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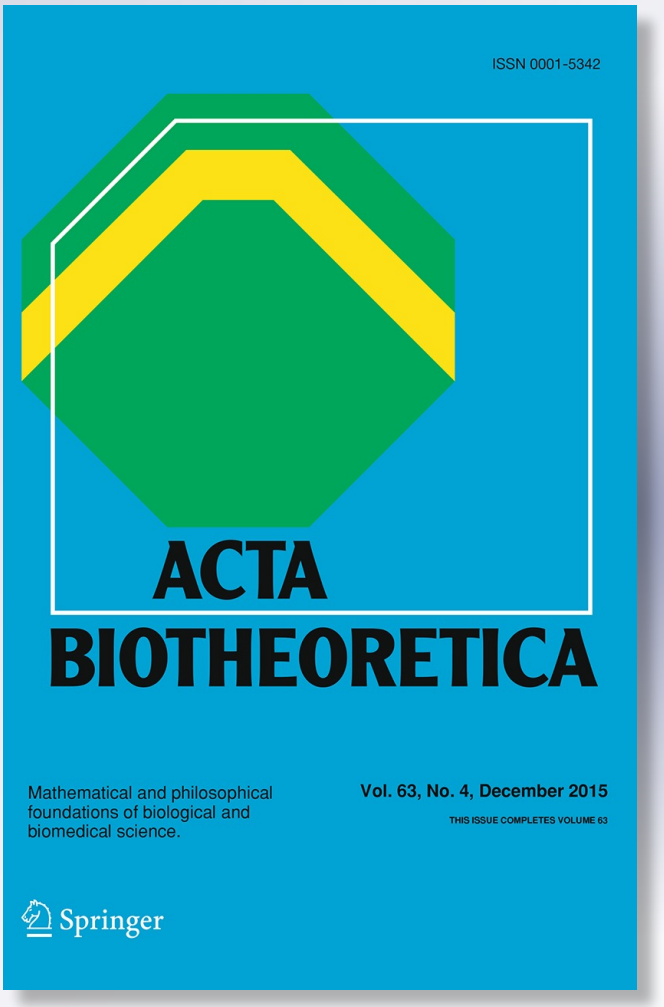

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BOOK REVIEW

The Asymmetrical Bridge

Book Review of James Tabery's Beyond Versus: The Struggle to Understand the Interaction of Nature and Nurture

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1 Introduction

More than a decade ago, the cognitive scientist Steven Pinker published *The blank slate*, a book that weighed in on the centuries-old debate about the contributions of nature and nurture to human psychological characteristics (Pinker 2002). When the eminent British biologist Sir Patrick Bateson needed a title for his review of the book in *Science*, he chose to call it "The corpse of a wearisome debate," because by 2002, Bateson already considered this debate to be "tedious and increasingly irrelevant" (Bateson 2002, p. 2212). But the public's reaction was different: Pinker's book was a bestseller that ultimately qualified as a finalist for the Pulitzer Prize. Today, published studies continue to compare the contributions of genes and environments to complex human traits (Plomin and Deary 2015; Polderman et al. 2015) even as numerous theorists insist that such comparisons are pointless and that the Nature–Nurture debate should be considered passé (Blumberg 2005; Gottlieb 1997; Moore 2002, 2013b; Weaver 2007). So the question is, why do some people continue to think the Nature–Nurture debate is still worthy of attention?

Into this morass wades James Tabery, an associate professor of philosophy at the University of Utah, whose admirable new book, *Beyond versus: The struggle to understand the interaction of nature and nurture,* explains the persistence of this debate by pointing out how the two groups of disputants in the Nature–Nurture debate have been talking past one another for more than 100 years. As Tabery sees it, by failing to agree on what is meant by the phrase "interaction between nature and nurture," the disputants have found themselves separated by an "explanatory

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divide," whereby they disagree about what sorts of natural phenomena need to be explained, what qualifies as suitable explanations for those phenomena, and how one should go about studying them (among other disagreements). As a result, when one group claims that nature and nurture interact to produce a particular trait—a phenotype—the other group remains unconvinced, so the debate continues, even as more and more empirical data pile up, data that would otherwise have been thought sufficient to end the debate. So, Tabery's book is fundamentally about how different theorists in the past 150 years have worked with different concepts of interaction. In an effort to make real progress on this front, Tabery endeavors to construct an "explanatory bridge" that could help researchers on each side of the explanatory divide understand how their work relates to the work of those laboring on the other side.

Tabery's book is a valuable contribution to the literature on gene-environment interaction, because he is certainly right that one reason for the resilience of the Nature–Nurture debate is the different approaches adopted by the two groups of disputants. Tabery calls these approaches the "variation-partitioning" and the "mechanism-elucidation" approaches respectively. The former approach has its roots in population genetics, and has traditionally been used to evaluate the extent to which genetic variation is associated with phenotypic variation (hence "variation-partitioning"); historically, behavior geneticists have used correlational studies of identical and fraternal twins to answer these kinds of questions. The latter approach has its roots in developmental biology, and has traditionally been used by experimental biologists and psychologists to discover how physical entities in the body (i.e., DNA, proteins, etc.) interact *in mechanistic ways* with physical entities in their environments (i.e., nutrients, sunlight, hormones, etc.) to build phenotypes (hence "mechanism-elucidation"); historically, these researchers have used experimental studies of non-human organisms to answer these kinds of questions. Because these two groups have different ideas about what it means for nature and nurture to interact, they have been failing to see eye-to-eye since scientific efforts to address the Nature–Nurture question first began in the 19th century. Thus, Tabery's effort to build a bridge between these camps is a worthwhile enterprise.

