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The Evolution of Interaction Shape in Differential Susceptibility

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***Child Development, 88,* 1897–1912 (2017).**

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Abstract

Expectations about the shape of statistical interactions play a crucial role in the study of differential susceptibility and other types of person-environment interplay. These expectations shape methodological guidelines and inform the interpretation of empirical findings; however, their logic has never been explicitly examined. This study is the first systematic exploration of the evolution of interaction shape in differential susceptibility. The model introduced here yields a number of novel insights; for example, interactions in differential susceptibility should usually be asymmetric, and likely to be biased toward the prototypical shape of diathesis-stress models. The paper also presents an exploratory analysis of interaction shape in recent empirical studies, and ends with a discussion of the theoretical and methodological implications of the present findings.

Keywords: Differential susceptibility; plasticity; proportion of interaction.

The theory of *differential susceptibility* is one of the main contemporary paradigms for the study of person-environment interactions (Belsky, 1997, 2005; Boyce et al., 1995; Ellis, Boyce, Belsky, Bakermans-Kranenburg & Van IJzendoorn, 2011). Conceived at the intersection of evolutionary and developmental psychology, the theory argues that many of the same individual factors that determine increased sensitivity to the effects of negative environments (e.g., high levels of stress, danger, and adversity) also confer enhanced responsivity to *positive* environments (e.g., high levels of safety and emotional support). In other words, susceptible individuals respond to the quality of their environment "for better *and* for worse" (Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007; Boyce et al., 1995). Differential susceptibility goes beyond the classic concept of vulnerability or *diathesis-stress*, whereby individual factors increase vulnerability in response to negative or stressful events (Belsky & Pluess, 2009, 2013). Differential susceptibility can also be distinguished from *vantage sensitivity*, in which individual factors amplify the effect of positive environments but not that of negative environments (Pluess & Belsky, 2013; Pluess, 2015).

One way to interpret empirical findings of differential susceptibility is to assume that outcomes in negative environments are detrimental to susceptible individuals. On this "normative" view, the downside of susceptibility is vulnerability to the damaging effects of the environment (e.g., Boyce et al., 1995). However, evolutionary models of differential susceptibility take a different perspective; specifically, they postulate that susceptible individuals respond to both positive and negative environments in a biologically *adaptive* way—that is, by developing traits that maximize the likelihood of survival or reproduction, and ultimately the replication of one's genes in subsequent generations (fitness). For example, prosociality and self-control may be adaptive in safe and nurturing environments, whereas aggression and impulsivity may enhance fitness in dangerous and unstable contexts. While the latter traits are usually regarded as undesirable and problematic from a mental health (normative) perspective, they can be biologically adaptive if they reliably increase survival or reproduction (see Frankenhuis & Del Giudice, 2012). From this perspective, outcomes in negative environments do not reflect vulnerability but rather adaptive matching: susceptible individuals have the ability to "match" their phenotype to the likely state of the environment, whereas non-susceptible individuals develop similar phenotypes regardless of the local conditions. If this is the case, susceptibility can be biologically advantageous in both positive and negative environments, and the question becomes why some individuals are *not* responsive (or at least less responsive) to their developmental context. Possible explanations for the evolution of individual differences in susceptibility include *negative frequency-dependent selection*, whereby the fitness of susceptible individuals increases with the proportion of non-susceptible individuals in the population (and vice versa), as well as reproductive *bet-hedging*, whereby individual variation in susceptibility works as "insurance" against unpredictable fluctuations in the environment (see Ellis et al., 2011; Frankenhuis et al., 2016). Individual differences in susceptibility are likely to reflect a combination of genetic and early environmental effects; different models of the development of susceptibility tend to emphasize different pathways and mechanisms (Ellis et al., 2011).

Levels of Analysis in Differential Susceptibility

The individual factors that determine susceptibility can be examined at various levels of analysis—genetic, neurobiological, temperamental, and so on. At the genetic level, differential

susceptibility occurs when certain alleles increase an individual's plasticity at both the positive and negative end of an environmental variable, giving rise to *crossover* or *disordinal* genotype-environment (G×E) interactions (Belsky et al., 2007). At the level of neurobiology and temperament, differential susceptibility is described by phenotype-environment (P×E) interactions of the same form. Figure 1 provides a schematic illustration of differential susceptibility with two types of individuals, susceptible (S) and non-susceptible (NS). The lines in the interaction plot can be thought of as *reaction norms*, that is, functions that link an individual's expected phenotype—for example aggression, self-control, or depressive symptoms—to the state of his or her environment. While the reaction norm of low-susceptibility individuals is by definition flatter than that of high-susceptibility ones, it is not necessarily horizontal as in Figure 1. Also, differential susceptibility models are not limited to two categories; empirical studies usually involve interactions with multiple genotypes (e.g., homozygous and heterozygous combinations of alleles), graded genotypic scores, or continuous phenotypic traits such as stress reactivity.

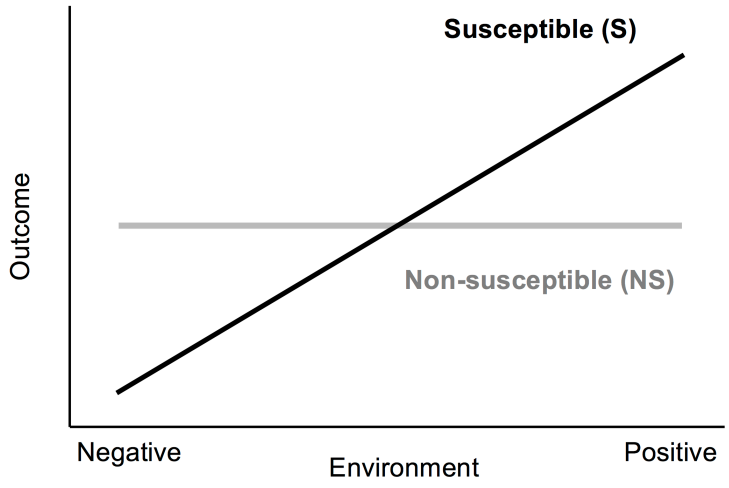

Figure 1. Schematic representation of differential susceptibility.

Research on differential susceptibility has investigated single-gene variants (e.g., Belsky et al., 2015; Bogdan, Agrawal, Gaffrey, Tillman, & Luby, 2014; Davies & Cicchetti, 2014; Daw et al., 2013; Elmore, Nigg, Friderici, Jernigan, & Nikolas, 2015; Kochanska, Kim, Barry, & Philibert, 2011; van IJzendoorn, Belsky, & Bakermans-Kranenburg, 2012) as well as "susceptibility scores" computed from multiple candidate genes (e.g., Belsky & Beaver, 2011; Cicchetti & Rogosch, 2012; Dalton, Hammen, Najman, & Brennan, 2014). In recent years, standard observational paradigms have been complemented by experimental G×E research (see Bakermans-Kranenburg & van IJzendoorn, 2015; van IJzendoorn & Bakermans-Kranenburg, 2015). Other studies have investigated putative phenotypic mediators of susceptibility, such as physiological reactivity to stress and negative emotionality (e.g., Beaver, Hartman & Belsky, 2014; Eisenberg et al., 2012).

