Differential susceptibility to the environment: Are developmental models compatible with the evidence from twin studies?

Differential Susceptibility to the Environment: Are Developmental Models Compatible with the Evidence from Twin Studies?

Marco Del Giudice

University of New Mexico

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Marco Del Giudice, Department of Psychology, University of New Mexico.
Address correspondence to Marco Del Giudice, Department of Psychology, University of New Mexico. Logan Hall, 2001 Redondo Dr. NE, Albuquerque, NM 87131, USA; email: marcodg@unm.edu

Abstract

According to models of differential susceptibility, the same neurobiological and temperamental traits that determine increased sensitivity to stress and adversity also confer enhanced responsivity to the positive aspects of the environment. Differential susceptibility models have expanded to include complex developmental processes in which genetic variation interacts with exposure to early environmental factors, such as prenatal stress hormones and family conflict. In this study I employed a simulation approach to explore whether, and under what conditions, developmental models of differential susceptibility are compatible with the cumulative findings from twin studies of personality and behavior, which consistently show sizable effects of genetic and nonshared environmental factors and small to negligible effects of the shared environment. Simulation results showed that, to a first approximation, current alternative models of differential susceptibility are all equally compatible with the evidence from twin research; that sizable interaction effects involving individual differences in plasticity are plausible, but only if direct environmental effects are correspondingly weak; and that a major role of shared environmental factors is plausible in early development (consistent with the developmental mechanisms postulated in the differential susceptibility literature), but not in later development. These results support the general plausibility of differential susceptibility models and suggest some realistic constraints on their assumptions.

Keywords: Biological sensitivity to context; differential susceptibility; genotype-environment interaction; plasticity; twin studies.

While early experience can have lasting effects on psychological development, individuals differ dramatically in how strongly they respond to their social and physical environments. Moving beyond classical conceptions of vulnerability and resilience, recent theoretical models and empirical findings converge in suggesting that many of the same factors that determine increased sensitivity to stress and adversity may also confer enhanced responsivity to the positive, supportive aspects of the environment (Belsky, Bakermans-Kranenburg & Van IJzendoorn, 2007; Belsky & Pluess, 2013; Boyce & Ellis, 2005; Ellis & Boyce, 2008; Ellis, Boyce, Belsky, Bakermans-Kranenburg & Van IJzendoorn, 2011).

Models of *differential susceptibility* postulate the existence of pervasive interactions between the quality of the environment and a set of neurobiological and temperamental traits—such as negative emotionality and physiological stress reactivity—that increase an individual's plasticity in response to both positive and negative experiences ("for better and for worse"). At present, the main alternative accounts of differential susceptibility are Differential Susceptibility Theory (DST; Belsky, 1997, 2005) and Biological Sensitivity to Context theory (BSC; Boyce & Ellis, 2005; Ellis & Boyce, 2008). While these models are based on a shared core of evolutionary principles, they make somewhat different assumptions about the genetic and environmental determinants of plasticity, the shape of the functions that describe the development of plasticity across environments, and so on (see below; Ellis et al., 2011).

Over the years, differential susceptibility models have expanded to include multi-stage developmental processes in which genetic variation interacts with exposure to early environmental factors, such as prenatal stress hormones and family conflict (e.g., Belsky & Pluess, 2013; Belsky et al., 2009; Ellis et al., 2011; Pluess & belsky, 2011). Clearly, these processes have the potential to generate remarkably complex patterns of interplay between genotypes, phenotypes, and environments. This raises the fundamental question of whether differential susceptibility models are compatible with the findings from behavior genetic research, including the large and well-established literature on twin studies. As explained in more detail below, twin studies paint a remarkably consistent picture of the relative contributions of genetic and environmental factors to personality and behavior (Plomin, DeFries, Knopik, & Neiderhiser, 2013; Polderman et al., 2015). However, they are not well equipped to detect the kinds of interactions that define differential susceptibility. Because of the divergent assumptions made by classical twin studies and differential susceptibility models, is still unclear to what extent the various developmental processes postulated in the differential susceptibility literature can be reconciled with the quantitative results from behavior genetics, and whether any of those processes are more plausible than others (i.e., they tend to produce patterns of correlations that resemble more closely those observed in empirical research).

In this paper I employ a simulation approach to explore the compatibility between developmental models of differential susceptibility and the findings from twin studies of personality and behavior. In a series of simulations, the assumptions of differential susceptibility models were used to generate virtual data for large samples of monozygotic and dizygotic twins, and the results were compared with those reported in the empirical literature. Importantly, this method sidesteps possible issues concerning the validity of twin designs and their assumptions (for recent discussions see Barnes et al., 2014; Johnson, Penke, & Spinath, 2011). The question

is whether the processes postulated by differential susceptibility models can reproduce the findings of twin studies when the data are analyzed in a comparable way, regardless of the validity of the underlying assumptions. In addition to providing an initial plausibility check of current theories of differential susceptibility, simulations results may inform the study of plasticity by placing realistic constraints on the assumptions of developmental models.

