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Gifts of the MAGI in schizophrenia and bipolar disorder

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These findings are not about the classic story of gift-giving, although the MAGI genes (officially named membrane associated guanylate kinase, WW and PDZ domain containing proteins) do influence brain function in important ways.

MAGI1 and MAGI2 are genes that code for the MAGI proteins. These proteins influence the development and function of synapses in the brain, the junctions where communication between nerve cells occurs.

Because they perform many important functions at brain synapses, researchers have made several attempts to tie these genes to psychiatric disease. So far, the efforts have been inconclusive, possibly because of insufficient statistical power, but now, authors of a new research study in *Biological Psychiatry* provide important evidence that MAGI1 and MAGI2 play a role in psychiatric disease.

Led by principal investigator and senior author Dr. Silvia Paddock, they examined genetic variations in families with bipolar affective disorder, schizophrenia, and schizoaffective disorder. These disorders have high overlapping genetic risk and are also highly heritable.

Using a multistage approach to assess and rank genetic variants, they identified rare mutations in MAGI1 and MAGI2.

Dr. John Krystal, Editor of Biological Psychiatry, commented, "We are searching for clues as to why the brain connections develop abnormally

in people diagnosed with schizophrenia and bipolar disorder. In this case, the authors have found a very rare signal that may shed light on the cause of this problem for a small group of people carrying these diagnoses."

"Our initial finding of mutated MAGI1 in a large, affected family may also indicate that it may have been premature by our field to declare linkage efforts failed," Dr. Paddock noted. "Valuable samples from large families have already been collected and previous linkage results can guide us where to look for mutations. We can and should go back to these samples and analyze them with the unprecedented accuracy that today's technology has to offer."

More information: The article is "MAGI1 Copy Number Variation in Bipolar Affective Disorder and Schizophrenia" by Robert Karlsson, Lisette Graae, Magnus Lekman, Dai Wang, Reyna Favis, Tomas Axelsson, Dagmar Galter, Andrea Carmine Belin, and Silvia Paddock (doi: 10.1016/j.biopsych.2012.01.020). The article appears in *Biological Psychiatry*, Volume 71, Issue 10 (May 15, 2012)

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