child. The implication, by inference, was that parental genes were affecting the child via environmental mechanisms. These so-called non-transmitted alleles provide an interesting bit of leverage for understanding the (parental) genetics of the rearing environment. Technically, if heritable confounds can be ruled out, the approach becomes a form of instrumental variable analysis for estimating the effects of the environment on the child's development, and hence gets us closer to causal inference. Studies using the Children of Twins (CoT) design, many of them published in this Journal, have for some time been investigating these kinds of processes, showing for example that despite being quite heritable in both parent and child, the transmission of depression from parent to child seems to be largely driven by the environment (Silberg, Maes, & Eaves, 2010) . Of course, for the CoT studies and studies using the non-transmitted alleles approach, lingering concerns about methodological artefacts and confounds may remain. One important way to enhance our confidence in these effects is to use theoretical models of environmental influence and measure the model-inferred environmental mechanisms directly. If the non-transmitted alleles, for example, not only associate with the child's outcome, but we can also see what it is that the parent is doing that is driving the association this is surely a more powerful demonstration, and one that leads more immediately to potential intervention strategies.

What all of this suggests is that we need to up our game in the conceptualization of environmental influence and, crucially, in the rich but scalable measurement of the environment, integrated, ideally, within genetically informative research designs. As Robert Plomin pointed out brilliantly in a commentary for this Journal in 2013 (Plomin, 2013), the environment is much more difficult to measure than DNA; we remain reliant on small numbers of indicators of relevant environments, often using crude instruments, often focused on a single domain or level of analysis; multiple environmental indicators are often

combined in simple linear, additive ways when the environmental state-space that affects psychobiological development is likely much more complex; and, as mentioned already, we typically measure the environment once every two to three years if we are lucky, often during periods where it is well established that development is progressing much more rapidly than that. The concept of the exposome, although not without its own challenges, helpfully encourages us to think about the plethora of multi-level influences embedded in a child's environment. Plomin also made the exceptionally important point that many indicators of the environment are rather passive (the 'imposed environment' as he called it), when in reality the environment is a very dynamic entity actively constructed or co-constructed between the organism and these so-called 'imposed' environments. Biological markers of the environment hold promise as a potent way to get closer to the dynamic interface where the causal action is.

This year's Annual Research Review, in that context, provides a wonderful synthesis of work in child psychology and psychiatry that is pushing our understanding of the environment to the next level. All the papers, considered collectively, focusing as they do on different areas and levels of analysis, culminate into a mini-textbook on the state of the art regarding key environmental processes and mechanisms relating to child psychopathology. From epigenetics, stress physiology, foetal and neonatal imaging, to domestic violence and bullying; ending with a focus on psychosocial, i.e., environmental, interventions for autism and suicide. For that reason, I gave the Special Issue the title: Re-imagining the environment in developmental psychopathology: from molecules to effective treatments.

The issue is kicked off by a fabulous overview by *Barker and colleagues* of the current state of the art of research on gene-regulation, and more specifically, the methylome, for understanding how the environment 'gets under the skin' and changes biological processes, including those implicated in psychopathology. Methylation is a biochemical mechanism in which methyl groups are added to segments of DNA mostly clustered in gene promoters that have the effect of switching off transcription, thereby silencing the gene. This mechanism is one of a number of dynamic processes that control the way the genome produces proteins that affect cell development and function, and appears to play a critical role in healthy and abnormal development. Studies in animals have shown that these changes can be triggered by environmental factors, and hence DNA methylation could be a mediating mechanism explaining how environments affect both physical health and mental disorder. The findings so far are complex, but the review points to tantalising evidence of DNA methylation sites mediating, at least in the statistical sense, the relationship between environmental exposures and childhood psychopathology. As the authors demonstrate, and Sonuga-Barke and I discuss in our commentary, there are many methodological challenges ahead for the next generation of studies of the methylome, but the prize, ultimately, is a rigorous picture of how the interface between genes, wider biology and the environment might work. One of the key areas that this field has focused on is gene-regulation of the stress system. The next review in the issue then couldn't be a neater fit. *Koss and Gunnar* (2018) provide a masterful synthesis of research on stress, the HPA axis and psychopathology. Again, the focus here is about understanding a biological process that may act as a mediator between adverse environments and risk for psychopathology. Like Barker et al, the authors highlight the role of DNA methylation as a key part of the causal chain. They also address the potential importance of sensitive periods in neurobiological development for setting the sensitivity of the HPA axis. Studies tackling this question in animals and humans are really homing in on the antenatal and early postnatal environment as key periods for epigenetic modification. Puberty, or peri-puberty, may be another crucial sensitive period.

