

Do The Ends Justify the Genes?

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Sex Differences in Variability for Cognitive Measures

Do the Ends Justify the Genes? (Commentary on Johnson et al., 2009)

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**ABSTRACT**—Theories about the origin of cognitive sex differences must address differences in three portions of ability distributions: low-tail variability, high-tail variability, and mean values. In addition, genetic theories must provide evidence that these three types of differences are (at least in large part) caused by alleles that are located on the *X* chromosome. It is well-established that there are more mentally retarded males than females, and this disparity is attributable to genes located on the *X* chromosome. By contrast, there are no known "intelligence genes" that can provide a parallel explanation for differences in variability in the high ability tail of distributions. Mean differences between males and females also defy any *X*-linked hypothesis about average intelligence because females and males excel on different cognitive measures. Thus, we conclude that *X*-linked genetic explanations of cognitive sex differences can only be substantiated as a causal explanation for the excess of males diagnosed with mental retardation.

Here are the facts on the genetics of human intelligence.

1. At the population level, intelligence is heritable. How heritable it is doesn't much matter.

2. At the molecular level, there are a number of alleles and mutations associated with low IQ.

This statement requires a little parsing. An observation that an allele is associated with low intelligence actually involves two statements about effect size and a hypothesis about etiology and development. The first statement about effect size involves a mean difference (e.g., individuals with allele *A* at a particular locus have a mean IQ of some value, whereas those with allele *a* have a different mean value). Notice that, in general, any allele that is associated with low intelligence has to be paired with another one associated with higher than average intelligence. The second statement about effect size involves percentage of variance explained, which is a function of the mean difference plus (or more accurately multiplied by) the frequencies of the alleles. By far the most common configuration, in fact the only configuration that has been observed reliably, involves a very rare allele associated with low intelligence and a much more common one associated with intelligence that is not discriminably different than average. This configuration produces a large effect size in terms of mean difference between allelic values, and a small effect size in terms of variance explained. This is what is meant by the statement that most known variants are associated with low IQ: Because the detrimental alleles are so rare, the complimentary alleles do not need to be associated with noticeably greater IQs in order to maintain the population mean. The hypothesis is that the association between ability and rare alleles of large effect is more than a mere association—it is causal and part of an identifiable developmental process. The observation of a large effect size for an allele implies a causal pathway from the allele,

presumably via neural development, to the brain and eventually to impaired intelligence.

3. Many of these detrimental alleles occur more frequently in males than females.

Males are therefore at greater risk than females for many forms of mental retardation.

4. Many such detrimental alleles are located on the X chromosome—more than would be predicted by chance.

5. There may also be a corresponding, but much smaller, overrepresentation of males at the high end of the ability distribution, independent of any gender difference in the mean.

These facts are well-known and relatively uncontroversial, with the possible exception of the last. On this last point, ironically, Johnson et al. (2009, this issue) ended up convincing us that the evidence for high-end gender differences in variances is weaker than we might have thought. They cite no independent evidence for the phenomenon, and their analysis of CAT and SMS scores is unconvincing, particularly because the numbers they report are confounded with mean differences that are not very clearly quantified. Assuming that tail probability ratios, which are never defined, represent the male–female ratio in the specified portion of the combined distribution, how large a value is unusual, and what do they make of the fact that the upper tail ratios are negative for verbal cognitive ability tests, on which females probably had a mean advantage? A quantitative model of group differences in low- and high-end variance differences would be very useful.

In any case, Johnson et al. provide an excellent summary of the known evidence on the first four points. The key questions, however, for both the genetics of intelligence in general and for consideration of the Johnson et al. article in particular, involve whether or how what is known about detrimental alleles can be extended to explain either normal variation or gender differences in intelligence or—even more challenging—unusually

high intelligence.

Notice that all the deeper controversies begin at this point. The extent to which males are at greater risk for mental retardation and the possible X-linked mechanisms that might confer that risk are both interesting empirical questions about which there is much more to be known, but they do not arouse fundamental philosophical or ethical concerns about the nature of human ability or the relationship between ability and gender. Our philosophical intuitions change when it comes to the determination of normal or high ability, and so do the empirical facts. In contrast to the many detrimental alleles and mutations that have been discovered for ability, many of them known long before the completion of the human genome, no alleles reliably associated with higher intelligence have been discovered, despite extensive and well-documented efforts to find them. So there are no rare alleles that confer high intelligence, and there are no common alleles that are known to be reliably associated with smaller advantages in ability. Thus there are, so far, no known neurodevelopmental pathways between the genotype and normal, let alone unusually high, intelligence. As far as anyone knows, normal intelligence emerges out of the complex interplay (to use the popular and intentionally vague term for such processes) of additive and nonadditive effects of many genes and many environments, with no single gene or environment possessed of a large enough effect to be reliably specified independent of the others.