While meta-analyses have shown reliable evidence of differential susceptibility in some domains (e.g., van IJzendoorn & Bakermans-Kranenburg, 2015; van IJzendoorn, Belsky, & Bakermans-Kranenburg, 2012), the findings of individual studies—especially those of candidate genes—remain considerably mixed. A likely reason is the low power of statistical tests for G×E interactions (Visscher & Posthuma, 2010); given the relatively small sample size of most studies in this area, important questions have been raised about the validity and replicability of candidate G×E findings (Dick et al., 2015; Duncan & Keller, 2011). Partly in response to such criticism, a recent wave of methodological work (Belsky, Pluess, & Widaman, 2013; Lee, Lei, & Brody, 2015; Roisman et al., 2012; Widaman et al., 2012) has provided researchers with more rigorous methods to identify differential susceptibility and distinguish it from other types of interaction.

Interaction Shape and the Symmetry Hypothesis

A crucial task in G×E and P×E research is to determine whether empirical interaction patterns conform to the assumptions of differential susceptibility (Belsky et al., 2007, 2013; Lee et al., 2015; Roisman et al., 2012; Widaman et al., 2012). For example, the expectations of most researchers in the field are based on what I label the *symmetry hypothesis*. According to the symmetry hypothesis, interactions showing differential susceptibility should have a symmetric shape, with the crossover point located at (or very close to) the mean of the environmental variable (Figure 1; Belsky et al., 2007, 2013; Roisman et al., 2012). While the symmetry hypothesis has never been explicitly stated or defended in the literature, it informs much of current thinking on differential susceptibility and lies at the core of standard methodological guidelines.

To discuss the implications of the symmetry hypothesis (and other key aspects of differential susceptibility theory), it can be useful to employ numerical indices that quantify the shape of different interaction patterns. The most widely adopted index in the literature is the *proportion of interaction* (PoI) proposed by Roisman and colleagues (2012). The PoI is the proportion of the total area between the lines of an interaction plot—conventionally bounded by ±2 standard deviations of the environmental variable—that lies on the positive side of the crossover point (Figure 2). Based on the symmetry assumption, the prototypical interaction shape for differential susceptibility would correspond to PoI = .50 (Figure 2c), that is, a shape in which the amount of change "for better" (area B in Figure 2) equals the amount of change "for worse" (area W). The prototypical shape predicted by diathesis-stress models has PoI = .00 (Figure 2a), whereas PoI = 1.00 corresponds to prototypical vantage sensitivity (Figure 2d). Roisman and colleagues (2012) suggested that PoI values between .40 and .60 indicate an interaction effect highly consistent with differential susceptibility (dashed lines in Figure 2c). Clearly, these guidelines rely strongly on the symmetry hypothesis; over the last few years, they have become standard in the literature and are routinely employed to evaluate the meaning of statistically significant G×E and P×E interactions.

While the symmetry hypothesis can be intuitively plausible, it is important to realize that it does not necessarily follow from theoretical models of differential susceptibility. The same qualitative pattern of "for better and for worse" susceptibility would obtain if the crossover point were located away from the environmental mean (as in Figure 2b). At present, it is simply not known whether the hypothesis is biologically justified. In fact, questioning the symmetry

hypothesis raises an even deeper issue in the study of susceptibility. While there is much discussion about different patterns of interaction and their developmental origin (e.g., Pluess, 2015), current models offer no principled way to predict whether a certain configuration of environmental factors will lead to the evolution of differential susceptibility (Figure 2c) or rather produce interaction patterns that match a "diathesis-stress" (Figure 2a) or "vantage sensitivity" prototype (Figure 2d). The consequence is a peculiar disconnect between empirical findings and their interpretation. For example, many studies in this area seek to determine whether significant interactions in the data match a differential susceptibility or diathesis-stress prototype (e.g., Cho & Kogan, 2015; Gallitto, 2015; Ludmer et al., 2015); however, they rarely advance predictions about which of these patterns should be expected and why.

The Present Paper

In this paper I perform the first systematic exploration of the evolution of interaction shape in differential susceptibility. The simple model I present provides novel insights into the evolution of person-environment interactions. It is important to stress at the outset that this model does not address the evolution of individual differences in susceptibility *per se* (as in the model by Frankenhuis et al., 2016). Rather, the model starts from the assumption that individual differences are favored by selection—which is itself a matter of theoretical debate—and asks what kinds of interaction patterns are likely to arise in different ecological scenarios. The applicability of the present model thus depends on the likelihood that patterns of differential susceptibility will evolve, for example through frequency-dependent selection or bet-hedging.

A key result of the model is that, contrary to widespread assumptions, the symmetry hypothesis (i.e., the expectation that prototypical patterns of differential susceptibility will have PoI = .50) is not warranted except in special cases. In addition, the model shows that patterns of differential susceptibility are more likely to be asymmetric with PoI < .50 (that is, shifted toward the diathesis-stress prototype). The bias toward lower PoI values also occurs when ecological conditions do not favor the evolution of crossover interactions. When this is the case, ordinal interactions with PoI = .00 (the diathesis-stress prototype in Figure 2a) evolve in a broader range of conditions than interactions with PoI = 1.00 (the vantage sensitivity prototype in Figure 2d). Finally, crossover interactions with PoI > .50 and ordinal patterns characteristic of vantage sensitivity (PoI = 1.00) can only evolve if negative environmental states occur more often than positive ones.

As a preliminary test of these evolutionary predictions, I present an exploratory analysis of published PoI values from recent empirical studies of G×E and P×E interactions. Consistent with model predictions, the empirical PoI distribution was not centered on .50 but on a lower value (mean PoI = .38, median PoI = .43). Moreover, PoI values close to 1.00 were absent from the studies included in the analysis, while there were several values close to .00. I also found that many PoI values reported in the published literature are incorrect, due to confusions about the position of areas B and W in Figure 2. I conclude the paper by discussing the broader theoretical and methodological implications of these findings.

