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# Beyond risk, resilience, and dysregulation: Phenotypic plasticity and human development

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**Abstract**

We provide a theoretical and empirical basis for the claim that individual differences exist in developmental plasticity and that phenotypic plasticity should be a subject of study in its own right. To advance this argument, we begin by highlighting challenges that evolutionary thinking poses for a science of development and psychopathology, including for the diathesis–stress framework that has (fruitfully) guided so much empirical inquiry on developmental risk, resilience, and dysregulation. With this foundation laid, we raise a series of issues that the differential-susceptibility hypothesis calls attention to, while highlighting findings that have emerged over just the past several years and are pertinent to some of the questions posed. Even though it is clear that this new perspective on Person × Environment interaction is stimulating research and influencing how hypotheses are framed and data interpreted, a great many topics remain that need empirical attention. Our intention is to encourage students of development and psychopathology to treat phenotypic plasticity as an individual-difference construct while exploring unknowns in the differential-susceptibility equation.

Empirical research on risk and resilience first emerged in the 1970s (e.g., Garmezy, 1974; Rutter, 1979; Werner & Smith, 1977) and has come to exert a major influence on the study of development and psychopathology (for reviews, see Luthar, Cicchetti, & Becker, 2000; Masten, 2007; Rutter, 2012). One of the most important and valuable insights that emerged over the past decades has been that individuals differ in the degree to which they are affected by contextual adversity. Whereas some "vulnerable" children and adults are likely to develop problematically in response to negative contextual conditions by becoming emotionally and/or behaviorally dysregulated, others are not and are thus regarded as "resilient."

Empirically observed variability in vulnerability to contextual adversity accords nicely with the widely embraced, if not always labeled, diathesis–stress framework (Gottesman & Shields, 1967; Monroe & Simons, 1991; Zuckerman, 1999). This perspective stipulates that some individuals are disproportionately, if not exclusively, likely to succumb to the negative effects of some contextual stressors (e.g., childhood maltreatment, insensitive parenting, poverty) and become psychologically and/or behaviorally disturbed and dysregulated, if not disordered. This heightened vulnerability to adversity may be due to organismic characteristics of the individual, such as genetic makeup, personality, or temperament, or even family factors and processes or extrafamilial conditions. Perhaps nowhere else has diathesis–stress thinking explicitly or implicitly guided recent empirical inquiry more than in the study of Gene × Environment (G × E) interaction (e.g., Caspi et al., 2002).

One of the challenging issues that arises with respect to diathesis–stress motivated G × E research has to do with understanding why natural selection would craft an organism to respond to adversity by becoming disordered or dysregulated. That is, what could be the pay-off of developmental dysfunction? As we clarify in the next section, the answer to this question emerges upon challenging another prevailing notion that is commonly encountered in the literature on development and psychopathology, that of "optimal development." Thus, the first major section of this paper raises some evolutionary-inspired challenges to diathesis–stress thinking and, more generally, the science of development and psychopathology. Although evolutionary theory has made inroads recently into these arenas of inquiry (see the 2011 Special Section of *Development and Psychopathology* edited by Ellis and Boyce and 2012 *Developmental Psychology* edited by Ellis and Bjorklund), it would still be fair to say that developmentally oriented scholars have been among the slowest to embrace an evolutionary perspective. We seek to change that and join the limited company of others, some of whom have encouraged such an orientation relatively unsuccessfully for quite some time (Belsky, Steinberg, & Draper, 1991; Bjorklund & Pellegrini, 2002; Daly & Wilson, 1980, 1981).

The evolutionary-inspired challenges to prevailing thinking about development and psychopathology that we highlight in the next section, including the diathesis–stress framework, lead to the conclusion that developmental plasticity should be regarded as a phenotype in its own right, that is, as an individual-difference construct, something students of animal behavior are becoming ever more appreciative of

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(Dingemanse, Kazem, Reale, & Wright, 2010; Mathot et al., 2011). This claim calls attention to a new and evolutionary-inspired way of thinking about Person × Environment interaction: the differential-susceptibility framework (Belsky, 1997, 2005; Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007; Belsky et al., 2009; Belsky & Pluess, 2009a; Boyce & Ellis, 2005; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011). In an attempt to further inquiry in this area, we highlight future directions for research and theory by highlighting some new empirical findings in the second major section of this paper. Then, we draw some general conclusions in the final section.

## Evolutionary Challenges to a Science of Development and Psychopathology

### *Optimal versus adaptive development*

Much theory, research, and writing about development and psychopathology today is based on what has been described recently as the "mental health model" (Belsky, 2008) or "developmental psychopathology model" (Ellis et al., 2012; Frankenhuis & Del Giudice, 2012). Central to this theoretical and empirical framework is the implicit if not explicit assumption that there is something ubiquitously referred to in the developmental literature as "optimal" development. The notion of optimal development more or less implies that it is the natural condition of humans from youth to later in life to become secure, autonomous, self-controlling, prosocial, achievement striving, intimate in the context of pair bonds, hardworking, sensitively responsive in parenting, and generative in the next generation, as well as physically healthy, happy, and long lived. Development goes awry (i.e., becomes dysregulated) when forces direct it from its natural or otherwise anticipated course. Thus, being insecure, dependent, impulsive, antisocial, a risk taker, an insensitive parent, and/or depressed are implicitly if not explicitly regarded as developmental outcomes that nature did not intend.

However, an evolutionary perspective challenges this prevailing view of so-called dysfunctional, dysregulated, or maladaptive development, especially when, consistent with diathesis–stress thinking, it arises within settings of adversity (Belsky, 2008; Daly & Wilson, 2005; Ellis, 2004; Ellis, Boyce, et al., 2011; Ellis et al., 2012; Hinde & Stevenson-Hinde, 1990). Because stressful and supportive environments have been part of human experience throughout our evolutionary history, evolutionists conceptualize developmental systems as shaped by natural selection to respond adaptively to both kinds of contexts. From this perspective, the experience of encountering stressful environments does not so much disturb, or dysregulate, development as direct, *or regulate*, it toward strategies that are or at least once were biologically adaptive under conditions of adversity. Moreover, by adaptive we mean functional and perhaps even optimal, given the circumstances in which the individual finds him/herself, in that they directly or indirectly promoted the individual's reproductive fitness. (See below for further discussion of this fundamental goal of all living things.)

Some of the most compelling evidence highlighting the validity of the adaptational perspective just outlined can be found in the much-heralded rodent work showing that what is regarded by many as "low-quality" maternal care in the rat, as reflected in limited licking and grooming of the newborn pup, modifies stress physiology and brain morphology, but in functional and strategic rather than maladaptive ways. Even though evidence of higher corticosterone levels, shorter dendritic branch lengths, and lower spine density in hippocampal neurons would appear to provide indisputable evidence of negative effects of early experience, such presumptively nonoptimal developments appear strikingly functional, given the conditions that gave rise to them. This is because the developmental experiences in question enhance learning and memory processes under stressful conditions (Champagne et al., 2008). Moreover, such putatively disturbed or dysregulated physiological and morphological changes promote central features of defensive and reproductive strategies (behavior under threat, open-field exploration, pubertal development, sexual behavior, and parenting; Cameron et al., 2005) in ways consistent with evolutionary models of adaptive reproductive strategies (Belsky et al., 1991; Chisholm, 1993), a subject we consider in greater detail below.

Ultimately, developmental adaptations to high-stress environments enable individuals to make the best of a bad situation (i.e., mitigate inevitable fitness costs), even though "the best" may still constitute a high-risk strategy that jeopardizes the person's health and survival (e.g., Mulvihill, 2005; Shonkoff, Boyce, & McEwen, 2009). It is certainly possible to view many of the developmental sequelae of child maltreatment in this manner. After all, it is not difficult to appreciate the developmental "wisdom" in being especially vigilant to threat, engaging in biased attributions or behaving aggressively if the lessons of a painful life have taught one to "act first and ask questions later" and "presume the worst rather than the best of people." By the same token, the indiscriminant friendliness of institutionally reared children (Bakermans-Kranenburg et al., 2011) could be regarded as a highly functional strategy for seeking help and support in a world that has offered little, even if it looks disturbed or disordered from the perspective of family-reared children.

Reflection on these observations should clarify why natural selection may have crafted human development to respond to certain conditions by making individuals behave in ways we now regard as disturbed, dysfunctional, dysregulated, psychopathological, and nonoptimal. As such, this analysis perhaps strengthens the theoretical foundations of diathesis–stress thinking that we questioned earlier. That is, one can now understand why nature may have crafted at least some individuals to respond to adversity by developing in putatively disturbed and dysregulated ways. Nevertheless, it remains our view that the potential costs of not responding to adversity in a putatively dysfunctional, dysregulated, and dis-

ordered manner merits more consideration by students of development and psychopathology than it has been given. Thus, in addition to considering the possible benefits of behavior regarded by many as dysregulated and problematic, students of development and psychopathology would be well advised to consider what the costs may be of behaving, given the circumstances some live in, in those ways that mainstream thinking labels as optimal.

The argument advanced here ultimately calls into question the use of the term *optimal* when discussing development and suggests that there could be substantial merit in thinking more in terms of why it may actually make good sense for children, adolescents, and adults to behave in the dysregulated and troubled ways in which they do. However, such a perspective does not mean abandoning efforts to reduce psychological pain and suffering. What it suggests is that to do so most effectively may require consideration of the payoffs and tradeoffs that may have resulted in natural selection crafting an organism to develop and behave in the way we observe them to, especially under conditions of adversity. We suspect that intervention efficacy could be enhanced if interventionists seriously considered "biological gravity" (natural selection has crafted phenotypes that serve to enhance fitness) when designing programs rather than think only in traditional mental health terms about what behavior is optimal and what is not. Much like the efforts of would-be aviators who predated the modern ones who eventually came to grips with physical gravity, thereby recognizing the need for lift and propulsion before they could fly, some intervention efforts reflect little more than attaching wings to the arms and jumping off cliffs. Without understanding the nature, origin, and function of disordered and dysregulated behavior, including its evolutionary basis (i.e., biological gravity), the likelihood of preventing or remediating it may be seriously compromised. Ellis and associates (2012) develop this point further in the case of adolescent risk taking, highlighting existing interventions that appear consistent or inconsistent with evolutionary thinking as well as offering novel, evolutionary-inspired ones.

### *Probabilism versus determinism*

It is widely appreciated by developmentalists today that factors that shape human development typically do so in a probabilistic rather than deterministic fashion. That is, forces that we expect to enhance or undermine human functioning, in the traditional mental health sense, will not always do so, even if they sometimes, or even often, do so. This probabilistic nature of development also needs to be appreciated in its evolutionary basis, something that seems forgotten when it is argued that disturbances in development could not reflect evolutionary adaptations because they so often lead to failure, including perhaps failure to disburse genes in future generations in the modern western world. Two points merit consideration in response to this seemingly reasonable observation.

The first is that natural selection is backward not forward looking, selecting phenotypes that have fostered fitness in the past. This means that what was once evolutionarily adaptive may no longer be so today. However, even if that is true, which should not necessarily be the default assumption, it would not "biologically" follow that the neurobiological and psychological processes that gave rise to them in the first place would have been short circuited in order to no longer engender the behavioral functioning that is typically regarded as problematic today. If that were the case, it would be easy to override the human proclivity to consume sugary foods. After all, this penchant for sweets evolved at a time when such substances were rarely or intermittently available, yet in the modern world today they are continuously available and abundant. Thus, even if a developmental process no longer achieves the goal it was selected to realize but instead engenders developmental problems in the modern world (e.g., obesity), the process itself likely remains operative because of the time it takes for evolution to engineer genetic change.

The second point regarding probabilism and nonoptimal development is that, for selection to take place, a phenotype does not have to always or often succeed in enhancing fitness; it only needs to have done so more often than alternative phenotypes once did (Frankenhuis & Del Giudice, 2012). Moreover, the costs of failure need to be weighed against the benefits of success (Ellis et al., 2012; Figueredo & Jacobs, 2010; Frankenhuis & Del Giudice, 2012). Thus, even if antisocial behavior or depression or teenage pregnancy seem counterproductive from either a mental health or fitness standpoint and could have proven so in the past (failing more often than succeeding), such putative disturbances in development could still have been selected, especially when a low-frequency success engendered a substantial payoff. What this implies, of course, is that some putatively dysregulated behavior will be of the high-stakes' variety: unlikely to succeed yet succeeding hugely when it does.

### *What is development trying to achieve?*

The concept of optimal development is most certainly intended to capture phenomena like health, happiness, security, longevity, and other indisputably highly valued life conditions. On the basis of much developmental writing, it would not seem misguided to infer that nature has crafted human development to achieve such outcomes. From an evolutionary perspective, however, this is certainly not (exclusively) the case. Although security, good health, happiness, and a long life may be the means by which some or many individuals successfully pass genes on to future generations and promote their more general inclusive fitness, especially when growing up and living under benign or benevolent conditions, there is no reason to presume that these phenotypes achieved or can achieve these same ends under all conditions, especially contrasting conditions. This observation was central to Belsky's (in press; Belsky et al., 1991) effort to recast socialization theory in evolutionary perspective two decades ago, which was built on Draper and Harpending's (1982) evolutionary insight

about why father absence may be related to "promiscuous" sexual behavior on the part of females.

Rather than presuming that development was crafted by natural selection to yield phenotypes reflective of optimal development, Belsky et al.'s (1991) psychosocial acceleration theory and its derivatives (Chisholm, 1993; Del Giudice, 2009; Del Giudice, Angeleri, & Manera, 2009; Ellis, 2004; Ellis & Garber, 2000; Frankenhuis & Panchanathan, 2011; James, Ellis, Schlomer, & Garber, 2012) are founded on the premise that the ultimate goal of all living things, including humans, is to disperse their genes to future generations and that the means of achieving this fitness end is contextually contingent. Thus, what works under certain developmental conditions does not necessarily work under others. It is ultimately for this reason that the notion of optimal development is fundamentally problematic: what is optimal in one (modern and well resourced?) context may not be so in another.