Models of Differential Susceptibility

In the differential susceptibility literature (e.g., Belsky et al., 2007; Ellis et al., 2011), the interplay between plasticity and environmental quality is described by a crossover phenotype-by-environment (P×E) interaction in which the developmental response to a given dimension of the environment (e.g., parental warmth, family conflict, early stress) depends on an individual's level of plasticity. The shape of the function that links the outcome trait (e.g., aggression, self-control, depression) to the quality of the environment is assumed to be approximately linear, with slope determined by plasticity; in the resulting interaction pattern, highly plastic individuals express lower than average levels of the trait in negative environments but *higher* than average levels of the same trait in positive environments (or vice versa, depending on the trait). This pattern captures the "for better and for worse" effect of susceptibility, as illustrated in the right panel of Figure 1. While DST and BSC make similar assumptions about the role of plasticity in the development of outcome traits—that is, they converge on the interaction shape shown in the right panel of Figure 1—they offer markedly different accounts of the origin of plasticity itself (left panel of Figure 1).

Differential Susceptibility Theory (DST). According to DST, the biological function of differential susceptibility is to limit the evolutionary costs of plasticity by making some individuals resistant to environmental influences, including those exerted by parents (Belsky, 1997). DST was derived from evolutionary considerations, and predicted the existence of differences in susceptibility as a form of "insurance" against developmental errors. The central idea of DST is that highly plastic individuals benefit when early environmental conditions correctly predict the later environment; however, the same individuals risk severe mismatch when conditions change or early cues about the state of the environment—including the parents' behavior in infancy and childhood—turn out to be inaccurate or misleading. Individual differences in plasticity spread the risk of mismatch and can be favored by natural selection in response to unpredictable fluctuations in the environment (Frankenhuis, Panchanathan, & Belsky, 2015).

In the original formulation of the model (Belsky, 1997), plasticity was assumed to be essentially a function of genetic factors. Under this assumption, the P×E interaction depicted in the right panel of Figure 1 becomes equivalent to a genotype-by-environment (G×E) interaction. As I explain below, extensive G×E interactions can account for the characteristic pattern of environmental influences observed in twin studies. The assumption that genotypes directly determine plasticity is depicted as DST-1 in the left panel of Figure 1. In model DST-1, different lines represent different genotypes, which in turn are associated with different levels of plasticity (P). The fact that lines are horizontal implies that plasticity does not depend on the quality of the environment. While the initial version of DST made no specific predictions about the phenotypic underpinnings of plasticity, later research suggested emotional and temperamental reactivity as

plausible mediators of plasticity at the phenotypic level (see Ellis et al., 2011). The DST model was later expanded to include both genetic factors and early environmental effects, such as prenatal exposure to stress hormones (Belsky, 2005; Belsky & Pluess, 2009; Pluess & Belsky, 2011). In its current version, DST acknowledges the possibility that genetic factors may amplify the effects of the early environment on plasticity, giving rise to G×E interactions between the early environment and plasticity-related genes in determining individual levels of plasticity (see Pluess & Belsky, 2011). This expanded and more complex set of assumptions is depicted as DST-2 in the left panel of Figure 1. In this version of the model, trait development involves a minimum of *two* interactions with the environment: an early G×E interaction that determines the child's plasticity (DST-2 in the left panel of Figure 1), and a later P×E interaction that determines the outcome trait (e.g., aggression; right panel of Figure 1).

Biological Sensitivity to Context Theory (BSC). The BSC model has it roots in developmental research on health and adversity. Boyce and colleagues (1995) found that children high in cardiovascular and immune reactivity have worse health outcomes in stressful environments, but better outcomes in positive and supportive environments. In short, Boyce et al. (1995) advanced a differential susceptibility hypothesis to explain their empirical findings, while Belsky (1997) independently proposed the same concept on a purely theoretical basis (see Ellis et al., 2011 for a detailed account). Later, Boyce and Ellis (2005) reframed the hypothesis in an evolutionary framework and developed the BSC model. According to BSC, plasticity is primarily mediated by individual differences in neurobiological traits. One of the key mediators of plasticity (or "sensitivity to context") is the stress response system, so that infants and children with a highly responsive stress physiology are more plastic than those who exhibit dampened stress reactivity. From an evolutionary standpoint, the central tenet of the model is that heightened plasticity is adaptive at both ends of the continuum of environmental quality—that is, in highly stressful *and* highly protected environments. In harsh environments, plasticity increases an individual's ability to detect and respond to dangers and threats; in safe and protected environments, it maximizes his/her ability to benefit from social resources and support. In moderately stressful environments, the costs of neurobiological susceptibility outweigh its benefits, and comparatively low levels of plasticity are favored (Boyce & Ellis, 2005).

In total, the BSC model predicts a U-shaped (i.e., approximately quadratic) relation between early adversity and plasticity. This prediction is consistent with recent simulation results suggesting that, in presence of crossover interactions such as those postulated by differential susceptibility models, it may be optimal to express higher levels of plasticity at both ends of the relevant environment variable (Del Giudice, 2015). In the simplest version of the model, plasticity is mainly determined by early environmental exposure; this simplified model with no genotypic effects is shown as BSC-1 in the left panel of Figure 1. In its complete formulation, however, the BSC model recognizes the significance of genetic variation in plasticity, as well as the possibility of G×E interactions between early adversity and an individual's genotype (Ellis, Jackson, & Boyce, 2006). These more complex assumptions are embodied by model BSC-2 (left panel of Figure 1). While the overall relation between environmental quality and plasticity is still U-shaped, the strength of the relation now depends on genotypic differences between individuals.

