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'Neurological work-arounds' offer hope to people with monoamine-related disorders

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Researchers have known for decades that the brain has a remarkable ability to "reprogram" itself to compensate for problems such as traumatic injury. Now, a research article published in the February 2009 issue of the journal *Genetics* suggests that the brain may also be able to compensate for problems with key neurotransmitters such as serotonin and dopamine. This finding may open the doors to entirely new lines of research and treatments for a wide range of brain disorders, including addiction, depression, Parkinson's disease, and schizophrenia.

David Krantz, Associate Professor at the University of California, Los Angeles and Anne Simon, now an Assistant Professor at York College of the City University of New York were the two lead investigators on the study. "Illnesses such as depression, addiction, schizophrenia and Parkinson's disease devastate millions of lives each year. Current treatment strategies often fail and remain poorly understood," said Krantz. "In our research, we have discovered a simple way to identify the functional changes that may be associated with these illnesses and to research new drugs."

To reach this conclusion, Krantz, Simon and colleagues bred fruit flies with what should have been a devastating, life-threatening mutation in the vesicular monoamine transporter gene. This mutation caused their brain cells to be unable to release monoamine neurotransmitters such as serotonin and dopamine. Fruit flies were used in the study because they are convenient for genetic experiments and have a set of neurotransmitters that is nearly identical to that of humans.

And as is the case with humans, monoamine neurotransmitters are considered necessary for the fly to function normally. The researchers observed that although the mutant fruit flies crawled less as larvae and were infertile as adults, they lived and were surprisingly healthy in many respects. This suggests that there is at least one neurological mechanism that helps them compensate for the lack of monoamine neurotransmitters. The next step is to identify the specific changes that take place in their brains to determine how much of this might be applicable to humans.

"We see this over and over: humans are not so different from the other animals," said Mark Johnston, PhD, Editor-in-Chief of *Genetics*. "By studying simple organisms like the fruit fly, we learn fundamental things about our makeup, even organs as complex as the brain."

More information: Anne F. Simon, Richard Daniels, Rafael Romero-Calderón, Anna Grygoruk, Hui-Yun Chang, Rod Najibi, David Shamouelian, Evelyn Salazar, Mordecai Solomon, Larry C. Ackerson, Nigel T. Maidment, Aaron DiAntonio, and David E. Krantz. Drosophila Vesicular Monoamine Transporter Mutants Can Adapt to Reduced or Eliminated Vesicular Stores of Dopamine and Serotonin. *Genetics* (2009) 181:525-541. www.genetics.org/cgi/content/abstract/181/2/525

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