We submit that students of development and psychopathology would do well to think in fitness terms when trying to understand phenotypes of concern. Upon doing so, what is regarded as dysregulated, dysfunctional, disturbed, or disordered may come to be seen in a new and informative light, a point recently made by Ellis and associates (2012) with respect to adolescent risk taking. Once again, however, an evolutionary perspective with its emphasis on selection of phenotypes that foster the dispersion of genes in future generations does not mean that nothing should be done. Such would reflect succumbing to the naturalistic fallacy, inferring what "ought to be" from what "is," a long-derided perspective. However, we do suggest that seeing development the way natural selection views it may facilitate efforts to address contemporary concerns.

### *Fast versus slow development*

Because of its grounding in evolutionary life-history theory (Kaplan & Gangestad, 2005; Stearns, 1992), psychosocial acceleration theory appreciated that growing up fast and behaving in putatively nonoptimal ways was sometimes advantageous when it came to dispersing genes in future generations. Although maturing early is known to carry numerous risks for females, including early sexual debut, early first birth, sexually transmitted disease, and breast cancer (Ellis, 2004), such "ontogenic risk taking" was theorized to make biological sense under conditions of adversity. It was for this reason that Belsky et al. (1991) proposed that rearing conditions that induced in the individual the sense that the future was risky and that supportive relationships were precarious would promote early maturation, early sexual debut, promiscuous sexual behavior, unstable pair bonds, limited parental investment, and the bearing of more rather than fewer offspring. After all, from the standpoint of reproductive fitness, it is better to "live fast and die young," having offspring along the way, than to die (or become disabled) before getting the chance to reproduce (Chisholm, 1993; Nettle, 2010). Thus, adolescents who, for example, respond to dangerous environments by developing insecure attachments; adopting opportunistic, advantage-taking interpersonal orientations; engaging in externalizing behavior; discounting the future; and experiencing early sexual debut are no less functional or even less regulated than are those responding to a well-resourced and supportive social environment by developing the opposing characteristics and orientations (Belsky et al., 1991; Ellis, Boyce, et al., 2011).

What this analysis highlights is that development involves trade-offs, a concept central to an evolutionary, life-history perspective. As just noted, a primary risk associated with waiting to mature, find a mate, and breed is that one may not survive long enough to achieve any or all of these ends. Additional risks include limits to ones' capabilities and competencies, as well as poor health, thereby making it difficult to attract mates and/or protect and facilitate the development of the offspring one eventually produces. Ellis and associates (in press) recently pointed out in this regard that the concept of allostatic load, which informs ever more developmental inquiry (e.g., Evans & Kim, 2012; Fuller-Rowell, Evans, & Ong, 2012), may need rethinking. Instead of conceptualizing this construct as part of a disease process, it could be better to think of it in terms of evolutionary and life-history trade-offs. Although there are indisputable costs associated with developing in certain ways under conditions of ecological stress, costs that seem to undermine child well-being, long-term health and even longevity, these costs may be compensated for by the increased likelihood that the individual incurring these costs would make it to maturity, find a mate, and produce offspring.

It is intriguing that the aforementioned rodent work once again proves consistent with the view just advanced: *life conditions can regulate the rate of development in the service of fitness goals*. Moreover, this is because it is not true that stressful rearing conditions that take the form of limited maternal licking of the rat pup increase fearful and defensive behaviors via the epigenetic regulation of the stress-response system. All too unappreciated by many developmentalists who (appropriately) herald this work for its documentation of such effects is that such putatively limited maternal care also accelerates sexual maturation, increases sexual behavior, and reduces parental investment. It would appear then that parental "neglect" in the form of limited licking and grooming serves as a means of regulating (not dysregulating) development in a biologically strategic manner. This is consistent with Belsky et al.'s (1991) psychosocial acceleration theory, as noted by Cameron and associates (2005). In this rodent context, neglect can be regarded as a mechanism through which rat mothers facilitate their offspring's development by accelerating it toward survival and reproductive strategies that are optimal under conditions of adversity. Therefore, it would seem mistaken to view diminished licking and grooming as "poor maternal care" or the development induced by such care as disturbed, dysregulated, or nonoptimal. From an evolutionary perspective, the care provided by the putatively neglectful parents may serve as appropriate preparation

of their offspring for the ecological conditions into which they are likely to mature.

### *Costs and limits of plasticity*

Like many theories and perspectives on human development, psychosocial acceleration theory presumes that development is contextually conditional and developmentally plastic. Developmental experiences and environmental exposures regulate growth and development such that how an individual turns out is at least partly based on environmental influences, shared or unshared, to use the terminology of behavior genetics (Plomin & Daniels, 1987). Evolutionists use the terminology *adaptive developmental plasticity* to characterize this process (Schlichting & Pigliucci, 1998; West-Eberhard, 2003), as do evolutionary-minded developmentalists (Belsky et al., 1991; Chisholm, 1993; Ellis, 2004; Kuzawa, 2005; Nettle, 2011; Quinlan, 2007).

However, what many developmentalists have failed to appreciate (and we include ourselves among this group, at least until recently) is that plasticity carries costs (DeWitt, Sih, & Wilson, 1998; Frankenhuis & Del Giudice, 2012; Schlichting & Pigliucci, 1998; Sih, 2011). There is the cost associated with the increased complexity that may be required of organisms in order to be capable of developing in diverse ways depending on contextual conditions. The costs derive from the idea that, as complexity increases, so does the risk of something going wrong, in the same way that a machine with more moving parts has more ways to break down than one with fewer parts. Consider the following and related costs of plasticity enumerated by DeWitt and associates (1998): energetic costs of the sensory and regulatory mechanisms of plasticity; the production cost of environmentally inducible structures and processes; the cost of acquiring information about the environment, including the energy expended and potential risks incurred; and the imprecision in "manufacturing" a phenotype based on environmental experience. Collectively, these would seem to imply that some individuals may manifest limited malleability, with their development highly canalized, trading off the benefits of being able to thrive in more than a single ecological niche against costs of a breakdown in the developmental machinery and processes needed to do so.

It is also important to appreciate with respect to the costs of plasticity that modifying development early in life in response to developmental experiences and environmental exposures may result in a "mismatch" between the developed organism and the environment in which it finds itself later in life (Nederhof & Schmidt, 2012; Sih, 2011). In this way, seemingly adaptive developmental plasticity, selected to allow the organism to be "programmed" on the basis of early experience so as to "fit" the later environment, can undermine developmental opportunity and eventual fitness rather than enhance it. Thus, here is another reason why there seem to be grounds for expecting individual differences in developmental plasticity. After all, those individuals whose development is more canalized and less programmable by environmental exposures would be less likely to experience a mismatch resulting from developmental plasticity. Of course, such highly canalized specialists with more or less fixed characteristics could end up mismatched to their environment, but for different reasons from that of the plastic, programmable generalist, who may develop in a manner guided by experiences earlier in development.

What these observations imply is that the being developmentally malleable should not be regarded, as it typically is, as an unmitigated good for the developing organism and, thus, as something that should be pronounced in all individuals. In some cases it would appear wiser not to be plastic or to be less malleable, manifesting a more canalized pattern of development, than others and thus less susceptible to environmental conditions. What this suggests, as noted repeatedly, is that we should expect individual differences in developmental plasticity. In other words, *developmental plasticity should be conceptualized as a phenotype in its own right*, something that will vary across individuals for a variety of reasons. For the most part, this possibility has not been appreciated by those studying development and psychopathology, at least not until recently. Where it has, questions can be raised about how those studying development and psychopathology have conceptualized the issue.

## New Directions for Theory and Research

Recall that central to the prevailing diathesis–stress model of environmental action and psychopathology is the view that some individuals are more susceptible than are others to the negative developmental effects of contextual adversity; these are the so-called vulnerable ones. We have already questioned whether it would make evolutionary sense for nature to craft a species in which some individuals were more susceptible than others, especially for organismic reasons, to having their development compromised by becoming disordered or dysregulated. Recall, however, that we then delineated why this could nevertheless occur, especially once we eschewed concepts like "developmentally compromised" and optimal development, while appreciating that what is often regarded as nonoptimal and dysregulated could enhance fitness or could have in our ancestral past under certain conditions.

An alternative, evolutionary-inspired way of thinking about Person × Environment interaction has recently gained a foothold in the developmental literature and psychopathological literature, one that is based on the appreciation of the costs of plasticity. It differs from the traditional diathesis–stress model by treating developmental plasticity as a phenotype while proposing that what appears to be evidence of disproportionate vulnerability to adversity may actually reflect more general and often undetected negative *and* positive susceptibility to environmental influences in the mental-health sense of these terms (Belsky, 1997, 2005; Belsky et al., 2007; Belsky et al., 2009; Belsky & Pluess, 2009a, 2009b; Boyce & Ellis, 2005; Ellis, Boyce et al., 2011). The argument has been advanced that the former viewpoint has

been more widely considered than the latter not only because of the absence of an evolutionary perspective when thinking about development and psychopathology but also because of the designs of many investigations (Belsky, 2005; Belsky et al., 2007; Belsky & Pluess, 2009a; Ellis, Boyce et al., 2011). Rather than studying the full range of environmental exposures and of development from negative to positive, there has been a disproportionate, even if understandable (from a humanitarian point of view), focus on contextual adversity and developmental dysfunction/dysregulation. This has resulted in individuals who may be disproportionately responsive to negative and positive developmental or other environmental experiences and exposures being regarded exclusively as disproportionately susceptible to the negative effects of adversity.

Fortunately, this situation is changing rapidly, but it remains that numerous issues related to developmental plasticity as a phenotype and differential susceptibility to environmental influences are in need of attention. In this section, we therefore highlight these as a way of outlining future directions for research. Along the way we also summarize some of the latest differential-susceptibility related findings, virtually all of which have appeared since our 2009 reviews of the literature (Belsky et al., 2009; Belsky & Pluess, 2009a).

### *Resilience or reduced plasticity?*

Implicit in the diathesis–stress model is the notion of resilience. After all, the resilient individual develops in a manner opposite that of the vulnerable one according to this theoretical perspective, because he or she is, by definition, "protected" from the anticipated negative effects of adversity (Cicchetti & Rogosch, 2012; Garmezy, Masten, & Tellegen, 1984; Masten, Best, & Garmezy, 1990; Rutter, 1987, 2012; Werner & Smith, 1982). Because diathesis–stress thinking focuses upon response to adversity, it makes no claims about differences in how resilient and vulnerable individuals develop under benign or supportive conditions. In this regard it differs substantially from differential-susceptibility thinking, because differential susceptibility presumes that the putatively vulnerable are generally plastic in a "for-better-and for-worse manner" (Belsky et al., 2007); whereas the putatively resilient will be relatively unresponsive to supportive conditions, just like they are to unsupportive ones, with their developmental pathways highly canalized. This view leads us to take issue with the use of the terms *buffer* and *protection* when discussing how more developmentally plastic individuals respond to positive circumstances; such individuals are not so much protected (against what?) when they experience good conditions, as some contend (e.g., Zimmermann et al., 2011), but they experience *enhanced* functioning, something not expected of those resilient to adversity (for a review, see Pluess & Belsky, 2013).

To the extent that this is the case, it would suggest that resilience, or at least that which derives from endogenous characteristics of the individual (e.g., temperament, genotype), is something of a misnomer, reflecting a highly canalized developmental process with limited developmental plasticity more than anything else (Pluess & Belsky, 2013). Unfortunately, too many investigations of risk and protection informed by diathesis–stress thinking have not only failed to entertain this possibility for theoretical reasons but have also not been well positioned to evaluate it for reasons previously outlined: a supportive environment in much resilience research often reflects little more than the absence of adversity (e.g., not impoverished, not maltreated), and positive functioning often reflects nothing more than the absence of dysfunction (e.g., not depressed, not aggressive). In order to be able to determine whether those resilient to adversity are also relatively unresponsive to environmental support and enrichment, as the differential-susceptibility framework presupposes, more will be required than merely expanding the range of measurements of environments and development.

### *Vantage sensitivity: Response to positive environmental influences*

According to differential susceptibility reasoning, diathesis–stress thinking only addresses the "dark side" of the Person × Environment equation, ignoring the "bright side." Recently, we adopted and promoted the term *vantage sensitivity*, originally introduced by Manuck and associates (Manuck, 2011; Sweitzer et al., 2013), to convey the notion that some individuals are more sensitive and positively responsive to the environmental advantages to which they are exposed and *vantage resistance* to describe the absence of such responsivity in other individuals (Pluess & Belsky, 2013). In that effort, we also reviewed emerging empirical evidence for vantage sensitivity as a function of behavioral, physiological, and genetic factors previously associated with differential susceptibility and diathesis–stress. Although the same factors seem to moderate effects of environmental influences, irrespective of whether they are exclusively negative (i.e., diathesis–stress), exclusively positive (i.e., vantage sensitivity), or range from the negative to the positive (i.e., differential susceptibility), it is important to caution against inferring that every risk factor will also, by default, function as a vantage-sensitivity and thus differential-susceptibility factor. Ultimately, this is an empirical question, as there may very well be specific factors that play a predominant role in diathesis–stress but not in vantage sensitivity and vice versa. Future research should address whether there are psychological, behavioral, or neurobiological factors and mechanisms that are specific to diathesis–stress or vantage sensitivity.

### *Competitive evaluation of models of Person × Environment interaction*

Much of the evidence cited in our earlier reviews of differential-susceptibility related evidence (Belsky et al., 2009; Belsky & Pluess, 2009a), as well as in subsections to follow, is based on "eye-ball" tests of graphed interactions between an environmental predictor and developmental outcome

moderated by a plasticity factor. The limits of this approach to "testing" the differential-susceptibility hypothesis led Belsky et al. (2007) to propose explicit empirical criteria. Subsequently, Kochanska, Kim, Barry and Philibert (2011) extended this effort by using the regions of significance approach (Preacher, Curran, & Bauer, 2006; Takane & Cramer, 1975) to separately evaluate the for-better and for-worse sides of the differential-susceptibility hypothesis upon documenting the required cross-over interaction.

