MedicalXpress

Avian influenza strain primes brain for Parkinson's disease

August 10 2009

At least one strain of the H5N1 avian influenza virus leaves survivors at significantly increased risk for Parkinson's disease and possibly other neurological problems later in life, according to new research from St. Jude Children's Research Hospital.

In the August 10 online early edition of the Proceedings of the National Academy of Sciences, researchers reported that mice which survived infection with an H5N1 flu strain were more likely than uninfected mice to develop brain changes associated with neurological disorders like Parkinson's and Alzheimer's diseases. Parkinson's and Alzheimer's involve loss of brain cells crucial to a variety of tasks, including movement, memory and intellectual functioning. The study revealed the H5N1 flu strain caused a 17 percent loss of the same neurons lost in Parkinson's as well as accumulation in certain brain cells of a protein implicated in both diseases.

"This avian flu strain does not directly cause Parkinson's disease, but it does make you more susceptible," said Richard Smeyne, Ph.D., associate member in St. Jude Developmental Neurobiology. Smeyne is the paper's senior author.

"Around age 40, people start to get a decline in brain cells. Most people die before they lose enough neurons to get Parkinson's. But we believe this H5N1 infection changes the curve. It makes the brain more sensitive to another hit, possibly involving other environmental toxins," Smeyne explained.

Smeyne noted the work involved a single strain of the H5N1 flu virus, the A/Vietnam/1203/04 strain. The threat posed by other viruses, including the current H1N1 pandemic flu virus, is still being studied.

Early indications are that the H1N1 pandemic strain carries a low neurologic risk, said Richard Webby, Ph.D., director of the World Health Organization Collaborating Center for Studies on the Ecology of Influenza in Animals and Birds, which is based at St. Jude. Webby, who is also an associate member of the St. Jude Department of Infectious Diseases, was not involved in the H5N1 study led by Smeyne.

This study also supports the theory that a hit-and-run mechanism is at work in Parkinson's disease. The investigators believe the H5N1 infection sparks an immune response that persists long after the initial threat is gone, setting patients up for further devastating losses from a second hit, possibly from another infection, drug or environmental toxin. In this case, researchers believe the flu virus is the first hit that sets up development of Parkinson's at a later time.

An estimated 4.1 million Americans, including 1 to 2 percent age 55 and older, have Parkinson's. Many suspect both genetic and environmental factors play a role in its development. The disease is linked to the death of dopamine-secreting cells in an area of the midbrain known as the substantia nigra pars compacta (SNpc). Dopamine is a neurotransmitter responsible for stimulating the motor neurons that control movement. Parkinson's is usually diagnosed after individuals lose 70 to 80 percent of the dopamine-producing cells. Treatment is available, but there is no cure.

Flu is primarily a respiratory disease, but indirect evidence dating back to 1385 links it to neurological problems, including the brain inflammation known as encephalitis. The association between flu and brain disorders like Parkinson's was strengthened by an outbreak of

encephalitic lethargic, also known as von Economo's encephalopathy, following the 1918 Spanish flu pandemic. Some of those patients developed Parkinson's symptoms.

St. Jude researchers launched this study nearly three years ago in response to the threat posed by avian flu. Smeyne said there was concern about possible long-term neurological risks facing H5N1 survivors.

Previous studies had isolated H5N1 in the nervous system. But this is the first to show the path the virus takes to enter the brain as well as the aftermath of the infection. Smeyne said the virus' path from the stomach through the nervous system and into the brain is reminiscent of how Parkinson's unfolds.

In this study, mice were infected with an H5N1 flu strain isolated in 2004 from a patient in Vietnam. Robert Webster, Ph.D., said the strain remains the most virulent of the avian flu viruses. Webster, a co-author of the study, holds the Rose Marie Thomas Chair in Infectious Diseases at St. Jude.

About two-thirds of the mice developed flu symptoms, primarily weight loss. After three weeks there was no evidence of H5N1 in the nervous systems of the mice that survived.

But the inflammation the infection triggered within the brain continued for months. It was similar to inflammation associated with inherited forms of Parkinson's. Although the tremor and movement problems disappeared as flu symptoms eased, investigators reported that 60 days later mice had lost roughly 17 percent of dopamine-producing cells in SNpc, a structure found in the midbrain.

Researchers also found evidence that the avian flu infection led to over-production of a protein found in the brain cells of individuals with both

Alzheimer's and Parkinson's diseases. The protein, alpha-synuclein, collected in H5N1-infected cells throughout the brain, including the midbrain where key dopamine-producing cells are located. There was little protein accumulation in the brain cells of uninfected mice.

The study marks the first time scientists were able to naturally trigger the protein build-up in an experimental Parkinson's system. "The virus activates this protein," Smeyne explained.

Source: St. Jude Children's Research Hospital