Tabery's book is very well written, helpful, clearly articulated (despite the conceptually complex subject matter), acutely reasoned, and thought provoking; it is an exceptionally valuable contribution to thinking about the interaction of nature and nurture. The book reads as good philosophy that has been written for an audience that might—and in fact, *should*—include non-philosophers.

2 Structure of the Book

After an introduction, Tabery begins with three chapters that present a history of debates about Nature–Nurture interaction. These chapters focus on (1) a debate about eugenics between Ronald A. Fisher and Lancelot Hogben in the 1930s, (2) a debate about IQ between Arthur Jensen and Richard Lewontin in the 1960s and 1970s, and (3) a debate about characteristics like depression and antisocial behavior between a research team led by Avshalom Caspi and Terrie Moffitt and a number of

their critics in the 2000s. Tabery's use of debates between individuals personalizes these debates in a way that makes for interesting reading; tracing the Nature–Nurture debate across the decades by focusing on raging disputes between individuals works well as a narrative device, so Tabery has wound up with an engaging chronicle. The approach also allows for a clear-sighted analysis; using Tabery's sources, one can see how the debate has persisted because of the way the two parties have talked past one another. And by treating the debate as he does, Tabery has written a balanced, non-polemical treatise. Of particular importance is the way he dismisses the long-running distraction wherein the two sides of the debate accuse each other of being either ignorant or motivated primarily by political concerns. He is clearly right that there is more to the debate's resilience than this. His strategy of tracking the controversy across historical periods allows him to weaken (if not outright dismiss) claims of sociopolitical bias.

In part II of his book, Tabery leaves behind the tools of the historian and takes up the tools of the philosopher of science, helping to clarify the relationship between mechanism-elucidation and variation-partitioning. This is the most important and valuable part of the book, and although I will take issue with some of Tabery's points below, I cannot find any outright errors in his work. In this part of the book, he does a superb job of characterizing the relationship between the variation-partitioning and the mechanism-elucidation approaches, and in particular, of clarifying what, exactly, the variation-partitioning approach can contribute to understanding; his efforts here represent a significant achievement. In particular, he illustrates how Kenneth Waters' (2007) concept of an "actual difference maker" can be used to make sense of what exactly it is that the variation-partitioning approach does (i.e., this approach is effectively a search for actual difference makers, factors whose variation accounts for phenotypic variation in a population). By combining this concept with ideas from the philosophy of mechanisms, Tabery has been able to describe "population thinking about mechanisms," which, he argues, bridges the work of variation-partitioners and mechanism-elucidators.

Tabery's final two chapters constitute a part III that concerns itself more with the future than with the past or present, and specifically with the bioethical implications of the existence of phenotypes that develop via gene-environment interactions. His decision to include this part in his book was a good one; these are important ideas to understand, particularly given how they might be used by states to monitor and intervene on innocent individuals, or by couples to make pre-implantation decisions in the wake of in vitro fertilization. Tabery's work is particularly strong where he clarifies how the results of Caspi and Moffitt's work do not support the idea that people with, for example, low levels of the MAOA protein are more prone to antisocial behavior; it all depends on both their genes *and* their developmental environments.

3 Variation-partitioning Versus Mechanism-elucidation

At the center of this book is the distinction Tabery makes between the variation-partitioning and the mechanism-elucidation approaches to explaining phenotypes. The former approach allows one to conclude that, for instance, genetic variation in a population can account for 80 % of the variation in height in that population; this kind of conclusion can be generated with correlational studies that do not require any experimental manipulations. In contrast, the latter approach *requires* experimental studies that seek to establish *how* an individual comes to have his or her body-length. Adopting an understandable pluralism, Tabery sees value in both approaches. In fact, he believes they co-inform one another. The idea here is that correlational studies can be used to generate hypotheses about which variables *might* play causal roles in the development of particular phenotypes, and that these hypotheses can then be used by experimentalists to elucidate the mechanisms that give rise to those phenotypes. Likewise, once mechanisms have been elucidated that explain how particular phenotypes arise in development, this understanding can be used to predict phenotypic variation in a population.

Tabery is right. There is no reason that variation-partitioning and mechanism-elucidation approaches must be considered exclusive enterprises; they *can* co-inform one another. Used properly—that is, in *conjunction* with mechanism-elucidation approaches—variation-partitioning approaches can add value to scientific endeavors. I do not grant these points lightly, because for more than a decade, I have been an outspoken critic of variation-partitioning approaches to causal explanation (Moore 2002, 2006, 2013a). Of course, I stand by my claim that behavior geneticists have *historically not* used their approach in conjunction with mechanism-elucidation approaches, and that instead they have typically black-boxed development, an approach that is of limited value. But these concerns notwithstanding, Tabery has made a strong case that variation-partitioning approaches are a tool that can be of use to scientists, specifically in steering the attention of mechanism-elucidators to hypotheses that might be worth exploring.

