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Author's Response

Understanding Heritability: What it is and What it is Not

WENDY JOHNSON[1,2]*, LARS PENKE[1] and FRANK M. SPINATH[3]

[1]*Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh, Edinburgh, Scotland, UK*
[2]*Department of Psychology, University of Minnesota—Twin Cities, Minneapolis, MN, USA*
[3]*Department of Psychology, Saarland University, Saarbruecken, Germany*

Abstract: Commentators generally found our exposition of the concept of heritability helpful for psychologists, suggesting that we largely accomplished our primary goal. Many provided supplemental and helpful perspectives on concepts we addressed. A few of the comments indicated that we may not have been completely successful in making clear our secondary goal, which was to outline how heritability estimates confound a plethora of influences. In this response, we thus emphasize that we do not claim that specific kinds of complexity, or, even worse, intractable complexity, pervade the genetics of behavioural traits. Rather, our claim is that genetics is riddled with complexity of many degrees and kinds, and heritability is a poor indicator of either degree or kind of underlying genetic complexity.

We were pleased to see the 13 thoughtful commentaries our target article received, coming as they did from people actively involved in exploring genetic influences on behavioural traits from both quantitative and molecular perspectives. We thank all the commentators for their engagement with the topic and their constructive remarks. This is currently a very active area of research, and new developments and findings are announced daily. While many of the developments take place in scientific disciplines far from psychology, interest in making use of them to unravel the origins of behavioural traits is high. We strongly believe that, as with most tools, background knowledge is important in using the quantitative and molecular genetic technologies now available. This is particularly important in this area because the new developments are not only limited to the technological but also extend to the conceptual as well. Our primary goal in writing this article was to provide this background knowledge, to avoid perpetuation of the oversimplifications of interpretation that have recently peppered some applications of these technologies in psychology and in other social sciences such as economics and sociology.

INSIGHTFUL VARIATIONS ON THEMES RAISED IN PURSUIT OF OUR PRIMARY GOAL

The commentaries suggest that we were largely successful in meeting our primary goal. All commentators expressed support for the general thrust of our discussion, with most providing additional perspectives elaborating on the themes we raised. Each of these contained an important insight that helps to flesh out the possible ways in which genetic influences may contribute to the heritability statistics that have become familiar to psychologists. *Asendorpf* noted the importance of recognizing that heritability estimates made at any point in time reflect the aggregation of the outcomes of individual developmental processes and that these developmental processes inevitably involve transactions between genetic and environmental influences. When genetic influences on one person act to shape the environments of relatives, they can create either similarity or differences between them, and the two kinds of influence will have different effects on heritability estimates depending on the specific genetic relationships the relatives in the sample on which the heritability estimates are based. This underlines the fact that even traits with high heritability are developmentally sensitive to environmental circumstances.

Burt raised several interesting points regarding gene-shared environmental correlation. The possible existence of this form of gene–environment correlation is arguably one of the most neglected subjects in psychology. The developmental process involving reinforcement loops to which Burt refers is well encompassed by Experience-Producing Drive Theory (Bouchard, 1997; Hayes, 1962; Johnson, 2010). This is the idea that, rather than contributing directly to behavioural traits, genetic influences contribute to motivation to pursue certain kinds of activities and respond to and seek out particular kinds of stimuli, and the traits develop as consequences of these experiences. To the extent such processes exist, they certainly constitute potential sources of active gene–environment correlation with strong developmental implications. Burt noted that the existence of this process implies that gene–environment interaction and correlation are linked in systematic ways, as discussed extensively by Johnson (2007).

*Correspondence to: Wendy Johnson, Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh, Edinburgh, Scotland, UK. E-mail: wendy.johnson@ed.ac.uk

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More generally, the neglect of gene–environment correlation in the field is a serious omission because, if it is present to any substantial degree, it is likely quite powerful. Its neglect is also no accident, because we currently have no good, commonly available methods either to detect or to measure it. Burt claimed that we can use comparisons of heritability results from adoptive and biological siblings to assess it, but we see two difficulties with this. Both surround what we perceive to be misunderstandings of the concept of passive gene–environment correlation. First, as we discussed in the target article, there is a tendency for people to equate passive gene–environment correlation with genetic-shared environment correlation, but this is an oversimplification. Genetic-shared environmental correlation is nothing more than the correlation between genetic influences and environmental influences that act to make twins or other pairs of family members similar. As with the subtleties of the definition of shared environmental influence itself, shared experiences can act to make these pairs different, thus acting as nonshared environmental influences. And different specific experiences can act to make family members similar, thus acting as shared environmental influences. When these are correlated with genetic influences, the result is a gene-shared environmental correlation, and it can be active or evocative as well as passive.

