INSIGHTS

PERSPECTIVES

GENETICS

Using nature to understand nurture

Genetic associations show how parenting matters for children's education

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Children resemble their parents in health, wealth, and well-being. Is parent-child similarity in traits and behaviors due to nature (the genes that children inherit from their parents) or nurture (the environment that parents provide for their children)? Answering this enduring question can directly inform our efforts to reduce social inequality and disease burden. On page 424 of this issue, Kong *et al.* (*1*) use genetic data from trios of parents and offspring to address this question in an intriguing way. By measuring parents' and children's genes, they provide evidence that inherited family environments influence children's educational success, a phenomenon termed genetic nurture.

Specifically, Kong *et al.* show that the part of the parental genotype that children

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Genetic nurture considers the influence of family environment on offspring.

do not inherit can nonetheless predict children's educational attainment. This genetic nurture effect is an indirect link between parental genotypes and children's characteristics, not caused by the children's own biology but rather by the family environment that covaries with parental genes. The concept of genetic nurture in human families extends previous work by behavioral ecologists and animal breeders on indirect genetic effects: environmentally mediated effects of one organism's genes on the phenotype of a related organism (*2*). For instance, one source of genetic variation in dung beetle body size is how large a brood mass the mother beetle produces (*3*). Interestingly, given how much of the animal research on indirect genetic effects has centered on offspring body size, Kong *et al.* found no evidence of genetic nurture on children's height and body mass index (BMI). For humans living in wealthy societies, genetic nurture might be more relevant for behavior and social achievements than for more biologically proximal outcomes such as body size.

Although the analyses of Kong *et al.* focus on a single child within a nuclear family, they are careful to remind us that family is more than one generation deep and often includes more than one child per generation. The environment that parents provide for their children could reflect the long arm of nurture by previous ancestors. And, siblings might create environments for each other. Genetic nurture could operate through any physical or social environment woven by genetic kin—a tangled web indeed.

The phenomenon of genetic nurture underscores that the results of genetic association studies cannot be interpreted as support for a biologically determinist account of human individual differences, as most social scientists who work with genetic data have stressed (*4*, *5*). Rather, results from genetic association studies are correlations that might point the way toward understanding causal mechanisms, but these mechanisms are likely to be complex and phenotype-specific. Genetic associations might depend on environmental context (*6*); for example, the alleles influencing educational attainment might differ between birth cohorts that have experienced different social and political institutions. And genetic effects can exert their influence via environmentally mediated channels, such as how teachers react to students with specific genotypes (*7*, *8*). Now, genetic nurture provides another compelling example of how tightly genetic and environmental mechanisms are entangled.

Genetic nurture also raises important methodological issues for future studies. Geneticists have long been concerned with population stratification (*9*), which is defined as the existence of systematic differences in gene frequency between groups that might also differ in environment and culture. Population stratification can induce a genotype-phenotype correlation that is, in fact, due to an unidentified group environment. The classic example is the chopsticks gene (*10*): Any genetic variant that differs in frequency between Asians and Europeans would come to be correlated with using chopsticks if population stratification were uncontrolled. Controlling for population stratification is typically accomplished by using statistical techniques that adjust for ancestry-specific genetic differences among people. However, there is no clear line between population stratification and genetic nurture, particularly once we realize that genetic nurture effects might themselves reproduce across generations: At what point does family history become ancestry? For researchers whose aim is to identify only those genetic effects that could be causally manipulated by changing an individual's own genotype, genetic nurture is, like population stratification, a source of false results.

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Genetic nurture also presents a new challenge for research designs such as Mendelian randomization (*11*) that aim to identify causal effects by using genes as if they were naturally occurring experiments. For example, a researcher might use the alleles associated with educational attainment to test whether going further in school has a causal effect on one's health. One of the assumptions of Mendelian randomization is that genes are not correlated with unobserved confounds, such as parental environment. The study of Kong *et al.* clearly shows that this assumption can be wrong. If alleles identified in genetic association studies are not, in fact, independent of the parental environment, then Mendelian randomization studies might detect causal effects that are not really there.

Yet, genetic nurture does not undermine the value of genetic associations for prediction purposes. For example, researchers who want to control for genetic effects in order to obtain more precise estimates of an environmental or medical treatment in a randomized controlled trial (*12*) do not care why the genes are correlated with the outcome. All that matters is that the genes used as control variables predict as much variance as possible in the target outcome.

Furthermore, for many scientists nurture, not nature, is the phenomenon of interest. The study from Kong *et al.* provides these scientists with a fascinating new tool for investigating the effects of the family environment. Until now, the primary tools to disentangle the effects of a parent's genes from their actual parenting were adoption studies (*13*) and children-of-twins studies (*14*). However, collecting such data is difficult, and these study designs rarely represent the entire range of environments. Kong *et al.* capitalize on the same logic as an adoption study. The nontransmitted parental alleles function like the genotype of an adoptive parent, in that they help to shape the rearing environment but are independent from the offspring's genotype. Data sets with genotyped trios and high-quality measurements of the family environment are, unfortunately, still rare. But because of low genotyping costs, the trio design developed by Kong *et al.* could become a valuable and cost-effective research paradigm for scientists interested in understanding the impact of family environments on human flourishing.

The ingenious analysis of genetic trio data by Kong *et al.* reminds us yet again of the methodological problems that plague scientists as we try to understand individual differences in complex human behaviors and diseases—but also illustrates how understanding nature can provide us with new tools for studying nurture. ■

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