Roisman and associates (2012) recently offered an even more demanding approach for evaluating differential susceptibility by providing two new quantitative metrics in combination with the regions of significance analysis: the *proportion of interaction* index, which represents the proportion of the total area of an interaction plot that is uniquely attributable to differential susceptibility, and the *proportion affected* index which quantifies the proportion of people in the sample who fall above the cross-over point (i.e., proportion of sample in the for-better condition). In addition, Roisman et al. (2012) recommend testing for nonlinear relationships between predictor and outcome and correction for multiple comparisons.

All of the approaches offered to date to evaluate differential susceptibility have involved conducting essentially exploratory tests of Organism × Environment interactions as a first step before further interrogating the data at hand. Widaman and associates (Belsky, Pluess, & Widaman, 2013; Widaman et al., 2012) recently advanced a strategy that sidesteps such approaches, moving directly to test competing theoretical models. In a first step, the cross-over point between high- and low-susceptible individuals is estimated with the help of a reparameterized regression equation (Widaman et al., in press). If the estimated cross-over point lies within the observed range of the predictor, four additional reparameterized regression models are applied: two constrained to reflect a weak and a strong version of diathesis–stress and two to reflect a weak and a strong version of differential susceptibility. Fit indices of the four models are then compared to evaluate whether the data fits better with a diathesis–stress or differential-susceptibility model (Belsky et al., 2013). The strong version of differential susceptibility presupposes that there are those who are susceptible to positive and negative contextual conditions and others who are not; the weak version presupposes that, although many may be susceptible to environmental influences to some extent, some are more affected than others.

The time has thus come to move beyond exploratory tests of Organism × Environment interaction in regression and analysis of variance designs and to more formally evaluate in a competitive manner the a priori hypotheses central to diathesis–stress and differential-susceptibility models of environmental action.

### *Temperament/negative emotionality as plasticity factor*

The first evidence Belsky (1997, 2005) could point to consistent with his evolutionary-inspired, differential-susceptibility hypothesis surprisingly indicated that a difficult temperament or high levels of negative emotionality (e.g., fear, inhibition) early in life not only function as a risk factor that increases the likelihood of problematic functioning when coupled with contextual risks (e.g., poverty, maternal depression), as long presumed, but also seemed to predispose individuals to benefit from benign or supportive experiences. Since our 2009 review, even more evidence to this effect has emerged in the case of children, as revealed in research linking maternal empathy (Pitzer, Jennen-Steinmetz, Esser, Schmidt, & Laucht, 2011) and anger (Poehlmann et al., 2012) with externalizing problems; mutual responsiveness observed in the mother–child dyad with effortful control (Kim & Kochanska, 2012); intrusive maternal behavior (Conway & Stifter, 2012) and poverty (Raver, Blair, & Willoughby, 2012) with executive functioning; and sensitive parenting with social, emotional, and cognitive–academic development (Roisman et al., 2012).

However, it is not just responsiveness to parenting that negativity seems to moderate in a for better and for worse manner, as documented in recent work examining the influence of teacher–child conflict on change in symptomology during the primary-school years (Essex, Armstrong, Burk, Goldsmith, & Boyce, 2011) and of marital quality on sensitive mothering (Jessee et al., 2010). The latter work also makes it clear that it is not just children who prove differentially susceptible to environmental effects. We would be remiss, however, if we failed to call attention to studies showing it was less rather than more negatively emotional or reactive children who proved highly responsive to environmental experiences in a manner consistent with differential susceptibility (Essex et al., 2011, see their figure 2, bottom; Du Rocher Schudlich, White, Fleischhauer, & Fitzgerald, 2011) and to other evidence showing that sometimes difficult temperament operates only in a manner consistent with the diathesis–stress rather than differential-susceptibility framework (Kochanska & Kim, 2013; Roisman et al., 2012; Yaman, Mesman, van IJzendoorn, & Bakermans-Kranenburg, 2010).

The cited research reveals that diverse indices of negative emotionality function as plasticity factors (e.g., fear, inhibition, distress, difficult temperament, negative affect), which raises several issues that future research should address. For example, is there a particular component or feature of negativity that is principally responsible for the moderational effects detected (Buss, 2011) or could more progress be made with regard to this issue by embracing the integrated, evolutionary, hawk–dove model of temperament (Korte, Koolhaas, Wingfield, & McEwen, 2005) that Sturge-Apple, Davies, Martin, Cicchetti and Hentges (2012) recently found to be empirically useful? Whereas hawklike strategies are characterized by approach, dominant–negative affect (e.g., anger), and activity, dovelike ones involving avoidance, inhibition, and vulnerable affect (e.g., fear) seem more consistent with heightened plasticity according to existing research.

We also wonder about the extent to which the moderational effect of negative emotionality depends on the origins

of this plasticity factor, given evidence that negativity is heritable (e.g., Buss & Plomin, 1984; Rhee et al., 2012) but also shaped by prenatal and postnatal experience (Belsky & Pluess, 2009b; Davis, Glynn, Waffarn, & Sandman, 2011; Glynn & Sandman, 2011; for a review, see Pluess & Belsky, 2011), although sometimes more so in some genotypes than others (Ivorra et al., 2010; Pluess et al., 2011). Thus, what may be particularly important is distinguishing negative emotionality that reflects an experience-induced failure to self-regulate and that which reflects a general hypersensitivity to the environment.

### *Physiological reactivity as a plasticity factor*

Belsky's (1997, 2005) differential-susceptibility hypothesis was based entirely on evolutionary reasoning, but Boyce and Ellis' (2005) evolutionary-oriented biological sensitivity to context (BSC) proposal emerged in response to an unanticipated finding that Boyce and associates (1995) generated a decade earlier. Central to the BSC framework is the claim that physiological reactivity is a plasticity factor regulated by environmental experience. The recently promulgated *adaptive calibration model* represents the further development of these ideas (Del Giudice, Ellis, & Shirtcliff, 2011).

The evidence indicating that physiological reactivity operates as a plasticity factor is diverse, with findings showing that more physiologically reactive children are more susceptible, in a for better and for worse fashion, to the effects of actual marital conflict (Obradovic, Bush, & Boyce, 2011), as well as simulated interparental aggression (Davies, Sturge-Apple, & Cicchetti, 2011), on externalizing problems; of family adversity on school achievement (Obradovic, Bush, Stamperdahl, Adler, & Boyce, 2010); and of teacher–child conflict on change in symptom severity (Essex et al., 2011). Work showing similar moderational effects of physiological reactivity with respect to family influences on female pubertal development by Ellis and associates (2011) is especially noteworthy, given the roots of this work in psychosocial acceleration theory (Belsky et al., 1991) and the way in which its findings proved consistent with the differential-susceptibility related revision of the theory (Belsky, 2000). After all, Belsky (2000) postulated that some females would be "alternative strategists" whose pubertal development proved unrelated to their rearing experiences, just as Ellis and associates (2011) found for girls low in physiological reactivity, whereas others would be "conditional strategists" susceptible to the accelerating and delaying effects of unsupportive and supportive rearing, respectively, just as Ellis et al. (2011) observed in the case of highly reactive girls. Once again, though, we would be remiss if we did not highlight some evidence inconsistent with the BSC thinking, such as that from the aforementioned Obradovic et al. (2011) investigation showing that it was young children with low rather than high respiratory sinus arrhythmia reactivity who seemed, in some analyses, to benefit from growing up under supportive family conditions characterized by little marital strife.

One of the key questions that still remains to be answered regarding BSC concerns its life span implications. More specifically, do those individuals who are induced to be highly physiologically reactive early in life, and thus developmentally plastic, remain that way over time? It seems hard to imagine that a child induced by supportive rearing to be highly physiologically reactive, in accordance with the theory (Boyce & Ellis, 2005), would remain highly reactive as the years go by. Of course, this is an empirical question, one that has implications for our understanding of the role physiological reactivity does or does not play as a plasticity factor as the individual develops.

### *Genetic polymorphisms as plasticity factors*

Perhaps nowhere has the diathesis–stress framework informed Person × Environment interaction research in recent years more than in the study of G × E interaction, launched by Caspi and associates (2002, 2003) a decade ago. In the time since our 2009 reviews of differential-susceptibility related evidence (Belsky et al., 2009; Belsky & Pluess, 2009a), ever more G × E findings have appeared consistent with the notion that there are individual differences in developmental plasticity. Much of the evidence to this effect comes from studies involving the serotonin transporter linked polymorphic region (*5-HTTLPR*) and the dopamine receptor D4 gene (*DRD4*).

Consider in this regard evidence showing for better and for worse results in the case of those carrying one or more *5-HTTLPR* short alleles when the rearing predictor and child outcome were maternal responsiveness and moral internalization (Kochanska et al., 2011), child maltreatment and antisocial behavior (Cicchetti, Rogosch, & Thibodeau, 2012), and supportive parenting and positive affect (Hankin et al., 2011), respectively. Differential-susceptibility related findings also emerged (among male, African American adolescents) when perceived racial discrimination was used to predict conduct problems (Brody et al., 2011), when life events were used to predict neuroticism (Pluess, Belsky, Way, & Taylor, 2010) and life satisfaction of young adults (Kuepper et al., 2012), and when retrospectively reported childhood adversity was used to explain aspects of impulsivity among college students (e.g., pervasive influence of feelings, feelings trigger action; Carver, Johnson, Joormann, Kim, & Nam, 2011).

To clarify, other *5-HTTLPR* related findings prove more consistent with the diathesis–stress than the differential-susceptibility framework (e.g., Bakermans-Kranenburg, Dobrova-Krol, & van IJzendoorn, in press; Brody et al., 2012), sometimes even in G × E studies that also chronicle differential susceptibility (e.g., Kochanska et al., 2011). Moreover, in apparently rare instances it is those with long rather than short alleles who prove most susceptible to environmental influences, even when differential-susceptibility related findings emerge (e.g., Cicchetti, Rogosch, & Oshri, 2011; Sulik et al., 2012). Therefore, the results of a recent meta-analysis

of G × E findings pertaining to children under 18 years of age are especially noteworthy; they show that short allele carriers are more susceptible to the effects of positive and negative developmental experiences and environmental exposures, at least in Caucasians (van IJzendoorn, Belsky, & Bakermans-Kranenburg, 2012).

Turning to *DRD4*, it is worth highlighting that recent differential-susceptibility related evidence showing heightened or exclusive susceptibility of individuals carrying the seven-repeat (7R) allele when the environmental predictor and developmental outcome were maternal positivity and prosocial behavior (Knafo, Israel, & Ebstein, 2011), early nonfamilial childcare and social competence (Belsky & Pluess, 2013), contextual stress and support and adolescent negative arousal (Beach et al., 2012), childhood adversity and young-adult persistent alcohol dependence (Park, Sher, Todorov, & Heath, 2011), and newborn risk status (i.e., gestational age, birth weight for gestational age, length of stay in neonatal intensive care unit) and observed maternal sensitivity (Fortuna et al., 2011), respectively. However, note that at least one investigatory team finds that it is those without the 7R allele who prove most responsive to childhood adversities in a diathesis–stress manner (Das, Cherbuin, Tan, Anstey, & Easteal, 2011). Nevertheless, a meta-analysis of G × E research involving dopamine-related genes revealed that children 8 years and younger respond to positive and negative developmental experiences and environmental exposures in a manner consistent with differential susceptibility (Bakermans-Kranenburg & van IJzendoorn, 2011).

Emerging evidence has also begun to suggest that the brain-derived neurotrophic factor gene (*BDNF*) may be a plasticity gene (e.g., Chen, Li, & McGue, 2012; Gunnar et al., 2012; Juhasz et al., 2011; Mata, Thompson, & Gotlib, 2010; Suzuki et al., 2011), as is the oxytocin receptor gene (*OXTR*; Johansson et al., 2012; Poulin, Holman, & Buffone, 2012; Sturge-Apple, Cicchetti, Davies, & Suor, 2012) and the FK506 binding protein 5 gene (Bevilacqua et al., 2012; Xie et al., 2010; Zimmermann et al., 2011). There are perhaps less frequent indications of this in the catechol-*O*-methyltransferase gene (Laucht et al., 2012; Nijmeijer et al., 2010) and, in the previously reviewed literature, the monoamine oxidase A gene (*MAOA*; Enoch, Steer, Newman, Gibson, & Goldman, 2010; Wakschlag et al., 2010). It will be worth monitoring these and other polymorphisms as more work emerges to see whether additional evidence proves consistent with differential susceptibility.

Given that virtually all of the polymorphisms just considered have been studied in G × E perspective as a result of the original interests of psychiatric geneticists in simple genotype–phenotype linkages, we cannot but wonder whether an entirely different set of polymorphisms reflecting sensitivity to the environment would have emerged had the phenotype of interest been not some psychiatric disorder but developmental plasticity itself. It therefore behooves investigators to expand the list of genetic "suspects" beyond those thought to be related to disturbances in functioning by thinking biologically about genes that could be related to physiological processes instantiating plasticity. An excellent recent example of this approach is found in Grazioplene, DeYoung, Rogosch, and Cicchetti's (2013) work showing that the neuronal acetylcholine receptor subunit α-4 genotype interacts with childhood maltreatment to predict features of personality in a differential-susceptibility related manner. This polymorphism was selected for investigation because it is involved in the production of the neurotransmitter acetylcholine, a component of the cholinergic system that is strongly involved in neural plasticity and learning.

### *Polygenetic plasticity*

Most G × E research has focused on one or another polymorphism. In recent years, however, work that we believe should be encouraged has emerged focusing on multiple polymorphisms, thus reflecting the operation of epistatic (i.e., G × G) interactions (e.g., Beaver, Sak, Vaske, & Nilsson, 2010; Conner, Hellemann, Ritchie, & Noble, 2010) as well as G × G × E polymorphisms. One can distinguish polygenetic G × E research in terms of the basis used for creating multigene composites. One strategy that seems fundamentally problematic to us involves identifying genes that show main effects and then compositing only these to then test an interaction with some environmental parameter (e.g., Docherty, Kovas, & Plomin, 2011). What leads us to question the wisdom of this approach is that genes or any other factors that do not exert main effects could still be involved in interactions with the environment, just as some recent G × E research reveals (e.g., Cicchetti & Rogosch, 2012; Cicchetti, Rogosch, & Oshri, 2011; Pluess et al., 2011).