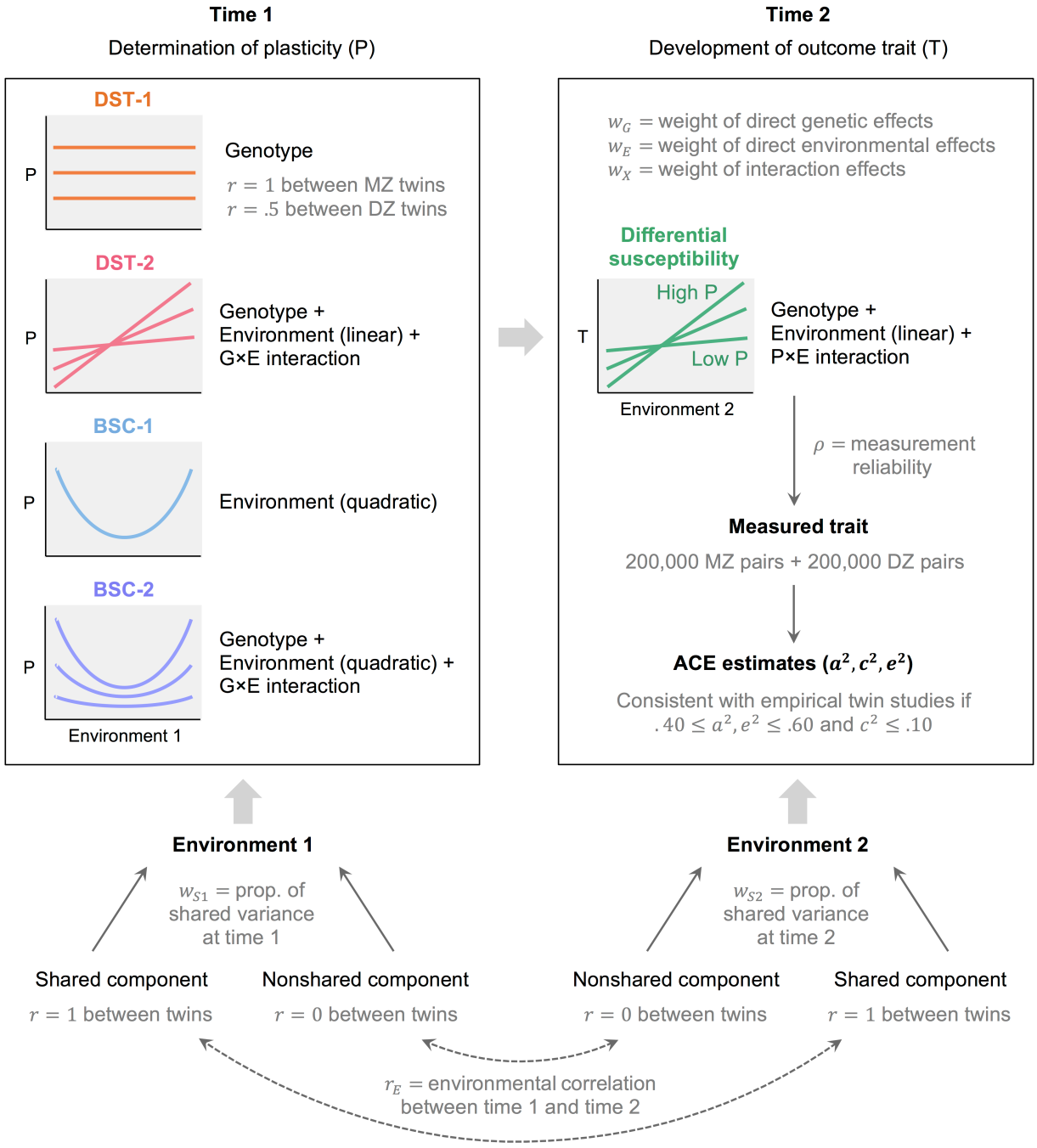

Figure 1. Structure of the simulation. See the main text for explanation. DST = differential susceptibility theory; BSC = biological sensitivity to context; DZ = dizygotic; MZ = monozygotic.

Evidence from Twin Studies

Twins studies have been the primary tool of behavior genetics for about a century, and continue to provide valuable information to this day (see Evans, Gillespie, & Martin, 2002; Plomin et al., 2013). In the classical twin design, correlations between monozygotic (MZ) and dizygotic (DZ) twins are employed to separate the variance of a trait into genetic and environmental components. This is possible because twins share the same familial environment and a known proportion of genetic variance. In most twin studies, trait variance is partitioned into three components: *additive genetic* variance or narrow-sense *heritability* (a^2); *shared environmental* variance (c^2), which captures environmental factors that make siblings within a family similar to one another; and *nonshared environmental* variance (e^2), which captures environmental factors that act independently on different siblings within a family (and tend to make them different from one another). This partitioning model is known by the acronym ACE. Importantly, ACE models assume the absence of G×E interactions. If such interactions do exist, they are absorbed into one of the other estimated components. Specifically, interactions between genotype and shared environmental factors inflate the estimated heritability (a^2), whereas interactions between genotype and nonshared environmental factors inflate the nonshared environmental variance (e^2). Finally, the e^2 term also absorbs the measurement error associated with the trait of interest, so that unreliable measurement ends up inflating the nonshared environmental variance (see Evans et al., 2002; Johnson et al., 2011).

Importantly, models of differential susceptibility often postulate a sizable role of family variables—such as conflict between parents, parental warmth and support, or maternal depression—in the early development of plasticity. These variables are likely to affect multiple siblings within a family, and should operate (at least in part) as shared environmental effects. In singletons, prenatal variables such as exposure to stress hormones are likely to have a large nonshared component; however, even those variables are mostly experienced as shared effects within twin pairs, and should be detected as such in twin designs. In total, the differential susceptibility literature often makes the accessory assumption that shared environmental effects should play a sizable role in the early development of plasticity. This is not necessarily true of later stages of development, and there are reasons to expect that the weight of shared effects will generally decline over time as siblings are exposed to different experiences with peers, partners, and other kinds of extra-familial environments.

