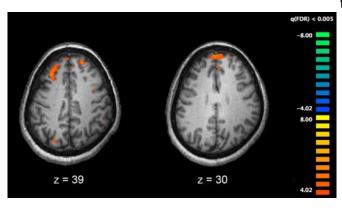


Cell types underlying schizophrenia identified

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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.

Scientists at Karolinska Institutet in Sweden and University of North Carolina have identified the cell types underlying schizophrenia in a new study published in *Nature Genetics*. The findings offer a roadmap for the development of new therapies to target the condition.

Schizophrenia is an often devastating disorder causing widespread human suffering. Genetic studies have linked hundreds of genes to schizophrenia, each contributing a small part to the risk of developing the disease. The great abundance of identified genes have made it difficult to design experiments. Scientists have been struggling to understand what links the genes and whether these genes affect the entire brain diffusely, or if they affect specific parts of the brain.

By combining new maps of all the genes used in different <u>cell types</u> in the brain with detailed lists of

the genes associated with schizophrenia, scientists in the current study identified the types of cells that underlie the disorder. The genetics implicate certain cell types more than others. One finding was that there appear to be a few major cell types contributing to the disorder, each of which originates in distinct areas of the brain.

"This marks a transition in how we can use large genetic studies to understand the biology of disease. With the results from this study, we are giving the scientific community a chance to focus their efforts where it will give maximum effect," says Jens Hjerling-Leffler, research group leader at the Department of Medical Biochemistry and Biophysics at Karolinska Institutet, one of the main authors.

The findings offer a roadmap for the development of new therapies.

"One question now is whether these <u>brain</u> cell types are related to the clinical features of schizophrenia. For example, greater dysfunction in one cell type could make treatment response less likely. Dysfunction in a different cell type could increase the chances of long-term cognitive effects. This would have important implications for development of new treatments, as separate drugs may be required for each cell type involved," says co-author Patrick Sullivan.

As a result of rapid progress in human genetics and single cell transcriptomics, it has only recently become possible to study diseases in this way. In coming years, the researchers suggest that the approach should lead to breakthroughs in the biological understanding of other complex disorders such as autism, major depression and eating disorders.

"Understanding which cell types are affected in a disease is of critical importance for developing new medicines to improve their treatment. If we do not



know what causes a disorder we cannot study how to treat it," says Nathan Skene, postdoc at the Department of Medical Biochemistry and Biophysics at Karolinska Institutet and UCL Institute of Neurology, UK, one of the lead authors.

More information: Genetic identification of brain cell types underlying schizophrenia, *Nature Genetics* (2018). DOI: 10.1038/s41588-018-0129-5

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