The sensitivity of antenatal and early postnatal development to environmental influence underlines how important it is to be able to study the dynamics of brain development during these phases. *Batalle, Edwards and O'Muircheartaigh* (2018) provide a brilliant review of recent advances in prenatal, neonatal and early postnatal brain imaging. The very fact that it has become possible to overcome the technical challenges of studying brain structure and function in utero is staggering and exciting, and opens up whole new vistas for investigating the earliest origins of neurodevelopmental disorder, and the genetic and environmental mechanisms shaping early brain development. In their far-reaching review, the authors explore the intriguing hypothesis that microstructural abnormalities associated with premature birth (and indeed other adverse neonatal exposures) may reflect changes in the brain's network topology that are 'designed' to compensate for energetic deficiencies (e.g., associated with hypoxia) in order to maintain functionality of core neural systems, at the expense of higher-order cognitive functions, like memory, attention and executive functions. Interestingly, findings so far in autism tend to implicate quite distinct brain alterations, largely occurring postnatally, in the first 6 months to three years, although prenatal imaging of at-risk populations is yet to be done.

The next paper in the special issue by *Harold and Sellers* (2018) provides a timely review of what we currently know about the impact of inter-parental conflict on childhood psychopathology, the mechanisms involved and what can be done to reduce or prevent it. The review highlights the spectrum of experiences that children may be exposed to under this broad category, from 'silence to violence'. The evidence of impact is quite clear, and increasingly researchers are asked nuanced questions about which children are most vulnerable to these environmental exposures and what the mediating psychological and biological mechanisms are. Inter-parental conflict is a crucial 'hidden' environment affecting children, and this review will, I am sure, spur further scientific investment in this area.

The next review by *Arsenault* (2018) also focuses on a key social environment that is increasingly recognised as a major determinant of children and young people's psychological health and wellbeing: bullying. Arsenault provides an authoritative summary of the current state of play on this important topic. The elegant use of longitudinal studies and particularly genetically informative studies, including MZ twin difference designs, has convincingly demonstrated the role of bullying in a number of psychopathology outcomes in children and young people, especially anxiety and depression, and suggests that the effects may be long-lasting. The review also details crucial studies identifying risk and protective factors, such as higher prior levels of self-blame, low family supports, and a family history of suicide (the latter increasing risk that bullying leads to self-harm (Fisher et al., 2012)). The review also highlights the role of prior victimisation (e.g., parental maltreatment) in increasing the risk of experiencing peer victimisation. In other words, one form of maltreatment may lead to another. The good news is that anti-bullying programmes, delivered rigorously, can be effective.

The next two reviews focus on the treatment of autism spectrum disorder and its associated impairments. Psychosocial treatment of ASD has become an area of intense interest in recent years, as retrospective studies and studies of infants at genetic risk have identified a number of early-appearing predictors of later diagnosis that may be amenable to some form of early intervention, as highlighted by the previous Annual Research Review by Johnson et al., (2015). One intriguing possibility highlighted by *Green's* wide-ranging review of the state of the field of treatment research in ASD, is that some early neurocognitive vulnerabilities may impact on, and impoverish, necessary environmental inputs to social brain development and

thereby compound or canalise the emerging ASD phenotype. These early social experiences, such as those embedded in early social interactions, are plausible targets for intervention. As the review by *French and Kennedy* shows, the evidence for the efficacy of ASD-focused psychosocial interventions is decidedly mixed and the studies are of variable quality. Nevertheless, there are enough positive signs to warrant some optimism and certainly further larger scale programmatic research. As Green outlines, more rigorous designs are urgently needed, and treatments may need to consider ways in which they can be more accurately targeted on neuroscientifically defined targets. They may also benefit from integrating effective treatment elements from different programmes, even perhaps integrating pharmacological and psychosocial approaches (especially if the mechanism of synergy can be well articulated and tested).

Last but by no means least, the Annual Research Review ends with an outstanding review by *Cha and colleagues* on what we know about the causes of suicide in young people and its prevention. As the second leading cause of death in young people, suicide is a major public health concern. As the authors outline, suicide presents a complex problem, with remarkable variability in prevalence across time, age groups, contexts and countries. Environmental risk factors have been well described in past research, including bullying and maltreatment, but the challenge remains to understand how these powerful but non-specific risk factors impact directly on suicidal ideation and behaviour. Work on both psychological and biological markers of proximal risk, described in the review, is therefore crucial. The review implies that while prevention strategies may be partially effective, the key may be the combination of prevention, screening and targeted intervention. To achieve this, we need to be able to measure and dynamically track key proximal risk mechanisms more effectively, drawing on methods coming out of the best available social, developmental and neuroscientific research.

So, there you have it. And to cap it all, all the papers in the Annual Research Review are accompanied by a commentary by a leading expert who highlights many of the key points and draws out crucial clinical and research implications. On behalf of all the editors of JCPP, I hope you enjoy this year's ARR.

This is the last Annual Research Review that I will edit, as I am handing over the reins to Sara Jaffee, who I know will be a fabulous editor. I would like to take this opportunity to thank all the authors and commentators that I have had the good fortune to work with over the years, it has truly been a pleasure and an honour.

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