With few exceptions, twin studies of personality and behavior in adulthood converge on a standard pattern of about 50% additive genetic variance (heritability), about 50% nonshared environmental variance, and a small amount of shared environmental variance, typically less than 10% and often close to zero (Bleidorn, Kandler, & Caspi, 2014; Jang & Yamagata, 2009; Malouff, Rooke, & Schutte, 2008; Plomin et al., 2013). Decades of research have shown that the same general pattern applies to most behavioral traits; observed differences in heritability between traits tend to be unsystematic and difficult to replicate (Polderman et al., 2015; Turkheimer, Pettersson, & Horn, 2014). The predominance of nonshared environmental effects in twin research is consistent with a number of alternative explanations. First, it may be the case that nonshared components of the environment play a large direct role in development. Second, there may be extensive G×E interactions between the nonshared environment and individual

genotypes. Third, some of the more complex developmental patterns postulated by DST and BSC models may lead to similar results when the data are filtered through the standard ACE model.

Of course, twin studies are not without limitations (see Johnson et al., 2011). For example, it has been shown that standard twin designs tend to systematically underestimate the contribution of shared environmental effects (Burt, 2014). At the same time, and despite their limitations, twin studies still represent the most robust source of knowledge about the genetic structure of behavioral traits (Polderman et al., 2015); for example, they do not suffer from the severe replication problems of candidate gene studies or require the very large samples of genomewide association studies (GWAS; see Chabris, Lee, Cesarini, Benjamin, & Laibson, 2015; Dick et al., 2015; Duncan & Keller, 2011). If differential susceptibility models are valid, they should be capable of successfully explaining and/or reproducing the results of twin studies, whatever the limitations and interpretive difficulties of the latter. At present, it is still unclear whether—and under what conditions—the developmental processes postulated by differential susceptibility models can be expected to yield results compatible with those reported in the literature on twin studies. The goal of the present study was to explore these questions with a simulation approach.

Method

Monte Carlo simulations were run in R™ 2.15 (R Core Team, 2012). The simulation structure is shown in Figure 1. In each simulation, the assumptions of one of four specific models of differential susceptibility (DST-1, DST-2, BSC-1, and BSC-2) were employed to generate trait scores in a virtual sample of 400,000 twin pairs (200,000 MZ pairs and 200,000 DZ pairs). Trait development was modeled as a two-step process. The first step (time 1) simulated the early determination of plasticity according to one of the four developmental models. The second step (time 2) simulated a crossover P×E interaction between plasticity and the later state of the environment, which in turn determined the outcome trait. As explained above, the shape of the interaction at time 2 is assumed to be the same in the four models. To make the simulation more realistic, measurement error was added to individual trait scores. Trait correlations in MZ and DZ twins were then used to compute estimates of a^2, c^2, and e^2. Finally, the estimated variance components were compared with the range of values commonly observed in twin studies. What follows is an overview of the simulation procedure and the underlying logic; a detailed description can be found in the online supporting information.

Time 1: Determination of Plasticity

At time 1, the state of the environment experienced by each twin was determined as a weighted sum of shared and nonshared environmental effects. Shared effects were identical between twins, whereas nonshared effects were specific to each member of the pair. Environmental states were modeled as normally distributed with $M = 0$ and $SD = 1$. The proportion of shared variance on the total environmental variance was determined by parameter w_{S1}, which could range between 0 and 1. Genotypic effects were also modeled as normally distributed with $M = 0$ and $SD = 1$. This is reasonable if one assumes that individual plasticity is not determined by a single gene, but rather by the joint effect of variation at multiple loci (e.g.,

Belsky & Beaver, 2011). In MZ pairs, the genotypes of the two twins were identical; in DZ pairs, the correlation between genotypic effects in the two twins was set to .50.

Plasticity was determined as a function of an individual's genotype and/or environment, according to four alternative models of differential susceptibility (left panel of Figure 1). Model DST-1 was based on the original version of DST, in which plasticity is fully determined by genotypic factors. Model DST-2 was based on the current version of DST, in which the early environment (e.g., prenatal hormones) can affect plasticity both directly and in interaction with the genotype. The relative contribution of direct genetic effects, direct environmental effects, and G×E interaction effects to the total variance of plasticity was determined by parameters w_G, w_E, and w_X. These parameters could range between 0 and 1, with $w_G + w_E + w_X = 1$.

Model BSC-1 represented a minimalist version of BSC, in which plasticity develops as a quadratic function of the early environment with no further contribution from the genotype. Model BSC-2 described a more complete version of BSC, in which plasticity results from the combination of a quadratic effect of the environment, a linear effect of the genotype, and a linear-by-quadratic G×E interaction. As in model DST-2, the relative contribution of direct genetic effects, direct environmental effects, and G×E interaction effects to the total variance in plasticity was determined by parameters w_G, w_E, and w_X.

In all models, plasticity scores were rescaled to a distribution with $M = 1$ and $SD = 0.20$, effectively restricting them to positive values. This was done to obtain the specific interaction shape postulated by differential susceptibility models, in which the environmental slope may become larger (higher plasticity) or smaller (lower plasticity), but does not change sign (right panel of Figure 1).

