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Study of Williams syndrome patients reveals specific gene's role in intelligence

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Although genetics is the most significant known determinant of human intelligence, how specific genes affect intelligence remains largely unknown. A multi-institution team led by a University of Utah (U of U) USTAR researcher has found that the brain gene STX1A plays a significant role in the level of intelligence displayed by patients with Williams Syndrome (WS). The study may have implications for the understanding of intelligence and treatment of neurological disease in the general population.

Researchers at UCLA, Cedars-Sinai Medical Center, Salk Institute, and the U of U found that variations in the expression of STX1A could account for 15.6 percent of cognitive variation in a group of 65 WS patients, a very high level of confidence in comparison to prior genetic studies. STX1A is involved in the electrochemical processes that occur at the brain's synapses.

The research team is under the direction of Julie R. Korenberg, Ph.D., M.D., Brain Institute USTAR investigator and professor of pediatrics at the U of U School of Medicine. The team published the study on April 21, 2010 in the open access / online scientific jounal *PLoS ONE*.

The study describes a new approach in determining the relationship between gene expression and intelligence in patients with WS, a neurodevelopmental disorder caused by the deletion of only two dozen genes from chromosome 7, a tiny fraction of the almost 30,000 genes found in humans. WS patients have one less copy each of the genes in

question than does the general population.

WS patients typically exhibit an IQ of 60, compared to an average of 100 for the general population. WS patients tend to be highly verbal and social, but have difficulty with numbers, visual-spatial perception and memory.

"Williams Syndrome patients are missing a very, very small amount of genetic material," said Korenberg. "In almost all other respects, their make-up is the same as the general population, so we knew to take a very close look at a small number of genes. We analyzed ten different genes, but the data spoke, and STX1A clearly stood out in relation to the different patients' intelligence levels," Korenberg said.

STX1A has a fundamental role in the brain's neurotransmission machinery. It supports the process by which electrical signals speed from one neuron to the next. "In terms of the brain, we're talking about a basic utility when we look at STX1A," Korenberg said.

The study points the way to further research that may have long-range benefits for WS patients as well as the general population. "This study shows in part how Nature's hand shapes intelligence at the synapse. Monitoring gene expression may provide unique insights into the neurobiology and genetics of intelligence in WS subjects and possibly the general population," Korenberg said.

Korenberg suggested there may be pharmaceutical treatments in the future that could help enhance synaptic function. "New studies could suggest ways to help people whose brain function is lacking, such as in Williams Syndrome, or people who are losing brain function, such as in Alzheimer's Disease," she said.

The research team overcame obstacles with some creative problem

solving, Korenberg said. Since brain cells from live patients were unavailable for study, lymphoblastoid cells from the lymph system grown in culture provided the genetic material to analyze.

In addition, the researchers developed a more precise measure of WS intelligence test data, using a technique called Principal Component Analysis (PCA). In comparison to standardized IQ tests best suited for the general population, the PCA approach was able to better represent a baseline pattern of intelligence in WS patients. The WS baseline adjusted for relative strengths and weaknesses in the study group, and was able to illuminate the impact of specific genes like STX1A more accurately.

More information: The full text of the paper, "Intelligence in Williams Syndrome is related to STX1A, which encodes a component of the presynaptic SNARE complex," is at tinyurl.com/237fdvp

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