Another approach is to composite genes for a secondary, follow-up analysis that has been found in a first round of inquiry to generate significant G × E interactions (e.g., Brody, Chen, & Beach, 2013; Sonuga-Barke et al., 2009). When Cicchetti and Rogosch (2012, see their figure 2) applied this approach using four different polymorphisms, they found that as the number of sensitivity to the environment alleles increased (i.e., short–short allele of *5-HTTLPR*, zero copies of the corticotropin releasing hormone receptor 1 gene TAT haplotype, the TT genotype of *DRD4-521C/T*, and A carrier of *OXTR*), so did the degree to which maltreated and nonmaltreated low-income children differed on a composite measure of resilient functioning in a for better and for worse manner.

A third approach that has now been used successfully a number of times to chronicle differential susceptibility involves compositing a set of genes selected on an a priori basis before evaluating G × E (e.g., Brody et al., 2013). Consider in this regard evidence indicating that two-gene composites moderate links between sexual abuse and adolescent depression/anxiety and somatic symptoms (Cicchetti, Rogosch, & Sturge-Apple, 2007), between perceived racial discrimination and risk-related cognitions reflecting a fast versus slow life-history strategy (Gibbons et al., 2012, see their figure 2), between contextual stress/support and aggression in

young adulthood (Simons et al., 2011), and between social class and postpartum depression (Mitchell et al., 2011); that a three-gene composite moderates the relation between a hostile–demoralizing community and family environment and aggression in early adulthood (Simons et al., 2011); and that a five-gene composite moderates the relation between parenting and adolescent self-control (Belsky & Beaver, 2011).

No matter how informative the approach to compositing polymorphisms on an a priori basis has proven to be when detecting differential susceptibility, we suspect that the wave of the future will be the "system-level genetic approach." This involves combining genes considered to collectively influence a particular biological process or pathway, such as the dopaminergic or serotonergic system (e.g., Brody et al., 2013; Conner et al., 2010; Nikolova, Ferrell, Manuck, & Hariri, 2011), or neurological endophenotypes for increased susceptibility, such as amygdala volume (Yap et al., 2008), hippocampus volume (Whittle et al., 2011), and ventral striatum reactivity (Nikolova, Bogdan, Brigidi, & Hariri, 2012), to list just a few possibilities. Further insight could be gained, conceivably, by even more refined analysis of such subsystems, including those reflecting synthesis, degradation/transport, receptor, and modulation (Chen et al., 2011). To date, these latter approaches have not been used in studies of G × E to our knowledge, whether evaluating or not evaluating the differential-susceptibility hypothesis. Of course, they could be.

### *G × E mechanisms*

There are likely multiple explanations as to why the mechanisms in the G × E findings prove consistent with differential susceptibility and thus our claim that developmental plasticity should be regarded as a phenotype in its own right. When considering mechanisms, however, we must remember that this term means quite different things to different scholars. For example, mechanism may refer to brain structure or function to a brain scientist; for an endocrinologically oriented investigator it may refer to a hormonal phenomenon, for a geneticist to an epigenetic cascade, and for a cognitive neuroscientist an attentional process. Thus, what may qualify for a cognitive scientist as a "proximate mechanism" (e.g., attentional bias) may well be regarded by a geneticist focused on the epigenome as a "distal predictor." Developmental and behavioral scientists should thus not be arrogant when stipulating what does and does not qualify as a mechanism. It ultimately depends on the level or levels of analysis at which one is working.

Based on recent empirical evidence, in the following we call attention to some possible differential-susceptibility related mechanisms at different levels of analysis. Instead of emphasizing the findings directly linking particular genes to particular psychological or biological processes as most genotype–phenotype and even G × E reports do, we highlight research showing that such processes are responsive to environmental exposures in a differential-susceptibility related manner.

In regard to *cognitive processes*, the following have been found to be moderated by *5-HTTLPR* and an environmental factor in a for better and for worse manner: positive and negative attentional biases (Fox, Zougkou, Ridgewell, & Garner, 2011; see also Pergamin-Hight, Bakermans-Kranenburg, van IJzendoorn, & Bar-Haim, 2012), reward sensitivity (Roiser, Rogers, Cook, & Sahakian, 2006), and accurate processing of emotional faces (Jacobs et al., 2011). The same is true of inattention in *DRD4* (Berry, Deater-Deckard, McCartney, Wang, & Petrill, 2013), working-memory accuracy and reaction time in *BDNF* (Gatt et al., 2009), and rumination in a two-gene composite (*5-HTTLPR*, *BDNF*; Clasen, Wells, Knopik, McGeary, & Beevers, 2011) and "street code," reflecting high value placed on being tough and aggressive, standing up for one's rights, and being ready to fight in the case of a three-gene composite (*5-HTTLPR*, *DRD4*, *MAOA*; Simons et al., 2012).

In regard to *physiological processes*, *5-HTTLPR* and an environmental factor have been found to interact in a differential-susceptibility related manner in predicting cortisol reactivity (Way & Taylor, 2010), with the same being true of *BDNF* when the dependent variable is heart rate (Gatt et al., 2009) or evening salivary cortisol (Vinberg et al., 2009). For *brain measurements*, Alexander and colleagues (2012) present evidence that *5-HTTLPR* interacts with stressful life events in a for better and for worse manner to predict left amygdala reactivity to fearful faces, whereas Gatt et al. (2009) document much the same when using *BDNF* to forecast grey matter volume in the hippocampus and the amygdala. In addition, Klucken and associates (2013) report that *BDNF* interacts with positive and negative feedback in a for better and for worse manner during appetitive conditioning when predicting hemodynamic response in the amygdala. Evidence also suggests that individuals homozygous for the isoallele of a polymorphism in the mineralocorticoid receptor gene (*rs5522*) manifest the most and least right amygdala reactivity relative to valine carriers when they (retrospectively) reported experiencing high and low levels, respectively, of emotional neglect in childhood (Bogdan, Williamson, & Hariri, 2012).

However, it may not be only adversity to which the amygdala of certain individuals proves especially sensitive. After all, an extensive meta-analysis showed that the amygdala responds to negative stimuli and even more strongly to positive stimuli (Sergerie, Chochol, & Armony, 2008). This suggests to us, as does the work cited in the preceding paragraph, that amygdala reactivity could be one of several central nervous mechanism by which differential susceptibility operates. This would certainly be consistent with the hypothesis proposed by the differential-susceptibility framework (Belsky & Pluess, 2009a) and the concept of sensory-processing sensitivity (Aron & Aron, 1997; Aron, Aron, & Jagiellowicz, 2012) that heightened susceptibility is the function of a more sensitive central nervous system on which experiences register more easily and deeply. According to this neurosen-

sitivity hypothesis, specific gene variants (e.g., *5-HTTLPR* short allele, *DRD4* 7R) contribute to the increased sensitivity and responsivity of specific brain regions that then manifests itself in increased negative emotionality and physiological reactivity (Pluess, Stevens, & Belsky, 2013), in part because highly sensitive individuals are more easily aroused.

What this brief summary of diverse findings related to putative plasticity genes should make clear is that a variety of plausible mechanisms at multiple levels of analysis may help to account for the G × E findings noted or referred to earlier. More such research is required, and the big challenge going forward will be to "put Humpty Dumpty together" (even if not "again") so that a multilevel system of causation can be illuminated (Hyde, Bogdan, & Hariri, 2011). This represents a huge agenda, perhaps the holy grail of inquiry.

### *Repeated measurements*

All of the differential-susceptibility related work cited herein, as well as in our earlier reviews, essentially presumes that children and adults who share the same characteristics, be they temperamental, physiological or genetic plasticity factors, would function in a manner opposite to what was observed were they also observed under contrasting conditions. For example, we have presumed that children carrying *DRD4* 7R and showing high levels of externalizing problems in the face of insensitive parenting would score low on such problems if they were raised by skilled caregivers; however, there is almost no research validating this assumption, in part because it is unethical to provide a child growing up under for-better, supportive conditions with for-worse, adverse ones just to test the differential-susceptibility hypothesis. One of the few studies that systematically addressed the repeated-measurement issue under consideration, even if not in such differential-susceptibility related terms or with children, examined the probability of taking a risk in a gambling-decision-making game when the chances of winning were high (i.e., for-better condition) and when they were low (i.e., for-worse condition; Roiser et al., 2006). The results revealed that the more short *5-HTTLPR* alleles an individual carried, the more likely the person was to make a bet (i.e., take a risk) when the chance of winning was high, and the less likely the individual was to make such a bet when the probability of winning was low.

In addition to constructing repeated-measurement experiments, future researchers would be well advised to take advantage of experiments in nature that could serve this purpose. Consider in this regard the imaginative work of Verschoor and Markus (2011), who took advantage of days in which undergraduates did and did not have examinations in order to see how those students homozygous for long and short *5-HTTLPR* alleles functioned. They found that the latter experienced the most tension, negative mood, and perceived stress on exam days, yet the least on nonexam days. Consider Schoebi, Way, Karney, and Bradbury's (2012) marital research, which indicated that spouses homozygous for short alleles proved more sensitive to their partner's positive *and* negative emotion during marital interactions.

### *Experimental evaluation of plasticity*

All of the research cited through this point has been observational, correlational, and often longitudinal in character. The common strategy employed in such work for discounting the possibility that organism–environment correlation is masquerading as Organism × Environment interaction is to insure that the temperamental, physiological, or genetic moderator under study is not correlated with the contextual predictor under consideration. However laudable such efforts are, they are not without limits. For example, just because the moderating polymorphism (e.g., *DRD4*) under investigation proves unrelated to the contextual predictor of interest (e.g., sensitive parenting) does not mean that this is true of all other unmeasured or unexamined organismic factors (e.g., *BDNF*). Ultimately, that environments have not been systematically manipulated in most plasticity-related research means that one cannot be certain, even in the case of the putatively malleable, that truly causal environmental effects are being detected (van IJzendoorn & Bakermans-Kranenburg, 2012).

As pioneered by Dutch investigators in genetic plasticity factors (Bakermans-Kranenburg, van IJzendoorn, Mesman, Alink, & Juffer, 2008; Bakermans-Kranenburg, van IJzendoorn, Pijlman, Mesman, & Juffer, 2008), one way around this problem involves conducting intervention experiments in which individuals are randomly assigned to a treatment condition. Because it is unethical to assign individuals, especially children, to conditions of adversity, this approach has only been used to evaluate differential response, as a function of some hypothesized plasticity factor, to an experience presumed to promote positive functioning. Such a design is limited, because it can only evaluate the for-better side of developmental plasticity. Nevertheless, it represents an ideal way to determine whether those considered to be resilient to adversity on the basis of observational research also prove relatively unresponsive to supportive conditions and whether those considered vulnerable to adversity disproportionately benefit from environmental enrichment; there is ever-growing experimental evidence that this is the case.

With regard to the plasticity factor of negative emotionality, consider findings showing that it is infants who score relatively low on irritability as newborns who fail to benefit from an otherwise security-promoting intervention (Cassidy, Woodhouse, Sherman, Stupica, & Lejuez, 2011) and infants who show few, if any, mild perinatal adversities (known to be related to limited negative emotionality) who fail to benefit from computer-based instruction otherwise found to promote preschoolers' phonemic awareness and early literacy (van der Kooy-Hofland, van der Kooy, Bus, van IJzendoorn, & Bonsel, 2012). In other words, only the putatively "vulnerable." those manifesting or likely to manifest high levels of negativity, experienced developmental enhancement as a function of the interventions cited. Similar results emerge among older

children, as Scott and O'Connor's (2012) parenting intervention resulted in the most positive change in conduct among emotionally dysregulated children (i.e., loses temper, angry, touchy). Van de Wiel, van Goozen, Matthys, Snoek, and van Engeland (2004) presented related results when the plasticity factor was physiological reactivity, finding that an intervention for children with disruptive behavior disorder proved effective but only for those displaying high cortisol related, stress reactivity.

Recent genetically informed intervention evaluations also indicate that alleles presumed to place individuals at risk in the face of adversity (*5-HTTLPR* short, *DRD4* 7R) or to promote resilience (i.e., not short/not 7R) are associated with them being respectively susceptible or not susceptible to the benefits of intervention (but, for counterevidence, see Cicchetti, Rogosch, & Toth, 2011). Consider in this regard Drury and associates' (2012) data showing that it was only children growing up in Romanian orphanages who carried *5-HTTLPR* short alleles who benefited, in terms of reductions in the display of indiscriminant friendliness, from being randomly assigned to high-quality foster care. Eley and associates (2012) also documented intervention benefits restricted to short allele carriers, but their design included only treated children (i.e., not a randomized clinical trial [RCT]). Turning to *DRD4*, Kegel, Bus, and van IJzendoorn (2011) tested and found support for the hypothesis that it would be *DRD4* 7R carriers who would benefit from specially designed computer games promoting phonemic awareness and, thereby, early literacy in their RCT. Other RCT results point in the same direction with regard to *DRD4* 7R, including research on African American teens in which substance use was the examined outcome (Beach, Brody, Lei, & Philibert, 2010; Brody et al., 2013, in press).

Last to be considered is research examining genetically moderated intervention effects by considering multigene composites rather than singular candidate genes. The Drury et al. (2012) findings show that even though *BDNF* did not operate as a plasticity factor when it came to distinguishing those who did and did not benefit from the foster-care intervention, the moderating effect of *5-HTTLPR* was amplified if a child carried methionine alleles *and* short *5-HTTLPR* alleles. In other words, the more plasticity alleles children carried, the more their indiscriminant friendliness declined over time when assigned to foster care and the more it increased if they remained institutionalized. Consider next Brody et al.'s (2013) confirmed prediction that the more GABAergic and dopaminergic genes African American teens carried, the more protected they were from increasing their alcohol use over time when enrolled in a whole-family prevention program. Such results once again call attention to the benefits of moving beyond single polymorphisms when operationalizing the plasticity phenotype. They also indicate that even if a single gene may not moderate an intervention (or other environmental) effect, in could still play a role in determining the degree to which an individual benefits. These are insights future investigators and interventionists should keep in mind when seeking to find "what works for whom?"

