

count for 0.50 of the variance in general cognitive ability, shared environmental agents account for 0.33, nonshared environmental agents 0.17, and error of measurement 0.10. Thus, genetic agents are indeed important in the determination of intellect and its closely related traits (such as working memory and spatial skills), but environmental and experiential agents are also critical.

Such a conclusion about the contributions of genetics to intellectual function validates and empowers the search for QTLs that underlie the genetic agents for complex traits (7). The figure is an adaptation of a cartoon from the work of Charlie Sing that originally described the contributions of genes to the differences among individuals in developing coronary artery disease (7). It substitutes a different end point—intellect—for coronary artery disease and shows the general relation among genes, the environment, and the passage of time in determining human traits. An article was published in 1996 with the title "Molecular genetic research on IQ: Can it be done? Should it be done?" (8). The answer to both questions was yes, and the authors went on to start the study with an association strategy, fully aware of the odds against finding genes that underlie IQ. But rapid improvements in the numbers of identified genes and markers permit a dense map of the human genome, a minimum requirement for identifying any gene that by itself may account for as little as 1% of the phenotypic variance, as is the case for the genetic determinants of variation in intellect. A stringent statistical conscience must be in place for such expeditions into the causes of complex diseases and traits (9) so as to avoid false promises and disappointments; statistical allowances must be made for genomewide scans, whether conducted or only implied.

What do we know so far about the specific genes? The genes in the cartoon, depicted as contributing to cognition, are from a larger set, all implicated by linkage or association strategies in humans, mouse, or *Drosophila* in some aspect of brain functioning relevant to cognitive abilities. Some appear to have a role both in single major locus conditions as well as be potential QTLs for IQ or cognitive decline (10). Various hypothetical "endophenotypes" are shown that mediate the impact of gene products on emergent systems and set the stage for being expressed on the "reaction surface" (11). Each person and each confirmed facet of cognitive ability will require its own such blueprint, but the constancy of heritability for *g* after adolescence reflected in the new information about octogenarian twins suggests that in this case we may not need to concern ourselves with marked age-dependent effects (12) that would frustrate QTL searching. Data from twin studies for complex traits can be used to screen for "candidate traits" that can become the focus for connecting to candidate genes. The high

heritabilities of traits such as general cognitive abilities and diseases such as schizophrenia tell us where to invest our efforts first.

Galton is credited with the enduring alliterative phrase "nature versus nurture," likely inspired by *The Tempest*, wherein Prospero says of Caliban (13): "A devil, a born devil, on whose nature nurture can never stick, on whom my pains, humanely taken, all, all lost, quite lost" (4.1.187–190). The true genetic nature of humans has still not been defined, but if you are looking for a place to invest your intellectual capital and have a high tolerance for risk, then the search for QTLs for complex behavioral traits and diseases can be recommended as a long-term buy—but beware of the near-term volatile oscillations in your investment.

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13. W. Shakespeare, *The Tempest*, 4.1.187–190. Caliban's mother was a witch, his father a devil, making the latter a dominant gene character in the Bard's view.



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<http://ispec.ucsd.edu/intro.html>

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Edited by David Voss

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