



Differential susceptibility to therapy

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Abstract

Evolutionary thinking leads to the proposition that individuals should differ in their susceptibility to environmental influences. Evidence consistent with this line of argument is reviewed, showing that certain individuals, as a function of their temperament and/or genetic make up, are more affected in a for-better-and-for-worse manner than others by, respectively, supportive and adverse contextual conditions. It is therefore proposed that therapy, be it attachment focussed or not, should not prove effective all the time, as some individuals manifest greater plasticity or malleability than others.

Why Therapy Should Fail (Sometimes):

Differential Susceptibility to Environmental Influences

Many a therapist, many a time, feels as if she is pushing on a string. No matter how hard he works, even an often effective therapeutic treatment fails to get the job done with some clients. Certainly attachment-based therapists are not immune to this experience. One consequence of this situation is the therapist coming to feel—and perhaps believe—that she has failed, even let the client down.

But perhaps, at least sometimes, an alternative analysis better characterizes the situation: The client is simply less susceptible to treatment—this treatment, perhaps any treatment. In this essay, which deals not directly with clinical treatment, we argue that this is, more or less, as it should be; and this is because individuals vary, for evolutionary biological reasons, in their susceptibility to environmental influences, including therapy.

We come to this view not as psychotherapists, but as developmental psychologists who have become ever more enamoured with viewing human development through an evolutionary lens. Perhaps the first author is particularly open to this way of seeing things because he has long been a student of attachment theory (e.g., Belsky & Nezworski, 1988; Belsky & Cassidy, 1994; Belsky, 1997). Bowlby (1969), of course, anchored his theory of attachment in evolutionary biology.

As most readers will be aware, Bowlby took issue with many fundamental precepts of classical Freudian analysis. One difference in view concerned why babies and young children develop close emotional bonds—attachments—to

their mothers (or principal caregivers). Whereas Freud believed that the reason the child formed such a strong bond was because the infant came to associate mother with the pleasure derived from nursing at the breast—essentially a classical-conditioning argument—Bowlby regarded the child's tie to mother as a consequence of evolutionary history: On ancestral times—what Bowlby referred to as the environment of evolutionary adaptedness—the establishment of a close, emotional bond to mother (or other primary caregiver) increased the likelihood the child would survive. Thus, infants who failed to establish attachment bonds were more like to die by, for example, wandering away from mother and falling into a fire or being consumed by a predator, whereas those who remained close, called out and/or clung to her were more likely survive. These latter children with a heritable, bioBehavioural tendency to become attached to mother were thus positioned to pass on their attachment-disposing genes to descendants. As a result, the proclivity to establish an attachment bond to mother or principal caregiver evolved and this, according to Bowlby, facilitated the survival of the species.

We no long talk about “survival of the species” as being the reason Behaviour (or anything else) evolves, basically because it is now appreciated that the unit of selection is not the species, but the gene (though there are debates on this matter), and so what evolves is that which promotes the reproductive fitness of the individual and, thereby, the gene. Survival is of fundamental importance not because living is so evolutionarily significant, but because it is the means to a much more important end—the passing on of genes to future generations, which is what defines reproductive fitness. Behaviour, including attachment Behaviour, evolves because it in some way facilitates reproduction, maybe not immediately, but eventually. Of course, the process may be convoluted, involving sex, pair bonding and parenting, to name but three relevant processes, but the accounting system we know as natural selection is more than capable of monitoring (reproductive) profit and loss.

Like Bowlby's analysis of the origins of attachment, our analysis of why attachment-oriented, or any therapies for that matter, should not succeed all the time derives from an evolutionary-biological analysis of human development. More specifically, it is based on a more general, evolutionarily-inspired hypothesis that individuals should vary in their susceptibility to environmental influences, perhaps of all kinds, though especially of rearing (Belsky, 1997; Belsky, 2005). And this view itself derives from a fundamental and indisputable precept of time: the future is uncertain. When this enduring reality is juxtaposed to an evolutionary biological perspective regarding human development, it leads to the conclusion that nature—meaning natural selection—should have crafted parents to bear children who vary in their susceptibility to rearing influences, thereby resulting in clients in therapy who vary in their susceptibility to treatment.

