Beyond Vulnerability: Attachment, Adversity, Gene-Environment Interaction, and Implications for Intervention

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The Bucharest Early Intervention Project (BEIP) is unique in its effort to determine whether a positive postinstitutional experience of high-quality foster care, experienced on a random basis by institutionalized children, prevents or ameliorates the anticipated adverse developmental consequences of growing up in an environment characterized by severe deprivation. The fact that experience in such deprived circumstances adversely affects children, especially regarding their social-emotional functioning, including attachment, has been appreciated for half a century (e.g., see Tizard and Rees[1]; for review, see Van IJzendoorn et al[2]). The more recent discovery stemming from prior BEIP investigations that at least some of these adverse effects prove more pronounced in the case of some children rather than others, and as a function of their genetic makeup, underscores the fact that children are not equally susceptible to the adverse consequences of institutionalization or to the benefits of intervention intended to ameliorate or prevent such sequelae. Whereas prior work has thus documented differential susceptibility, or sensitivity, to the negative effects of institutional rearing and the positive effects of high-quality foster care after such adverse early experience, what the BEIP team's most recent report reveals is that such a differential legacy of atypical and typical attachment also applies to some more than others, and once again this seems to be accounted for, at least in part, by children's genetic makeup, specifically, whether they are homozygous for the short *5-HTTLPR* allele.

Two things make these latest BEIP results especially noteworthy. First, and once again, gene-X-environment (GXE) interaction evidence indicates that the disproportionate, even if understandable, concern of psychiatric geneticists for the negative effects of adversity risks misrepresenting the nature of human development. Rather than it just being the case that those carrying putative "risk" alleles prove disproportionately likely to function problematically when exposed to a stressor, as stipulated by the classic diathesis-stress model[3] of person-X-environment interaction, which has informed, implicitly or explicitly, much GXE work, at least until Belsky et al[4,5] challenged this view, what the report by Humphreys et al[6] makes evident again is that those most vulnerable to adversity are also most likely to benefit from contextual support or enrichment. In other words, they are more developmentally plastic or malleable, for better and for worse,[7] disproportionately succumbing in the face of stressors but thriving under good conditions.

The second reason why the latest BEIP results are especially notable is because of the very condition that is revealed to affect children in a for-better and for-worse manner, depending on their genetic makeup, namely attachment. Ever since attachment theory and research emerged, 2 things have been more or less assumed by developmental scholars: first, all children are equally susceptible to the effects of sensitive care in promoting attachment security and insensitive care in promoting attachment insecurity; second, the anticipated developmental benefits of security and costs of insecurity apply equally to all children. But what Humphreys et al[6] make crystal clear, as have a few studies before them,[8–10] is that at least in the case of atypical attachment vis-a-vis the prediction of externalizing problems, the latter presumption regarding the developmental sequelae of attachment simply does not hold. Indeed, as the central finding of Humphreys et al[6] indicates, the developmental legacy of atypical attachment proves not to be the same for all BEIP children. That is because it only forecasts elevated levels of externalizing problems among children homozygous for the short allele of the serotonin transporter gene, whereas typical attachment forecasts lower levels of problem behavior only for genetically similar short/short children. Thus, consistent with differential susceptibility theorizing,[5,11,12] the for-better and for-worse patterning of findings emerged with those carrying 2 putative "risk" alleles proving most likely to experience the presumed developmental benefits and costs of typical and atypical attachment, respectively. In line with prior meta-analytic evidence from GXE investigations involving children,[13] short alleles do not simply reflect, or confer, vulnerability and thus a diathesis condition, but developmental plasticity more generally (i.e., for better and for worse).

It seems especially notable that Humphreys et al[6] found that the GXE involving attachment proved

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significant even with the GXE interaction involving the intervention taken into account (along with main effects of attachment, genotype, and intervention), with the reverse being true as well. But one must wonder why no effort was made, or at least reported, to illuminate a 3-way G-X-attachment-X-intervention interaction. Would it not be of interest to learn whether the benefits of typical attachment and costs of atypical attachment apply equally to short/short carriers, irrespective of whether their attachment figure was a single foster care parent or one of several institutional caregivers, specifically, their "favorite"? One might imagine that the discerned gene-X-attachment effect would prove stronger when the child was relating to only a single caregiver (i.e., the foster parent) rather than to many. But would it not also prove interesting were this not the case? In the absence of the appropriate analyses, there is no way of knowing how these 3 important factors interact. However meritorious it might have been to address this issue empirically, it is certainly conceivable that Humphreys et al[6] refrained from doing so due to concerns about statistical power and thus the risks of prematurely embracing the null should no evidence of a 3-way interaction emerge in their modest-sized sample.