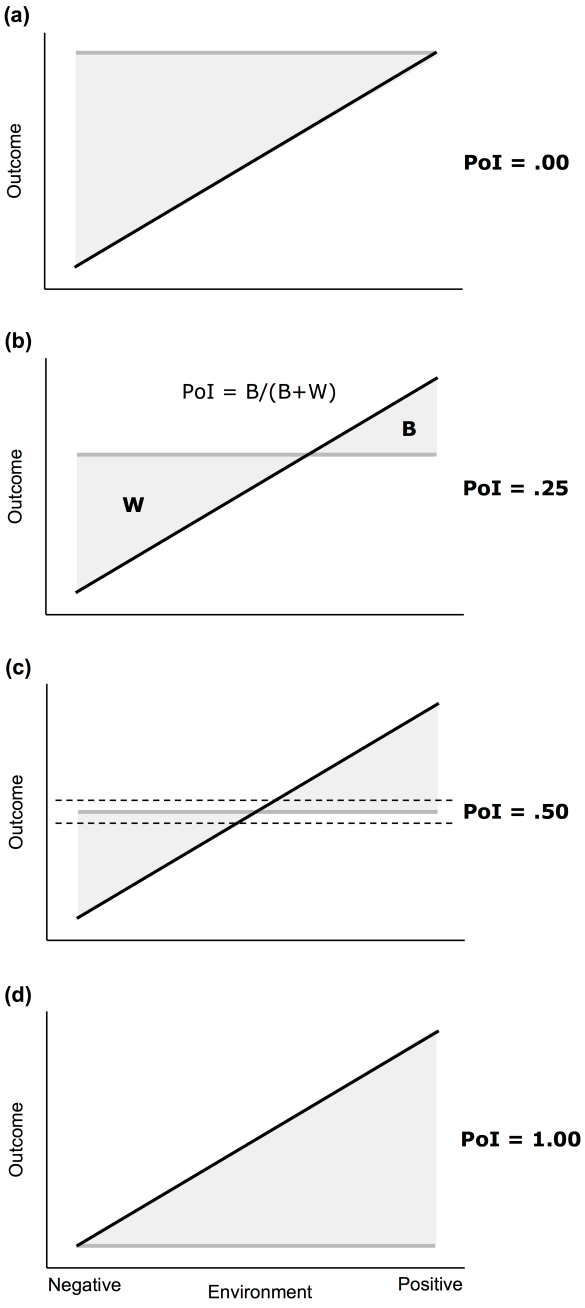

Figure 2. Interaction shape and the PoI index (proportion of interaction). Dashed lines in panel (c) show the region from PoI = .40 to PoI = .60. PoI values in this region are typically regarded as providing strong evidence of differential susceptibility.

The Evolution of Interaction Shape

To examine the evolution of interaction shape I will consider a basic scenario with two types of individuals (susceptible and non-susceptible), each characterized by an evolving

reaction norm, and an environment with two states (positive and negative). An example of this would be a G×E interaction involving a single genetic locus with two alleles in an asexually reproducing organism. The model further assumes that environmental variation is spatial rather than temporal; more specifically, environmental states are uncorrelated both between generations and between individuals in a generation (other assumptions of the model are reviewed in Section S1 of the supplementary material).

In the 2×2 model considered here, the reaction norm of non-susceptible individuals consists of a single value of the outcome trait, whereas that of susceptible individuals consists of two values, one for each state of the environment. The shape of the interaction and the corresponding PoI are determined by the position of the non-susceptible reaction norm relative to that of the susceptible reaction norm (Figure 2). Assuming for the moment that the state of the environment can be detected with certainty (i.e., the individual has access to perfectly reliable cues), the susceptible reaction norm will evolve to match the optimal values of the outcome trait (e.g., self-control) for each environmental state. These are the values of the trait that result in the highest expected fitness; in other words, they are perfectly *matched* to the state of the environment (e.g., high self-control in the positive environment and low self-control in the negative environment). As an individual's trait moves away from the optimal value, the individual will experience a degree of *mismatch* and a reduction in expected fitness.

Crucially, non-susceptible individuals are unable to match both environmental states. If the non-susceptible reaction norm evolves so as to match the positive environment (e.g., by producing systematically high levels of self-control), non-susceptible individuals will become mismatched to the negative environment, and vice versa. A compromise between the two environments—that is, an intermediate value of the trait—will result in a partial mismatch in both environments. Note that for differential susceptibility to evolve, there has to be some mechanism limiting the fitness of susceptible individuals, such as a physiological cost of plasticity, imperfect reliability of cues, and so on (e.g., Frankenhuis et al., 2016); otherwise, susceptible individuals would simply replace non-susceptible ones in the population because of their superior matching ability, and differential susceptibility would be lost. The exact mechanism is not important for the purpose of this paper and is not explicitly included in the model; it is sufficient to assume that susceptibility has certain costs that counterbalance its adaptive benefits.

Given these premises, the key question becomes: what is the optimal trait value for non-susceptible individuals? For the symmetry hypothesis to hold, the optimal non-susceptible phenotype must lie at the midpoint between the optimal phenotype for the positive environment and that for the negative environment. With perfect cue reliability, this only occurs if the fitness benefits of matching the negative environment are exactly equivalent to the fitness benefits of matching the positive environment. However, differential susceptibility theory explicitly assumes that environmental states differ in quality: *by definition*, positive states are safe, supportive, and rich in social and material resources, whereas negative states are dangerous, stressful, resource-scarce, and so on (Belsky et al., 2007; Ellis et al., 2011). On average, negative conditions can be expected to reduce an individual's prospects of successful survival and reproduction. For example, mortality rates increase dramatically with poverty; in the USA, both adult and infant mortality approximately *double* as one moves from the highest to the lowest

level of socioeconomic status (Adler et al., 1994). While modern socio-economic dynamics have changed the relation between fertility and resource availability in most countries, across our evolutionary history it has been consistently the case that fertility was reduced in resource-poor contexts (e.g., Shenk, 2009; Shenk, Towner, Kress, & Alam, 2013). This long-term pattern is most relevant to the evolutionary scenarios explored in the present model.

Because of the fitness implications of environmental quality, it follows from the assumptions of differential susceptibility theory that, even accounting for phenotypic matching, the maximum potential fitness in positive environments is going to be higher than the maximum potential fitness in negative environments. Stated otherwise, a well-matched individual in a positive environment enjoys better prospects of survival and reproduction than an equally well-matched individual in a negative environment. On average, non-susceptible individuals whose trait values happen to be well matched to the positive environment will leave more offspring than non-susceptible individuals whose trait values happen to be well matched to the negative environment. As a result, selection is expected to shift the non-susceptible reaction norm toward the optimal trait value for the positive environment.

To summarize: all else being equal, if alternative states of the environment differ in their maximum potential fitness—an assumption that flows from the very definition of differential susceptibility—non-susceptible individuals should evolve so as to match positive (higher-fitness) states better than negative (lower-fitness) ones. The resulting person-environment interactions would be shifted toward lower PoI values (compare Figures 2b and 2c), thus violating the symmetry hypothesis. Moving beyond this general prediction, the exact outcome of the evolutionary process will depend on a number of factors, including the ratio of the maximum fitness in positive vs. negative environments, the distribution of environmental states, the reliability of cues about the state of the environment, and the shape of the function linking an individual's trait value to its expected fitness in a given environment. I now consider these factors in more detail.