Why would it be that parents bear children who prove differentially susceptible to rearing and presumably other influences on development? Because parents can be wrong! Thus, inadvertently, even if not intentionally, parents can lead their progeny and most certainly have done so across human evolutionary history down developmental blind alleys, including literal, not just figurative, dead ends. So to hedge against this ever present risk, the argument is that Darwinian

processes of natural selection molded humans to vary in their susceptibility to parental and presumably other environmental influences as well. Nothing, of course, from an evolutionary biological perspective would have been more costly—than having all one's offspring fail to reproduce—because they all followed parental leads. So it stands to reason, at least evolutionary biological reason, that natural selection protected genomes from falling off this (fitness) cliff.

If this biological analysis sounds unconvincing or seems too far fetched, consider the Killing Fields of Cambodia. Who did the Khmer Rouge first murder when they filled the power vacuum that emerged in parts of Southeast Asia soon after the withdrawal of American troops from Vietnam? People like us; that is, those whose hands were not calloused and/or who wore eyeglasses. Why such people? Because these kind of people were likely to be educated and thus resist efforts by the Khmer Rouge to "re-educate" the Cambodian nation.

What this implies, then, is that Cambodian parents who had in earlier decades encouraged their children to study hard, do well in school and become educated, perhaps so they would avoid lives of manual labor, toiling in the fields, ended up consigning their children to an early death. Those recalcitrant offspring who did not "get with the (educational) program", however, being not interested in school or willing to study hard, who perhaps attracted their parent's approbation at the time, were more likely to survive the killing fields and, most significantly, breed another day than were their parentally-influenced siblings.

Needless to say, this is a dramatic example. But it serves to illustrate the point that even the best laid plans can prove

misguided—because the future is uncertain. Thus, effects that families have on children, whether consciously or unconsciously pursued, can engender outcomes never intended. By bearing and rearing some offspring—and thus adults who might show up in therapy some day—who are not responsive to parental influence, a family essentially secures an insurance policy against this most unforeseen and undesirable circumstance. What this may further imply, interestingly, is that such individuals who show up in therapy and prove unaffected by it may actually be there in the first place not for reasons of upbringing or other challenges or traumas they have experienced, but just because they were more or less born a certain way.

Essentially, what this line of argument leads to is the theoretical proposition that some people, using evolutionary-biological terminology, are "fixed strategists" when it comes to making their way in the world, whereas others are "plastic strategists". Or, thinking dimensionally rather than categorically, some individuals are more plastic or malleable and thus shaped by their experiences than others who are less shaped by experience and thus more the way they are because they were born that way rather than made that way. Please appreciate that use of the term "strategist" here does not imply and thus should not be read to imply that a person consciously follows a particular strategy, only that he may be developing and behaving as if he were. Just as important to

appreciate is that all so-called fixed strategists do not function in the same way. Whereas some should do very well, whether we are speaking about functioning in relationships, at work or in life more generally, others should do rather poorly, perhaps showing up in therapy. Some should also function more or less at average levels. That is, fixed does not mean fixed at an average (or high or low) level of functioning. It simply means that whatever the persons talents, limitations, etc., these are not particularly susceptible to environmental influence.

From Theory To Evidence

Unfortunately, we know of no empirical evidence pertaining to effects of therapy, be it attachment-based or not, consistent with the argument being advanced, other than the wealth of research showing that effects of therapy vary (Dobson, 1989; Crits-Christoph, 1992; Imel, Malterer, McKay, & Wampold, 2008) Of course, this is not something that therapists need research to reveal to them. Their regular professional activity documents this clearly enough, perhaps all too clearly sometimes.

But, importantly, there is evidence consistent with our theoretical claim that individuals should differ in their susceptibility to environmental influences and, thus, there should exist individual differences in plasticity or malleability. Some of it derives from developmental research on children, especially with regard to parenting, and some of it from genetics, especially pertaining to gene-environment-interaction (GXE) in the etiology of psychopathology. We, therefore, summarize

in the remainder of this essay select and illustrative research findings demonstrating that some individuals appear more malleable than others and that they do so in a for-better-and-for-worse manner. That is, so-called plastic strategists not only are more negatively affected by adversity, but they benefit more from supportive environmental conditions (Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2007).