### *Domain specific versus domain general*

Conceptualizing plasticity as a phenotype would seem to imply, particularly as we have discussed it, that some individual differences will be more and some less developmentally malleable. However, should this be broadly interpreted to mean that some individuals will be more and some less malleable to any and all environmental inputs and with respect to any and all developmental sequelae? Is it more likely that a narrow conceptualization holds, such that plasticity will prove domain specific rather than domain general? Thus, instead of some being more plastic in general, individuals will vary in terms of what they are susceptible to (e.g., parents, not peers; peers, not parents) and with regard to particular developmental outcomes but not others (e.g., social but not academic competence; Belsky et al., 2007; Belsky & Pluess, 2009a, 2009b)?

However more likely the latter prospect would seem, two new sets of evidence underscore the domain generality of plasticity. The first involves the nature and effects of two dramatically different Dutch interventions that used different indirect and direct approaches to influence children and that focused on different developmental outcomes yet revealed that children sharing the same plasticity factor were the primary beneficiaries of each. More specifically, even though one intervention promoted sensitive parenting via video feedback in order to reduce toddler's externalizing behavior (Bakermans-Kranenburg, van IJzendoorn, Pijlman, et al., 2008) and cortisol-related stress reactivity (Bakermans-Kranenburg, van IJzendoorn, Mesman, et al., 2008) and the other relied on a computerized instructional program to promote preschooler's phonemic awareness and thereby early literacy (Kegel et al., 2011), it was children carrying the *DRD4* 7R allele who disproportionately or exclusively benefited in both cases. There is also the longitudinal data evaluated by Roisman and associates (2012) showing that infants with difficult temperaments measured in the first 6 months of life proved more susceptible to the respective positive and negative effects of sensitive and insensitive mothering experienced during their first 3 years of life when it came to predicting teacher-reported social competence, behavior problems, and academic skills across the primary school years; this was so even with different teachers rating the children each and every year. Moreover, even though a diathesis–stress rather than differential-susceptibility model fit the data best when it came to predicting performance on objective tests of academic performance through 15 years of age, it once again proved to be children who as infants had difficult temperaments who were disproportionately susceptible to the shorter and longer term effects of early mothering. Of interest may be recent work showing that even though *DRD4* and negative emotionality early in life are related (Holmboe, Nemoda, Fearon, Sasvari-Szekely, & Johnson, 2010; Ivorra et al., 2010), the moderating effect of

*DRD4* does not account for a parallel moderating effect of negative emotionality, at least in a study of effects of child care on children's social functioning (Belsky & Pluess, 2013).

Despite such evidence, it still seems premature to embrace the broad domain-general interpretation of developmental plasticity. Nevertheless, the results just summarized caution against its premature dismissal. Ultimately, further work is called for before any firm conclusions can be drawn. Our suspicion is that there will be variation across individuals in that some will prove highly susceptible to many developmental experiences and environmental exposures (i.e., extremely plastic) and that some will prove susceptible to virtually none (i.e., extremely fixed) but that most will prove to be intermediate between these extremes. One could even envision a bell curve with regard to the degree of plasticity that individuals manifest.

### *Environmental cue reliability*

Whether children develop in a generally supportive or unsupportive environment, it is likely that the reliability of environmental cues indicative of the valence of the rearing milieu will vary. One can imagine in this regard two different hostile environments: one in which conflict is constant and thus highly predictable and another in which conflict is episodic and unpredictable. Frankenhuis and Panchanathan (2011) have insightfully observed that highly plastic individuals growing up in these two environments may differ in terms of when they "commit" to a developmental strategy, with the former "deciding" to specialize early, having high confidence about the state of the environment, but the latter deferring commitment and choosing to keep sampling the environment until a better estimate of the environment can be established. Whether this is actually the case is an issue that should be pursued empirically in the future. Frankenhuis and Panchanathan's (2011) intriguing ideas lead us to wonder whether it is when cue reliability is low that individuals "call upon" the epigenome to infer from markings passed down across multiple generations what past environments were like and thus what is the best developmental pathway to pursue. Such a process would be consistent with Kuzawa's (2005) notion of "intergenerational phenotypic inertia," which highlights that it is the experiences of not only the immediately preceding generation to which developing organisms are sensitive but also generations preceding that.

### *Parent–child conflict of interest*

Like many developmental scientists lacking foundational knowledge about evolutionary theory, virtually all of our thinking and writing about differential susceptibility to date has presumed that malleable children will have their development regulated by their rearing experiences. However, as Trivers (1974) pointed out more than four decades ago, that parents and children share an average of 50% of their genes means that their biological interests are not the same and thus that they often experience a conflict of interest (see also Schlomer, Del Giudice, & Ellis, 2011). In discussing the influence of prenatal stress on development, Del Giudice (2012) recently pointed out that it is because of this that children, even highly malleable ones, may not simply take instructions from their parents. What are the implications of this observation for understanding developmental plasticity?

### *Family dynamics*

However intrigued we have become with theory and evidence pertaining to differential susceptibility and the notion that individual differences exist in developmental plasticity, one issue has always caused us concern. We have *never* heard a parent characterize one of their children as more susceptible to their influence than another, which we regard as distinct from saying that their children are temperamentally different, with perhaps one being more "sensitive" to challenging or stressful situations than others or even being more "difficult" to care for. Why is that? Evolutionary reasoning would seem to imply that parents should detect for whom their socialization efforts, implicit or explicit, pay off and for whom they do not and so adjust those efforts accordingly. However, we are aware of no evidence suggesting or indicating this to be the case. Should not more malleable siblings seek to alert their parents that they are more responsive to rearing inputs in order to obtain more attention and other resources? However, could it be that such children do engage in such efforts but that they do not prove effective because less malleable children employ tactics to camouflage this characteristic of theirs in some way? Perhaps it is such children who prove most likely to claim "it's not fair" within families when siblings are perceived as being treated better as a way of "throwing their parents off track." At the very least, it would be interesting to study parental awareness or perception of variation in susceptibility across siblings within a family.

### *Timing of susceptibility*

It is widely assumed by many developmentalists that it is during the early years of life that human development is most susceptible to environmental influences, for better and for worse (e.g., Blair & Raver, 2012; Ganzel & Morris, 2011), as plasticity is presumed to be greatest when biological systems are being laid down. Even if this is true in general, does it mean that it is true in the case of each and every individual? It certainly seems conceivable that, at times in the ancestral past, individuals who were especially susceptible to environmental influence at some point in their life span could have experienced an adaptive advantage, leading perhaps to the selection of genes for later rather than earlier plasticity. If this is so, it implies that variation should exist in terms of *when* children and even adults are especially developmentally plastic. If this is the case, does it not imply that those who appear not to be especially malleable may simply not be so at the

developmental point in time when developmental experiences and environmental exposures are measured? Could it be that some are especially susceptible to contextual regulation early, others later, others at all times, and still others more or less never?

## Conclusion

Our ultimate goal in this essay was to provide a theoretical and empirical basis for our claim that there exists individual differences in developmental plasticity and, thus, that phenotypic plasticity should be a subject of study for developmentalists and psychopathologists. To advance this argument, we began by highlighting challenges that evolutionary thinking poses for a science of development and psychopathology, including for the diathesis–stress framework that has (informatively) guided so much empirical inquiry implicitly or explicitly on risk, resilience, and dysregulation. With this foundation, we raised a series of issues that the differential-susceptibility hypothesis calls attention to, while highlighting findings that have emerged over just the past several years and that are pertinent to some of the questions posed. Even though it remains clear that this new perspective is stimulating research and influencing how hypotheses are framed and data interpreted, it should be clear that there are a great many topics in need of empirical attention. Our hope is that this essay will encourage students of development as well as psychopathology to treat phenotypic plasticity as an individual-difference construct while exploring unknowns in the differential-susceptibility equation.

## References


Alexander, N., Klucken, T., Koppe, G., Osinsky, R., Walter, B., Vaitl, D., et al. (2012). Interaction of the serotonin transporter-linked polymorphic region and environmental adversity: Increased amygdala-hypothalamus connectivity as a potential mechanism linking neural and endocrine hyperreactivity. *Biological Psychiatry*, *72*, 49–56. doi:10.1016/j.biopsych.2012.01.030

Aron, E. N., & Aron, A. (1997). Sensory-processing sensitivity and its relation to introversion and emotionality. *Journal of Personality and Social Psychology*, *73*, 345–368.

Aron, E. N., Aron, A., & Jagiellowicz, J. (2012). Sensory-processing sensitivity: A review in the light of the evolution of biological responsivity. *Personality and Social Psychology Review*, *16*, 262–282. doi:10.1177/1088868311434213

Bakermans-Kranenburg, M. J., Dobrova-Krol, N. A., & van IJzendoorn, M. H. (in press). Impact of institutional care on attachment disorganization and insecurity of Ukrainian pre-schoolers: Protective effect of the long variant of the serotonin transporter gene (5HTT). *International Journal of Behavioral Development*.

Bakermans-Kranenburg, M. J., Steele, H., Zeanah, C. H., Muhamedrahimov, R. J., Vorria, P., Dobrova-Krol, N. A., et al. (2011). Attachment and emotional development in institutional care: Characteristics and catch-up. *Monographs of the Society for Research in Child Development*, *76*, 62–91. doi:10.1111/j.1540-5834.2011.00628.x

Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2011). Differential susceptibility to rearing environment depending on dopamine-related genes: New evidence and a meta-analysis. *Development and Psychopathology*, *23*, 39–52. doi:10.1017/s0954579410000635

Bakermans-Kranenburg, M. J., van IJzendoorn, M. H., Mesman, J., Alink, L. R., & Juffer, F. (2008). Effects of an attachment-based intervention on daily cortisol moderated by dopamine receptor D4: a randomized control trial on 1- to 3-year-olds screened for externalizing behavior. *Development and Psychopathology*, *20*, 805–820.

Bakermans-Kranenburg, M. J., van IJzendoorn, M. H., Pijlman, F. T., Mesman, J., & Juffer, F. (2008). Experimental evidence for differential susceptibility: Dopamine D4 receptor polymorphism (DRD4 VNTR) moderates intervention effects on toddlers' externalizing behavior in a randomized controlled trial. *Development and Psychopathology*, *44*, 293–300.

Beach, S. R. H., Brody, G. H., Lei, M.-K., & Philibert, R. A. (2010). Differential susceptibility to parenting among African American youths: Testing the DRD4 hypothesis. *Journal of Family Psychology*, *24*, 513–521. doi:10.1037/a0020835

Beach, S. R. H., Lei, M. K., Brody, G. H., Simons, R. L., Cutrona, C., & Philibert, R. A. (2012). genetic moderation of contextual effects on negative arousal and parenting in African-American parents. *Journal of Family Psychology*, *26*, 46–55. doi:10.1037/a0026236

Beaver, K. M., Sak, A., Vaske, J., & Nilsson, J. (2010). Genetic risk, parent–child relations, and antisocial phenotypes in a sample of African-American males. *Psychiatry Research*, *175*, 160–164.

Belsky, J. (1997). Variation in susceptibility to rearing influences: An evolutionary argument. *Psychological Inquiry*, *8*, 182–186.

Belsky, J. (2000). Conditional and alternative reproductive strategies: Individual differences in susceptibility to rearing experience. In J. Rodgers, D. Rowe, & W. Miller (Eds.), *Genetic influences on human fertility and sexuality: Theoretical and empirical contributions from the biological and behavioral sciences* (pp. 127–146). Boston: Kluwer.

Belsky, J. (2005). Differential susceptibility to rearing influences: An evolutionary hypothesis and some evidence. In B. Ellis & D. Bjorklund (Eds.), *Origins of the social mind: Evolutionary psychology and child development* (pp. 139–163). New York: Guilford Press.

Belsky, J. (2008). War, trauma and children's development: Observations from a modern evolutionary perspective. *International Journal of Behavioral Development*, *32*, 260–271. doi:10.1177/0165025408090969

Belsky, J. (in press). The development of human reproductive strategies: Progress and prospects. *Current Directions in Psychological Science*.

Belsky, J., Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2007). For better and for worse: Differential susceptibility to environmental influences. *Current Directions in Psychological Science*, *16*, 300–304.

Belsky, J., & Beaver, K. M. (2011). Cumulative-genetic plasticity, parenting and adolescent self-control/regulation. *Journal of Child Psychology and Psychiatry*, *52*, 619–626.

Belsky, J., Jonassaint, C., Pluess, M., Stanton, M., Brummett, B., & Williams, R. (2009). Vulnerability genes or plasticity genes? *Molecular Psychiatry*, *14*, 746–754.

Belsky, J., & Pluess, M. (2009a). Beyond diathesis–stress: Differential susceptibility to environmental influences. *Psychological Bulletin*, *135*, 885–908.

Belsky, J., & Pluess, M. (2009b). The nature (and nurture?) of plasticity in early human development. *Perspectives on Psychological Science*, *4*, 345–351.

Belsky, J., & Pluess, M. (2013). Genetic moderation of early child-care effects on social functioning across childhood: A developmental analysis. *Child Development*, *84*, 1209–1225. doi:10.1111/cdev.12058

Belsky, J., Pluess, M., & Widaman, K. F. (2013). *Confirmatory and competitive evaluation of alternative gene–environment interaction hypotheses*. Manuscript submitted for publication.

Belsky, J., Steinberg, L., & Draper, P. (1991). Childhood experience, interpersonal development, and reproductive strategy: An evolutionary theory of socialization. *Child Development*, *62*, 647–670.

Berry, D., Deater-Deckard, K., McCartney, K., Wang, Z., & Petrill, S. A. (2013). Gene–environment interaction between dopamine receptor D4 7-repeat polymorphism and early maternal sensitivity predicts inattention trajectories across middle childhood. *Development and Psychopathology*, *25*, 291–306.

Bevilacqua, L., Carli, V., Sarchiapone, M., George, D. K., Goldman, D., Roy, A., & Enoch, M.-A. (2012). Interaction between FKBP5 and childhood trauma and risk of aggressive behavior. *Archives of General Psychiatry*, *69*, 62–70.

Bjorklund, D., & Pellegrini, A. (2002). *The origins of human nature: Evolutionary developmental psychology*. Washington, DC: American Psychological Association.

