

SOUTHWESTERN NEWS

Media Contact: Mindy Baxter

214-648-3404 or

Theresa.Merola@utsouthwestern.edu

BRAIN CELL DAMAGE UNDERLYING GULF WAR SYNDROME CAUSES ABNORMAL BRAIN DOPAMINE PRODUCTION, STUDY SHOWS

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DALLAS – Sept. 14, 2000 – In a study released today, researchers say they have found a strong link between brain cell loss on the left side of the brain in sick Gulf War veterans and abnormal over-production of dopamine, a neurotransmitter chemical important in such conditions as degenerative brain diseases.

The UT Southwestern Medical Center at Dallas study, published in the American Medical Association's *Archives of Neurology*, links brain cell loss in the left basal ganglia of sick Gulf War veterans with out-of-control production of a brain neurotransmitter chemical called dopamine. With fewer total brain cells, the remaining dopamine-producing cells become over-responsive and produce too much dopamine.

"This finding gives increased importance to our earlier brain scan evidence of brain damage in these veterans," said Dr. Robert Haley, professor of internal medicine and holder of the U.S. Armed Forces Veterans Distinguished Chair for Medical Research, Honoring America's Gulf War Veterans. "Showing that the degree of brain cell injury directly affects the level of brain dopamine production suggests that the brain damage may be having a real effect on these veterans' brain function and is not just a coincidental finding."

In the June issue of *Radiology*, UT Southwestern researchers reported that sick Gulf War veterans had 9 percent fewer brain cells in the left basal ganglia than healthy veterans. Previous research has shown that brain damage in the left basal ganglia causes a dramatic increase in dopamine production, while brain damage in the right basal ganglia has less effect. The latest study found dopamine production was approximately twice as high in the sick veterans with the worst brain cell damage as in the normal veterans.

The UT Southwestern researchers said more study is necessary to determine the significance of this finding, but one possibility is that long-term neuro-degenerative illness may occur in some people as a result.

"We hypothesize that with injury to the brain cells that normally control dopamine production, the cells at first go wild, overproducing dopamine," said Dr. Frederick Petty, a UT Southwestern professor of psychiatry and staff psychiatrist at the Dallas Veterans

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Affairs Medical Center. "The question is whether, over time, these over-stimulated cells will wear out and die. If so, these patients could develop degenerative brain diseases such as Parkinson's disease."

Petty, holder of the Wesley Gilliland Professorship in Biomedical Research, said knowing that veterans could develop such diseases gives researchers time to pursue effective treatments.

Doctors performed magnetic resonance (MR) spectroscopy imaging on 12 sick veterans and 15 well veterans to measure the amount of neuron damage in the basal ganglia. A series of blood tests performed by Petty measured levels of various breakdown products of dopamine, which showed the dopamine production problems.

The researchers decided to study basal ganglia neurons and dopamine production because the symptoms of Gulf War syndrome strongly resemble early symptoms of well-studied degenerative diseases of the basal ganglia like Huntington's, Wilson's and Fahr's diseases. Typical symptoms of Gulf War syndrome include chronic fatigue, dizziness and attacks of vertigo, general body pain, attention and concentration problems, personality changes, depression, and tremor.

In 1997 Haley and colleagues defined three Gulf War syndromes in the *Journal of the American Medical Association*. Syndrome 1, commonly found in veterans who wore pesticide-containing flea collars, is characterized by impaired cognition. Syndrome 2, called confusion-ataxia, the most severe and debilitating of the syndromes, is found among veterans who said they were exposed to low-level nerve gas and experienced side effects from anti-nerve gas, or pyridostigmine bromide (PB), tablets. Syndrome 3, characterized by central pain, is found in veterans who wore insect repellent with high concentrations of DEET and experienced side effects from the PB tablets.

Other UT Southwestern authors of the study include Dr. James L. Fleckenstein, professor of radiology; Dr. W. Wesley Marshall, clinical instructor of internal medicine; Dr. George G. McDonald, a former assistant professor of radiology; and Gerald L. Kramer, a research biologist at the Dallas VA Medical Center.

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