

pression. Baron, for example, places the disease gene close to the gene for color blindness, on the long arm of the X chromosome. Other researchers have reported that the gene is at the opposite end of the X chromosome. Gershon and his colleagues do not find evidence for X-linkage in their families at either end of the chromosome.

Despite the discrepancies, most researchers still contend that depression, particularly manic depression, has a genetic basis. The notion was fueled by a 1987 report by Janice Egeland of the University of Miami School of Medicine in Florida, David Housman of Yale University School of Medicine in New Haven, Connecticut, and their colleagues. They reported that a dominant gene at the tip of the short arm of chromosome 11 conferred "a strong predisposition to manic depressive disease" (*Nature*, 26 February, 1987, page 783). In the same issue, however, two other reports failed to find the same linkage (pages 805 and 806).

Also, recent studies of families with Alzheimer's do not confirm that the disease gene is on the region of chromosome 21 reported by Gusella and his colleagues (*Science*, 20 February 1987, page 885). And new studies, some still unpublished, fail to find that a gene predisposing people to schizophrenia is on chromosome 5 (*Science*, 18 November 1988, page 1009). Do the discrepancies in data mean that researchers are wrong, or do they point to evidence of genetic heterogeneity?

"You shouldn't come to the conclusion that it's heterogeneity if you haven't replicated someone else's data," says Gershon. The first step is to confirm the linkage in one study. Then researchers have to do specific statistical tests to show that a particular disease has multiple genetic causes.

The ultimate test, however, is isolating the actual disease-causing genes. "The only way to prove heterogeneity is to localize or isolate all the different genes," says Gusella. "And this would be tremendously difficult with current approaches."

Some investigators are now suggesting a revision in the statistical criteria used to establish linkage of a disease gene to a particular chromosome. Linkage analysis depends on the use of chromosome markers that are thought to be close to the disease gene. The markers are either RFLPs (restriction fragment length polymorphisms), which are short, detectable stretches of DNA that have no known function, or other genes of known function. Researchers "score" how often the symptoms of disease occur together with its markers. Currently, a logarithmic ratio (called a lod score) of 3 is taken as evidence for linkage. It means that the likelihood is 1000 to 1 that the

pattern of the disorder and the markers in a family pedigree result from gene linkage rather than from random distribution. It is a measure that the disease gene is linked to, and therefore physically close to, the marker under study. Gershon thinks that a higher lod score should be required to establish linkage in most psychiatric disorders because of genetic heterogeneity or variation in the degree to which someone is affected.

Kenneth Kidd of Yale University School of Medicine raises another fundamental issue about methodology. "A linkage analysis cannot be done without specifying a mode of inheritance, without specifying that a single gene causes the disease, without specifying how penetrant the gene is," he says. And for neuropsychiatric disorders this information is simply not known. Instead, researchers make assumptions about these parameters before they begin to do the statistical analysis of family pedigree data.

"We are trying to associate a known gene marker with an unknown, hypothesized gene," Kidd says. "And the results we get are correct or incorrect to the degree that our assumptions are correct."

Everyone agrees that more data are required to resolve present inconsistencies. Ideally, researchers will be able to find several, large, multigenerational families that share a common genetic defect and exhibit similar behavioral symptoms. Failing that, they will collect data from many smaller families. The task has recently been undertaken at NIMH in its Genebank initiative.

Researchers who seek the chromosome location of a disease-causing gene ultimately want to find the gene itself and somehow correct the defect. Whether they ultimately accomplish this by gene therapy or by improved treatment remains to be seen. In either case, the overall goal now seems to be feasible.

■ **DEBORAH M. BARNES**

More Math Means More Money

If earning potential is your criterion in picking a spouse, a good place to start is by counting your lover's college math credits.

There is a positive correlation between the number of mathematics courses a person takes and earnings in the first decade of employment, according to two researchers at the U.S. Department of Education. Clifford Adelman and Nabeel Alsalam have analyzed the mathematics component of a data set known as the National Longitudinal Study, which tracked a sample of young people from high school graduation in 1972 to their early thirties in 1986.

Adelman and Alsalam presented their findings at a symposium on mathematics education and U.S. industrial competitiveness, sponsored by the Mathematical Sciences Education Board of the National Research Council. Employers recognize the importance of algorithmic and algebraic thinking on the job, Adelman says. "Our study shows how many people are prepared to do that."

Not surprisingly, students who took more mathematics in high school or college earned substantially more than others in their first decade of employment, Adelman and Alsalam find. The relationship is particularly strong for men. It is strong for women as well, but women studied substantially less mathematics after high school, and at more basic levels. The best predictor of high income is earned credits in calculus and advanced mathematics. "Baldly stated, more math means more money," the study says.

It is somewhat surprising, though, how

little mathematics the sample of students took in college. Among those earning bachelor's degrees, 62% earned six or fewer math credits (three credits roughly equal a one-semester course)—and 21% studied no math at all, even when computer science and statistics courses taught in other departments are included.

On the other hand, there seems to be little relationship between the amount of mathematics studied in high school and the number of math credits earned in college. Some of this is due to colleges filling a void: 30% of all earned college math credits were in precollegiate-level courses. (The figure is 50% for 2-year colleges and 22% for 4-year colleges.) A higher percentage of business and education majors studied precollegiate mathematics than did students majoring in other fields.

The National Longitudinal Study consists of data on a sample of 22,500 students who were high school seniors in 1972, with follow-up survey data from 1973, 1974, 1976, 1979, and 1986, and a postsecondary transcript sample for 12,600 members of the original sample who attended college or other institutions at any time up to February 1984. The 1986 survey contained career data for 12,800 members of the original survey, with 7,500 of these overlapping with the transcript sample. Mathematics is the first course area to be analyzed from the study.

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