Time 2: Development of Outcome Trait

Trait development at time 2 was modeled as the combination of a linear effect of the genotype, a linear effect of the environment at time 2, and a P×E interaction between the environment at time 2 and plasticity P (itself the product of development at time 1). The relative contribution of direct genetic effects, direct environmental effects, and P×E interaction effects to trait variance was determined by parameters w_G, w_E, and w_X. For the sake of parsimony these parameters were set to the same value at time 1 and time 2, as there was no reason to assume that the contribution of different kinds of effects would differ systematically between early and late development. Note that the model does not include a direct effect of plasticity, but only the interaction between plasticity and the environment. This aspect of the model reflects the key assumption that plasticity has no *independent* effects on trait development besides moderating the effect of the environment. Fitting a regression model to the interaction data would require one to include all the lower-order terms (including a main effect for the hypothesized moderator) in order to properly estimate the interaction term. However, this requirement does not apply to a generative model such as the one presented here.

As with the environment at time 1, the state of the environment at time 2 was determined as a weighted sum of shared and nonshared effects. The correlation between environmental states at time 1 and time 2 was controlled by parameter r_E, which could range between 0 and 1 (bottom

of Figure 1). With $r_E = 0$, early and later states of the environment were uncorrelated; with $r_E = 1$, the environment was completely stable between time 1 and time 2. Parameter w_{S2} determined the proportion of shared environmental variance at time 2. As I discussed above, the relative importance of shared and nonshared environmental effects may change considerably between early and later development; in the simulation, the weights of shared environmental factors at time 1 and time 2 could be controlled separately through parameters w_{S1} and w_{S2}.

Trait Measurement

Trait scores obtained at time 2 were standardized ($M = 0$; $SD = 1$); measured scores were computed by adding normally distributed random error ($M = 0$; $SD = 1$) to the true value of the trait. Parameter ρ determined measurement reliability, i.e., the proportion of true score variance on the total variance of the measured trait. Note that ρ represents the overall reliability of a measure, which is captured only partially by indices of internal consistency and test-retest stability. Well-validated, full-length personality scales achieve high levels of reliability, with coefficients of stability and internal consistency around .90 (e.g., McCrae, Kurtz, Yamagata, & Terracciano, 2011). Shorter scales tend to have lower reliabilities, often in the .70−.80 range; reliability coefficients below .70 are often considered problematic (Viswesvaran & Ones, 2000).

Variance Components

For each simulated sample, correlations between trait scores in MZ and DZ pairs were computed and used to estimate ACE variance components with Falconer's method (see Falconer & MacKay, 1996). Model results were judged to be compatible with the findings from twin studies if they met the following criteria: estimated heritability between 40% and 60% ($.40 \leq a^2 \leq .60$), nonshared environmental variance between 40% and 60% ($.40 \leq e^2 \leq .60$), and no more than 10% of shared environmental variance ($c^2 \leq .10$). These criteria reflect the general pattern of empirical results for most behavioral traits in adulthood—about 50% heritability, 50% nonshared environmental variance, and less than 10% shared environmental variance (Ploderman et al., 2015; Plomin et al., 2013). It should be stressed that these criteria were intended as rules of thumb for evaluating the plausibility of different models and parameter combinations, not as rigid thresholds of model correctness. The same qualitative results would obtain with a different range of acceptable estimates (e.g., $.30 \leq a^2 \leq .70$).

Simulation Plan

In each simulation run, parameters w_G, w_E, and w_X were varied systematically from 0 to 1 in steps of 1/30th (under the constraint $w_G + w_E + w_X = 1$). For each combination of w_G, w_E, and w_X, four samples of 400,000 twin pairs were generated, one for each model of differential susceptibility (DST-1, DST-2, BSC-1, and BSC-2). Simulation runs were performed for values of w_{S1} and w_{S2} ranging from 0 to 1 in steps of 0.1 to explore the effect of shared environmental influences in early vs. later development; in those simulations, the environmental correlation was set at $r_E = .50$. This procedure was repeated at three realistic levels of measurement reliability ($\rho = .70$, .80, and .90), for a total of 363 simulation runs. Finally, the effect of changing the environmental correlation between time 1 and time 2 was explored at various levels of w_{S1} and w_{S2}, by varying r_E from 0 to 1 in steps of 0.1.

Results

Simulation results showed that some parameters had small or negligible effects on the outcomes of the simulated twin studies. Specifically, the proportion of shared environmental variance in early development (w_{S1}) had virtually no influence on the size of ACE variance components, whereas the correlation between early and later environmental states (r_E) had only a small effect in the models based on BSC theory (discussed below; see the online supplementary figures). Figures 2 and 3 show simulation results for different values of shared environmental variance at time 2 (w_{S2}) and measurement reliability (ρ).

General Compatibility Results

For various combinations of parameters, the virtual data generated by differential susceptibility models were found to be compatible with the empirical findings from twin studies. In all those cases, there was a substantial direct effect of genotype (w_G). In quantitative terms, direct genetic effects accounted for about 45% to more than 90% of the true variance in the outcome trait. (Note that these figures refer to the generative model; they do not correspond to the partial R^2 one would obtain from a fitted regression model, as regression estimates would also include error variance.) At the same time, some parameter combinations allowed for relatively large P×E interaction effects (w_X), up to 40-55% of true variance in the outcome trait. (Note that the partial R^2 for the interaction term in a fitted regression model would be much smaller, after accounting for measurement error and the shared variance between the interaction term and the main effect of the environment.) Predictably, simulation results showed a clear trade-off between the weight of interaction effects (w_X) and that of direct environmental effects (w_E), so that strong interactions between environmental factors and individual plasticity were plausible only in presence of small to negligible direct effects of the environment. (Note that, even if the generative model included no direct effect of the environment, regression models would still detect an environmental main effect because of the shared variance between the interaction and the environmental variable.)

