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Schizophrenia: An Evolutionary Explanation for a Maladapted Modern Environment

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The Paradox of Inheritable, Detrimental Disorders

Schizophrenia is a particularly fascinating topic in the realm of evolution because it persists in the population despite its detrimental effects. In an evolutionary context, the high mortality rate and reduced fertility rate in patients with schizophrenia are at odds with the fact that there is a genetic component and high prevalence rate associated with this disorder.[1]

A Unique Human Disorder

Early evolutionary theories of schizophrenia focused on characteristics unique to the human species such as intelligence, language, social relationships and creativity.

It has been argued that the genetic components underlying language and schizophrenia are related, since these have been present in populations separated for thousands of years. In support of this, schizophrenia does involve an indiscriminate sense of external (speech) versus internal language (thought).[2,3] However, schizophrenia involves much more than language and other theories have tried to account for changes in social behaviour and executive function.[4] For example, humans, even more so than other primates, are able to interact with their social environment in complex ways and one suggestion has been that schizophrenia may arise as a disconnect with a harmful social world.[5,6]

The creativity aspect of schizophrenia is one that has long piqued curiosity on potential benefits to mental health disorders. Relatives of people with schizophrenia are more likely to hold positions in academic or artistic professions and have been found to have greater cognitive flexibility.[7,8,9]

Theories related to creativity include Horrobin's neuronal membrane phospholipid theory in which an evolution near a source of water, with access to essential fatty acids, allowed for enhanced neuronal connectivity and flexibility in our reactions.[10] This allowed for cognition, memory and creativity, but also for conditions like schizophrenia, dyslexia and manic depressive disorder.[4,10]

In the past, our diet may have counteracted effects of mutations in phospholipid metabolism to produce a milder form of disorder but our deviation from traditional diets may have made the disorder more harmful.[10]

General Evolutionary Theories

Three main categories of evolutionary theory include ancestral neutrality, balancing selection and polygenic mutation-selection balance.

Ancestral neutrality is the concept that a condition was not harmful in the past, but as our ancestral alleles interact with our modern-day world there is a mismatch between those alleles and our current context. It is unknown the extent to which schizophrenia was fitness reducing in the past, but based on

its current effects on fitness it is highly unlikely that schizophrenia was either neutral or produced a significant advantage to the individual in the past.[11]

Balancing selection occurs in conditions that decrease fitness under some circumstances, but increase fitness under other circumstances. Another form of balancing selection is antagonistic pleiotropy where an allele affects multiple traits, having positive effects on some and negative effects on others. Yet this is likely to occur only in special circumstances and provides no protection against genetic drift.[11]

Balancing selection also implies there must be a benefit and even non-affected relatives of those with schizophrenia have been argued not to have a reproductive advantage over the general population.[11] In addition, the presence of a paternal age effect is more consistent with what is expected under a mutation-selection model.[11]

In the model of polygenic mutation-selection balance, schizophrenia results from mutations at many places in the genome. This model explains *why* people with schizophrenia present in different ways. Traits important to fitness rely on the functioning of many complex processes, and so rely on a large number of genes.[11,12]

While mutations might be only mildly harmful on their own, they can cumulatively create a propensity for disease.[13,14] These mutations would be selected against, but their removal would be slow. Such a situation reflects the few reliable and replicable susceptibility alleles found in schizophrenia.[13]

Clinical Implications from an Evolutionary Perspective

While genes increase susceptibility to schizophrenia, environmental factors are still at work in allowing for the manifestation of the disorder. Recognizing this is important because it reveals where interventions can be made. These interventions include areas of diet, lifestyle and targeted supplementation.

As Western grain products were introduced to areas of traditionally low wheat consumption, rates of schizophrenia increased.[15] World War II food shortages revealed that areas of wheat shortage saw a drop in hospitalizations for schizophrenia, whereas areas of increased wheat consumption (such as the United States) saw an increase in hospitalizations during that time.[16]

Promising results have been seen in a number of trials where removal of gluten resulted in a dramatic improvement of schizophrenia and it is suggested that such an intervention is beneficial for a subgroup of patients.[17]

Patients with schizophrenia have also been seen to undergo a resolution of symptoms during periods of high fever only to relapse once the fever subsides. Horrobin made a connection between fever and phospholipid metabolism. It is thought that supplementing with eicosapentanoic acid (EPA) creates an effect similar to that of a fever by adjusting the ratio of arachidonic acid to EPA. In support of this, schizophrenia has a milder presentation in populations in which there is an inverse relationship between lifetime severity and the ratio of essential fatty acids to other fats in the diet.[18]

Considering theories centered around socialization, language and creativity, lifestyle-related therapies may be useful for improving quality of life. Existing trials suggest art therapy, music

therapy, animal-assisted therapy and dance movement therapy each have benefits for patients with schizophrenia.[19–28] In particular, dance movement therapy is linked to a 20% reduction in negative symptoms.[27,28]

Summary

Overall, an evolutionary perspective provides insight into why schizophrenia persists in the population and direction on therapeutic strategies.

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