Evolutionary Outcomes

Outcomes when positive and negative environmental states are equally probable. I begin by considering the case in which positive and negative environmental states occur with equal probability. This scenario is implicitly assumed in much of the differential susceptibility literature, both empirical and methodological. For example, the assumption that environmental states follow a symmetric (and approximately normal) distribution underlies the interpretation of the *proportion affected* (PA) index proposed by Roisman and colleagues (2012). While differential susceptibility theory does not provide any *a priori* reasons why positive states should be more or less common than negative states, it is worth stressing that symmetry in the distribution of environmental states is not a necessary component of the theory, and is not assumed by evolutionary models such as the one by Frankenhuis and colleagues (2016).

Assuming for the moment that positive and negative states are equally likely makes it easier to focus on a critical determinant of the evolutionary outcome: the shape of the function that links individual phenotypes to their expected fitness (Figure 3). Figure 3a illustrates the case in which phenotypic matching has increasing fitness returns. With increasing returns, the

expected fitness is an accelerating function of the degree of matching (the benefits of a matching phenotype increase more steeply as one moves closer to the optimal level of the trait). Figure 3b shows the case of linear fitness returns, in which fitness increases or decreases linearly as one moves along the range of possible trait values. In both cases, the optimal phenotype for non-susceptible individuals (NS) is the trait value that maximizes fitness in the positive environment (positive optimum), that is to say, the same phenotype expressed by susceptible individuals (S) in the positive environment. It is easy to verify from the figure that all other possible values of the trait have lower average fitness across positive and negative environmental states. In sum, if fitness returns are linear or increasing (and positive and negative estates are equally likely), the expected interaction shape corresponds to PoI = .00, the prototypical pattern postulated by diathesis-stress models (Figures 3a and 3b).

The crossover interaction patterns that define differential susceptibility can only evolve when fitness has *diminishing* returns, as illustrated in Figure 3c. Diminishing returns imply that fitness benefits increase rapidly as one moves away from grossly mismatched phenotypes, but grow less and less steeply as one moves closer to the optimal level of the trait. Consider how the fitness of a NS individual changes as trait value moves toward the high end in the left panel of Figure 3c. The fitness gains associated with matching the positive environment become smaller, while at the same time the costs of mismatch in the negative environment become larger. At some point, moving closer to the S optimum results in a net reduction in average fitness. The reverse happens with low values of the trait. In total, the average fitness of NS individuals is maximized at an intermediate value of the trait; and since the positive environment makes a larger contribution to the average fitness, the NS optimum is going to be closer to the positive S optimum than to the negative S optimum. The exact position of the NS optimum depends on the ratio of the maximum fitness in positive vs. negative environments, or *fitness ratio*. The outcome is a crossover interaction with $.00 < PoI < .50$, with higher fitness ratios leading to smaller PoI values (right panel of Figure 3c).

The key role of diminishing fitness returns in the evolution of differential susceptibility is a notable result of this model. In the supplementary material I explore additional scenarios that combine different types of fitness functions. If fitness returns are diminishing in the positive environment but linear in the negative environment (section S5 in the supplementary material), model predictions are qualitatively similar to those associated with diminishing returns in both environments (i.e., there is scope for crossover interactions to evolve). If fitness returns are diminishing in the positive environment but increasing in the negative environment (section S6 in the supplementary material), the model yields the same predictions as with increasing returns in both environments (i.e., crossover interactions are not expected to evolve, except in the special cases discussed below).

Outcomes when positive and negative environmental states occur with unequal probabilities. If positive and negative environmental states occur with unequal probabilities, evolutionary predictions become more complex. All else being equal, selection will shift the NS phenotype toward matching those states of the environment that occur more often. If positive states are more frequent than negative states, this effect will simply reinforce that of environmental quality. If, on the contrary, negative states occur more often than positive states, the effect of state distribution will attenuate or even reverse that of state quality.

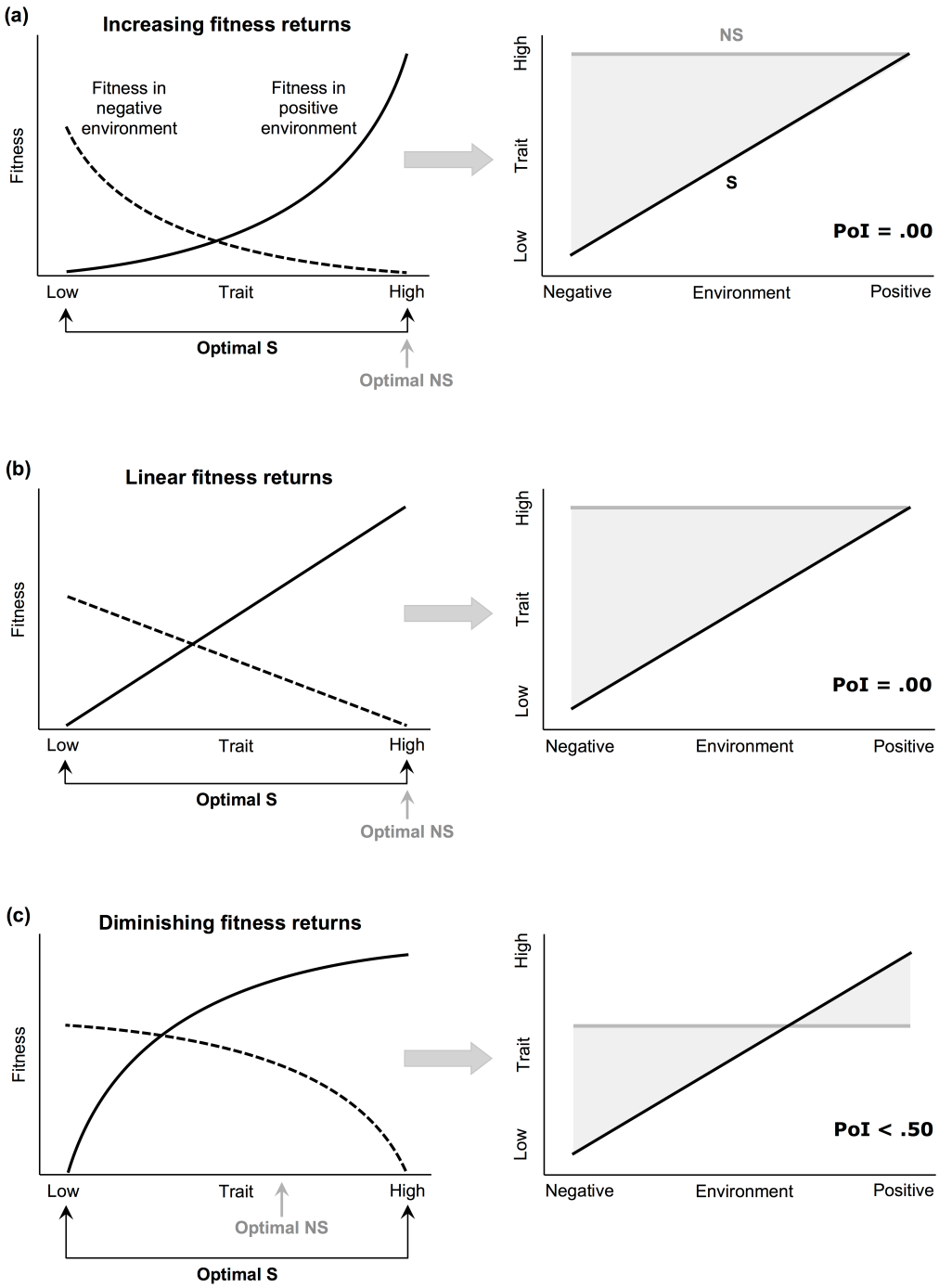

Figure 3. Evolution of interaction shape when positive and negative environments occur with equal probability and cues to the state of the environment are perfectly reliable. S = reaction norm for susceptible individuals; NS = reaction norms for non-susceptible individuals. PoI = proportion of interaction.