Nonetheless, I still believe that the tools on either side of Tabery's explanatory bridge are not of equal value, even if Tabery might see them that way. For example, of the variation-partitioners, Tabery writes that they are "certainly allowed to stay on their side and ignore the causal mechanisms…" (p. 146). But the variation-partitioning approach—because it cannot by itself contribute to our understanding of causal mechanisms—will always yield only a partial story about why things are as they are, a story that cannot offer any practical information about how to influence the development of children, crops, or livestock in beneficial ways; at best, these approaches allow for *prediction* at better-than-chance rates. In contrast, the world on the other side of the bridge is more self-contained; by itself, the mechanism-elucidation approach can identify tools that can be used to intervene in development in beneficial ways *and* can identify actual difference makers that can help explain variation across a population. This is true because if you understand a causal mechanism, you can both explain variation in a population and potentially alter it. There is no particular reason why a variation-partitioning approach is

required as a first step to identify an actual difference maker, so mechanism-elucidators really can stay on their side of the bridge, confident that their work will yield information that can be used to improve the human condition. To refer to work cited by Tabery, even if a variation-partitioning study like that conducted by Hariri and colleagues (2003) had been unable to find any naturally-occurring variation in memory performance in human populations, mechanism-elucidation studies like those conducted by Mizuno and colleagues (2000) would still have identified how the system being studied works, and in a way that has the potential to improve memory performance. Seen in this light, it should be clear that the work of mechanism-elucidators is of more value than the work of variation-partitioners.

Tabery and I agree that human behavior geneticists have historically black-boxed the causal mechanisms responsible for phenotypes. But we also agree that history need not dictate the future; if advocates of variation-partitioning begin "crossing the bridge" to consider questions of mechanism, by all means, advocates of the mechanism-elucidation approach should welcome them. I certainly do! Nonetheless, I continue to harbor concerns about the variation-partitioning approach as it is practiced by contemporary researchers, for a couple of reasons.

In the absence of the kind of comprehensive understanding that Tabery both possesses himself and has tried to disseminate in his book, the results of variation-partitioning studies can very easily—and erroneously!—be taken as having revealed more than they have actually revealed. For example, imagine a researcher who studies how variation in parental socioeconomic status (SES) is related to variation in IQ. If, in this imaginary study, the researcher finds that she can account for *all* of the variation in IQ by looking at variations in parental SES, it would be easy to conclude that IQ is not affected by other variables. But this would be a mistake, because variation-partitioning approaches cannot reveal the effects of factors that do not vary, *even if those factors play important causal roles in phenotype development*. So for example, in a population where everyone is exposed to the same diet, nutritional factors will not *look* like they influence IQ, even if they do. This is a problem, because the variation-partitioning approach allows us to easily miss ways of influencing an outcome, ways that would involve intervening on variables that are either relatively stable in a population or that have simply not drawn a researcher's attention. Of course, if some of these variables are easy to manipulate, failing to see their mechanistic roles could represent a fairly serious missed opportunity.

This problem could be in evidence whenever a variation-partitioning study fails to find that variation in a factor accounts for much of the phenotypic variation in a population. In one section of his book, Tabery writes about how twin and adoption studies conducted in the 1970s and 1980s implicated a genetic component in depression. This result should not have surprised anyone, because depression—like any psychological condition—is manifested in the brain and body, entities that are built with the help of the genome. But consider for a moment what it would have meant if the behavior geneticists had found that variation in depression could *not* be accounted for by variation in genetic factors. Obviously, such a finding would mean that all of the variation in depression in the studied population could be accounted for by variation in *non*-genetic factors, such as exposure to divorce, death of a

spouse, or the onset of a serious physical illness. But, would such a finding have meant that depression could occur in a person without any help from the person's genome? Of course not! For depression to manifest in a brain, engagement of the genome will be required. As any molecular biologist would affirm, all phenotypes—depression included—arise from interactions between genetic and non-genetic factors. So if the genome is not implicated in a behavior genetic study, that simply means that there's little to no *variation* in the population in the genetic factors that contribute to the studied phenotype; it does *not* mean that there are no genetic factors that contribute to that phenotype.

Much as the absence of a main effect of genes cannot be taken to mean that genetic factors are unimportant in the development of a phenotype, the absence of an interaction in a variation-partitioning study is equally hard to interpret. Ultimately, this reflects an important asymmetry in how the results of analyses of variance (ANOVA) should be understood. While statistically significant main effects or interactions are meaningful, *failures* to find such effects are *not* necessarily meaningful, for the usual reasons that null results cannot be clearly interpreted. Particularly when we do not yet know what the relevant genetic and nongenetic factors are in the development of a phenotype—which is the case for virtually all complex phenotypes, at present—it is impossible to be sure if a variation-partitioning project is studying the proper factors. For example, Tabery describes how Turkheimer found gene × environment interactions contributing to IQ only after decades of earlier studies had failed to find such interactions. (We should not be surprised that an appropriately broad population—in this case, one that included poor children—revealed interactions, because only populations characterized by sufficiently variable environments would be able to reveal the effect.) This is a case study in why we should recognize "no interaction" as a null result, one that carries with it all of the usual problems of interpretation. The failure to find a statistically significant interaction between two variables ought not be taken as evidence that these two variables are not interacting; other ways of conducting the study could very well reveal an effect that was there all along.