Despite the (apparent) failure to address this issue, there can be no doubt that the research under consideration is of importance. Perhaps most impressively, it builds on a huge effort undertaken by the investigatory team to provide not just foster care but high-quality foster care to children whose prior lives in Romanian institutions no one would wish on any child. Then, there is the fact that when it came to investigating intervention effects, the investigators relied on state-of-the-art intention-to-treat analyses making their findings conservative in character. Most notable, of course, is the authors' appreciation, based on differential susceptibility theory and their own prior work, that children not only vary in their sensitivity to their developmental experiences and environmental exposures, but also that it may not be the case that some are simply more vulnerable to adversity than others. In fact, in finding that genetic makeup seems to make some more susceptible to both adversity and enrichment in the form of atypical and typical attachment, with others seemingly not affected at all, their work raises, like related research, a most pressing intervention issue: With whom should one intervene?

In a world of limited resources, if we keep discovering that some prove more susceptible to developmental experiences, environmental exposures, and now to attachment, should we consider "targeting" for intervention those most likely to benefit from support and enrichment, who are also most likely to have their development compromised when not provided with such, even if the basis of targeting is a child's genotype? Consider in this regard that emerging evidence does indeed indicate that intervention effects are genetically moderated[14,15] including prior research by the BEIP study team (e.g., see Refs. 16,17). If ever more such evidence emerges, how should we manage the tension between equity or treating all the same and efficacy, that is, providing services disproportionately to those most likely to benefit from them?

My own view on this is two-fold. First, every child deserves a decent quality of life irrespective of whether he or she reaps detectable developmental benefits from it. Children's lives are not exclusively about preparation for the future; the present counts too. Clearly then, no child should be exposed to the kind of care that Romanian and many other institutions provide. It is simply not humane.

But once the issue is not whether care qualifies as humane, I believe an emphasis on efficacy over equity is called for with one proviso. To my way of thinking, there is nothing ethical about (1) providing services to those who do not benefit, (2) especially if limited-resource conditions mean that those who could and would benefit are denied the service when equity is the primary guiding principle, and (3) when taxpayers are asked to pay for the services being provided.

But now for the proviso: evidence that a particular service or even multiple services only benefit some and not others should not be a license for abandoning efforts to benefit those who prove nonresponsive to the services being provided. Efforts need to be made to determine whether the nonresponders are whom I would call "fixed" as opposed to "plastic" strategists, ones whose development is not, for genetic or other reasons, shaped by their developmental experiences and environmental exposures, or whether they just appear that way. After all, it may be that even if this or that or even multiple interventions do not seem to benefit some seemingly "fixed" strategists, treatments that have not been considered or investigated still might. Even if my theoretical leanings incline me to believe that some will prove relatively impervious to most interventions, I suspect that this will not be the case for many nonresponders.

The question becomes, in fact, whether susceptibility should be conceptualized in categorical or dimensional terms. Are some developmentally susceptible (e.g., short/short homozygotes) and others not (e.g., l/l homozygotes) or are some simply more susceptible and others less so? As it turns out, GXE research[11] and even gene-X-intervention research from the BEIP project[16,17] makes clear that when one considers multiple genetic moderators using polygenic scores, rather than single candidate genes as in Humphreys et al,[6] that dose-response relations obtain between environmental exposures and developmental consequences. That is, individuals carrying more rather than fewer "plasticity genes" seem to be more affected than others. This clearly implies that a dimensional rather than categorical view of susceptibility is called for. In other words, there appears to be a plasticity "gradient."

Finally, one should not lose sight of theory suggesting that plasticity itself can be induced by developmental experiences.[5,12,18] To the extent that this proves to be

the case, then it may be that even when genetic evidence suggests otherwise, those seemingly impervious to anticipated effects of developmental experiences and environmental exposures can have their development shaped by them.

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