Commentary: Variation and Causation in the Environment and Genome

Eric Turkheimer

Department of Psychology, University of Virginia, Charlottesville, VA, USA. E-mail: ent3c@virginia.edu

Science is about causes, period. For too many years, mainstream behavioural genetics was based on a watery version of classical population genetics that entailed partitioning the variation of a trait into three (or occasionally a few more) components. I presume the basics of the process are familiar to readers of this comment. Using pairs of twins or other variation in genetic relatedness, variation in a trait can be partitioned into a component (denoted A) ‘attributable to’ (the vagueness of this half statistical, half biological phrase protected the field from recognizing its limitations) the additive effects of genes; a component called C, for common environment, attributable to environmental effects making children raised in the same family similar to each other, and finally a component E, attributable to environmental effects making children in the same family different.

Whether this exercise has any scientific content has been the subject of debate for more than a century, and here is a summary of why I think it does not: it is not about cause. Practitioners of the art wanted it to be about cause, in the sense that the relative magnitudes of the various components were supposed to tell us something about the importance of genetic and environmental causes underlying a trait, but they do not. The reason they do not, which appears at first to be a technical concern but which actually lies at the heart of the matter, is that biometric components are not invariant across the genetic, environmental and phenotypic variances of uncontrolled traits in their naturally occurring populations. The proportions of variance attributable to A, C and E depend on the variances of A, C and E, and the variances of A, C and E have no ‘true’ values to be estimated. In populations of cloned organisms, all differences are environmental; in a genetically diverse population of rats raised in identical laboratory conditions, all differences are genetic. In the real world of humans, in a given context everything is heritable to some extent and environmental to some other extent, but the magnitudes of the proportions are variable from situation to situation, and have nothing whatsoever to do with the causal properties of genes and environment for the trait in question, unless one is interested in the pointless null hypothesis that one of the components is zero. This message has taken 100 years to soak in to genetic social science, and it has not fully soaked in yet: not a month goes by without another outbreak of credulous surprise that one trait or another has turned out to be 50% heritable, often now at the new frontiers of population genetics in economics or politics.

Plomin and Daniels marked the beginning of the end of variance partitioning as a useful endeavour in human developmental science. The famous three-step research programme—quantify the effects of non-shared environment, identify the relevant non-shared variables and then assess their causal effects—represented...
a new direction for behavioural genetics. We know, in a very general way, that something non-genetic is making children in the same family different from each other, but what? What specific environmental events cause real developmental outcomes?

Putting it that way makes it clear that Plomin and Daniels’s famous question changed the field in another way as well. When the object of study changes from the decomposition of the variation of a phenotype to the identification of causes and effects, the field of study is enlarged from the insulated domain of twin pairs to the more causally relevant world of parents and their children. Twins had not been the object of behavioural genetic research because anyone was interested in how one twin caused outcomes in the other. Twins were simply a means to the end of variance partitioning; the interesting causal arrows, both genetically and environmentally, run from the genes and behaviours of parents to the development of children.

The work that followed from Plomin and Daniels’s call to action was an exercise in quasi-experimental identification of causal effects in a matrix of non-experimental familial associations. Suppose you have an observation that, in the population, maternal depression is associated with problems in the social development of children. This might occur because depressed behaviour in mothers ‘causes’ problems in children, but it also might not; there are two important classes of competing hypotheses to the causal interpretation. It might be that genes predisposing mothers to depression are passed to the mothers’ children, and predispose them to problems in social development. The important consideration is that under the genetic predisposition hypothesis, the association between mothers’ depression and children’s outcomes is not causal. Had the children been adopted away from their mothers at birth, they would have had the same risk for social development problems, because they would still have the relevant genes from their biological mothers. The other class of non-causal explanations of the observed association is environmental, specifically ‘shared’ environmental. If poor mothers are at greater risk for depression and poor children are at greater risk for social development problems, an association will be induced even if there is no causal relationship between the two.

The remaining possibility can be seen in two nearly equivalent ways. If genetic and shared environmental pathways between mother and child have been ruled out, the alternative is the non-shared environmental pathway. It is easiest to understand what this means by considering the difference between identical twin pairs as a concrete estimate of the non-shared environment. Suppose you have a pair of identical twin mothers, and one of them is depressed. This difference in depression is by definition non-shared environmental. The within-pair association between the mothers’ depression difference and the difference in the social development of the mothers’ children is the non-shared environmental association between depression and social development. Within maternal twin pairs, is the more depressed mother also the one whose children are at greater risk for problems in social development? Since most of the plausible uncontrolled non-causal confounds of the association are either genetic or shared environmental, confirmation that the non-shared environmental association remains significant after the A and C confounds have been controlled helps to convince us that the association is really causal. (It is not, however, probative, and there is ultimately no way to recover the epistemological certainty of the randomized experiment from non-experimental data. Specifically, there is always the possibility of ‘non-shared environmental’ confounds that explain the within-pair association.)

Equivalently, one can look at non-shared environmental associations as an embodiment of the co-twin control design. We are presented with a depressed identical twin mother who has a child with social development problems. Her non-depressed co-twin controls for certain classes of possible confounds of a causal interpretation of the association. Ultimately, then, Plomin and Daniels’s interest in the non-shared environment was based on an issue far more important than the quantification of biometric variance components. Asking about the non-shared environmental associations between developmental events is a way of asking whether the myriad non-experimental associations observed by developmentalists are still plausibly causal after they have been exposed to risk of disconfirmation via genetic and shared environmental confounds. Does non-experimental, correlational psychology, the softer of Cronbach’s two worlds, really work as a method of identifying developmental causes? That is what Plomin and Daniels were asking, and put that way it is no wonder that the question cut so deep.