Despite the strengths of his argument, I believe Tabery has not adequately considered this asymmetry. For example, after asking "should we assume depression arises from this case of gene-environment interaction, or should we assume depression does not arise from this case of interaction?", Tabery answers: "we shouldn't assume anything" (p. 159). But here, he is missing an opportunity to clarify for readers what the statistical analyses *do not* mean. Tabery comes to his noncommittal conclusion because he is giving the same weight to null results as to significant results, but the two kinds of results are *not* symmetrical: null results do not permit strong conclusions, whereas significant results do. Also, his writing in this section of the book fails to take seriously the claim of mechanism-elucidators that the absence of a *statistical* interaction in a given variation-partitioning study of a phenotype does not mean the phenotype develops in the absence of *mechanical* interactions between DNA segments and their contexts (more on this in the next section). Because it is possible for two factors to interact in the development of a phenotype without an ANOVA revealing any statistical interaction (owing to

insufficient variability across the population), Tabery's analysis underestimates the role of interaction in the development of depression.

4 Two Kinds of Interaction

By clarifying the differences between the kind of interaction traditionally explored by variation-partitioners (i.e., a statistical interaction) and mechanism-elucidators (i.e., a causal–mechanical interaction), Tabery has provided a needed service for theorists concerned with the interaction of nature and nurture. The distinction he draws is very important, because without it, we are all at risk of misunderstanding any null results that might emerge from variation-partitioning studies; specifically, we might misunderstand null results as meaning that the phenotype being studied actually emerges in the *absence* of interactions between genetic and non-genetic factors, even though such a conclusion would be inconsistent with the known facts of biology (Eisenberg 2004; Gottlieb et al. 1998; Johnston 2010; Lewkowicz 2011; Michel and Moore 1995; Moore 2002, 2013a; Noble 2006). However, despite Tabery's valuable contribution here, there are a number of places in his book where he seems to lose sight of the distinction, thereby highlighting the dangers of variation-partitioning approaches.

Beginning in chapter 6, Tabery considers the "empirical evidence for interaction." Unfortunately, in this section he is exclusively focused on *statistical* interactions, as if these are the only important kinds of interactions. He presents evidence for and against the existence of interaction, but in each case, it is *statistical* interaction he's reporting on, even though he is not explicit about this. Such an approach risks confusing readers who are still just beginning to make the conceptual distinction between statistical and causal–mechanical interactions.

For instance, on page 157, Tabery gives his answer to the evidential question about interaction: "it's a mixed bag, and we should not assume one way or the other whether interaction exists for any particular trait…" But this is only a valid conclusion if one is concerning oneself strictly with *statistical* interaction! Failure to explicitly note this fact implies that some phenotypes really emerge in the absence of interactions between genes and environments, and that is simply never the case; genes always interact with non-genetic factors to produce phenotypes, whether our statistical analyses reveal those interactions or not.[1] Tabery goes on to say that there is "plenty of empirical evidence against" interaction, but that really is a misleading statement, because although there is some *statistical* evidence against interaction, there is no empirical evidence whatsoever to suggest that genes are capable of influencing phenotypic outcomes without mechanically interacting with other factors in their environments.

The failure of writers to distinguish clearly between statistical and causal–mechanical kinds of interaction is probably at least partially to blame for the

[1] There are at least two reasons why statistical analyses might fail to reveal interactions that are present: (1) if the correct factors are not tested, or (2) if the correct factors are tested but do not vary sufficiently in the tested population.

extraordinary persistence of the Nature–Nurture debate (Keller 2010; Moore 2013b). We can see how problematic it is to lose sight of the distinction by looking at Tabery's treatment of "Brunner syndrome" in chapter 7. There, he writes that in an infamous Dutch family with a lot of extremely aggressive men, "MAOA deficiency…was responsible for their low intelligence and proneness to aggression" (p. 170). But here, Tabery has used causal–mechanical language even though the studies on this family were done using a correlational, variation-partitioning method. In fact, there is a strong *statistical* relationship between the genetic mutation associated with Brunner syndrome and aggressive behavior. But because no experimental studies were done on this family, we have no idea *how* the reduced MAOA that is associated with the mutation brings about aggressive behavior. And in the absence of this kind of mechanistic understanding, it is misleading to say that the mutation is "responsible for" the behavior, when in fact the behavior would almost certainly be attenuated (or absent) in some contexts and amplified in others. Aggressive behavior is a complex phenotype, and it is unlikely to be caused single-handedly, in a deterministic way, by a particular DNA segment. After describing a different study, Tabery notes that 85 % of participants who both carried a particular variant of the MAOA gene *and* had been severely maltreated were antisocial in one way or another. But what of the other 15 % of this population? Although 15 % is a relatively small number, its non-zero nature makes it clear that there is more going on here than a simple deterministic relationship between low MAOA levels and aggression, *even when controlling for one aspect of experience*. So, to state that MAOA deficiency "was responsible for" the aggressive behavior in the Dutch family is overstating the case, because this deficiency alone could not have single-handedly caused the aggression. This example highlights the trouble that can arise when a clear distinction is not maintained between statistical and causal–mechanical effects.