An example may help make this clear. Suppose parents with two children believe strongly, possibly for genetic reasons of some kind, that learning to swim is an important life skill, and their children should learn to do it. At some appropriate age, they enrol them in swimming lessons. One of the children takes to it like the proverbial duck to water and takes every opportunity to swim, possibly for genetic reasons of some kind, although not necessarily the same ones that contributed to the parents' goal of seeing their children learn to swim. For this child, there is a passive gene–environment correlation: genetic influences in the parents provide an environment to which the child responds genetically. The other child sinks like a stone and freezes in the pool, making the lessons tortuous, possibly for genetic reasons of some kind. The parents are committed, however, and find some lessons in a warmer pool, persuade the parents of the child's best friend to enrol their child in the same lessons and make opportunities to give the child positive experiences in the water. Eventually, the child learns to swim and in the process even learns to enjoy it and to do it regularly, with adaptation to the initial unpleasant experience possibly having some genetic basis. For this child, there is an evocative gene–environment correlation: the parents respond environmentally to the child's genetically influenced difficulty with swimming. For both children, there is ultimately some kind of active gene–environment correlation, as they both regularly go swimming and do it well. For both children as well, the result is a gene-shared environmental correlation, although the genes and the environments involved for the two children may have little overlap.

Second, passive gene–environment correlation is a process, not a state focused on a result as is shared gene–environment correlation. Definitions often given for passive gene–environment correlation refer explicitly to children inheriting genetic influences from their parents that contribute to both the environment the parents create and the children's responses to that environment. The requirement of direct genetic transmission from parents to children is, however, overly restrictive. The important aspect of the process is that it takes place, to the extent it does, passively for genetic reasons. This may occur most readily in biological families, but it can also occur in adoptive parent–child relationships as long as it is passive. That is, the parents are creating some aspect of the environment for their own genetically influenced reasons without regard to the children's responses to it (it is not evocative), and the children are adapting to it (positively or negatively) for their own genetically influenced reasons, without in any active way either pursuing it or avoiding it, for example, if they cannot. This kind of passive gene–environment correlation may be rarer in adoptive families, but it is in no way impossible and could even be common, especially in normally distributed traits for which most people, both parents and children, tend to fall in the middles of the ranges.

Importantly, we agree with Burt that looking at the magnitudes of shared environmental influences remains important in the field today in a way that examining magnitudes of genetic influences does not. Our reasons, however, are different and have little to do with underlying biology. The idea of genetic influences on behaviour was so controversial for so long that behaviour geneticists formed the habit of testing the significance of parameters estimating genetic, shared and nonshared environmental influences in their models and dropping those that were not significant. At least partly because, in twin samples, there is less power to pick up shared environmental influences, this commonly resulted in the so-called AE model incorporating only genetic and nonshared environmental influences being identified as best. In turn, this has led to an impression in the field that shared environmental influences are often completely absent, when in reality, they are merely smaller than estimates of genetic influences. As long as this impression predominates, we agree that some focus on the magnitudes of shared environmental influences are important, even when they are not statistically significant.

Cramer, Kendler and Borsboom pointed out that one reason for the lack of success in identifying specific genes involved in behavioural traits, despite substantial heritability, may be that the behavioural traits and especially the syndromes that have been identified as important may be networks of causally interrelated behaviours or symptoms. Gene-hunting methods for behavioural traits tend to rely on the assumptions that one set of genes plays a causal role in all the behaviours defining a trait, especially a syndrome, and that we can measure the severity of the syndrome by summing symptom counts. As Cramer, Kendler, and Borsboom note, if the symptoms instead exist in network clusters that have reciprocal causal effects on each other, this is much less likely: each symptom may have its own set of causally related genes. In such a case, the sum score approach may produce robust heritability estimates, but the effects of individual genes may be too blurred in population samples because some people in each sample with similar syndrome

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levels have one pattern of causal relations among symptoms, and others have other patterns. This is one way of saying that the phenotype, syndrome or behavioural traits that have been identified may be genetically emergent rather than latent, or formative rather than reflective. The difference is that the heritability we estimate in an emergent trait is evidence of a result of gene action, whereas the heritability we estimate in a latent trait is evidence of a genetic cause for the trait. Individual traits can of course have aspects that are both emergent and latent. Whereas the implicit and likely oversimplified assumption in differential psychology today is that genetic influences are single latent causal factors, right now, we simply do not know the ratio of latent to emergent aspects for any trait or syndrome. This could be an important direction for future personality and individual differences research, but heritability estimates cannot be used to make this distinction. *Grigorenko* discussed this blurring of the trait concept in some detail.

