Potts bases his estimations on the physical state of the fossilized bone fragments, a measure that was developed a few years ago by Anna K. Behrensmeyer, also of the National Museum. Under the influence of daily fluctuations in temperature, humidity, exposure to sunlight, and bacterial action on organic material, fresh bones pass through a series of stages of deterioration. For instance, initial fine cracks eventually become more extensive and abraded; layers of surface bone begin to peel off; and finally the whole thing disintegrates. The process of deterioration, which takes about 15 years from first to last stage, is halted once the bone is buried.

Now, if all the bone had been deposited at the various Olduvai sites within very short periods of time, as would happen with a typical hunter-gatherers' home base, then the degree of deterioration in the individual pieces in each site would be roughly similar. In fact, Potts finds that there is a considerable spread of stages of deterioration, showing that bone deposition took place over a 5- to 10-year period. He also analyzed bones from the den of a spotted hyena in Kenya, and found a similar pattern.

Potts is careful to point out that the similarity in the dynamics of bone deposition between the Olduvai sites and the spotted hyena den should not be taken to imply that the Olduvai hominids were more like hyenas than humans. Instead, he suggests that the sites might have been formed in the way they apparently were because they included a cache of raw material for making stone tools. Because such material is often not widely distributed, it would have made sense to make collections of it, which would then become the focus of occasional butchering events. Such an activity could indeed have been carried out intermittently over a period of several years.

Archeological sites further north, at Koobi Fora in Kenya, generally do not have the appearance of the long-term bone accumulation seen at Olduvai. Although deposition analysis has not yet been carried out on them, some do look like briefly occupied sites. Potts points out that these sites are later in time than those at Olduvai—dated at about 1.5 million years—and therefore might be the work of more advanced hominids. But it is possible that a difference in environment, which includes availability and nature of raw material for making stone tools, might have some influence too. ■

ROGER LEWIN

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Manic-Depression: Is It Inherited?

Preliminary evidence from a study on the Amish indicates that manic-depression might be caused by a single dominant gene

It sounds almost simplistic. Mental disorders are complex and relatively common in the population. It would be too much to ask that their genetics be straightforward, that they be caused by single aberrant genes.

Yet there is a precedent. Huntington's disease is caused by a single gene and whoever inherits the gene sooner or later develops the disease. In about half of all cases, the first symptoms of this progressive neurological disease are psychiatric ones. Patients may be depressed or irrational, forgetful or disoriented. Those who do not start out with psychiatric symptoms start with movement disorders—clumsiness and an unsteady gait. So the example of Huntington's disease at least raises the possibility that complex psychiatric syndromes are caused by single genes.

No one expects the genetics of true psychiatric disorders to be as straightforward as that of Huntington's disease. But there are reasons to believe that some psychiatric disorders are largely inherited and that the means exist to find the genes involved. In particular, researchers are on the trail of a gene that may cause many cases of manic-depression.

As Elliott Gershon of the National Institute of Mental Health points out, it has been suspected for years that there is a strong genetic component to manic-depression, which also is called bipolar disorder. For example, if one identical twin has manic-depression, the other has a nearly 80% chance of having it too. If one member of a pair of fraternal twins has the illness, the other member has about a 20% chance of having it. When adopted persons with manic-depressions were studied, investigators found that more than 30% of their biological parents also had manic-depressions, but only 2% of the adoptive parents did.

But it is difficult to go from studies such as these to a search for a gene that causes this mental illness. What would be most useful is large families whose members develop the disease, such as the families studied by the Huntington's disease researchers when they found a genetic marker for that disease. The researchers begin with blood samples from family members. Using the tools of molecular biology, they then chop up the DNA from these blood cells. Then they use molecular probes to search for a piece of DNA so near to the manic-depression gene that it is inherited along with it. If such a genetic marker is found, researchers can start homing in on the gene itself.

Fortunately, in the case of manic-depression, researchers actually have such large families. Living in Lancaster County, Pennsylvania, are 12,500 Old Order Amish, an isolated group of people who are descended from around 50 couples who arrived in Pennsylvania from Germany between 1720 and 1750. They have large families, live by farming, and avoid contact with the rest of the world. Most important for geneticists, the Amish, because they have isolated themselves from the rest of society, constitute a closed population.

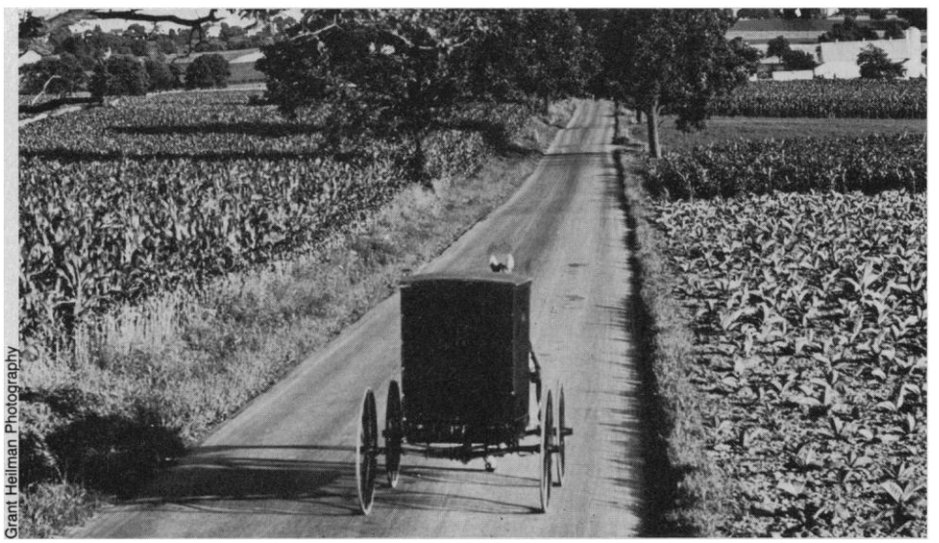
An extensive genetic study of the Amish is headed by Janice Egeland of the University of Miami School of Medicine. Egeland, who lived among the Amish for years, finds that although the Amish as a group have no more mental illness than the rest of the population, they do have social values that make mental illnesses easier to diagnose.