What makes this latter observation of such importance is that it suggests that prevailing diathesis-stress

views of psychopathology may seriously misrepresent human development. This view which guides so much research, especially work on temperament and parenting and GXE work, regards some individuals as being "vulnerable" or "at risk" for reasons pertaining to their own Behavioural or biological make up (e.g., difficult temperament, risk allele) and thus being disproportionately, if not exclusively likely, to be adversely affected by negative experiences. For example, insensitive parenting may promote attachment insecurity in children vulnerable due to their difficult temperament. Or an individual carrying a particularly version of a particular gene may be the one who succumbs to depression upon confronting uncontrollable life stressors. According to the diathesis-stress view of psychopathology, then, those lacking the putative "vulnerability factor" are far less and even perhaps not at all adversely affected by the very experiences which prove so damaging to their at-risk brethren.

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Thus, to be clear, a differential-susceptibility perspective, in contrast to a diathesis-stress one, stipulates that the very individuals who appear most vulnerable and thus adversely affected by environmental stressors are, simultaneously, most likely to benefit from supportive environmental conditions, including ones in which contextual risk factors are simply absent. Basically because so many psychopathologist concentrate virtually exclusively upon clinical conditions and environmental risk factors, they stand to misconstrue a heightened and general susceptibility to environmental influences of all kinds to a particular sensitivity—that is, vulnerability—to adversity. One of the interesting issues this argument raises, of course, is that those who benefit the most from therapy may be so-called plastic strategists who are most affected, for better and for worse, by environmental conditions.

In what follows work on parent-X-temperament interaction and on GXE is considered which, at the least, is not inconsistent with this possibility, even though none of the research cited addresses therapy per se, especially attachment-based therapy. As will become evident, however, some of it does pertain to intervention efforts designed to enhance the functioning of children at risk of developing Behaviour problems. Furthermore, some evidence that differential susceptibility plays a role in how adult state of mind regarding attachment influences infant attachment is presented.

Temperament as a Phenotypic Marker of Differential Susceptibility

Some of the earliest and most suggestive evidence of differential susceptibility to environmental influences emerged in research on temperament-X-parenting interaction (Belsky, 1997), a long-standing focus of developmental inquiry (Rothbart & Bates,

2006). Belsky's (2005) review of relevant research revealed that predictive links between rearing experience and a variety of Behavioural outcomes often were consistently

greater for a subgroup of children characterized by a temperamental propensity for high negative affectivity, whether operationalized in terms of difficult temperament, irritability, fearfulness, or inhibition. But even though most of the work considered revealed that greater variance in a variety of developmental outcomes could be explained by rearing experiences in the case of more negatively emotional children, statistical analyses in the studies in question often did not afford determination of whether this result was itself a function of a for-better-and-for-worse parenting effect. Fortunately, the situation is different today, with numerous new studies chronicling such individual differences in developmental plasticity.

Consider, for example, Van Aken, Junger, Verhoeven and Dekovic's (2007) evidence that 16-to-19 month boys with difficult temperament manifest the smallest increase six months later in externalizing problems scores when reared by highly sensitive mothers who only infrequently used negative control, but the largest increase when highly insensitive mothers relied heavily on negative control. These striking parenting effects simply did not occur in the case of other children. Consider next work by Kochanska, Aksan, and Joy (2007) focused on father's reliance on power assertion (15 months), children's fearfulness (7 and 15 months) and their rule compatible conduct (38 months). Whereas high vs. low power assertiveness made no apparent difference for children scoring low in fearfulness (at 7 and 15 months), children who had been highly-fearful infants proved less obedient than all

others when fathers' power assertion was high, yet more obedient than all others when fathers' power assertion was low.

Drawing on data of the large scale longitudinal NICHD



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Study of Early Child Care and Youth Development (NICHD Early Child Care Research Network [ECCRN], 2005) and focusing upon maternally-reported difficult temperament at one and six months (composited), Bradley and Corwyn (2008) also discerned evidence of differential susceptibility when it came to evaluating effects of observed and reported maternal sensitivity, harshness and productive activity on teacher-reported Behaviour problems: Children with more difficult temperaments had more Behaviour problems in first grade than all other children if they experienced low-quality parenting across the infant, toddler and preschool years, but fewer problems than all other children if they experienced high-quality parenting; the anticipated effect of parenting quality was weaker in the case for children with intermediate levels of difficult temperament and weaker still in the case of children scoring very low on difficult temperament (i.e., easy temperament). Pluess and Belsky (in press-a) extended this work by showing that the differential-susceptibility effects in question extended through the end of the elementary school years. Moreover, their research further demonstrated that it was not just the case that infants with difficult temperaments were more affected—in a for-better-and-for-worse manner—by, respectively, sensitive and insensitive parenting, but that the same was true with regard to the quality of nonmaternal care. That is, it was infants who had the most difficult temperaments whose early and later social functioning was most influenced by whether or not they experienced care that was attentive, responsive, warm and stimulating across their first 54 months of life (Pluess & Belsky, in press-b; in press-a).