Similarly, *Jackson, Hill and Roberts* listed some additional ways that heritability has been misinterpreted and stressed the importance of recognizing that gene expression can both change with development and be responsive to environmental circumstance. This indicates that some variance attributed to heritability may reflect more similar genetic responses to environmental circumstances by monozygotic than by dizygotic twins, rather than genetic variance *per se*. And *Jaffee and Price* emphasized that it is not just environmental circumstances, objectively measured, that may influence gene expression but our perceptions of those circumstances. *Lukaszewski* took this theme of contributions to heritability from environmental circumstances a step further by noting that environment may also include the presence of other genetically influenced traits. That is, one's status on one genetically influenced trait may influence the extent to which one develops other characteristics, causing what has been termed 'reactive heritability'. One example that may be pervasive among social animals might be how genetically influenced physical size and strength influence the development of dominance behaviours. Such adaptive facultative adjustments of behavioural strategies to independently inherited traits theoretically can evolve, but only if the link between the heritable trait and the fitness payoff of the behavioural strategy is stably reliable over long evolutionary time spans (Penke, 2010). *Trumbetta and Gottesman* also elaborated on a similar theme, pointing out that many different genetically influenced characteristics may contribute to diverse developmental trajectories that nevertheless lead to similar outcomes. They stressed that identification of underlying endophenotypes may help articulate these developmental trajectories and the genetic mechanisms involved more clearly. Taken together with the developmental processes outlined by Asendorpf and the possibility of emergent traits highlighted by Cramer et al. (where differences in the strength of network relations might well be the outcomes of developmental processes), these commentaries nicely illustrate that causal heterogeneity and developmental equifinality might be widespread. This underlines, as *Mitchell* reminds us, that we should not think of genes 'for' a trait.

Mitchell turned the discussion towards identification of the specific genetic variants involved in behavioural traits. He noted that many of the techniques we currently use to identify specific genes involved in traits of interest are based on the assumption that the variants to be identified are common in the population. There is, however, increasing evidence that many important genetic variants may actually be rare, and techniques under development will be able to identify these rare variants as well. We agree with Mitchell that a large number of individual rare genetic variants could collectively make substantial contribution to heritability estimates derived on population levels, as we noted on page 261 of the target article and in earlier publications (Deary, Penke, & Johnson, 2010; Penke, 2010; Penke, Denissen, & Miller, 2007). Rare variants with substantial effects by definition exert those effects on only a few individuals in the population, and these variants only remain rare if they reduce evolutionary fitness. This makes the recent observation that genetic variants are more likely to be functionally meaningful the rarer they are in the population (Zhu et al., 2011) exactly what we should expect. Therefore, rare variants are more likely important contributors to the genetic architecture of traits that consistently decrease fitness (such as physical and mental disorders or perhaps low intelligence) than of traits with less clear or variable fitness associations (as is arguably true for normal range personality traits generally construed; Penke, 2010; Penke et al., 2007).

Munafo and Flint focused more on the roles of common genetic variants (as studied in current genome-wide association studies) and pointed out that, even if the number of genetic variants involved in a trait is very large, and no one gene has more than a tiny effect, with the large samples being accumulated, our methods should eventually reveal these variants as well. As it stands, molecular genetic research suggests that quasi-infinite numbers of common variants or loads of rare variants (or a mixture of both) are the most likely genetic architectures of behavioural traits as we study them. If this is correct, because evolutionary genetic considerations render it unlikely that rare variants contribute much to personality traits, soft balancing selection (Pritchard, Pickrell, & Coop, 2010) might maintain a large number of common variants in personality.