Effect of Measurement Reliability

As measurement reliability (ρ) increased, the upper limit of the size of interaction and/or environmental effects increased as well, ranging from about 40% of true trait variance with $\rho = .70$ to about 55% with $\rho = .90$. As noted above, measurement error is absorbed by the e^2 component of ACE estimates; higher amounts of error leave less room for genuine nonshared effects, which in turn include both the direct effects of nonshared environmental factors and their interaction with genotypic and/or phenotypic factors. It is worth stressing that, when measurement reliability is low, plasticity interactions can generate twin correlation patterns similar to those produced by pure genetic effects (left column in Figures 2 and 3).

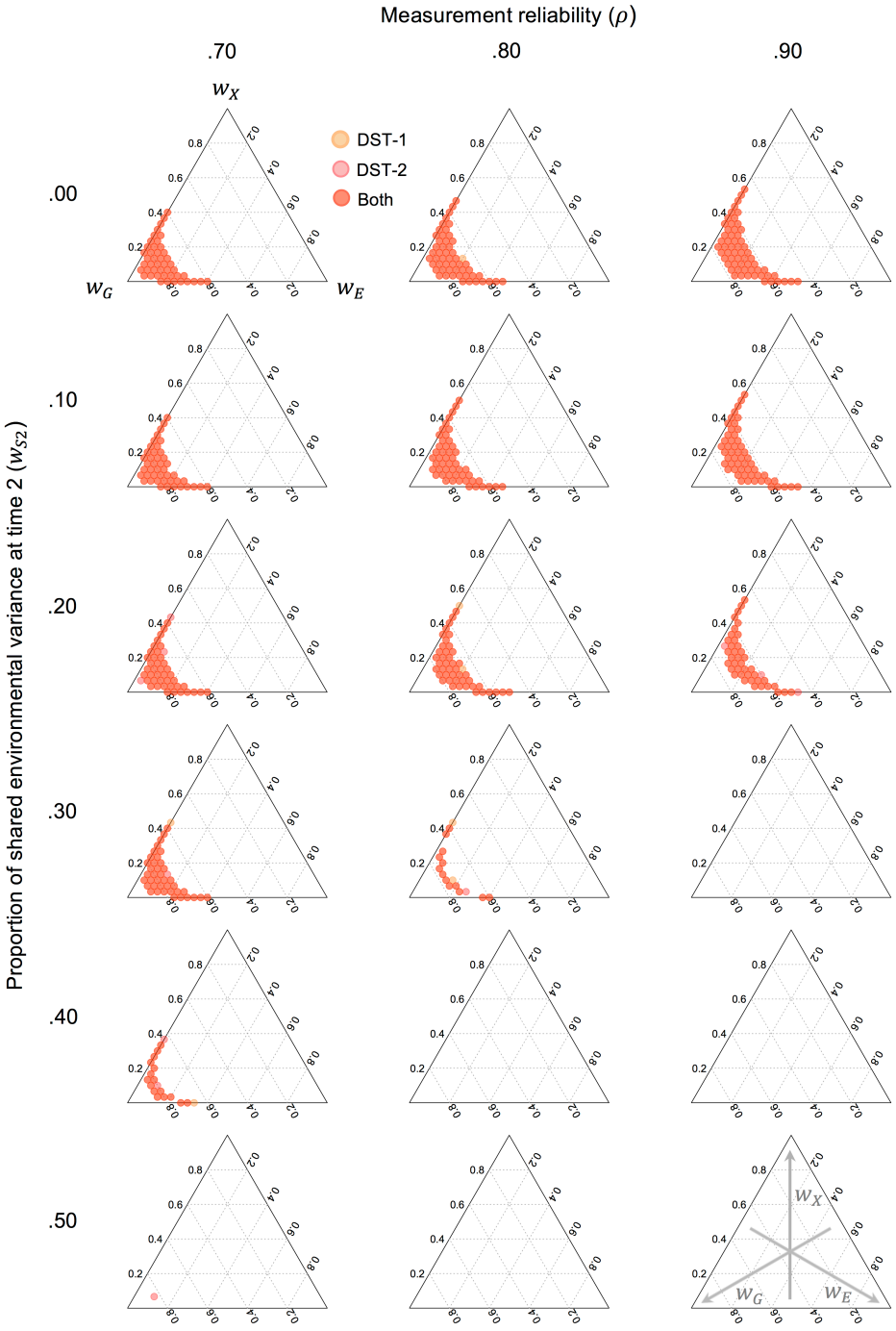

Figure 2. Simulation results for models based on differential susceptibility theory (DST-1 and DST-2). Dots show combinations of parameters for which model results were compatible with the empirical results of twin studies (see the main text for details). The position of a dot within the triangle is determined by the values of w_G, w_E, and w_X (bottom right plot), where w_G is the weight of direct genetic effects, w_E is the weight of direct environmental effects, and w_X is the weight of interaction effects. The top corner of the triangle corresponds to a pure interaction effect with no direct effects of either genotype or environment ($w_X = 1$); the bottom left corner corresponds to a pure genetic effect ($w_G = 1$); the bottom right corner corresponds to a pure environmental effect ($w_E = 1$). Each dot is based on 400,000 simulated twin pairs. In all the simulations, $w_{S1} = .50$ and $r_E = .50$.