Blair, C., & Raver, C. C. (2012). Individual development and evolution: Experiential canalization of self-regulation. *Developmental Psychology*, *48*, 647–657. doi:10.1037/a0026472

Bogdan, R., Williamson, D. E., & Hariri, A. R. (2012). Mineralocorticoid receptor iso/val (rs5522) genotype moderates the association between previous childhood emotional neglect and amygdala reactivity. *American Journal of Psychiatry*, *169*, 515–522. doi:10.1176/appi.ajp.2011.11060855

Boyce, W. T., Chesney, M., Alkon, A., Tschann, J. M., Adams, S., Chesterman, B., et al. (1995). Psychobiologic reactivity to stress and childhood respiratory illnesses: Results of two prospective studies. *Psychosomatic Medicine*, *57*, 411–422.

Boyce, W. T., & Ellis, B. J. (2005). Biological sensitivity to context: I. An evolutionary–developmental theory of the origins and functions of stress reactivity. *Development and Psychopathology*, *17*, 271–301.

Brody, G. H., Beach, S. R. H., Chen, Y.-F., Obasi, E., Philibert, R. A., Kogan, S. M., & Simons, R. L. (2011). Perceived discrimination, serotonin transporter linked polymorphic region status, and the development of conduct problems. *Development and Psychopathology*, *23*, 617–627. doi:10.1017/s0954579411000046

Brody, G. H., Chen, Y., & Beach, S. R. H. (2013). Differential susceptibility to prevention: GABAergic, dopaminergic and multilocus effects. *Journal of Child Psychology and Psychiatry*, *54*, 863–871. doi:10.1111/cdev.12058

Brody, G. H., Chen, Y., Beach, S. R. H., Kogan, S. M., Yu, T., DiClemente, R. J., et al. (in press). Differential sensitivity to prevention programming: A dopaminergic polymorphism-enhanced prevention effect on protective parenting and adolescent substance use. *Health Psychology*.

Brody, G. H., Yu, T., Chen, Y. F., Kogan, S. M., Evans, G. W., Windle, M., et al. (2012). Supportive family environments, genes that confer sensitivity, and allostatic load among rural African American emerging adults: A prospective analysis. *Journal of Family Psychology*. doi:10.1037/a0027829

Buss, A., & Plomin, R. (1984). *Temperament: Early developing personality traits*. Hillsdale, NJ: Erlbaum.

Buss, K. A. (2011). Which fearful toddlers should we worry about? Context, fear regulation, and anxiety risk. *Developmental Psychology*, *47*, 804–819. doi:10.1037/a0023227

Cameron, N. M., Champagne, F. A., Parent, C., Fish, E. W., Ozaki-Kuroda, K., & Meaney, M. J. (2005). The programming of individual differences in defensive responses and reproductive strategies in the rat through variations in maternal care. *Neuroscience & Biobehavioral Reviews*, *29*, 843–865.

Carver, C. S., Johnson, S. L., Joormann, J., Kim, Y., & Nam, J. Y. (2011). Serotonin transporter polymorphism interacts with childhood adversity to predict aspects of impulsivity. *Psychological Science*, *22*, 589–595. doi:10.1177/0956797611404085

Caspi, A., McClay, J., Moffitt, T. E., Mill, J., Martin, J., Craig, I. W., et al. (2002). Role of genotype in the cycle of violence in maltreated children. *Science*, *297*, 851–854.

Caspi, A., Sugden, K., Moffitt, T. E., Taylor, A., Craig, I. W., Harrington, H., et al. (2003). Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. *Science*, *301*, 386–389.

Cassidy, J., Woodhouse, S. S., Sherman, L. J., Stupica, B., & Lejuez, C. W. (2011). Enhancing infant attachment security: An examination of treatment efficacy and differential susceptibility. *Development and Psychopathology*, *23*, 131–148. doi:10.1017/s0954579410000696

Champagne, D. L., Bagot, R. C., van Hasselt, F., Ramakers, G., Meaney, M. J., de Kloet, E. R., et al. (2008). Maternal care and hippocampal plasticity: Evidence for experience-dependent structural plasticity, altered synaptic functioning, and differential responsiveness to glucocorticoids and stress. *Journal of Neuroscience*, *28*, 6037–6045. doi:10.1523/jneurosci.0526-08.2008

Chen, C., Moyzis, R., Stern, H., He, Q., Li, H., Li, J., et al. (2011). Contributions of dopamine-related genes and environmental factors to highly sensitive personality: A multi-step neuronal system-level approach. *PLoS ONE*, *6*(7), e21636. doi:10.1371/journal.pone.0021636

Chen, J., Li, X., & McGue, M. (2012). Interacting effect of BDNF Val66Met polymorphism and stressful life events on adolescent depression. *Genes, Brain and Behavior*. doi:10.1111/j.1601-183X.2012.00843.x

Chisholm, J. S. (1993). Death, hope, and sex: Life-history theory and the development of reproductive strategies. *Current Anthropology*, *34*, 1–24. doi:10.1086/204131

Cicchetti, D., & Rogosch, F. A. (2012). Gene × Environment interaction and resilience: Effects of child maltreatment and serotonin, corticotropin releasing hormone, dopamine, and oxytocin genes. *Development and Psychopathology*, *24*, 411–427. doi:10.1017/s0954579412000077

Cicchetti, D., Rogosch, F. A., & Oshri, A. (2011). Interactive effects of corticotropin releasing hormone receptor 1, serotonin transporter linked polymorphic region, and child maltreatment on diurnal cortisol regulation and internalizing symptomatology. *Development and Psychopathology*, *23*, 1125–1138. doi:10.1017/s0954579411000599

Cicchetti, D., Rogosch, F. A., & Sturge-Apple, M. L. (2007). Interactions of child maltreatment and serotonin transporter and monoamine oxidase A polymorphisms: Depressive symptomatology among adolescents from low socioeconomic status backgrounds. *Development and Psychopathology*, *19*, 1161–1180.

Cicchetti, D., Rogosch, F. A., & Thibodeau, E. L. (2012). The effects of child maltreatment on early signs of antisocial behavior: Genetic moderation by tryptophan hydroxylase, serotonin transporter, and monoamine oxidase A genes. *Development and Psychopathology*, *24*, 907–928.

Cicchetti, D., Rogosch, F. A., & Toth, S. L. (2011). The effects of child maltreatment and polymorphisms of the serotonin transporter and dopamine D4 receptor genes on infant attachment and intervention efficacy. *Development and Psychopathology*, *23*, 357–372. doi:10.1017/s0954579411000113

Clasen, P. C., Wells, T. T., Knopik, V. S., McGeary, J. E., & Beevers, C. G. (2011). 5-HTTLPR and BDNF Val66Met polymorphisms moderate effects of stress on rumination. *Genes, Brain and Behavior*, *10*, 740–746. doi:10.1111/j.1601-183X.2011.00715.x

Conner, B. T., Hellemann, G. S., Ritchie, T. L., & Noble, E. P. (2010). Genetic, personality, and environmental predictors of drug use in adolescents. *Journal of Substance Abuse Treatment*, *38*, 178–190. doi:10.1016/j.jsat.2009.07.004

Conway, A., & Stifter, C. A. (2012). Longitudinal antecedents of executive function in preschoolers. *Child Development*, *83*, 1022–1036. doi:10.1111/j.1467-8624.2012.01756.x

Daly, M., & Wilson, M. I. (1980). Discriminative parental solicitude: A biological perspective. *Journal of Marriage and the Family*, *42*, 277–288. doi:10.2307/351225

Daly, M., & Wilson, M. I. (1981). Child maltreatment from a sociobiological perspective. *New Directions for Child Development*, *198*, 93–112. doi:10.1002/cd.23219811107

Daly, M., & Wilson, M. (2005). Carpe diem: Adaptation and devaluing the future. *Quarterly Review of Biology*, *80*, 55–60. doi:10.1086/431025

Das, D., Cherbuin, N., Tan, X., Anstey, K. J., & Easteal, S. (2011). DRD4-exonIII-VNTR moderates the effect of childhood adversities on emotional resilience in young-adults. *PLoS ONE*, *6*. doi:10.1371/journal.pone.0020177

Davies, P. T., Sturge-Apple, M. L., & Cicchetti, D. (2011). Interparental aggression and children's adrenocortical reactivity: Testing an evolutionary model of allostatic load. *Development and Psychopathology*, *23*, 801–814. doi:10.1017/s0954579411000319

Davis, E. P., Glynn, L. M., Waffarn, F., & Sandman, C. A. (2011). Prenatal maternal stress programs infant stress regulation. *Journal of Child Psychology and Psychiatry*, *52*, 119–129. doi:10.1111/j.1469-7610.2010.02314.x

Del Giudice, M. (2009). Sex, attachment, and the development of reproductive strategies. *Behavioral and Brain Sciences*, *32*, 1–21. doi:10.1017/s0140525x09000016

Del Giudice, M. (2012). Fetal programming by maternal stress: Insights from a conflict perspective. *Psychoneuroendocrinology*, *37*, 1614–1629. doi:10.1016/j.psyneuen.2012.05.014

Del Giudice, M., Angeleri, R., & Manera, V. (2009). The juvenile transition: A developmental switch point in human life history. *Developmental Review*, *29*, 1–31. doi:10.1016/j.dr.2008.09.001

Del Giudice, M., Ellis, B. J., & Shirtcliff, E. A. (2011). the adaptive calibration model of stress responsivity. *Neuroscience & Biobehavioral Reviews*, *35*, 1562–1592. doi:10.1016/j.neubiorev.2010.11.007

DeWitt, T. J., Sih, A., & Wilson, D. S. (1998). Costs and limits of phenotypic plasticity. *Trends in Ecology & Evolution*, *13*, 77–81. doi:10.1016/s0169-5347(97)01274–3

Dingemanse, N. J., Kazem, A. J., Reale, D., & Wright, J. (2010). Behavioural reaction norms: Animal personality meets individual plasticity. *Trends in Ecology & Evolution*, *25*, 81–89. doi:10.1016/j.tree.2009.07.013

Docherty, S. J., Kovas, Y., & Plomin, R. (2011). Gene–environment interaction in the etiology of mathematical ability using SNP sets. *Behavior Genetics*, *41*, 141–154. doi:10.1007/s10519-010-9405-6

Draper, P., & Harpending, H. (1982). Father absence and reproductive strategy: An evolutionary perspective. *Journal of Anthropological Research*, *38*, 255–273.

Drury, S. S., Gleason, M. M., Theall, K. P., Smyke, A. T., Nelson, C. A., Fox, N. A., et al. (2012). Genetic sensitivity to the caregiving context: The influence of 5HTTLPR and BDNF Val66Met on indiscriminate social behavior. *Physiology and Behavior*, *106*, 728–735. doi:10.1016/j.physbeh.2011.11.014

Du Rocher Schudlich, T. D., White, C. R., Fleischhauer, E. A., & Fitzgerald, K. A. (2011). Observed infant reactions during live interparental conflict. *Journal of Marriage and Family*, *73*, 221–235. doi:10.1111/j.17413737.2010.00800.x

Eley, T. C., Hudson, J. L., Creswell, C., Tropeano, M., Lester, K. J., Cooper, P., et al. (2012). Therapygenetics: The 5HTTLPR and response to psychological therapy. *Molecular Psychiatry*, *17*, 236–241. doi:10.1038/mp.2011.132

Ellis, B. J. (2004). Timing of pubertal maturation in girls: An integrated life history approach. *Psychological Bulletin*, *130*, 920–958.

Ellis, B. J., & Bjorklund, D. F. (2012). Beyond mental health: An evolutionary analysis of development under risky and supportive environmental conditions: An introduction to the special section. *Developmental Psychology*, *48*, 591–597. doi:10.1037/a0027651

Ellis, B. J., & Boyce, W. T. (2011). Differential susceptibility to the environment: toward an understanding of sensitivity to developmental experiences and context. *Development and Psychopathology*, *23*, 1–5. doi:10.1017/s095457941000060x

Ellis, B. J., Boyce, W. T., Belsky, J., Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2011). Differential susceptibility to the environment: An evolutionary–neurodevelopmental theory. *Development and Psychopathology*, *23*, 7–28. doi:10.1017/s0954579410000611

Ellis, B. J., Del Giudice, M., Dishion, T. J., Figueredo, A. J., Gray, P., Griskevicius, V., et al. (2012). The evolutionary basis of risky adolescent behavior: implications for science, policy, and practice. *Developmental Psychology*, *48*, 598–623. doi:10.1037/a0026220

Ellis, B. J., Del Giudice, M., & Shirtcliff, E. A. (in press). Beyond allostatic load: The stress response system as a mechanism of conditional adaptation. In T. P. Beauchaine & S. P. Hinshaw (Eds.), *Child and adolescent psychopathology* (2 ed.). New York: Wiley.

Ellis, B. J., & Garber, J. (2000). Psychosocial antecedents of variation in girls' pubertal timing: Maternal depression, stepfather presence, and marital and family stress. *Child Development*, *71*, 485–501. doi:10.1111/1467-8624.00159

Ellis, B. J., Shirtcliff, E. A., Boyce, W. T., Deardorff, J., & Essex, M. J. (2011). Quality of early family relationships and the timing and tempo of puberty: Effects depend on biological sensitivity to context. *Development and Psychopathology*, *23*, 85–99. doi:10.1017/s0954579410000660

Enoch, M. A., Steer, C. D., Newman, T. K., Gibson, N., & Goldman, D. (2010). Early life stress, MAOA, and gene–environment interactions predict behavioral disinhibition in children. *Genes, Brain and Behavior*, *9*, 65–74. doi:10.1111/j.1601-183X.2009.00535.x

Essex, M. J., Armstrong, J. M., Burk, L. R., Goldsmith, H. H., & Boyce, W. T. (2011). Biological sensitivity to context moderates the effects of the early teacher–child relationship on the development of mental health by adolescence. *Development and Psychopathology*, *23*, 149–161. doi:10.1017/s0954579410000702

Evans, G. W., & Kim, P. (2012). Childhood poverty and young adults' allostatic load: The mediating role of childhood cumulative risk exposure. *Psychological Science*. doi:10.1177/0956797612441218

Figueredo, A. J., & Jacobs, W. J. (2010). Aggression, risk-taking, and alternative life history strategies. In M. Frias-Armenta & V. Corral-Verdugo (Eds.), *Bio-psycho-social perspectives on interpersonal violence* (pp. 3–28). Hauppauge, NY: NOVA Science.