Unhappily, the answer to the question has for the most part turned out to be no. I will only review briefly here my own contribution to the Plomin and Daniels phenomenon, in the form of a meta-analysis I conducted with Mary Waldron. We collected all of the studies published up until that time in which genetically informative data were collected on actual, observed environmental differences between and within families and their associations with actual, observed outcomes in children. The results were startling: although the population-based variance component called non-shared environment indisputably accounted for upwards of 50% of the variation in most outcomes, assessments of the effects of specific, measured environmental variables were rarely significant, accounting for a median of ~3% of the observed variation in specific measured behavioural outcomes.

Plomin and Daniels’s premise that a substantial proportion of differences among siblings is attributable
to the non-shared environment, combined with Turkheimer and Waldron’s finding that specific environmental differences among siblings account for practically none of the differences among siblings for specific outcomes, leads to a very specific conclusion. Something, and presumably something that can be broadly characterized as environmental, makes siblings, even identical twins, different from each other. But whatever that something is, attempts to decompose it into an additive collection of systematic environmental causes that produce systematic differences in outcome almost always end in disappointment. Non-shared environment is a catch-all name for a catch-all variance component comprising all the uncountable and uncontrollable events that accumulate over a lifetime to make us different from each other. As a result, a principle emerges: much of the variability of a ‘single’ variable is non-shared environmental, but the covariance among multiple variables is rarely non-shared among siblings, and for this reason most of the associations we observe between developmental events dry up and blow away when the appropriate familial controls are put in place. Developmental events are correlated within lives because they share a very general familial background, but plausible causation, in the form of non-shared environmental links among life events, is damnably hard to find.

Plomin’s powerful influence on the direction of developmental behaviour genetics did not end with this paper. Soon after Plomin and Daniels’s was published, the human genome project was reaching its conclusion, molecular genetic technology was making quantum leaps forward and Plomin’s attention was turning to what he would call ‘DNA’, meaning the human genome project was reaching its conclusion, molecular genetic technology was making quantum leaps forward and Plomin’s attention was turning to what he would call ‘DNA’,5 meaning the causal effects of actual genetic structures, as opposed to population-based aggregations of genetic variation. This quest has precisely the same structure as the Plomin and Daniels enterprise with the non-shared environment. Start with a variance component—in this case the endlessly replicated heritability of everything—and a resolution to decompose it into its individual causal effects. Then, the three steps of the Plomin and Daniels research programme can be transformed effortlessly into a description of genome wide association studies: quantify the overall effect of genes (already done); identify the relevant alleles, quantitative trait loci (QTLs) or single nucleotide polymorphism (SNPs) and document their causal effects.

And to the great surprise of almost everyone, the molecular genetic project has foundered on the same shoals of developmental complexity that sank the non-shared environment. The other thing that makes children raised in the same family so different, of course, is the 50% of their genes that they do not share. But are there causal effects of individual genes that make one sibling more depressed, intelligent or extraverted than the other? All the frustrations of the hunt for the real non-shared environment have recently been re-enacted in genomics, but this time with a gloss of high technology that has disguised the real problem. For example, in a recent special issue of Nature Genetics,6 conceding the difficulty of finding genes ‘for’ depression or intelligence or schizophrenia, researchers turned to something that really ought to work: height. Height has a heritability upwards of 0.9; it can be measured almost without error; it has straightforward analogues in lower organisms; and it can be acquired from tens of thousands of participants without great effort. And when all the 65 000 participants were pooled together, half a million SNPs each, the specific associations between SNPs and height accounted for about 3% of the variance. The unexplained genetic variation in traits has come to be known as ‘genetic dark matter’. It has been less often noted that the obstacles currently faced by genomics were foreshadowed by the long struggles of environmental social science to establish systematic environmental cause and effect relations between individual developmental events. Plomin and Daniels3 provided the bridge between the frustrations of environmental and genomic social science.

The conclusion of Plomin’s ongoing efforts to decompose reliable but vague biometric components into meaningful causal elements may not be what he wanted or expected, but it is nevertheless hugely important: individual differences in complex human characteristics do not, in general, have causes, neither genetic nor environmental. Complex human behaviour emerges out of a hyper-complex developmental network into which individual genes and individual environmental events are inputs. The systematic causal effects of any of those inputs are lost in the developmental complexity of the network. Causal explanations of complex differences among humans are therefore not going to be found in individual genes or environments any more than explanations of plate tectonics can be found in the chemical composition of individual rocks. Some new paradigm, unlimpsed at present, will be required before meaningful progress can be made on the causal structure of either the family dynamics or genomics underlying the parent–child relationship. This writer doubts that present company will be around to see that paradigm emerge, but when it does it is sure to be noted that Plomin and Daniels started us down the road that eventually led there.

Conflict of interest: None declared.

References
1 Cesarini D, Dawes C, Fowler J, Johannesson M, Lichtenstein P, Wallace B. Heritability of cooperative


5 Plomin R, Crabbe J. DNA. Psychol Bull 2000; 126:806.