5 Interaction in the 21st Century

When he considers more recent work on the interaction between nature and nurture, Tabery highlights research by Caspi and Moffitt (2002, 2003, 2005) as paradigmatic of the modern approach of mechanism-elucidators. Although Caspi and Moffitt's studies are extremely important, they arguably have more in common with the variation-partitioning approach than Tabery suggests. Specifically, Caspi and Moffitt's studies were strictly correlational; they *measured* the status of their participants' genomes, environments, and behavioral outcomes, and looked for statistical relationships between them. In no case did they *manipulate* any of these factors using an experimental design. Therefore, although these researchers studied particular genes rather than entire genomes, their work nonetheless has quite a lot in common with the whole-genome studies traditionally conducted by behavior geneticists.

As a result, Caspi and Moffitt have not escaped the problems of traditional behavior genetics. Because their studies were still merely correlational, they were not able to elucidate any mechanisms, but instead sought to explore how various genetic and environmental factors were *associated* with behavioral outcomes.

Tabery has argued that individual variation-partitioning and mechanism-elucidating studies are "*all* correlational" (p. 128, emphasis in original), and that's true in a Humean sense, but there is still an important distinction—a crucial distinction, really—to be made between studies that involve a manipulation and studies that merely measure: the former can reveal practical interventions that can influence outcomes, whereas the latter cannot. The best a non-experimental study can do is permit some predictions. Tabery thinks that Caspi and Moffitt's "appeals to experimental research" (p. 93) identify them as mechanism-elucidators, and those appeals do suggest that Caspi and Moffitt are not strict variation-partitioners. But the research they are best known for is *not* experimental, so when Tabery writes "Moffitt and Caspi's studies of gene-environment interaction are the modern-day exemplar of the mechanism-elucidation approach to understanding interaction" (p. 93), I have to disagree. A much better candidate for a modern day exemplar of the mechanism-elucidation approach is the research undertaken by Michael Meaney and Moshe Szyf, who have been *experimentally* studying the molecular mechanisms by which early-life experiences cause different behaviors in adulthood (Meaney 2001, 2010; Szyf and Bick 2013; see also Moore 2015). On a hypothetical continuum between variation-partitioning and mechanism-elucidation, Caspi and Moffitt would probably be relatively far from the mechanism-elucidation pole staked out by Hogben and Lewontin in the 20th century. Whereas I doubt that Hogben or Lewontin would have ever acceded to the claim that phenotype development might *not* involve an interaction—because a "mechanism" for biologists can fairly be *defined* as a system of causally *interacting* parts—had Caspi and Moffitt not detected a statistically significant interaction in their initial ANOVAs, there is a chance they would have abandoned their search.

Tabery's treatment of Caspi and Moffitt's work offers a particularly good opportunity to examine the risks that characterize variation-partitioning studies. Tabery, like some other theorists, seems to take the Caspi and Moffitt work to be an example of the kind of interactionist thinking promoted by developmental systems theorists (such as Lickliter 2013; Moore 2002, 2015; Oyama et al. 2001; Spencer et al. 2009; Thelen and Smith 1994). However, developmental systems theorists recognize that phenotypes always emerge from mechanical interactions between genes and their contexts, and a close look at Tabery's writing (and the writing of Caspi and Moffitt) reveals a willingness to accept a form of genetic determinism that is decidedly at odds with a developmental perspective.

For example, on page 140, Tabery offers a portrait built around how variations in the serotonin transporter gene (5-HTTLPR) are associated with variations in neuroticism. His portrait details how differences in this DNA segment lead to differences at higher levels of analysis, from the molecular level to the cellular level to the organ level, and thereby results in individuals having—or not having—the "stable trait of negative affectivity [or neuroticism]." Tabery's goal here is to elaborate on Caspi and Moffitt's story about how people with a lot of negative affectivity *may or may not* develop major *depression*, depending on the experiences they have as they develop; as both Tabery and Caspi and Moffitt tell it, this looks like a story about interaction, because different outcomes depend on both different 5-HTTLPR genes *and* on different life events. But Tabery's depiction of the

mechanism underlying *neuroticism itself* shows no such subtlety; in that portrait, a genetic difference leads directly to a difference in neuroticism. Nevertheless, I am not aware of any data to support the claim that neuroticism is genetically determined, that is, insensitive to the contexts in which development takes place. Instead, neuroticism—like the major depressions that depend on it—must develop in some *context*, and there are good reasons to believe the development of this phenotype depends on more than just the 5-HTTLPR gene. So, Tabery's example here illustrates the risks associated with variation-partitioning; unless we are always thinking in terms of mechanism-elucidation, we are at risk of unwittingly starting to think like a genetic determinist. This is risky, because genetic determinism black-boxes development and effectively encourages researchers to give up the search for answers about how to *affect* phenotypic outcomes by intervening in development (Johnston 1987; Lehrman 1953; Lickliter and Berry 1990; Moore 2009).

