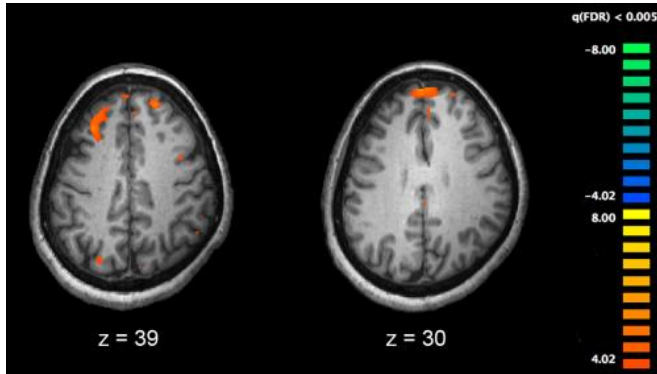


# Gene fault identified in people with schizophrenia

15 March 2016, by Bob Yirka



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.

(Medical Xpress)—A large team of researchers from the U.S., Sweden, Finland and the U.K. has identified a gene fault that appears to be unique to people with schizophrenia and other neural diseases. In their paper published in the journal *Nature Neuroscience*, the team describes the large genomic study they undertook that included people with and without the disorder and what they found in doing so.

Schizophrenia is a mental disorder characterized by a variety of thinking and emotional problems—its cause is not known, but is believed to come about due to both genetic and environmental factors. In recent years, scientists have come closer to identifying the genetic components involved in the disorder, narrowing down the regions in the genome that are believed to contain genetic changes that are related to it. In this new effort, the researchers have found the first example of a

single risk gene, though it is still not clear how or to what degree the gene is involved in causing problems.

To find the gene, or genes that may be responsible for causing at least some instances of [schizophrenia](#), the researchers performed sequencing on the genomes of 8,534 people in Finland and the U.K. and combined those results with data that had been obtained from 5,074 people in a study conducted in Sweden and from another 1,078 people that had participated in a separate family study. In so doing the researchers found a gene, SETD1A, that was faulty in 10 [schizophrenia patients](#) but not in any of the people without a neurological disorder—though it did appear in 6 other patients who had other neuropsychiatric disorders.

Because the [faulty gene](#) was not found in all, or even most of the people with the schizophrenia, it cannot be described as the cause of the disorder—it is more aptly described, the researchers note as one of the contributing factors in some cases. They also note that because the same faulty gene was found in people with a variety of neurological problems, there appears to be a shared common biological pathway. And, because the faulty gene has been isolated, it is possible that a therapy can be developed to help treat patients that have symptoms attributable to the fault, perhaps reducing some or all of those symptoms making for a better life for them.

**More information:** Tarjinder Singh et al. Rare loss-of-function variants in SETD1A are associated with schizophrenia and developmental disorders, *Nature Neuroscience* (2016). [DOI: 10.1038/nn.4267](#)

## Abstract

By analyzing the whole-exome sequences of 4,264 schizophrenia cases, 9,343 controls and 1,077 trios, we identified a genome-wide significant

association between rare loss-of-function (LoF) variants in SETD1A and risk for schizophrenia ( $P = 3.3 \times 10^{29}$ ). We found only two heterozygous LoF variants in 45,376 exomes from individuals without a neuropsychiatric diagnosis, indicating that SETD1A is substantially depleted of LoF variants in the general population. Seven of the ten individuals with schizophrenia carrying SETD1A LoF variants also had learning difficulties. We further identified four SETD1A LoF carriers among 4,281 children with severe developmental disorders and two more carriers in an independent sample of 5,720 Finnish exomes, both with notable neuropsychiatric phenotypes. Together, our observations indicate that LoF variants in SETD1A cause a range of neurodevelopmental disorders, including schizophrenia. Combining these data with previous common variant evidence, we suggest that epigenetic dysregulation, specifically in the histone H3K4 methylation pathway, is an important mechanism in the pathogenesis of schizophrenia.

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