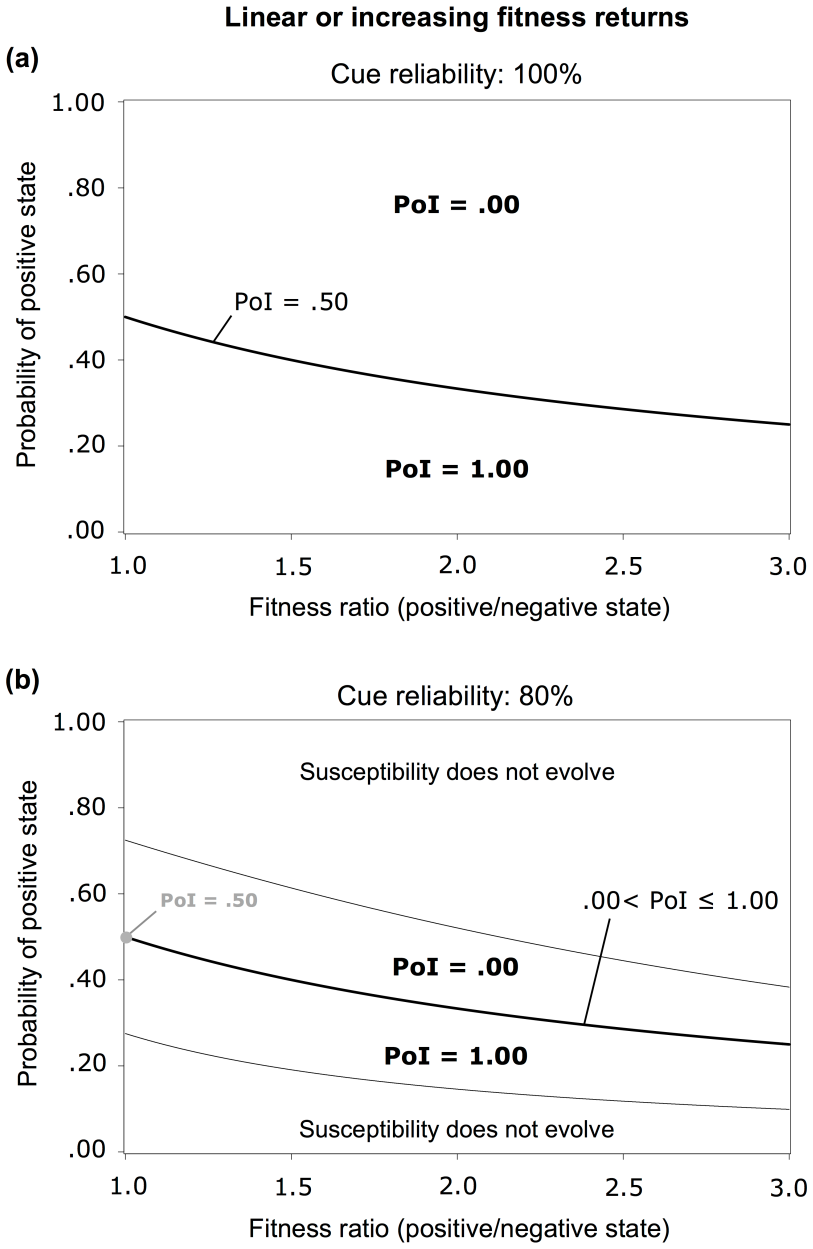

Figure 4. Model results showing predicted interaction shape when fitness functions have linear or increasing returns. (a) Cues to the state of the environment are perfectly reliable (cue reliability: 100%). (b) Cues correctly predict the state of the environment with 80% probability (cue reliability: 80%). Regions in the plots show predicted values of the PoI index (proportion of interaction) based on the fitness ratio between positive and negative states of the environment (horizontal axis) and the probability of positive states (vertical axis). Thick lines correspond to a weighted fitness ratio of 1(see the main text for discussion).

The joint effect of state distribution and quality can be easily determined by weighting the fitness ratio by the ratio between the probabilities of the two environmental states (*probability ratio*). For example, consider a case in which the maximum fitness in the positive environment is twice as high as that in the negative environment (fitness ratio = 2). If the positive state occurs 40% of the times and the negative state occurs 60% of the times, the probability ratio is 2/3. The *weighted fitness ratio* is the product of the fitness ratio by the probability ratio, that is, 4/3 or approximately 1.33. Since the weighted fitness ratio still favors the positive environment (i.e., is higher than 1), the predicted outcomes remain qualitatively the same as when environmental states are equally probable. Now consider the case in which the fitness ratio is 2 but the positive state occurs 30% of the times while the negative state occurs 70% of the times (probability ratio = 3/7). The weighted fitness ratio becomes 6/7, or approximately 0.86. Now the positive environment has lower *expected* fitness despite yielding higher *maximum* fitness.

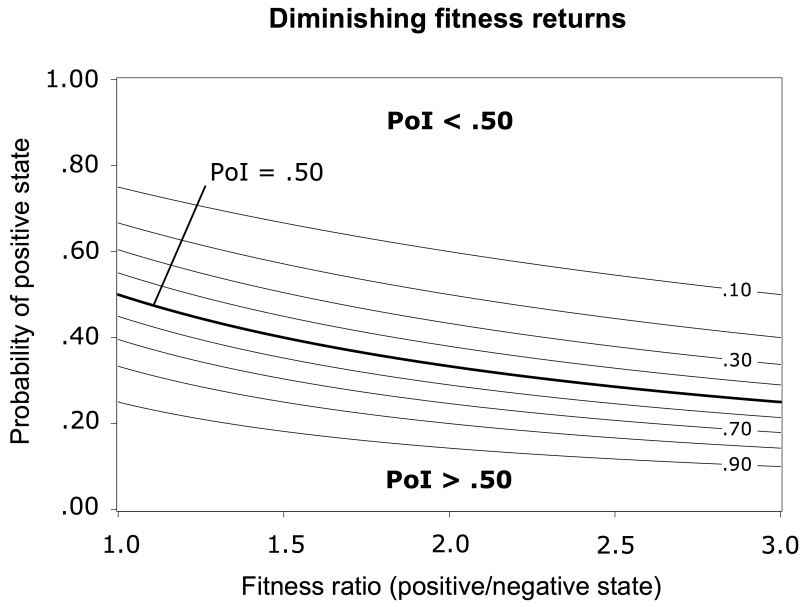

Figure 5. Model results showing predicted interaction shape when fitness functions have diminishing returns. Regions in the plot show predicted values of the PoI index (proportion of interaction) based on the fitness ratio between positive and negative states of the environment (horizontal axis) and the probability of positive states (vertical axis). The thick line corresponds to a weighted fitness ratio of 1 (see the main text for discussion).