Although the Pluess and Belsky (in press-b; in press-a) work indicates that differential-susceptibility effects pertaining to early parenting and child-care experience and involving temperament-based susceptibility factors extend beyond the early childhood years, the question arises as to whether rearing and related experiences in later childhood operate in a similar manner. Some suggestive evidence that it does comes from Lengua's (2008) temperament-X-parenting interaction study which sought to explain change in externalizing problems using a community sample of 8-12 year olds. Children's reports of their mothers' parenting style (i.e., rejection/acceptance, inconsistent discipline) predicted change over a one-year period in mother-reported internalizing and externalizing problems, but differentially as a function of temperament. Children highly prone to frustration increased in externalizing problems over time when mothers were rejecting, but decreased when mothers manifested little rejection, with no such apparent effects of rejection evident in the case of children scoring low on frustration.

Intriguingly, there is also suggestive evidence of the legacy or even operation of differential susceptibility in early adulthood. Of importance in this regard is work testing hypothesized interactions between sensory-processing sensitivity, a personality characteristic measurable by means of the Highly Sensitive Person

Scale (see Aron & Aron, 1997), and various environmental factors in predicting adult shyness and negative affectivity (Aron, Aron, & Davies, 2005). According to Aron and Aron (1997), about 20% of the population are characterized by a high-sensitive personality which encompasses a sensitive nervous system, awareness of subtleties in surroundings, and a tendency to be more easily overwhelmed when in a highly stimulating environment. The study with perhaps the most relevant results showed that a problematic (and retrospectively reported) childrearing history predicted

high levels of (self-reported) shyness and negative affectivity in a sample of undergraduate students, whereas its absence predicted low levels of these same outcomes, but principally in the case of those students scoring high on sensory-processing sensitivity.

The repeatedly discerned moderational effect of negative emotionality/difficult temperament (sensory-processing sensitivity) in the case of parenting, child care quality, and other environmental experiences

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raises the question of why this should be the case. This would seem especially important to address in view of the fact that even though Belsky (1997; 2005) theorized that children should vary in their susceptibility to environmental influences (i.e., plasticity), his differential-susceptibility hypothesis did not stipulate that more negatively emotional children or those with difficult temperament (or with high sensory-processing sensitivity) would prove especially malleable; this was an empirical observation (Belsky, 2005). As it turns out, several non-mutually exclusive explanations have been advanced with regard to the issue at hand. Kochanska (1993) drew explicitly on Dienstbier's (1985) thinking on anxiety to account for her results, arguing that more negatively emotional/fearful/inhibited infants have lower thresholds for anxiety, thereby making them more easily aroused by discipline and thus responsive to it. Not unrelatedly, Belsky (2005) contended that a negatively emotional/difficult temperament reflects a highly sensitive nervous system on which experience—of both the positive and negative variety—registers especially strongly (see also Aron & Aron, 1997).

Whatever the mechanisms involved in making more negatively emotional children seemingly more malleable—in an often for-better-and-for-worse manner—it would be mistaken to conclude that this is the most important phenotypic marker of plasticity. Even though this could turn out to be the case, it could also be an artifact of the disproportionate attention that investigators guided by diathesis-stress perspective pay to so-called "risk factors" that interact with contextual adversity in producing problematic functioning (Belsky & Pluess, in press). If this is so, then it certainly behooves us to consider other potential behavioural markers of plasticity/malleability rather than reify one.

Genetic Markers of Differential Susceptibility

Whereas almost all the evidence considered through this point derives from studies of children, GXE findings consistent with the differential-susceptibility hypothesis often comes from research with adults; this is especially true of psychiatric research focused upon pathological outcomes (e.g., depression, antisocial Behaviour). The fact that most of this work has been guided by traditional diathesis-stress thinking means that on many occasions evidence that those carrying a putative “risk allele” actually function better than others when not exposed to the risk condition being studied (e.g., negative life events) is not even noted by investigators who, instead, exclusively herald evidence consistent with diathesis-stress thinking. In what follows, we call attention to GXE findings involving a variety of polymorphisms.