Alcohol and drug abuses, for example, are unheard of among the Amish. Psychiatrists suspect that many cases of depression and of manic-depression in the non-Amish, especially among men, are hidden by alcoholism. There are virtually no crimes or acts of violence in the Amish community, so the increased death rate from suicide that is associated with manic-depression can be ascertained.

Egeland, who is a behavioral scientist, called on psychologist Jean Endicott of Columbia University College of Physicians and Surgeons and a team of four independent psychiatrists to diagnose manic-depression in the Amish. "The diagnostic procedure is rather elaborate," says Endicott. She and the four-member psychiatric review board independently receive clinical data and independently make diagnoses. Because their diagnostic criteria are very specific—they use the well-accepted Research Diagnostic Criteria, which were written by Endicott, Robert Switzer of Columbia University, and Eli

Robbins of Washington University in St.Louis in 1973—they usually agree on diagnoses. "We have very good agreement," Endicott says.

The Amish provide classic descriptions of symptoms of manic-depression. Describing depression, for example, a woman told Endicott that her brother had spells when he "seemed down." Endicott asked how she could tell and the sister remarked that he usually played with his children and was



Grant Heilman Photography

Amish families live as they did two centuries ago

interested in his dogs. Now, the sister said, he just sits after work and stares into space, he no longer laughs, and he does not pay attention to what is going on around him.

When an Amish man is manic, his friends and relatives will say that he talks so fast that no one can understand him, that he is up all night and on the go, that he drives his horse and buggy too fast, and that he is loud, boastful, and intrusive. They frequently say the man has a driven quality, "as if he was running too fast," according to Endicott.

In order to make diagnoses of depression, for example, the team of investigators look for evidence that a person has four or five of nine symptoms. These include sleep disturbances, changes in energy level, a pervasive loss of interest in former pleasures, appetite changes, and a preoccupation with death or dying. These symptoms must persist for at least 2 weeks for a definite diagnosis of depression.

The Amish themselves had noticed that manic-depression seems to run in families. It was "in the blood," they said. In fact, the 26 suicides reported since 1880 occurred in just four of the extended families. Now David Pauls and his colleagues at Yale University School of Medicine have evidence from the pedigrees and diagnoses supplied by Endicott and her associates and by Egeland that, at least in this population, manic-depression seems to be inherited as though it is carried by a dominant gene with incomplete penetrance, meaning that not everyone who inherits the gene develops the disease. Pauls estimates that 35 to 55% of those who inherit the gene eventually develop manic-depression.

Pauls and his associates used a mathematical model to decipher the inheritance patterns of manic-depression in the Amish. Using computer programs based on population statistics, Pauls says, he tried to "see if fairly simple genetic mechanisms could account for inheritance patterns seen in the families. We wanted to see if the pattern could be explained by a single gene." Essentially, a disease that is carried by a single dominant gene will show up in each generation. A disease that is caused by a recessive gene, such as cystic fibrosis, will almost never show up in subsequent generations. Manic-depression appears in virtually every generation of the affected Amish families.

If manic-depression were like Huntington's disease, which is 100% penetrant, everyone who inherits the gene would get the disease. So, on average, half of all the children of an affected parent would get the disease. With manic-depression in the Amish, however, only about a quarter of the children of an affected parent get the disease, so the disease is said to be incompletely penetrant. What this means, says Pauls, is that "you may have the gene, but because of the effects of other, modifying genes or factors in the environment, you may not express it."

The next step is to start looking for a genetic marker. So far, Pauls, David Housman and Daniela Gerhard of the Massachusetts Institute of Technology have preliminary evidence that the gene may be on chromosome 11. "We didn't pick chromosome 11 for any particular reason except that we were already doing recombinant studies on chromosome 11 and once we had these data it seemed obvious to use them [in looking for a manic-depression gene]," says Gerhard. The MIT researchers did not expect the gene to be on chromosome 11 but, says Gerhard, "we reasoned that it would be useful to know where the gene *isn't* as well as where it is." To their surprise, they could not rule the chromosome out. The group also looked at many sites on other chromosomes and concluded that the manic-depression gene probably is not there.

Although suggestive, the chromosome 11 data are far from conclusive. As more data are analyzed the linkage may not hold up. "This would not be the first time that linkage data have gone through the floor," Gerhard says.

Suppose the manic-depression gene found in the Amish really is on chromosome 11. Will that be the end of the story? Pauls and Housman think not. Since manic-depression is very common in the general population, the researchers suspect that more than one gene may be involved. To determine whether other genes cause manic-depression, investigators will have to look at families other than the Amish.

Nonetheless, an understanding of the function of the gene they are now tracking may lead to effective strategies to find other manic-depression genes, according to Housman. "If we can identify an enzyme in a neurotransmitter pathway, for example, then it would be logical to look for other defects in that pathway," he says.

The real payoff from this work, says Housman, is that it should enable researchers to "get to the gene level to understand the physiological basis of this illness. It is a tremendous mystery what the biochemical basis is. And our treatments are far from perfect. But we don't really understand what's going on. That's what's most important." ■ GINA KOLATA

This is the third in a series of articles on the development of genetic tests to determine susceptibility to disease. The first two articles appeared in the 18 April and 27 April issues.

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