Fortuna, K., van IJzendoorn, M. H., Mankuta, D., Kaitz, M., Avinun, R., Ebstein, R. P., et al. (2011). Differential genetic susceptibility to child risk at birth in predicting observed maternal behavior. *PLoS ONE*, *6*. doi:10.1371/journal.pone.0019765

Fox, E., Zougkou, K., Ridgewell, A., & Garner, K. (2011). The serotonin transporter gene alters sensitivity to attention bias modification: Evidence for a plasticity gene. *Biological Psychiatry*, *70*, 1049–1054. doi:10.1016/j.biopsych.2011.07.004

Frankenhuis, W. E., & Del Giudice, M. (2012). When do adaptive developmental mechanisms yield maladaptive outcomes? *Developmental Psychology*, *48*, 628–642. doi:10.1037/a0025629

Frankenhuis, W. E., & Panchanathan, K. (2011). Individual differences in developmental plasticity may result from stochastic sampling. *Perspectives on Psychological Science*, *6*, 336–347. doi:10.1177/1745691611412602

Fuller-Rowell, T. E., Evans, G. W., & Ong, A. D. (2012). Poverty and health: The mediating role of perceived discrimination. *Psychological Science*, *23*, 734–739. doi:10.1177/0956797612439720

Ganzel, B. L., & Morris, P. A. (2011). Allostasis and the developing human brain: Explicit consideration of implicit models. *Development and Psychopathology*, *23*, 955–974. doi:10.1017/s0954579411000447

Garmezy, N. (1974). The study of competence in children at risk for severe psychopathology. In E. J. Anthony & C. Koupernik (Eds.), *The child in his family: Children at psychiatric risk* (Vol. 3, pp. 77–97). New York: Wiley.

Garmezy, N., Masten, A. S., & Tellegen, A. (1984). The study of stress and competence in children: A building block for developmental psychopathology. *Child Development*, *55*, 97–111. doi:10.1111/j.1467-8624.1984.tb00276.x

Gatt, J. M., Nemeroff, C. B., Dobson-Stone, C., Paul, R. H., Bryant, R. A., Schofield, P. R., et al. (2009). Interactions between BDNF Val66Met polymorphism and early life stress predict brain and arousal pathways to syndromal depression and anxiety. *Molecular Psychiatry*, *14*, 681–695.

Gibbons, F. X., Roberts, M. E., Gerrard, M., Li, Z., Beach, S. R. H., Simons, R. L., et al. (2012). The impact of stress on the life history strategies of African American adolescents: Cognitions, genetic moderation, and the role of discrimination. *Developmental Psychology*, *48*, 722–739. doi:10.1037/a0026599

Glynn, L. M., & Sandman, C. A. (2011). Prenatal origins of neurological development: A Critical period for fetus and mother. *Current Directions in Psychological Science*, *20*, 384–389. doi:10.1177/0963721411422056

Gottesman, I., & Shields, J. (1967). A polygenic theory of schizophrenia. *Proceedings of the National Academy of Sciences*, *58*, 199–205.

Grazioplene, R. G., DeYoung, C. G., Rogosch, F. A., & Cicchetti, D. (2013). A novel differential susceptibility gene: CHRNA4 and moderation of the effect of maltreatment on child personality. *Journal of Child Psychology and Psychiatry*, *54*, 872–880. doi:10.1111/jcpp.12031

Gunnar, M. R., Wenner, J. A., Thomas, K. M., Glatt, C. E., McKenna, M. C., & Clark, A. G. (2012). The brain-derived neurotrophic factor Val66Met polymorphism moderates early deprivation effects on attention problems. *Development and Psychopathology*, *24*, 1215–1223. doi:10.1017/s095457941200065x

Hankin, B. L., Nederhof, E., Oppenheimer, C. W., Jenness, J., Young, J. F., Abela, J. R. Z., et al. (2011). Differential susceptibility in youth: Evidence that 5-HTTLPR × Positive Parenting is associated with positive affect "for better and worse." *Translational Psychiatry*, *1*, e44. doi:10.1038/tp.2011.44

Hinde, R. A., & Stevenson-Hinde, J. (1990). Attachment: Biological, cultural and individual desiderata. *Human Development*, *33*, 62–72.

Holmboe, K., Nemoda, Z., Fearon, R. M., Sasvari-Szekely, M., & Johnson, M. H. (2010). Dopamine D4 receptor and serotonin transporter gene effects on the longitudinal development of infant temperament. *Genes, Brain and Behavior*. doi:10.1111/j.1601-183X.2010.00669.x

Hyde, L. W., Bogdan, R., & Hariri, A. R. (2011). Understanding risk for psychopathology through imaging gene–environment interactions. *Trends in Cognitive Sciences*, *15*, 417–427. doi:10.1016/j.tics.2011.07.001

Ivorra, J. L., Sanjuan, J., Jover, M., Carot, J. M., Frutos, R., & Molto, M. D. (2010). Gene–environment interaction of child temperament. *Journal of Developmental and Behavioral Pediatrics*, *31*, 545–554. doi:10.1097/DBP.0b013e3181ee4072

Jacobs, R. H., Pine, D. S., Schoeny, M. E., Henry, D. B., Gollan, J. K., Moy, G., et al. (2011). Maternal depressive history, teen 5HTTLPR genotype, and the processing of emotional faces: Exploring mechanisms of risk. *Behaviour Research and Therapy*, *49*, 80–84. doi:10.1016/j.brat.2010.10.004

James, J., Ellis, B. J., Schlomer, G. L., & Garber, J. (2012). Sex-specific pathways to early puberty, sexual debut, and sexual risk taking: Tests of an integrated evolutionary–developmental model. *Developmental Psychology*, *48*, 687–702. doi:10.1037/a0026427

Jessee, A., Mangelsdorf, S. C., Brown, G. L., Schoppe-Sullivan, S. J., Shigeto, A., & Wong, M. S. (2010). Parents' differential susceptibility to the effects of marital quality on sensitivity across the first year. *Infant Behavior & Development*, *33*, 442–452.

Johansson, A., Bergman, H., Corander, J., Waldman, I. D., Karrani, N., Salo, B., et al. (2012). Alcohol and aggressive behavior in men-moderating

effects of oxytocin receptor gene (*OXTR*) polymorphisms. *Genes, Brain and Behavior*, *11*, 214–221. doi:10.1111/j.1601-183X.2011.00744.x

Juhasz, G., Dunham, J. S., McKie, S., Thomas, E., Downey, D., Chase, D., et al. (2011). The CREB1-BDNF-NTRK2 pathway in depression: Multiple gene–cognition–environment interactions. *Biological Psychiatry*, *69*, 762–771. doi:10.1016/j.biopsych.2010.11.019

Kaplan, H. S., & Gangestad, S. W. (2005). Life history theory and evolutionary psychology. In D. M. Buss (Ed.), *The handbook of evolutionary psychology* (pp. 68–95). New York: Wiley.

Kegel, C. A. T., Bus, A. G., & van IJzendoorn, M. H. (2011). Differential susceptibility in early literacy instruction through computer games: The role of the dopamine D4 receptor gene (DRD4). *Mind, Brain, and Education*, *5*, 71–78. doi:10.1111/j.1751-228X.2011.01112.x

Kim, S., & Kochanska, G. (2012). Child temperament moderates effects of parent–child mutuality on self-regulation: A relationship-based path for emotionally negative infants. *Child Development*, *83*, 1275–1289. doi:10.1111/j.1467–8624.2012.01778.x

Klucken, T., Wehrum, S., Schweckendiek, J., Merz, C. J., Hennig, J., Vaitl, D., et al. (2013). The 5-HTTLPR polymorphism is associated with altered hemodynamic responses during appetitive conditioning. *Human Brain Mapping*, *34*, 2549–2560. doi:10.1002/hbm.22085

Knafo, A., Israel, S., & Ebstein, R. P. (2011). Heritability of children's prosocial behavior and differential susceptibility to parenting by variation in the dopamine receptor D4 gene. *Development and Psychopathology*, *23*, 53–67. doi:10.1017/s0954579410000647

Kochanska, G., & Kim, S. (2013). Difficult temperament moderates links between maternal responsiveness and children's compliance and behavior problems in low-income families. *Journal of Child Psychology and Psychiatry*, *54*, 323–332. doi:10.1111/jcpp.12002

Kochanska, G., Kim, S., Barry, R. A., & Philibert, R. A. (2011). Children's genotypes interact with maternal responsive care in predicting children's competence: Diathesis–stress or differential susceptibility? *Development and Psychopathology*, *23*, 605–616.

Korte, S. M., Koolhaas, J. M., Wingfield, J. C., & McEwen, B. S. (2005). The Darwinian concept of stress: Benefits of allostasis and costs of allostatic load and the trade-offs in health and disease. *Neuroscience & Biobehavioral Reviews*, *29*, 3–38. doi:10.1016/j.neubiorev.2004.08.009

Kuepper, Y., Wielpuetz, C., Alexander, N., Mueller, E., Grant, P., & Hennig, J. (2012). 5-HTTLPR S-allele: A genetic plasticity factor regarding the effects of life events on personality? *Genes, Brain and Behavior*. doi:10.1111/j.1601-183X.2012.00783.x

Kuzawa, C. W. (2005). Fetal origins of developmental plasticity: Are fetal cues reliable predictors of future nutritional environments? *American Journal of Human Biology*, *17*, 5–21. doi:10.1002/ajhb.20091

Laucht, M., Blomeyer, D., Buchmann, A. F., Treutlein, J., Schmidt, M. H., Esser, G., et al. (2012). Catechol-*O*-methyltransferase Val158Met genotype, parenting practices and adolescent alcohol use: Testing the differential susceptibility hypothesis. *Journal of Child Psychology and Psychiatry*, *53*, 351–359. doi:10.1111/j.1469-7610.2011.02408.x

Luthar, S. S., Cicchetti, D., & Becker, B. (2000). The construct of resilience: A critical evaluation and guidelines for future work. *Child Development*, *71*, 543–562.

Manuck, S. B. (2011). *Delay discounting covaries with childhood socioeconomic status as a function of genetic variation in the dopamine D4 receptor (DRD4)*. Paper presented at the Society for Research in Child Development, Montreal.

Masten, A. S. (2007). Resilience in developing systems: Progress and promise as the fourth wave rises. *Development and Psychopathology*, *19*, 921–930. doi:10.1017/s0954579407000442

Masten, A. S., Best, K., & Garmezy, N. (1990). Resilience and development: Contributions from the study of children who overcome adversity. *Development and Psychopathology*, *2*, 425–444.

Mata, J., Thompson, R. J., & Gotlib, I. H. (2010). BDNF genotype moderates the relation between physical activity and depressive symptoms. *Health Psychology*, *29*, 130–133. doi:10.1037/a0017261

Mathot, K. J., van den Hout, P. J., Piersma, T., Kempenaers, B., Reale, D., & Dingemanse, N. J. (2011). Disentangling the roles of frequency- vs. state-dependence in generating individual differences in behavioural plasticity. *Ecology Letters*, *14*, 1254–1262. doi:10.1111/j.1461-0248.2011.01698.x

Mitchell, C., Notterman, D., Brooks-Gunn, J., Hobcraft, J., Garfinkel, I., Jaeger, K., et al. (2011). Role of mother's genes and environment in postpartum depression. *Proceedings of the National Academy of Sciences*, *108*, 8189–8193. doi:10.1073/pnas.1014129108

Monroe, S. M., & Simons, A. D. (1991). Diathesis–stress theories in the context of life stress research: Implications for the depressive disorders. *Psychological Bulletin*, *110*, 406–425.

Mulvihill, D. (2005). The health impact of childhood trauma: An interdisciplinary review, 1997–2003. *Issues in Comprehensive Pediatric Nursing*, *28*, 115–136. doi:10.1080/01460860590950890

Nederhof, E., & Schmidt, M. V. (2012). Mismatch or cumulative stress: Toward an integrated hypothesis of programming effects. *Physiology & Behavior*, *106*, 691–700. doi:10.1016/j.physbeh.2011.12.008

Nettle, D. (2010). Dying young and living fast: Variation in life history across English neighborhoods. *Behavioral Ecology*, *21*, 387–395. doi:10.1093/beheco/arp202

Nettle, D. (2011). Flexibility in reproductive timing in human females: integrating ultimate and proximate explanations. *Philosophical Transactions of the Royal Society*, *366B*, 357–365. doi:10.1098/rstb.2010.0073

Nijmeijer, J. S., Hartman, C. A., Rommelse, N. N. J., Altink, M. E., Buschgens, C. J. M., Fliers, E. A., et al. (2010). Perinatal risk factors interacting with catechol-*O*-methyltransferase and the serotonin transporter gene predict ASD symptoms in children with ADHD. *Journal of Child Psychology and Psychiatry*, *51*, 1242–1250. doi:10.1111/j.1469-7610.2010.02277.x

Nikolova, Y. S., Bogdan, R., Brigidi, B. D., & Hariri, A. R. (2012). Ventral striatum reactivity to reward and recent life stress interact to predict positive affect. *Biological Psychiatry*, *72*, 157–163. doi:10.1016/j.biopsych.2012.03.014

Nikolova, Y. S., Ferrell, R. E., Manuck, S. B., & Hariri, A. R. (2011). Multilocus genetic profile for dopamine signaling predicts ventral striatum reactivity. *Neuropsychopharmacology*, *36*, 1940–1947. doi:10.1038/npp.2011.82

Obradovic, J., Bush, N. R., & Boyce, W. T. (2011). The interactive effect of marital conflict and stress reactivity on externalizing and internalizing symptoms: The role of laboratory stressors. *Development and Psychopathology*, *23*, 101–114. doi:10.1017/s0954579410000672

Obradovic, J., Bush, N. R., Stamperdahl, J., Adler, N. E., & Boyce, W. T. (2010). Biological sensitivity to context: The interactive effects of stress reactivity and family adversity on socio-emotional behavior and school readiness. *Child Development*, *81*, 270–289.