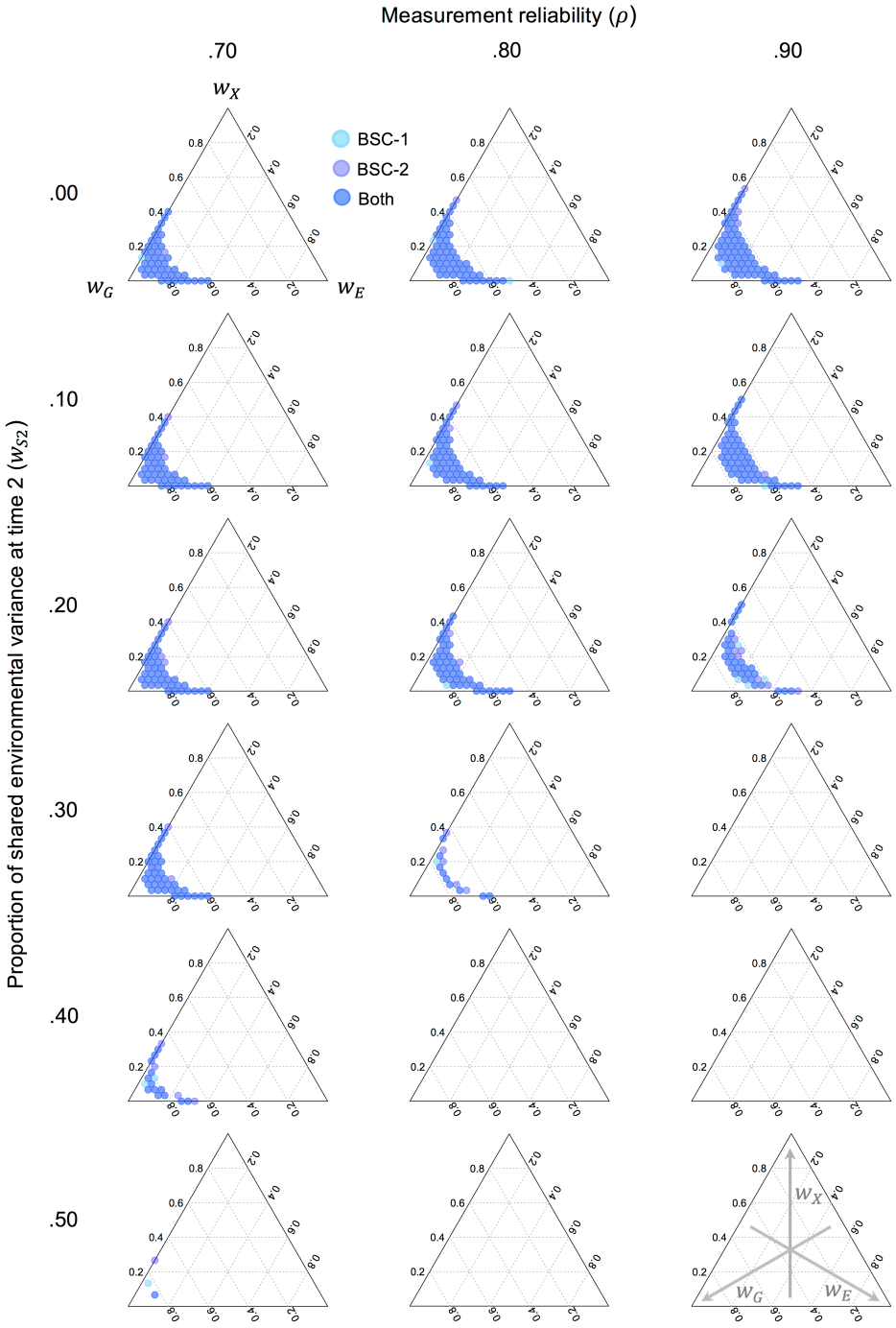

Figure 3. Simulation results for models based on biological sensitivity to context theory (BSC-1 and BSC-2). Dots show combinations of parameters for which model results were compatible with the empirical results of twin studies (see the main text for details). The position of a dot within the triangle is determined by the values of w_G, w_E, and w_X (bottom right plot), where w_G is the weight of direct genetic effects, w_E is the weight of direct environmental effects, and w_X is the weight of interaction effects. The top corner of the triangle corresponds to a pure interaction effect with no direct effects of either genotype or environment ($w_X = 1$); the bottom left corner corresponds to a pure genetic effect ($w_G = 1$); the bottom right corner corresponds to a pure environmental effect ($w_E = 1$). Each dot is based on 400,000 simulated twin pairs. In all the simulations, $w_{S1} = .50$ and $r_E = .50$.

Effect of Shared Environmental Variance

In contrast with time 1, the amount of shared environmental variance at time 2 (w_{S2}) had a substantial effect on the range of plausible parameter values. In particular, the range of plausible parameter combinations narrowed as the proportion of shared variance at time 2 increased, reflecting the tight constraint on the maximum permissible value of c^2. The maximum proportion of shared environmental variance compatible with the findings from twin studies ranged from about 40% of the total environmental variance when $\rho = .70$ to about 20% with $\rho = .90$. In total, simulation results indicate that, in early development, the contribution of shared environmental factors can range from very small to very large without affecting the compatibility of differential susceptibility models with the results of twin studies. However, the relative weight of the shared environment must decrease to comparatively low levels in later development.

