

Biologists link Huntington's disease to health benefits in young

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For years researchers in neurology have believed that people with Huntington's disease have more children than the general population because of behavioral changes associated with the disease that lead to sexual promiscuity.

In a new Tufts University study, three biologists have challenged that notion by suggesting that people with Huntington's have more children because they are healthier - not more promiscuous - during their peak reproductive years. "A Darwinian Approach to Huntington's Disease: Subtle Health Benefits of a Neurological Disorder" is published in the August 8, 2007 online issue of the journal *Medical Hypothesis* and will soon appear in print.

"Huntington's is a disease that may have beneficial health effects on people early in life, but dire health costs later when symptoms express themselves," said Philip T. Starks, assistant professor of biology in the School of Arts and Sciences at Tufts. "Ironically, these early health benefits may contribute to an increased prevalence of the disease."

Huntington's disease is a genetic disease involving degeneration of the central nervous system (CNS), leading to uncontrolled muscle movements, emotional instability and dementia. Folk musician and songwriter Woody Guthrie died from complications of the disease in 1967.

Link Between Huntington's and Immune System

Along with Dr. Starks, former Tufts undergraduate Benjamin R. Eskenazi and present doctoral student Noah S. Wilson-Rich reviewed 75 published studies in forming their hypothesis. They focused on the tumor suppressor protein p53, which maintains normal cell growth and is found at levels above normal in Huntington's sufferers. At these elevated levels, p53 appears to increase

resistance to cancer by causing cancerous cells to destroy themselves. Previous research has linked increased production of p53 to the mutant form of the Huntington (htt) protein that is found in the CNS of individuals with the disease. In this new hypothesis, the Tufts researchers suggest that p53 not only reduces the incidence of cancer in those affected by Huntington's disease but by improving overall health may also contribute to increased offspring production.

The Tufts team analyzed the often-noted fertility gap between people who have Huntington's and those who do not. Studies comparing family members indicated that individuals with the disease had between 1.14 and 1.34 children for every child born to an unaffected sibling. In explaining this difference, previous researchers have theorized that psychological deterioration and difficulty in discriminating between right and wrong - both symptoms associated with Huntington's - are reasons for promiscuous behavior in people who had the disease. But Eskenazi, Wilson-Rich and Starks observed that such behavior takes place later in life - not during peak reproductive age. They noted that the onset of Huntington's disease occurs, on average, at 41.5 years of age.

In their alternative hypothesis the Tufts researchers suggested that individuals affected with Huntington's have better health earlier in life at the time when their fertility is highest. "We've raised the possibility that the high birth rates are a result of better health," explained Starks. "We know that healthy people have more offspring than those who are sick."

Starks and his team suggested that one key factor behind these health benefits may be p53, and pointed to a 1999 study by doctors at the Danish Huntington Disease Registry at the University of Copenhagen that found lower age-adjusted cancer rates for individuals affected by Huntington's. "Research has shown that individuals with

Huntington's produce higher levels of cancer-suppressing p53, and we hypothesize that they may also reap the health benefits associated with a generally more vigilant immune system," said Starks. "These individuals also suffer from the negative impacts of heightened immune function, as they are more likely than those without Huntington's to suffer from autoimmune diseases."

Starks said that the hypothesis pointing to health benefits of people with Huntington's requires significant additional research. "This is a hypothesis that still needs strong support through more studies," he said.

Marriage of Evolutionary Biology and Medicine

Starks, whose research areas include behavior and evolution in a wide range of organisms, noted that Huntington's disease may be an example of antagonistic pleiotropy, in which one gene creates multiple and conflicting effects. Another example of this phenomenon includes a gene that appears to decrease the incidence of Alzheimer's disease while increasing the chance of elevated lipids in the blood. The convergence of evolutionary biology and medicine can reap many benefits, he believes. "This marriage has already shed light on phenomena such as fever and morning sickness," he noted. Huntington's disease may be one more beneficiary of this synergy.

Source: Tufts University

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