MAOA.

The neurotransmitter-metabolizing enzyme monoamine oxidase A or MAOA gene is located on the X chromosome. It encodes the MAOA enzyme, which metabolizes neurotransmitters such as norepinephrine, serotonin, and dopamine, rendering them inactive. Two sets of evidence, one linking the low-activity MAOA allele to antisocial Behaviour, and another linking abuse and neglect in childhood to the same developmental outcome, led Caspi and associates (2002) to hypothesize that inconsistency in findings in both literatures could be a result of the fact that maltreatment effects are moderated by genotype; and this is exactly what they discovered in their groundbreaking and widely cited GXE research carried out on a New Zealand birth cohort followed into young adulthood. More specifically, it was principally young men—females were not studied—with one form of the gene, that associated with low MAOA activity, who proved more violence prone when subject to child maltreatment. For those children with the high-MAOA-activity allele, a substantially smaller effect of child maltreatment emerged.

Although most have interpreted these findings, not unreasonably, in diathesis-stress terms, few have noticed that those most vulnerable to the adverse effects of maltreatment actually scored lowest in antisocial Behaviour when not exposed to maltreatment, suggesting perhaps greater plasticity—for better and for worse—rather than just greater vulnerability to adversity in the case of those with the low-activity MAOA allele. This interpretation would seem substantiated by results of a significant number of efforts to replicate the Caspi et al. (2002) findings. For example, Kim-Cohen et al. (2006) studied a

large number of boys to determine whether the MAOA polymorphism moderated effects of mother-reported physical abuse in early childhood on later mental health problems. At age 7 years boys with the low-MAOA-activity variant were rated by mothers and teachers as having more mental health problems—and specifically ADHD symptoms—if they had been victims of abuse, but fewer problems if they had not, compared to boys with the high-MAOA-activity genotype. In another longitudinal study, this of adolescent twin boys aged 8 to 17 years, Foley et al (2004) found that childhood adversity—based on parent and child report—predicted three-month history of conduct disorder (DSM-III) differently for children with the low- and high-activity MAOA allele. Once again, boys with the low-MAOA-activity allele were more likely to be diagnosed with conduct disorder if

exposed to higher levels of childhood adversity and less likely if exposed to lower levels of adversity, compared to boys with the high-MAOA-activity allele. Similar results emerged in Nilsson and associates’ (2006) cross-sectional investigation of 81 adolescent boys when the predictor was psychosocial risk, operationalized in terms of maltreatment experience and living arrangement. Only boys with the low-MAOA-activity allele



were affected by such risk, such that those with a history of adversity engaged in more criminal Behaviour (composite of vandalism, violence, stealing) and those lacking this history engaged in less.

5-HTTLPR

Far more investigated than GXE interactions involving MAOA have been those involving 5-HTTLPR. The serotonin-transporter-linked polymorphic region (5-HTTLPR) is a degenerate repeat polymorphic region in SLC6A4, the gene that codes for the serotonin transporter. Most research focuses on two variants—those carrying at least one short allele (s/s, s/l) and those homozygous for the long allele (l/l)—though more variants than these have been identified (Nakamura, Ueno, Sano, & Tanabe, 2000). The short allele has generally been associated with reduced expression of the serotonin transporter molecule—which is involved in the reuptake of serotonin from the synaptic cleft—and thus considered to be related to depression, either directly or in the face of adversity.

Again breaking empirical ground in GXE research, Caspi and associates (2003) were the first to show that the 5-HTTLPR moderates effects of stressful life events during early adulthood on depressive symptoms, as well as on probability of suicide ideation/attempts and of major depression episode at age 26 years. Individuals with two short alleles (s/s) proved most adversely affected whereas effects on those with two long alleles (l/l) were weaker or entirely absent. Of special significance given our focus on differential susceptibility, is that those homozygous for the short allele scored best on the outcomes just mentioned when stressful life events were absent, though just as was true among low-MAOA activity individuals in Caspi et al. (2002), not by very much.

