The Role Of Ancient DNA In Modern Traits

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An international team of researchers examined 732 post-mortem brain samples and identified variations in DNA associated with different psychiatric conditions, which they cross-referenced with data from large genetic studies. The research appears in Nature Communications, May 22, 2024.

In a summary of their work for a nonspecialist audience, three of the study authors report that their research is the first to show that ancient viral DNA is one of the avenues through which genetic susceptibility to psychiatric disorders may occur. They are careful not to attribute causality here, but to note that their findings "suggest" a link that deserves further exploration.

Human Endogenous Retroviruses

The ancient viral DNA is called human endogenous retroviruses, or HERVs, and makes up about 8 percent of the human genome. HERVs are DNA sequences that originated as viral infections millions of years ago and evolved in mammals through genetic mutations and deletions over time. Retroviruses are those that infect cells by inserting a copy of their own genes into the cell DNA.

First identified in the 1980s, HERVs have been characterized as "viral fossils"that continue to be passed on to modern generations. At first, HERVs were considered

to be “junk DNA,” with no known functions. As genomic technology advanced, scientists identified some specific roles for HERVs, such as producing RNA (ribonucleic acid) molecules that lead to proteins, and possibly regulating neighboring genes.

Most HERVs are thought to be inert, but some are known to play an active role in human physiology. For example, two known beneficial HERVs are those involved in the formation of the placenta and in embryogenesis, helping to make pregnancy possible. Other HERVs have been detected in some types of cancer, and research is beginning to look at how to target and possibly control these HERVs to treat the cancer.

HERV Variations and Mental Illness

The new findings reported in Nature Communications looked at how variations in HERVs are involved in regulating neighboring neurological genes in specific, finely mapped locations in the genome known to be associated with psychiatric conditions. Their approach identified HERVs in the adult brains of Africans and Europeans who had a psychiatric diagnosis at the time of their death.

“It is not clear yet how the expression of the high confidence risk HERVs may play a role in psychiatric disorders,” the authors write. However, they found that some of the 1,238 HERVs identified in the brain were associated with “risk for complex psychiatric traits.”

The new research is important for advancing our understanding of mental illness and possibly finding new ways to treat it. Older studies dating back to the 1960s identified a link between genetics and mental illness, but no specific mechanism for heritability. Much of the research came from adoption and twin studies carried out in Denmark over a decade by a joint U.S. and Danish research team.

Led by psychiatrist Seymour S. Kety at Harvard Medical School, the Danish studies spanned 1968 to 1994. Although the studies are generally accepted in the field as supporting a genetic basis for schizophrenia, there are some who challenge this, questioning the methodology and subjective interpretation of the data. Criticisms of the Danish twin studies point to the fact that control group adoptees were placed in more favorable environments than the study subjects, that the study did not include environmental variables, and that the definition of schizophrenia and its spectrum was not rigorous.

More recently, scientists have used genome-wide association studies to analyze genetic links to psychiatric disorders. A 2023 review of these studies stressed that "…there is no single 'disease-gene' for psychiatric disorders, but thousands of genetic variants that act together and collectively influence the risk of illness. Given that most of these genetic variants are commonly occurring, every human being has a genetic risk to each psychiatric disorder, from low to high."

Another factor to consider is the possibility of infection from viruses or bacteria that triggers neurological, immune system, and psychological changes, in association with schizophrenia in particular.

I*mplications for Human History*

We know the effects of severe mental illnesses and how society has dealt with those persons severely affected, often in inhumane ways. But are there any possible benefits to individuals who may have smaller numbers of genetic variants linked to a particular mental disorder?

Stanford biologist Robert Sapolsky has a provocative answer to this question, in his analysis of how individuals with a moderate number of genetic links to schizophrenia might have provided the ancient basis for modern religions.

Sapolsky begins a Stanford University class on the biological underpinnings of religiosity by outlining the positive adaptive value for people who have some genes linked to certain genetic disorders, but not enough to cause full-blown illness. Sickle-cell anemia, for example, conveys protection from malaria to those with some of its marker genes. Similarly, cystic fibrosis, crippling when full-blown, is associated with protection from cholera and dehydration in those who have some of its marker genes. In that lecture, Sapolsky makes the point that it's about too much allocation/expression of the genes. Just the right amount, and you have protection. Too much, and you have a chronic health issue.

In the same way, Sapolsky says, individuals who are on the spectrum of schizophrenia may have used their particular qualities of schizophrenia—seeing visions, hearing voices, obsessive-compulsive ritualistic behavior, intrusive thoughts, anxieties, and superstitions—positively in ancient societies.

Sapolsky bases his analysis on the data from the adoption studies in Denmark by Harvard psychiatry professor Seymour S. Kety and his U.S. and Danish research team, noted above. The Danish adoption studies found that schizophrenics often

had family members who were a little "off," not severely ill, but not quite "normal"—people whom they termed schizotypical.

Religion, Good Works, and Metamagical Thinking

In the appropriate context, Sapolsky says, a schizotypical individual could play a unifying role in an ancient society. Think of the shaman or medicine man in more recent native cultures, or the founding stories and rituals of today's Christian, Jewish, Muslim, and Eastern religions, which all have similar elements.

Sapolsky reviews in detail the similarity in the outline of the ritual, numerology, and anxiety-calming behavior of religions. For all religious beliefs, the description of religious behavior—its "structural steel" and "building blocks" as Sapolsky terms it—is on the mark. How the beginnings of theology mesh with the particular qualities of schizotypicals, from the metamagical to ritualist, is eerily recognizable.

The positives for society also ring true: Good works are motivated, and ritual behaviors (think holiday celebrations) are unifying and calming. Religious believers today, Sapolsky notes, live longer and are healthier than nonbelievers.

As Sapolsky emphasizes, a schizotypical person has to get it "just right" in order to succeed, and a society has room for just one such person at a time. Failed schizotypical leaders often branch off into cults, and have bad endings, like the Manson or Waco cults.

Sapolsky also reminds us that today's society still harbors metamagical thinking. A Gallup poll he quotes, for example, found that 25 percent of Americans believe in ghosts and 50 percent believe in the influence of the devil.

A New Frontier?

Sapolsky's presentation on the biological underpinnings of religiosity is mesmerizing. If you have an interest in human behavior on any level, the ideas provoke more serious thinking, which is always a good thing.

This area of research and discussion is a sensitive one, with considerable history associated with some of humanity's darkest chapters; genetic determinism in the form of eugenics and racism was an ugly feature of the World War II era.

How ancient HERVs (and modern microbial infection) influence the genetics of

schizophrenia and other mental illnesses is an important subject for research and a necessary one if we are to find better treatments.

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Source: Human Bridges

Credit Line: This article was produced by Human Bridges.