Alternative Susceptibility Models

As is apparent from Figures 2 and 3, the four models of differential susceptibility examined in the simulations gave virtually identical results for the same combination of parameters. (The two models based on DST allowed for slightly stronger interaction effects, but the difference was minimal). Regardless of how plasticity was determined at time 1, the P×E interaction at time 2 always behaved like a simple G×E interaction (as in DST-1) from the standpoint of the twin-based analysis. In other words, the complexity of the initial processes involved in the development of plasticity at time 1 was effectively "hidden" behind the P×E interaction at time 2; even when plasticity was entirely environmental in origin (as in BSC-1), twin correlations were almost undistinguishable from those produced by purely genetic effects (as in DST-1). A minor difference between DST and BSC models was that, in models based on BSC, high levels of environmental autocorrelation (about $r_E > .50$) determined a small decrease in the maximum weight of interaction effects (see supplementary figure S4).

Discussion

The goal of this study was to determine whether, and under what conditions, the developmental processes postulated by models of differential susceptibility yield results compatible with those reported in the empirical literature on twin studies. The answer to the first question is affirmative: simulated twin data based on four alternative models could easily reproduce the standard pattern in which trait variance is explained in about equal parts by additive genetic and nonshared environmental effects, with a minor or negligible contribution of the shared environment (Plomin et al., 2013; Polderman et al, 2015; Turkheimer et al., 2014). This is an important point, as findings from twin studies can be easily (and incorrectly) interpreted as if they refuted the possibility of extensive person-environment interaction effects. The present results refine this point by showing that specific developmental models (DST and BSC) can generate realistic patterns of results in a range of conditions.

Some of the simulation results are intuitive, and follow directly from the logic of twin studies and ACE partitioning. First, all the plausible scenarios for differential susceptibility

involve a substantial role of direct genetic effects, above and beyond environmental and interaction effects. Second, strong interactions between environmental factors and individual plasticity are plausible, but only if direct environmental effects (shared and nonshared combined) are correspondingly weak. As noted above, this result should be interpreted with care to avoid incorrect predictions about the results of empirical G×E or P×E studies. In particular, even a strong interaction may explain little *unique* variance (e.g., partial R^2 in a regression model) if the plasticity-by-environment product correlates with the environmental variable itself. This is exactly the pattern predicted by differential susceptibility models, since the slopes associated with different levels of plasticity are assumed to have the same sign (right panel of Figure 1). For the same reason, empirical data may show a main environmental effect even if the environment has no direct effect on trait development. In other words, finding that G×E or P×E interactions are associated with small effect sizes does not necessarily mean that they play a minor role in the development of psychological traits (McClelland & Judd, 1993). The fact that differential susceptibility can be expected to result in comparatively small effects underscores the need to carefully consider sample size when planning empirical studies in this area (for an extended treatment see Del Giudice, under review). Third, the findings from twin studies are *not* consistent with a major role of shared environmental factors in later development. Specifically, when traits are measured with reliabilities in the .80-.90 range, shared factors cannot account for more than 20-30% of the total variance of the environmental variable.

A less intuitive finding was that the proportion of shared environmental effects in *early* development had virtually no effect on simulated outcomes. In other words, twin studies are consistent with the possibility that the development of plasticity in infancy and childhood is largely determined by shared environmental factors. This is an important result for differential susceptibility models, considering that most of the early determinants of plasticity hypothesized in the literature—from prenatal stress hormones to family conflict—can be expected to behave as partly or fully shared influences within twin pairs. Stated otherwise, when the shared environment contributes to the development of early plasticity instead of directly determining the adult phenotype (see Del Giudice, 2015), it effectively disappears from view when variance is partitioned according to the classical twin design. Thus, the lack of shared environmental effects on adult phenotypes should not be reflexively interpreted as a lack of shared environmental effects on plasticity during early development.

Finally, simulations showed that—to a first approximation—alternative models of differential susceptibility are equally compatible with the results of twin studies. In most conditions, the widely divergent mechanisms postulated by DST and BSC produce almost identical patterns of twin correlations. Even when plasticity is entirely determined by early environmental factors (as in model BSC-1), interactions between plasticity and the later environment behave very much like simple G×E interactions when viewed through the lens of the classical twin design. Conversely, these results demonstrate that twin studies of adults provide virtually no information about the developmental nature of plasticity; standard ACE estimates are equally consistent with plasticity being determined entirely by the genotype, entirely by the early environment, or by various combinations of the two. In principle, genetic loci associated with plasticity are very difficult to detect owing to low statistical power (Visscher & Posthuma, 2010); these results suggest that a substantial proportion of individual variation in plasticity might be environmentally induced rather than genetically determined (see also Del

Giudice, 2015; Ellis et al., 2011). Of course, these considerations only apply to classical studies of adult twins; more complex designs (for example longitudinal twin studies) may be able to discriminate between the different developmental processes postulated by DST and BSC, or pinpoint the role of different environmental components in the development of plasticity.

In conclusion, the present results support the general plausibility of differential susceptibility models vis à vis the remarkably consistent empirical pattern that has emerged from a century of twin studies. At the same time, it suggests some realistic constraints on their assumptions. Hopefully, this initial study will contribute to further the integration of behavior genetic evidence into the emerging field of evolutionary-developmental psychology.

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