We can see this problem in relief a few pages later. There, Tabery writes that "Moffitt and Caspi combined … research on a genetic actual difference maker with … research on an environmental actual difference maker and ultimately proposed a 'unifying mechanism' that pulled the various threads together—a genetic actual difference maker that *leads to* actual differences in neuroticism *regardless of exposure to stressful life events*, but only actual differences in depression when exposed to actual differences in stressful life events" (p. 144, emphasis added). By failing to identify what sorts of non-genetic events contribute to the development of neuroticism itself, Caspi and Moffitt have still failed to provide a mechanism for the development of depression. What they have done—now with Tabery's help—is move genetic determinism back one level: now, rather than seeing depression itself as genetically determined, it is merely neuroticism that is characterized as genetically determined, with depression arising from a gene × environment interaction. This example is a good illustration of the persistence of the problem of thinking about genes as factors that are able to single-handedly determine phenotypes. When one loses sight of a developmental perspective and therefore sees a phenotype like negative affectivity as inevitable in the presence of a certain genotype, one can wind up *looking like* an interactionist (in this case, with respect to depression) while nonetheless implying that genes can deterministically cause a neurotic phenotype independently of the contexts in which development takes place.

Because there have been more than one large meta-analysis suggesting that the Caspi and Moffitt interaction is not replicable (Munafò et al. 2009; Risch et al. 2009), it would be easy to draw the conclusion that the experience of stress does not play an important role in the development of major depression. However, as Tabery helpfully points out, these results might merely "speak to a potential for refining the environmental variable" (p. 162). Of course, this is correct; "stress exposure" might be a variable that is simply too non-specific to allow for reasonably accurate predictions of depression. So in the end, Tabery saves the day by acknowledging that "we're talking about the potential discovery of a complicated relationship—between a gene that is still being understood at the molecular level, an environment that is difficult to quantify, and a complex psychiatric disorder" (p. 163). But he made it harder than necessary on himself by initially taking some null ANOVA results more seriously than was warranted.

Because of the differences in approach between the Caspi-Moffitt team and both Hogben and Lewontin, I had a difficult time believing Tabery's claim that the 21st century controversy over Caspi and Moffitt's findings mirrors the earlier debates between Fisher and Hogben or between Jensen and Lewontin. Nonetheless, Caspi and Moffitt's critics do seem to hearken back to Fisher when they reject gene-environment interactions as unlikely *in general* (p. 89). And notwithstanding my concerns about Caspi and Moffitt being treated as true mechanism-elucidators, I do think Tabery has written an impressive treatment of their findings and the ensuing controversy.

6 Envisioning the Future

The final two chapters of *Beyond versus* use the tools of the bioethicist to consider the significance of some recent findings regarding interaction between nature and nurture. Tabery is in top form in these chapters, conveying to readers the meaning of these findings, warning us of ways they can be misinterpreted, and alerting us to issues that deserve thought at this juncture. He makes a compelling argument in chapter 7 for not spending public funds to screen children for low MAOA and instead using any money available for such projects to extend to children in general an intervention to reduce maltreatment in childhood. Likewise, his points here about the need to remain aware of the power of self-fulfilling prophecies are worth taking seriously, because knowing what is in a child's genome—and having a *partial* understanding of what that might mean—would almost certainly influence people's thoughts and behaviors in ways that could negatively affect the child.

In chapter 8, Tabery focuses on the potential value of providing parents with information about their children's genomes *when that information could inform decisions that parents are going to make whether they have the information or not*. Parents make all sorts of decisions about the contexts in which their children develop, so Tabery is right that genetic information could potentially help them make more *informed* decisions. But he is also right that this approach is not without risks, as there could be downsides to empowering parents in this way, such as the increased responsibility that this empowerment would thrust upon them. Regardless, Tabery has done all of us a favor by beginning to consider the ethical implications of this work today, before the $1000-genome is actually available to us.

Ultimately, I share Tabery's concern that genetic determinism might be replaced by a new kind of "interactionist determinism," wherein a child with a particular genome who has been subjected to certain kinds of experiences comes to see himself or herself as *inevitably* possessed of a certain kind of mental or behavioral status. The fact is, we still understand very little about the development of characteristics like aggression or depression, and it would be a blunder to convey to the general public a mistaken impression that we know more than we do. The fact is, developmental outcomes remain largely unpredictable, to date.

As I see it, the most important take-away message from *Beyond versus* is a message that is not new, but that nonetheless bears repeating: given the fact that phenotypes reflect the *mechanical interaction* of genetic and non-genetic factors,

the idea that someone is "genetically predisposed" to a particular outcome is simplistic. Tabery does an outstanding job of explaining why this phrase is inappropriate in cases of gene × environment interaction that involve a "change in rank," but his argument is weaker than it needs to be, since he condones the use of the phrase in some cases (e.g., when an interaction involves only a "change in scale"). Biologists have understood for decades that there really are never any cases where we can be sure an interaction does *not* involve a change in rank, because even if there is no change in rank across a studied range of environments, a change in rank could still be discovered in some other range of environments; an interaction that involves merely a change of scale could involve a change of rank if the environments studied fell in a different range on the continuum.