The somewhat mysterious nature of the causal processes underlying normal variation in intelligence is a crucial part of our ethical intuition: Because normal intelligence emerges out of a complex background of genetic and environmental influences, it cannot be appropriated by particular groups of people and is not amenable to easy remediation or amelioration. The asymmetry in the explanation of low, normal, and high intelligence is reflected precisely in the domain of gender differences in ability.

Gender differences in retardation are well-established and uncontroversial; consideration of gender differences in normal or high intelligence requires carefully worded introductions about values in science and leads to the dismissal of presidents of great universities.

We should not be too quick to believe that such cautions and unfortunate outcomes are only the result of delicate sensibilities unable to maintain the distinction between values and science. There are profound differences between the ethical implications of genetic explanations based on large-scale structural effects of known genes, as opposed to the complex genetic and environmental background null model that is all we have to go on now. The null model allows us to accept the observed gender differences in the mean and variance of ability at face value and to agree that this outcome must involve genetic and neurological processes in one form or another while maintaining the expectation that the current status of male and female abilities are contingent on a complex web of small and unknown genetic and environmental effects that are prone to shift as various aspects of the system change. By way of comparison, no one expects that the low IQs of persons with Downs syndrome are a contingent consequence of a complex status quo. We understand that the developmental consequences of trisomy 21, while perhaps not immutable, are wired deep into the developmental system and unlikely to change short of very radical interventions. Gene therapy might work someday, but pills and special education programs, as helpful as they might be with the symptoms of Down syndrome, are unlikely to address the core deficits.

Despite Johnson et al.'s careful review, as their argument proceeds from rare genetic syndromes to processes in the normal range, it becomes almost entirely speculative. How could it be otherwise? As no major genes of any kind have been shown to be associated with normal or high ability, how could they possibly form the basis of

gender differences or be located on the *X* chromosome? Johnson et al. do entertain one possibility other than the existence of major genes on the *X* chromosome. Under the radically polygenic model that is the only plausible alternative to a major gene, perhaps the observed gender difference in variance (which is smaller than would be predicted if all the relevant genes were on the *X*) can at least be used to estimate the proportion of the uncounted genes of small effect that reside on the *X* chromosome. The resulting exercise in quantitative genetic algebra is interesting, but it essentially requires an assumption that nothing else—not other chromosomes and not the environment—has anything else to do with the variance phenomenon. The authors acknowledge that the result could take almost any value at all in the parameter space.

So the Johnson et al. argument consists of an observation that there are genes of large negative effect for ability, that these genes are disproportionately located on the *X* chromosome, and that males are therefore at greater risk for many of the resulting syndromes. They then speculate that either (a) there are undiscovered genes of large positive effect for ability and that these might be located on the *X* chromosome as well, or (b) if there are no genes of large positive effect, genes of small effect might also be disproportionately located on the *X* chromosome. There is currently no evidence at all for the first hypothesis regarding either the existence or location of genes of large positive effect. And although there is nothing inherently wrong with scientific speculation when it is clearly labeled, the ethical implications of discovering a gene of large positive effect will be profound and, we expect, unhappy. And if genes of large positive effect turn out to be the cause of observed differences between the genders, they will be examined for other group differences as well, with even more dire implications. Science will proceed either way, but in the meantime the lack of evidence for such genes is not exactly bad news. In our view, the second hypothesis is much more likely to be true, and the stakes

are much lower. Perhaps the "chromosome-wide association scan" Johnson et al. propose would show that the tiny effect sizes that are identified for alleles associated with ability are a little higher on the X chromosome than they are elsewhere in the genome, and perhaps that could explain the high-end difference in variation, if indeed that phenomenon continues to hold up. This would be a useful scientific advance that would not entail the world-changing consequences of major genes for high ability.

#### REFERENCES

Johnson, W., Carothers, A., & Deary, I.J. (2009). A role for the X chromosome in sex differences in variability in general intelligence? *Perspectives on Psychological Science, 4*, xxx–xxx.