THEN THERE WAS OUR SECONDARY GOAL

Within our primary goal of providing background knowledge to psychologists on the concept of heritability, we also had an important secondary goal. This was to make clear that there are many possible genetic, psychometric, environmental and interactive mechanisms that can explain the presence of substantive heritability estimates on behavioural traits, but the presence or the magnitude of the heritability estimates is no clue at all as to which of these explanations might be accurate in any one situation. Crucially, this means that we were not advocating any one explanation for 'missing heritability', nor waving our hands at complexity, but arguing that we need to look well beyond heritability estimates and avoid focusing on any single explanatory mechanism in order to understand how genes contribute to the manifestation of behavioural traits. In particular, we think it likely that the genetic influences

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indicated by heritability estimates will prove to have different kinds of explanations, from among those we discussed, those raised by some of the commentators and many others not yet discovered.

Several of the comments suggest that we may not have made our point about the limitations of heritability as a guide to underlying genetic mechanisms clearly enough. *De Moor and Boomsma*, for example, saw us as stressing the importance of gene–environment interplay in explaining heritability, whereas Jackson, Hill and Roberts charged us with not going far enough in recognizing the implications of gene–environment interplay and the ability of the environment to modify gene expression. It was not our objective to estimate to what extent this kind of interplay or any of the other possible explanations might account for 'missing heritability' but to note that, beyond genetic variants of small effect acting additively, these other possibilities likely are important. Similarly, *Riemann, Kandler and Bleidorn* maintained that our discussion of the effectiveness of measurement on heritability estimates was unnecessary because it is obvious that ineffective measurement distorts estimates of all effects. This is of course correct, but the implications of ineffective measurement on heritability estimates, especially some of the subtleties we described, are often disregarded. It was also not our aim, as they claimed, to turn heritability into a dichotomy but rather to highlight that the influences on the size of heritability estimates are so diverse that there is no straightforward interpretation for the size of any individual estimate. Of course, the more some of these influences can be controlled in well-designed studies (e.g. by all the reliability-increasing and validity-increasing means they list), the better they can be ruled out as factors distorting the magnitudes of the resulting heritability estimates. But because it is hardly possible to control all such influences on heritability in any single study, sizes of heritability estimates will never be direct indicators of any one biological quantity.

In contrast, *Visscher and Keller* defended the idea that genetically influenced variance is largely made up of additive effects. In the process, they appear to have misunderstood several of the points we raised. First, we in no way meant to deny that substantial heritability is associated with greater similarity among genetically related people than among people not genetically related to each other. The point we wanted to make, which is often missed by many, is that even quite high pair correlations allow for substantial differences between individuals within the pairs. Similarly, with respect to rare Mendelian diseases, our point in noting that their heritability in population samples is essentially zero was that, because most heritability estimates are made in such samples, we have no way of using them to identify traits where rare Mendelian genetic variants are important. And we quibble over wording regarding the issue of epistasis causing the appearance of additive genetic variance. Hill, Goddard, and Visscher (2008) demonstrated that even completely nonadditive (epistatic and/or dominant) genetic models generate substantial genetic variance that can be characterized as additive. To us, this means that we cannot use correlations among relatives that generate heritability estimates that appear to indicate primarily additive genetic variance to infer that epistasis and dominance (never mind other sources of interplay and/or genetic complexity) are *not* present and/or important. Are Visscher and Keller really prepared to disagree with this?

Finally, Visscher and Keller pointed to recent successes in demonstrating that, in addition to identifying many genes that contribute to height but explain little of its variance, additional common additive genetic variants in the aggregate contribute as much as half the outstanding genetic variance (Visscher, Yang, & Goddard, 2010; Yang et al., 2010). Presuming this is correct and, as Visscher and Keller appear to have implied, applicable to most behavioural traits, this indicates that literally thousands of genes are likely involved in each trait, with no single polymorphism having substantial effect, which is the quasi-infinite model to which Munafo and Flint refer. Whatever would we as psychologists do with such information?

CONCLUSION

Our target article was intended to provide background knowledge to psychologists and other social scientists on the subject of heritability. This statistic, in many ways so basic, is both extremely powerful in revealing the presence of genetic influence and very weak in providing much information beyond this. Many forms of measurement error, statistical artefact, violation of underlying assumptions, gene–environment interplay, epigenetic mechanisms and no doubt processes we have not yet even identified can contribute to the magnitudes of heritability estimates. If psychologists and other social scientists want to understand genetic involvement in behavioural traits, we believe that it is going to be necessary to distinguish among these possibilities to at least some degree. Heritability estimates alone are not going to help us do this.

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