Several research groups have attempted to replicate Caspi et al.'s findings (2003) of increased vulnerability to depression in response to stressful life events for individuals with one or more copies of the s allele, with most succeeding. Going unnoticed in most even if not all of this work to be summarized below, however, is that those carrying one or two short alleles (s/l, s/s) did not just function most poorly when exposed to many stressors, but best—showing least problems—when

encountering few or none. Consider, for example, Taylor and associates' (2006) findings (appreciated by the investigators) indicating that young adults homozygous for short alleles (s/s) manifested greater depressive symptomatology than individuals with other allelic variants when exposed to early adversity (i.e., problematic childrearing history), as well as many recent negative life events, consistent with a diathesis-stress framework, yet the fewest symptoms when they experienced a supportive early environment or recent positive experiences, that is, not just the absence of adversity. A similar for-better-and-for-worse pattern of environmental effects is evident—and noted—in Brummett et al.'s (2008) investigation of middle-aged and aging adults who differed in whether or not they served as caregiver of a relative with Alzheimer's disease and in Eley et al.'s (2004) research on adolescent girls who were and were not exposed to risky family environments. As in the case of those with the low-MAOA-activity allele, one cannot but wonder whether those carrying the s 5-HTTLPR allele might be more likely to benefit from therapy, or at least some types of therapy.



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DRD4

Moving from the serotonergic to the dopaminergic system, which is engaged in attentional, motivational, and reward mechanisms, a polymorphism of the dopamine receptor D4 (DRD4) gene also has stimulated much GXE research. Variants of the DRD4 differ by the number of 48-base pair tandem repeats in exon III, ranging from 2-11. The 7-repeat variant has been identified as a vulnerability factor due to its links to ADHD (Faraone, Doyle, Mick, & Biederman, 2001), high novelty seeking Behaviour (Kluger, Siegfried, & Ebstein, 2002), and low dopamine reception efficiency (Robbins & Everitt, 1999), among other correlates.

As it turns out, a number of studies indicate that children carrying this putative risk allele are not only more adversely affected by poorer quality parenting than other children, but also benefit more than others from good-quality rearing. Of special importance is that some of this work reflects efforts to determine whether intervention efficacy varies by genetic make up. But, before considering such research, the next investigation to be considered may be regarded as particularly important for another reason—because a “good” environment is not just operationalized as the absence of adversity, as in much of the GXE research already cited, but in terms of high quality parenting. In a longitudinal study

of infants, maternal insensitivity observed when children were 10 months predicted externalizing problems reported by mother more than two years later, but only for children carrying the 7-repeat DRD4 allele (Bakermans-Kranenburg & van Ijzendoorn, 2006). Moreover, although children with the 7-repeat DRD4 allele displayed, consistent with a diathesis-stress model, the most externalizing Behaviour of all children when mothers were judged insensitive, they also manifested the least externalizing Behaviour when mothers were highly sensitive.

Experimental intervention research designed to enhance parenting also documents a moderating effect of the 7-repeat allele on parenting. When Bakermans-Kranenburg, van Ijzendoorn, Pijlman, Mesman, and Juffer (2008) looked at change over time in parenting—from before to well after a video-feedback parenting intervention was provided on a random basis to mothers of 1-3 year olds who scored high on externalizing problems—they not only found that the intervention succeeded in promoting more sensitive parenting and positive discipline, but that experimental effects extended to improvements in child Behaviour, but only for those children carrying the DRD4 7-repeat allele.

The same team of Dutch of investigators also reported that the DRD4 7-repeat allele moderated the effect of maternal unresolved loss or trauma, as measured by means of the Adult Attachment Interview, on early infant development. More specifically, unresolved loss predicted infant attachment disorganization, an early developmental marker of psychological disturbance later in life (Carlson, 1998), but only in the case of infants carrying the 7-repeat allele (van Ijzendoorn & Bakermans-Kranenburg, 2006). Indeed, these infants manifest both the most and least disorganized attachment Behaviour when stressed depending on whether their mothers had or had not experienced unresolved loss or trauma in their own lives.

Conclusion

More than anything else, perhaps, what the selection of findings cited indicate is that it is not just that some individuals are more vulnerable to adversity than others, as the traditional diathesis-stress model of psychopathology has presumed, but that in some, perhaps many cases these same putatively vulnerable individuals are actually highly susceptible to the benefits of positive environmental conditions, even when this just means the absence of adversity. This raises the obvious question, of course, whether the same applies to the therapeutic experience. More pointedly, are there clients who simply are unresponsive to therapy, including attachment-based therapy? And, if so, are these also individuals whose psychological difficulties are less a function of experience

than often presumed by many etiological models guiding treatment? By the same token, are there some individuals who have not only been greatly—and adversely—affected by their experience, but who, as a result of their general susceptibility to environmental influences, benefit the most from therapy? Certainly if one generalizes broadly from the parenting intervention studies in the preceding paragraphs dealing with the prevention of child Behaviour problems, this would seem to be the case.