Park, A., Sher, K. J., Todorov, A. A., & Heath, A. C. (2011). Interaction between the DRD4 VNTR polymorphism and proximal and distal environments in alcohol dependence during emerging and young adulthood. *Journal of Abnormal Psychology*, *120*, 585–595. doi:10.1037/a0022648

Pergamin-Hight, L., Bakermans-Kranenburg, M. J., van IJzendoorn, M. H., & Bar-Haim, Y. (2012). Variations in the promoter region of the serotonin transporter gene and biased attention for emotional information: A meta-analysis. *Biological Psychiatry*, *71*, 373–379. doi:10.1016/j.biopsych.2011.10.030

Pitzer, M., Jennen-Steinmetz, C., Esser, G., Schmidt, M. H., & Laucht, M. (2011). Differential susceptibility to environmental influences: The role of early temperament and parenting in the development of externalizing problems. *Comprehensive Psychiatry*, *52*, 650–658. doi:10.1016/j.comppsych.2010.10.017

Plomin, R., & Daniels, D. (1987). Why are children in the same family so different from one another? *Behavioral and Brain Sciences*, *10*, 1–16.

Pluess, M., & Belsky, J. (2011). Prenatal programming of postnatal plasticity? *Development and Psychopathology*, *23*, 29–38.

Pluess, M., & Belsky, J. (2013). Vantage sensitivity: Individual differences in response to positive experiences. *Psychological Bulletin*, *139*, 901–916. doi:10.1037/a0030196

Pluess, M., Belsky, J., Way, B. M., & Taylor, S. E. (2010). 5-HTTLPR moderates effects of life events on neuroticism: Differential susceptibility to environmental influences. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *34*, 1070–1074.

Pluess, M., Stevens, S., & Belsky, J. (2013). Differential susceptibility: Developmental and evolutionary mechanisms of gene and environment interactions. In M. Legerstee, D. W. Haley, & M. H. Bornstein (Eds.), *The infant mind: Origins of the social brain*. New York: Guilford Press.

Pluess, M., Velders, F. P., Belsky, J., van IJzendoorn, M. H., Bakermans-Kranenburg, M. J., Jaddoe, V. W., et al. (2011). Serotonin transporter polymorphism moderates effects of prenatal maternal anxiety on infant negative emotionality. *Biological Psychiatry*, *69*, 520–525. doi:10.1016/j.biopsych.2010.10.006

Poehlmann, J., Hane, A., Burnson, C., Maleck, S., Hamburger, E., & Shah, P. E. (2012). Preterm infants who are prone to distress: Differential effects of

parenting on 36-month behavioral and cognitive outcomes. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. doi:10.1111/j.1469-7610.2012.02564.x

Poulin, M. J., Holman, E. A., & Buffone, A. (2012). The neurogenetics of nice: Receptor genes for oxytocin and vasopressin interact with threat to predict prosocial behavior. *Psychological Science*, *23*, 446–452.

Preacher, K. J., Curran, P. J., & Bauer, D. J. (2006). Computational tools for probing interactions in multiple linear regressions, multilevel modeling, and latent curve analysis. *Journal of Educational and Behavioral Statistics*, *31*, 437–448.

Quinlan, R. J. (2007). Human parental effort and environmental risk. *Philosophical Transactions of the Royal Society*, *274B*, 121–125. doi:10.1098/rspb.2006.3690

Raver, C. C., Blair, C., & Willoughby, M. (2012). Poverty as a predictor of 4-year-olds' executive function: New perspectives on models of differential susceptibility. *Developmental Psychology*, *49*, 292. doi:10.1037/a0028343

Rhee, S. H., Corley, R. P., Friedman, N. P., Hewitt, J. K., Hink, L. K., Johnson, D. P., et al. (2012). The etiology of observed negative emotionality from 14 to 24 months. *Frontiers in Genetics*, *3*, 9. doi:10.3389/fgene.2012.00009

Roiser, J. P., Rogers, R. D., Cook, L. J., & Sahakian, B. J. (2006). The effect of polymorphism at the serotonin transporter gene on decision-making, memory and executive function in ecstasy users and controls. *Psychopharmacology*, *188*, 213–227. doi:10.1007/s00213-006-0495-z

Roisman, G. I., Newman, D. A., Fraley, R. C., Haltigan, J. D., Groh, A. M., & Haydon, K. C. (2012). Distinguishing differential susceptibility from diathesis–stress: Recommendations for evaluating interaction effects. *Development and Psychopathology*, *24*, 389–409. doi:10.1017/S0954579412000065

Rutter, M. (1979). Protective factors in children's responses to stress and disadvantage. In M. W. Kent & J. E. Rolf (Eds.), *Primary prevention of psychopathology* (Vol. 3, pp. 49–74). Hanover, NH: University Press of New England.

Rutter, M. (1987). Psychosocial resilience and protective mechanisms. *American Journal of Orthopsychiatry*, *57*, 316–331.

Rutter, M. (2012). Resilience as a dynamic concept. *Development and Psychopathology*, *24*, 335–344. doi:10.1017/s0954579412000028

Schlichting, C. D., & Pigliucci, M. (1998). *Phenotypic evolution: A reaction norm perspective*. Sunderland, MA: Sinauer.

Schlomer, G. L., Del Giudice, M., & Ellis, B. J. (2011). Parent–offspring conflict theory: An evolutionary framework for understanding conflict within human families. *Psychological Review*, *118*, 496–521. doi:10.1037/a0024043

Schoebi, D., Way, B. M., Karney, B. R., & Bradbury, T. N. (2012). Genetic moderation of sensitivity to positive and negative affect in marriage. *Emotion*, *12*, 208–212. doi:10.1037/a0026067

Scott, S., & O'Connor, T. G. (2012). An experimental test of differential susceptibility to parenting among emotionally dysregulated children in a randomized controlled trial for oppositional behavior. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. doi:10.1111/j.1469-7610.2012.02586.x

Sergerie, K., Chochol, C., & Armony, J. L. (2008). The role of the amygdala in emotional processing: A quantitative meta-analysis of functional neuroimaging studies. *Neuroscience & Biobehavioral Reviews*, *32*, 811–830.

Shonkoff, J. P., Boyce, W. T., & McEwen, B. S. (2009). Neuroscience, molecular biology, and the childhood roots of health disparities building a new framework for health promotion and disease prevention. *Journal of the American Medical Association*, *301*, 2252–2259.

Sih, A. (2011). Effects of early stress on behavioral syndromes: An integrated adaptive perspective. *Neuroscience & Biobehavioral Reviews*, *35*, 1452–1465. doi:10.1016/j.neubiorev.2011.03.015

Simons, R. L., Lei, M. K., Beach, S. R., Brody, G. H., Philibert, R. A., & Gibbons, F. X. (2011). Social environmental variation, plasticity genes, and aggression: Evidence for the differential susceptibility hypothesis. *American Sociological Review*, *76*, 833–912. doi:10.1177/0003122411427580

Simons, R. L., Lei, M. K., Stewart, E. A., Beach, S. R. H., Brody, G. H., Philibert, R. A., et al. (2012). Social adversity, genetic variation, street code, and aggression: A Genetically informed model of violent behavior. *Youth Violence and Juvenile Justice*, *10*, 3–24. doi:10.1177/15412040114 22087

Sonuga-Barke, E. J., Oades, R. D., Psychogiou, L., Chen, W., Franke, B., Buitelaar, J., et al. (2009). Dopamine and serotonin transporter genotypes moderate sensitivity to maternal expressed emotion: The case of conduct and emotional problems in attention deficit/hyperactivity disorder. *Journal of Child Psychology and Psychiatry*, *50*, 1052–1063.

Stearns, S. (1992). *The evolution of life histories*. Oxford: Oxford University Press.

Sturge-Apple, M. L., Cicchetti, D., Davies, P. T., & Suor, J. H. (2012). Differential susceptibility in spillover between interparental conflict and maternal parenting practices: Evidence for *OXTR* and 5-HTT genes. *Journal of Family Psychology*, *26*, 431–442. doi:10.1037/a0028302

Sturge-Apple, M. L., Davies, P. T., Martin, M. J., Cicchetti, D., & Hentges, R. F. (2012). An examination of the impact of harsh parenting contexts on children's adaptation within an evolutionary framework. *Developmental Psychology*, *48*, 791–805. doi:10.1037/a0026908

Sulik, M. J., Eisenberg, N., Lemery-Chalfant, K., Spinrad, T. L., Silva, K. M., Eggum, N. D., et al. (2012). Interactions between serotonin transporter gene haplotypes and quality of mothers' parenting predict the development of children's noncompliance. *Developmental Psychology*, *48*, 740–754. doi:10.1037/a0025938

Suzuki, A., Matsumoto, Y., Shibuya, N., Sadahiro, R., Kamata, M., Goto, K., et al. (2011). The brain-derived neurotrophic factor Val66Met polymorphism modulates the effects of parental rearing on personality traits in healthy subjects. *Genes, Brain and Behavior*, *10*, 385–391. doi:10.1111/j.1601–183X.2010.00673.x

Sweitzer, M. M., Halder, I., Flory, J. D., Craig, A. E., Gianaros, P. J., Ferrell, R. E., et al. (2013). Polymorphic variation in the dopamine D4 receptor predicts delay discounting as a function of childhood socioeconomic status: Evidence for differential susceptibility. *Social Cognitive and Affective Neuroscience*, *8*, 499–508. doi:10.1093/scan/nss020

Takane, Y., & Cramer, E. M. (1975). Regions of significance in multiple-regression analysis. *Multivariate Behavioral Research*, *10*, 373–383. doi:10.1207/s15327906mbr1003_10

Trivers, R. L. (1974). Parent–offspring conflict. *American Zoologist*, *14*, 249–264.

van der Kooy-Hofland, V. A. C., van der Kooy, J., Bus, A. G., van IJzendoorn, M. H., & Bonsel, G. J. (2012). Differential susceptibility to early literacy intervention in children with mild perinatal adversities: Short- and long-term effects of a randomized control trial. *Journal of Educational Psychology*, *104*, 337–349. doi:10.1037/a0026984

van de Wiel, N. M., van Goozen, S. H., Matthys, W., Snoek, H., & van Engeland, H. (2004). Cortisol and treatment effect in children with disruptive behavior disorders: A preliminary study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *43*, 1011–1018.

van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2012). Differential susceptibility experiments: Going beyond correlational evidence: Comment on beyond mental health, differential susceptibility articles. *Developmental Psychology*, *48*, 769–774. doi:10.1037/a0027536

van IJzendoorn, M. H., Belsky, J., & Bakermans-Kranenburg, M. J. (2012). Serotonin transporter genotype 5HTTLPR as a marker of differential susceptibility? A meta-analysis of child and adolescent gene-by-environment studies. *Translational Psychiatry*, *2*, e147. doi:10.1038/tp.2012.73

Verschoor, E., & Markus, C. R. (2011). Affective and neuroendocrine stress reactivity to an academic examination: Influence of the 5-HTTLPR genotype and trait neuroticism. *Biological Psychology*, *87*, 439–449. doi:10.1016/j.biopsycho.2011.06.001

Vinberg, M., Trajkovska, V., Bennike, B., Knorr, U., Knudsen, G. M., & Kessing, L. V. (2009). The BDNF Val66Met polymorphism: Relation to familiar risk of affective disorder, BDNF levels and salivary cortisol. *Psychoneuroendocrinology*, *34*, 1380–1389.

Wakschlag, L. S., Kistner, E. O., Pine, D. S., Biesecker, G., Pickett, K. E., Skol, A. D., et al. (2010). Interaction of prenatal exposure to cigarettes and MAOA genotype in pathways to youth antisocial behavior. *Molecular Psychiatry*, *15*, 928–937. doi:10.1038/mp.2009.22

Way, B. M., & Taylor, S. E. (2010). The serotonin transporter promoter polymorphism is associated with cortisol response to psychosocial stress. *Biological Psychiatry*, *67*, 487–492.

Werner, E. E., & Smith, R. (1977). *Kauai's children come of age*. Honolulu, HI: University of Hawaii Press.

Werner, E. E., & Smith, R. (1982). *Vulnerable but invincible: A study of resilient children*. New York: McGraw–Hill.

West-Eberhard, M. J. (2003). *Developmental plasticity and evolution*. New York: Oxford University Press.

Whittle, S., Yap, M. B. H., Sheeber, L., Dudgeon, P., Yuecel, M., Pantelis, C., et al. (2011). Hippocampal volume and sensitivity to maternal aggressive behavior: A prospective study of adolescent depressive symptoms. *Development and Psychopathology*, *23*, 115–129. doi:10.1017/s0954579410000684

Widaman, K. F., Helm, J. L., Castro-Schilo, L., Pluess, M., Stallings, M. C., & Belsky, J. (2012). Distinguishing ordinal and disordinal interactions. *Psychological Methods*, *17*, 615–622.

Xie, P., Kranzler, H. R., Poling, J., Stein, M. B., Anton, R. F., Farrer, L. A., et al. (2010). Interaction of FKBP5 with childhood adversity on risk for post-traumatic stress disorder. *Neuropsychopharmacology*, *35*, 1684–1692. doi:10.1038/npp.2010.37

Yaman, A., Mesman, J., van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2010). Parenting and toddler aggression in second-generation immigrant families: The moderating role of child temperament. *Journal of Family Psychology*, *24*, 208–211. doi:10.1037/a0019100

Yap, M. B., Whittle, S., Yucel, M., Sheeber, L., Pantelis, C., Simmons, J. G., et al. (2008). Interaction of parenting experiences and brain structure in the prediction of depressive symptoms in adolescents. *Archives of General Psychiatry*, *65*, 1377–1385. doi:10.1001/archpsyc.65.12.1377

Zimmermann, P., Brueckl, T., Nocon, A., Pfister, H., Binder, E. B., Uhr, M., et al. (2011). Interaction of *FKBP5* gene variants and adverse life events in predicting depression onset: Results from a 10-year prospective community study. *American Journal of Psychiatry*, *168*, 1107–1116. doi:10.1176/appi.ajp.2011.10111577

Zuckerman, M. (1999). *Vulnerability to psychopathology: A biosocial model*. Washington, DC: American Psychological Association.