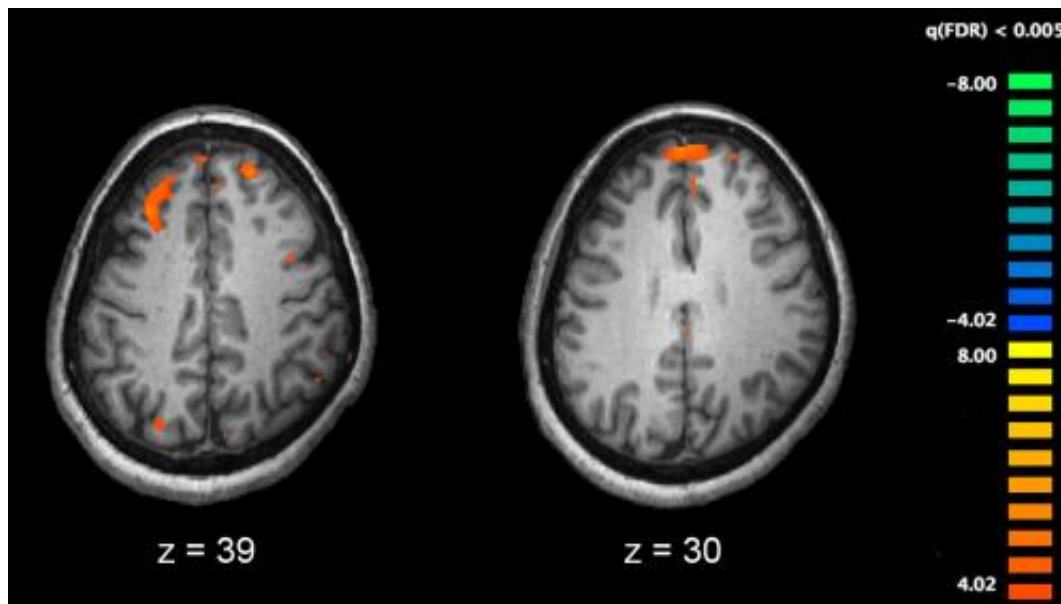


Computational model finds new protein-protein interactions in schizophrenia

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Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory. Credit: Kim J, Matthews NL, Park S./PLoS One.

Using a computational model they developed, researchers at the University of Pittsburgh School of Medicine have discovered more than 500 new protein-protein interactions (PPIs) associated with genes linked to schizophrenia. The findings, published online today in *npj*

Schizophrenia, a Nature Publishing Group journal, could lead to greater understanding of the biological underpinnings of this mental illness, as well as point the way to treatments.

There have been many genome-wide association studies (GWAS) that have identified gene variants associated with an increased risk for [schizophrenia](#), but in most cases there is little known about the proteins that these [genes](#) make, what they do and how they interact, said senior investigator Madhavi Ganapathiraju, Ph.D., assistant professor of biomedical informatics, Pitt School of Medicine.

"GWAS studies and other research efforts have shown us what genes might be relevant in schizophrenia," she said. "What we have done is the next step. We are trying to understand how these genes relate to each other, which could show us the biological pathways that are important in the disease."

Each gene makes proteins and proteins typically interact with each other in a biological process. Information about interacting partners can shed light on the role of a gene that has not been studied, revealing pathways and biological processes associated with the disease and also its relation to other complex diseases.

Dr. Ganapathiraju's team developed a [computational model](#) called High-Precision Protein Interaction Prediction (HiPPIP) and applied it to discover PPIs of schizophrenia-linked genes identified through GWAS, as well as historically known risk genes. They found 504 never-before known PPIs, and noted also that while schizophrenia-linked genes identified historically and through GWAS had little overlap, the model showed they shared more than 100 common interactors.

"We can infer what the [protein](#) might do by checking out the company it keeps," Dr. Ganapathiraju explained. "For example, if I know you have

many friends who play hockey, it could mean that you are involved in hockey, too. Similarly, if we see that an unknown protein interacts with multiple proteins involved in neural signaling, for example, there is a high likelihood that the unknown entity also is involved in the same."

Provided by University of Pittsburgh Schools of the Health Sciences

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