One of the most striking features of the preceding analysis is how diverse the evidence base is which suggests that individuals differ in their plasticity. That pertaining to environmental factors highlighted differential-susceptibility-related effects of parenting, child-care quality, and life events, to name but some of the predictors considered in the research cited. That pertaining to outcomes seemingly affected by these diverse environmental influences included disorganized infant attachment; externalizing problems in the toddler, preschool and childhood years; antisocial Behaviour in adolescence, young adulthood and even middle age; and depression throughout adulthood. And, of course, that pertaining to moderators of diverse environmental effects

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on these diverse outcomes, so-called susceptibility (not just vulnerability) factors, included temperamental attributes of children and genotypic ones. This latter point highlights what might be regarded as one of the unknowns in the differential-susceptibility equation. Is the research conducted by investigators often working in different fields actually identifying, by different means, the very same more-and-less-susceptible individuals? Consider in this regard that the very infants who score high in negative emotionality and who have short alleles on the 5-HTTLPR gene are often be one

and the same (Auerbach, Faroy, Ebstein, Kahana, & Levine, 2001).

Another unknown concern is whether it makes the most sense to regard more and less plasticity as a global, macro trait-like characteristic of individuals or consider it in more domain-specific terms? This should be an important issue for therapists, as it would seem to have bearing on whether certain individuals are unlikely or less likely to benefit from certain therapies or, instead, virtually any and all of them. Are some people simply more malleable than others across the board, almost irrespective of the environmental factor and aspect of functioning under consideration, or are people a complex mosaic of components that are more and less susceptible to environmental influence, thus making them both more and less malleable relative to (different sets of) others? Whereas the latter conceptualization might make more intuitive sense, of interest is a recent computer modeling effort designed to determine whether individual differences in susceptibility to environmental influences could evolve through natural selection (Wolf, van Doorn, & Weissing, 2008). Not only did it

show that it could, but it further indicated that it would occur in a more domain-general, across-the-board manner rather than domain-specific one. Nevertheless, were it to prove to be the case empirically that plasticity varied across domains, this might translate into some individuals being responsive to some therapies, but not to others—and vice versa, a view that probably resonates with many clinicians.

A final issue of the many that could be raised for further investigation and consideration is whether plasticity should be regarded as principally born or made, that is, a function of nature or nurture. Certainly the GXE evidence cited calls attention to heritable individual differences in plasticity, as well as to the fact that so-called “vulnerability genes” or “risk alleles” might in many cases be better conceptualized as “plasticity genes”. But just because GXE studies are replete with evidence, often unnoticed, of differential-susceptibility findings, not just genetic-vulnerability and thus diathesis-stress ones, should not lead to the presumption that plasticity is only born, a function of genotype, never made by experience (Belsky & Pluess, in press). Indeed, Boyce and Ellis (2005) have advanced a theory of “biological sensitivity to context” based on the premise that variation in susceptibility to environmental influences is shaped by early experience in life.

Especially notable with regard to the possibility that heightened susceptibility to environmental influences may be made is recent research on the putatively adverse effects on the developing child of maternal stress during pregnancy. This is because so-called “fetal programming” appears to influence several of the very susceptibility factors mentioned earlier in this essay that seem to be markers of differential susceptibility, including difficult temperament (Huizink, de Medina, Mulder, Visser, & Buitelaar, 2002) and emotional reactivity (Möhler, Parzer, Brunner, Wiebel, & Resch, 2006). Such data suggest that very early experience—in the womb—may shape plasticity, not just genetics, as these “outcomes” are among the very child characteristics found in work cited herein to demarcate heightened susceptibility to environmental influences.

In conclusion, even though current understanding of the mechanisms underlying differential susceptibility remain limited, there is much evidence consistent with the contention that individuals differ in degree—if not kind—of their response to environmental influences, be those influences of parenting, child care, life events or some other potential determinant of human development and psychological functioning. To the extent that such differences are rooted in biology and shaped by natural selection, there is reason to believe that similar differential response should characterize therapy, too. Only future research will determine the truth value of this claim.

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