To clarify this point, consider Tabery's definition of "a genetic predisposition": "the presence of a genetic difference between various groups *consistently* increases the probability of individuals from one group, in comparison to individuals from the other group(s), developing a particular trait *regardless of* the measured environmental condition" (p. 177, emphasis in the original). This definition works, but it contains a problem that could mislead readers. Tabery's reference is to a *measured* environmental condition, but the fact is that it is never possible to measure all environmental conditions. So, we can picture a situation in which the individuals in one study group are consistently more likely than the individuals in other groups to develop a trait in a hundred different environments. But there is always the possibility that a test conducted in the 101st environment would reveal individuals in the first group to be *less* likely than individuals in other groups to develop the trait *when reared in that environment*. So as a practical matter, it is really never appropriate to speak of a genetic predisposition without also specifying the contexts in which development will unfold. For this reason, the concept of "genetic predisposition" (as we intuitively think about it, at least) is suspect; because phenotypes always develop via the collaborative actions of genes and their contexts, and because it is impossible to test genomes in all possible contexts, we can never be sure we have a comprehensive understanding of what a given genome is (or is not) capable of producing. The geneticist Theodosius Dobzhansky concluded in the 1950s that knowing the limits that could be expected of a particular genotype would require testing that genotype in all possible environments, which is obviously an impossible task. To drive home his argument, Dobzhansky pointed out that "the existing variety of environments is immense, and new environments are constantly produced. Invention of a new drug, a new diet, a new type of housing, a new educational system, a new political regime introduces new environments" (Dobzhansky 1955, p. 75). And as a result of this situation, we can never state with confidence that a given genetic state predisposes an individual to a particular outcome *in general*; only by having information about *both* an organism's genes *and* environment can we make strong claims about predispositions. Put into Tabery's language about changes in rank versus changes in scale, any time we discover an interaction as a change in scale, the addition of another environment to be tested could reveal a previously-unseen change in rank; therefore, risk is almost always best understood as dependent on both genetic and environmental variables.

Notwithstanding my criticisms, Tabery's book is a welcome addition to the literature on the interaction of nature and nurture. In fact, I would argue that his presentation of Hogben's intellectual assault on eugenics should be required reading for all scientists, because it is so generally applicable to the problem of interpreting data, and it makes it clear how Fisher's *statistical* interaction differs from the kinds of causal–mechanical interactions that were of concern to Hogben (Griffiths and Tabery 2008). This is an extremely important message, as it bears on the question of what sort of information is of practical value. Fisher dismissed Hogben's concerns as "academic," because Hogben was interested in what might be possible; in contrast, Fisher considered his own work to be "practical," because he remained focused on partitioning variation in "real" populations of organisms like potato plants. Somewhat paradoxically, to understand "practical" problems facing farmers, Fisher-the-statistician wound up resorting to abstractions; in contrast, Hogben used real observations to make his points about what would be theoretically possible. Of course, Fisher used the word "practical" as meaning "relating to real life as we know it," but accepting the status quo is only practical in one sense. In contrast, to a developmentalist, what is "practical" is a tool that can be used to intervene in a way that can influence outcomes, thereby *changing* the status quo. As I see it, there can be little of more *practical* importance than using a mechanism-elucidation approach to discover ways to improve the human condition.

Ultimately, I agree with Hogben and Lewontin, and I believe Tabery does as well: the variation-partitioning approach is dangerous only if the conclusions generated by this approach are "treated as an end point, rather than as a starting point to other more interventionist experiments designed to investigate the developmental relationship between nature and nurture" (Tabery 2014, p. 69). It is via the analysis of development that behavioral scientists and life scientists can most effectively make positive contributions to people's lives.

References

Bateson P (2002) The corpse of a wearisome debate: review of Steven Pinker's the blank slate: the modern denial of human nature. Science 297:2212–2213

Blumberg MS (2005) Basic instinct: the genesis of behavior. Thunder's Mouth Press, New York

Caspi A, McClay J, Moffitt TE, Mill J, Martin J, Craig IW, Poulton R (2002) Role of genotype in the cycle of violence in maltreated children. Science 297:851–854

Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, Harrington H, Poulton R (2003) Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science 301:386–389

Caspi A, Moffitt TE, Cannon M, McClay J, Murray R, Harrington H, Craig IW (2005) Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene × environment interaction. Biol Psychiatry 57:1117–1127

Dobzhansky T (1955) Evolution, genetics, and man. Wiley, New York

Eisenberg L (2004) Social psychiatry and the human genome: contextualising heritability. Br J Psychiatry 184:101–103

Gottlieb G (1997) Synthesizing nature-nurture: prenatal roots of instinctive behavior. Lawrence Erlbaum Associates, Mahwah