If negative environmental states are so common that the weighted fitness ratio is lower than 1, the predictions made in the previous section need to be reversed. Specifically, if fitness returns are linear or increasing (as in Figures 3a and 3b), the NS reaction norm will match the phenotype expressed by susceptible individuals in the *negative* environment; the corresponding interaction shape will have PoI = 1.00, the prototypical pattern for vantage sensitivity. With diminishing fitness returns (as in Figure 3c), the NS reaction norm is still expected to evolve toward an intermediate value of the trait, but this time the value will be closer to the negative optimum than to the positive optimum (.50 < PoI < 1.00). If deviations from equal probabilities are small, interactions showing differential susceptibility will usually have PoI < .50, and

prototypical diathesis-stress patterns (PoI = .00) will be more common than prototypical vantage sensitivity patterns (PoI = 1.00).

Figures 4a and 5 present model results when cues are perfectly reliable. The figures show the predicted PoI for different values of the fitness ratio (from 1 to 3) and different probabilities of the positive state (from 0 to 1). If fitness returns are linear or increasing (Figure 4a), the predicted outcome is either PoI = .00 or PoI = 1.00, except when the weighted fitness ratio is exactly 1. In this (unlikely) special case, the expected interaction shape has PoI = .50 and the symmetry hypothesis holds, at least as an expected average across populations (see the supplementary material for details). With diminishing fitness returns (Figure 5), the predicted value of PoI depends on the exact combination of model parameters; as in the case of linear and increasing returns, symmetric interactions (PoI = .50) only evolve if the weighted fitness ratio is exactly 1 (see above). Note that (a) interactions with PoI < .50 (i.e., shifted toward the diathesis-stress prototype) evolve in a broader range of conditions than interactions with PoI > .50 (i.e., shifted toward the vantage sensitivity prototype); and (b) interactions with PoI > .50 can only evolve if negative environmental states are more frequent than positive states (that is, if the probability of positive states is less than .50).

Imperfect Cue Reliability. Until now, I have made the simplifying assumption that environmental states can be detected or predicted with perfect reliability. This allows susceptible individuals to accurately match the optimal trait value in both environments. If cue reliability is less than perfect, however, susceptible individuals also suffer a certain risk of mismatch. As reliability decreases, the adaptive strategy is to discount cues and rely more strongly on the prior probabilities of positive and negative states (this is a general result in Bayesian models of development; see Stamps & Frankenhuis, 2016). This means that susceptible individuals will develop similar phenotypes in response to positive and negative cues, and effectively behave more and more like NS individuals as cues become less reliable. With linear or increasing fitness returns, imperfect reliability leads to scenarios in which the S reaction norm becomes identical to the NS reaction norm, and susceptibility fails to evolve altogether (i.e., all individuals follow the same strategy and there are no person-environment interactions of any shape).

Figure 4b shows model results when cues are 80% reliable (that is, cues correctly predict the state of the environment with 80% probability) and fitness returns are linear or increasing. Susceptibility does not evolve when positive environmental states occur with either high or low probability. Symmetric interactions (PoI = .50) become even more unlikely than in the case of perfect reliability, as they can only evolve if the weighted fitness ratio is 1 *and* positive and negative states are equally probable (gray dot in Figure 4b; see the supplementary material for details). When the fitness function has diminishing returns, cue reliability has no effect on the evolution of interaction shape, and model results are the same as in Figure 5. However, unreliable cues mean that S and NS reaction norms become more similar to one another, and individual differences in the population vanish as reliability decreases (even if the shape of the resulting interactions remains the same). Thus, sizable individual differences can only evolve if cue reliability is sufficiently high.

Table 1. Values of the PoI index (proportion of interaction) for statistically significant interactions in recent studies of differential susceptibility.

			PoI	
Study	Environmental variable	Candidate genes/traits	Reported	Corrected
Beach et al. (2014)	Socioeconomic risk	*5-HTT*	(.45)	.55
			(.49)	.51
Belsky & Pluess (2013)	Child care quality	*DRD4*	.43	–
Belsky et al. (2014)	Maternal sensitivity	*DRD4*	.53	–
		BDNF	.18	–
			.19	–
		HTR2A	.24	–
		OPRM1	.10	–
			.47	–
			.21	–
			.53	–
			.63	–
Cho & Kogan (2015)	Community disadvantage	*DRD4*	(.58)	.42
	Protective parenting		.25	–
Dalton et al. (2014)	Family discord	*BDNF + 5-HTT*	(.42)	.57
			(.72)	.28
			(.78)	.22
Davies & Cicchetti (2014)	Maternal unresponsiveness	*5-HTT*	.32	–
			.50	–
Davies et al. (2015)	Maternal unresponsiveness	*DAT1*	.10	–
			.14	–
Elmore et al. (2015)	Family cohesion	*5-HTT*	.59	–
	Family conflict		(.51)	.49
Kogan et al. (2014)	Neighborhood disadvantage	*DRD4*	(.57)	.43
Ludmer et al. (2015)	Maternal depression	*DRD2*	.15	–
			.33	–
		SLC6A3	.31	–
			.35	–
Swann et al. (2014)	Stressful life events	*OPRM1*	.50	–
			(.59)	.41
			(.39)	.61
			(.27)	.73
			(.29)	.71
Zhang et al. (2015)	Negative parenting	*DRD2*	(.48)	.52
			(.56)	.44
Beaver et al. (2014)	Parental sensitivity	Irritable/difficult temperament	.45	–
			.47	–
			.46	–
			.49	–
			.46	–
Gallitto (2015)	Positive parenting	Irritable/difficult temperament	.02	–
			.07	–
Roisman et al. (2012)	Maternal sensitivity	Irritable/difficult temperament	.40	–

.00	–
.46	–
.39	–
.08	–

Note. Values in parentheses were incorrectly reported in the original papers. For the Roisman et al. (2012) study, the table reports PoI values computed across age groups (time intercepts). Additional information on the analysis in Elmore et al. (2015) was kindly provided by the authors upon request.

Empirical Data

To perform an initial test of the predictions made in the previous section, I searched the literature for studies reporting PoI values for G×E and P×E interactions. Specifically, I performed a Google Scholar search for published papers citing Roisman and colleagues (2012) or containing the phrases "PoI" and "proportion of interaction" (February 6, 2016). I excluded intervention studies, as well as studies testing interactions between traits within a person (e.g., genotype by coping style, genotype by sleep duration) instead of person-environment interactions. Finally, I excluded studies in which the measured environmental variables were not plausible indicators of environmental quality (i.e., harshness or unpredictability in the child's environment). For example, excluded studies investigated the effects of peer pressure and smoking; while peer pressure can have undesirable consequences and smoking has long-term detrimental effects on health, these variables do not reflect harshness or unpredictability in the sense postulated by theories of differential susceptibility.