Gottlieb, G., Wahlsten, D., & Lickliter, R. (1998). The significance of biology for human development: a developmental psychobiological systems view. In W. Damon (Series Ed.) & R. M. Lerner (Vol. Ed.), Handbook of child psychology: Vol. 1. Theoretical models of human development (5th ed., pp. 233–234). New York: Wiley

Griffiths PE, Tabery J (2008) Behavioral genetics and development: historical and conceptual causes of controversy. New Ideas in Psychology 26:332–352

Hariri AR, Goldberg TE, Mattay VS, Kolachana BS, Callicott JH, Egan MF, Weinberger DR (2003) Brain-derived neurotrophic factor val66met polymorphism affects human memory-related hippocampal activity and predicts memory performance. J Neurosci 23:6690–6694

Johnston TD (1987) The persistence of dichotomies in the study of behavioral development. Dev Rev 7:149–182

Johnston TD (2010) Developmental systems theory. In: Blumberg MS, Freeman JH, Robinson SR (eds) Oxford handbook of developmental behavioral neuroscience. Oxford University Press, New York, pp 12–29

Keller EF (2010) The mirage of a space between nature and nurture. Duke University Press, Durham

Lehrman DS (1953) A critique of Konrad Lorenz's theory of instinctive behavior. Quarterly Review of Biology 28:337–363

Lewkowicz DJ (2011) The biological implausibility of the nature–nurture dichotomy and what it means for the study of infancy. Infancy 16:331–367

Lickliter R (2013) Biological development: theoretical approaches, techniques, and key findings. In: Zelazo PD (ed) Oxford handbook of developmental psychology. Oxford University Press, New York, pp 65–90

Lickliter R, Berry TD (1990) The phyologeny fallacy: developmental psychology's misapplication of evolutionary theory. Dev Rev 10:348–364

Meaney MJ (2001) Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. Annu Rev Neurosci 24:1161–1192

Meaney MJ (2010) Epigenetics and the biological definition of gene × environment interactions. Child Dev 81:41–79

Michel GF, Moore CL (1995) Developmental psychobiology: an interdisciplinary science. MIT, Cambridge

Mizuno M, Yamada K, Olariu A, Nawa H, Nabeshima T (2000) Involvement of brain-derived neurotrophic factor in spatial memory formation and maintenance in radial arm maze test in rats. J Neurosci 20:7116–7121

Moore, D. S. (2002). The dependent gene: the fallacy of "nature vs. nurture." New York: Times Books/ Henry Holt & Co.

Moore DS (2006) A very little bit of knowledge: re-evaluating the meaning of the heritability of IQ. Hum Dev 49:347–353

Moore DS (2009) Probing predispositions: the pragmatism of a process perspective. Child Dev Perspect 3:91–93

Moore DS (2013a) Behavioral genetics, genetics, & epigenetics. In: Zelazo PD (ed) Oxford handbook of developmental psychology. Oxford University Press, New York, pp 91–128

Moore DS (2013b) Current thinking about nature and nurture. In: Kampourakis K (ed) The philosophy of biology: a companion for educators. Springer, New York, pp 629–652

Moore DS (2015) The developing genome: an introduction to behavioral epigenetics. Oxford University Press, New York

Munafò MR, Durrant C, Lewis G, Flint J (2009) Gene × environment interactions at the serotonin transporter locus. Biol Psychiatry 65:211–219

Noble D (2006) The music of life: biology beyond genes. Oxford University Press, New York

Oyama S, Griffiths PE, Gray RD (2001) Cycles of contingency: developmental systems and evolution. MIT Press, Cambridge

Pinker S (2002) The blank slate: the modern denial of human nature. Viking, New York

Plomin R, Deary IJ (2015) Genetics and intelligence differences: five special findings. Molecular Psychiatry 20:98–108

Polderman TJC, Benyamin B, de Leeuw CA, Sullivan PF, van Bochoven A, Visscher PM, Posthuma D (2015) Meta-analysis of the heritability of human traits based on fifty years of twin studies. Nat Genet 47:702–709

Risch N, Herrell R, Lehner T, Liang K, Eaves L, Hoh J, Merikangas KR (2009) Interaction between the serotonin transporter gene (5–HTTLPR), stressful life events, and risk of depression: a meta-analysis. J Am Med Assoc 301:2462–2471

Spencer JP, Blumberg MS, McMurray B, Robinson SR, Samuelson LK, Tomblin JB (2009) Short arms and talking eggs: why we should no longer abide the nativist-empiricist debate. Child Dev Perspect 3:79–87

Szyf M, Bick J (2013) DNA methylation: a mechanism for embedding early life experiences in the genome. Child Dev 84:49–57

Tabery J (2014) Beyond versus: the struggle to understand the interaction and nature and nurture. MIT Press, Cambridge

Thelen E, Smith LB (1994) A dynamic systems approach to the development of cognition and action. MIT Press, Cambridge

Waters CK (2007) Causes that make a difference. Journal of Philosophy 104:551–579

Weaver ICG (2007) Epigenetic programming by maternal behavior and pharmacological intervention: nature versus nurture: let's call the whole thing off. Epigenetics 2:22–28