In total, fifteen papers reported PoI values for statistically significant interactions involving various candidate genotypes and phenotypes, for a total of 47 values (Table 1). Whenever possible, I checked the reported PoI values against the corresponding interaction plots or recomputed them from regression coefficients (for details see Roisman et al., 2012). This led to the surprising discovery that many PoI values reported in the literature are incorrect. Reporting errors occur when investigators fail to reverse the direction of the environmental variable when higher values indicate a more *negative* (or less positive) environment rather than a more positive environment (e.g., higher scores of family discord or socioeconomic adversity; see footnote 9 in Roisman et al., 2012). This is equivalent to switching the B and W areas in Figure 2. When this is the case, the correct PoI value can be obtained by subtracting the published value from 1 (e.g., PoI = .60 becomes PoI = .40). Future reviews examining published PoI values will need to take into account the high rate of misreporting in the literature. Table 1 shows both the original values reported in the papers and the corrected ones.

The distribution of the PoI values listed in Table 1 is shown graphically in Figure 6. While this is an exploratory survey rather than a formal meta-analysis, the available evidence indicates that PoI values tend to cluster below .50; the unweighted mean of the distribution was .38, while the median was .43. Although these figures may seem close to .50 one should consider that, according to current guidelines, values below .40 provide equivocal evidence for differential susceptibility (Roisman et al., 2012). A binomial test confirmed that the proportion of PoI values falling below .50 was larger than expected by chance (p = .002).

These initial findings are consistent with the idea that, all else being equal, the expected interaction shape for differential susceptibility is asymmetric with PoI < .50. This is especially interesting considering that, when interactions are mistakenly detected because of type I errors, they are usually disordinal (see Dick et al., 2015). Since symmetric interactions are maximally disordinal, type I errors can be expected to bias the distribution of statistically significant interactions toward a PoI of .50 (i.e., when interactions happen to be statistically significant by chance, they are also more likely to have a symmetric shape). Moreover, it is clear from Figure 6 that low values of PoI tend to occur much more frequently than high ones; while 6 out of 47 interactions in Table 1 had PoI ≤ .10, there were none with PoI ≥ .90 (or even PoI ≥ .80). This pattern is consistent with the prediction that ordinal interactions matching the prototype of diathesis-stress should evolve under a broader range of conditions than interactions with a shape characteristic of vantage sensitivity.

It is important to stress that these data are preliminary and open to alternative interpretations. In particular, PoI values smaller than .50 may reflect a truncated distribution of the environmental variable if the measurement range is largely restricted to negative states. For example, low scores on a variable measuring family stress may not indicate an especially positive environment, but only the absence of negative conditions. While this interpretation is plausible, it is not supported by the data in Table 1: if anything, studies measuring negative variables such as maternal unresponsiveness and socioeconomic risk tended to report somewhat *larger* PoI values (unweighted mean = .42, median = .43) than studies measuring positive variables such as maternal sensitivity and childcare quality (unweighted mean = .34, median = .42).

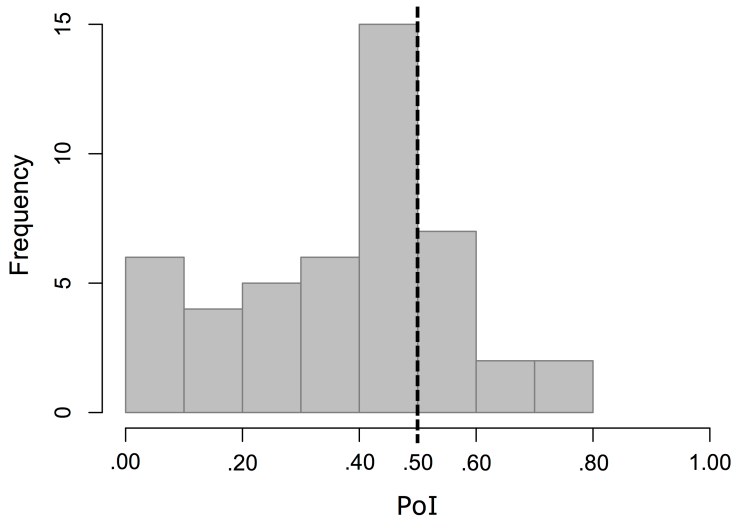

Figure 6. Distribution of published values of the PoI index (proportion of interaction) in recent studies of differential susceptibility (see Table 1).

Discussion

Expectations about interaction shape play a central role in the study of differential susceptibility (Pluess, 2015; Roisman et al., 2012; Widaman et al., 2012). However, the evolutionary logic underlying the various interaction patterns described in the developmental literature has never been explored systematically. In this paper I have taken a step in this direction by presenting a simple model of how person-environment interactions can be expected to evolve when the environment has a positive-negative polarity, as postulated by differential susceptibility theory. Based on the assumption that positive (safe, resource-rich) environments allow individuals to achieve higher maximum fitness than negative (dangerous, resource-scarce) ones, the model clarifies the conditions for the evolution of various types of ordinal and crossover interactions. Results indicate that the symmetry hypothesis is not warranted except in unlikely special cases, and that when crossover interactions evolve, they are more likely to be asymmetric with PoI < .50 (that is, shifted toward the prototype of diathesis-stress models) rather than asymmetric with PoI > .50 (closer the prototype of vantage sensitivity). The reason is that, all else being equal, non-susceptible phenotypes should evolve so as to match positive environments better than negative ones, as the former are potentially conducive to higher fitness. A preliminary survey of published PoI values from studies targeting a variety of candidate genotypes and traits showed that interaction shapes tend to cluster below .50 (Figure 6). These findings have both theoretical and methodological implications for research on person-environment interactions.

Methodological Implications

As discussed earlier, current guidelines for the interpretation of PoI values are based on the symmetry hypothesis and its corollary that PoI = .50 is the prototypical shape for differential susceptibility. However, both model results and existing data suggest that the actual distribution of PoI may be centered on a lower value. In addition, the model indicates that the evolution of interaction shape is likely to depend critically on factors such as the probability of positive vs. negative states and the corresponding fitness ratio. In other words, researchers should expect a *distribution* of interaction shapes rather than a single prototype for differential susceptibility. If this is correct, the .40 to .60 window proposed by Roisman and colleagues (2012) is problematic in two ways: first, it is centered on .50 even if the actual PoI distribution is likely to be centered on a lower value, possibly closer to .40 than to .50; second, it is rather narrow (Figure 2c), and therefore likely to exclude many interactions that are in fact theoretically consistent with a differential susceptibility model (e.g., Figure 4b).

At present, it is difficult to go beyond this qualitative statement and make precise quantitative predictions about the theoretically plausible range of PoI values. Doing so would require a more detailed evolutionary model and—just as importantly—empirical data about crucial factors such as the shape of fitness functions, the reliability of developmental cues, and the distribution of environmental states (both in the present and in the evolutionary past). More generally, it is important to realize that methodological guidelines for the interpretation of person-environment interactions should not be regarded as set in stone, but as evolving heuristics that are bound to change over time as the underlying theory gets more sophisticated.

Theoretical Implications

Differential Susceptibility. The implications of the model I presented go beyond the issue of interaction symmetry, and raise some important yet unaddressed questions about the nature of differential susceptibility. To begin, the model highlights diminishing fitness returns as a crucial condition for the evolution of crossover person-environment interactions (Figure 3). Diminishing fitness returns to phenotype matching are intuitively plausible; small deviations from the optimal phenotype may entail relatively small costs, especially in benign environments. In the model, diminishing returns in the positive state may still favor the evolution of differential susceptibility when combined with linear returns in the negative state, but not when combined with increasing returns in the negative state (see the supplementary material, sections S5 and S6). Given the centrality of fitness functions—not just in relation to interaction shape but also in the evolution of other phenomena, such as experience-dependent plasticity and sensitive periods (Frankenhuis & Panchanathan, 2011a, 2011b; Panchanathan & Frankenhuis, 2016)—it would be extremely important to collect empirical data on the likely shape of fitness functions in human development. This is clearly an urgent topic for future research. Another is the distribution of fitness-relevant environmental variables, including the symmetry (or lack thereof) between the probabilities of positive and negative states.

Diathesis-Stress. The core assumption of diathesis-stress models is that susceptible individuals are *vulnerable* to negative environmental conditions such as stress and lack of resources, but do not benefit more than others from being exposed to positive conditions. The concept of diathesis-stress originates from a normative view that regards outcomes in negative environments as "maladaptive," even if the underlying idea of maladaptation has more to do with health and well-being than with biological fitness. A diathesis-stress scenario in which vulnerable individuals suffer more severe damage in negative environments does indeed predict the appearance of ordinal interactions, with PoI = .00 as the prototypical case (Figure 2a). However, the converse is not necessarily true; as I showed in this paper, the same interaction shape can evolve not as a result of vulnerability or predisposition to dysfunction in susceptible individuals, but rather as a result of adaptive phenotype-environment matching in susceptible individuals. Specifically, when environments differ in quality and phenotypic matching has linear or increasing returns, non-susceptible individuals are selected to express the same phenotype that susceptible individuals express in the positive environment (Figures 3a and 3b). The outcome of this evolutionary process is also an interaction with PoI = .00, but the underlying mechanism is adaptive matching rather than vulnerability. Similar patterns characterized by small PoI values may also evolve with diminishing fitness returns, depending on ecological parameters such as the fitness ratio and cue reliability (Figures 4 and 5).

It follows that, in and of themselves, low PoI values provide only weak support for diathesis-stress hypotheses that involve dysregulation as opposed to adaptive developmental plasticity. The contrast—implicit in much literature—between differential susceptibility hypotheses involving adaptive matching and diathesis-stress hypotheses involving vulnerability should be reconsidered in light of these findings. Indeed, the present model shows that, unless fitness functions have diminishing returns, PoI = .00 is an evolutionary attractor over a large portion of the parameter space; even with diminishing fitness returns, outcomes with small PoI

values are more likely than outcomes with large PoI values (Figures 4 and 5). In total, one should expect ordinal interactions of this kind to be common even if phenotypic matching is the only developmental mechanism in play. This expectation fits with the relatively high number of interactions with PoI values close to .00 in Table 1 (see also Figure 6). Of course, "true" diathesis-stress scenarios in which environmental factors such as stress and adversity interfere with developmental processes are quite possible, and may coexist to some extent with adaptive plasticity in response to the same factors (e.g., Ellis & Del Giudice, 2014). However, finding evidence of ordinal interactions with low PoI values is not a strong reason to favor dysregulation hypotheses over hypotheses involving adaptive plasticity. Distinguishing between these alternatives requires in-depth consideration of the functions and constraints of the relevant developmental mechanisms, and—ideally—evidence bearing on the likely fitness costs and benefits of different phenotypes in different contexts (see Ellison & Jasienska, 2007).

Vantage Sensitivity. The evolutionary analysis described in this paper sheds light on the logic of vantage sensitivity, a recently described interaction pattern in which susceptible individuals are disproportionally sensitive to positive but not negative conditions (Pluess & Belsky, 2013; Pluess, 2015). The model I presented predicts that interactions matching the prototype of vantage sensitivity (PoI = 1.00) should evolve in a more restricted range of conditions than other patterns, and only when negative environmental states occur with a higher probability than positive ones. (Note that this is not a *sufficient* condition for the evolution of vantage sensitivity; if the fitness ratio is sufficiently high, selection can favor interactions with PoI = .00 even when negative states occur with higher probability than positive ones. See Figures 4 and 5.)

The rationale for this prediction is straightforward. For vantage sensitivity to evolve, non-susceptible individuals must specialize so as to match negative, lower-fitness environments instead of positive, higher-fitness ones. This strategy, however, is self-defeating unless negative states occur with sufficient probability to offset the fitness premium of positive environments. These constraints on the evolution of vantage sensitivity may explain why this interaction pattern has not been described until very recently, and why large PoI values consistent with strong vantage sensitivity are rarely found in the empirical literature. For example, none of the interactions reported in Table 1 had PoI ≥ .80 (see also Figure 6).

Conclusion

Differential susceptibility theory has made a lasting contribution to developmental science by looking at person-environment interactions through the lens of adaptive evolutionary processes. Until now, however, the theory has lacked the ability to make predictions about the evolution of interaction shape. Recent theoretical reviews emphasize that interactions can take a number of distinct forms (e.g., Belsy & Pluess, 2013a; Pluess, 2015), but do not explain when and why selection is expected to favor one over the others. My goal in this paper has been to extend and refine the theory by clarifying the logic underlying the evolution of person-environment interactions when the environment has a positive-negative polarity. While much work remains to be done, the present findings have several potentially useful implications for theory and methodology; among other things, they raise questions about current conventions for the interpretation of empirical data.

In future studies, it would be useful to combine the present insights into the evolution of interaction shape with models that address the evolutionary origins of individual differences in plasticity (e.g., Frankenhuis et al., 2016). The model I presented also shines a spotlight on the crucial role of the distribution of environmental variables. In the literature on person-environment interactions, environmental variables have received little attention compared with personal factors such as genotypes, temperamental traits, and neurobiological profiles. The present results suggest that a better quantitative understanding of present and past environments may hold the key to more realistic models of plasticity and more accurate evolutionary predictions. Hopefully, future studies in this fascinating area will continue to foster ever-deeper integration between theory, methodology, and empirical research.

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