Scientists discover novel therapeutic approach against genetic forms of schizophrenia

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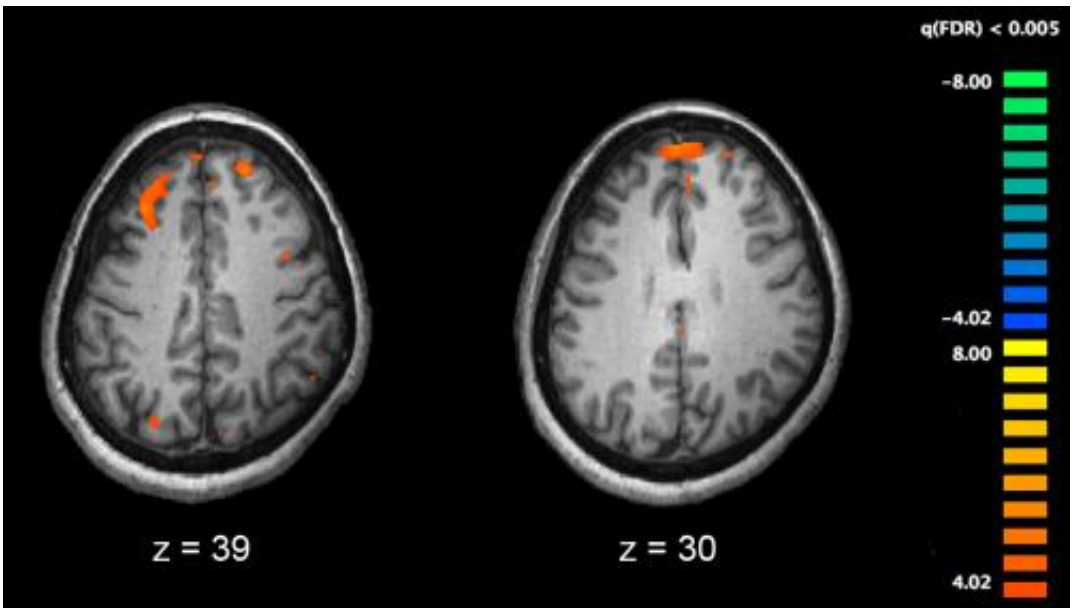

Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown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

Research led by the University of Glasgow has made a breakthrough in developing a possible future treatment of schizophrenia and related

psychiatric conditions.

Studies currently show that people with a hereditary form of schizophrenia, or a subset of the general schizophrenic population, are deficient in the brain protein DISC1, an important multi-function 'scaffolding' protein vital to key brain functions.

This groundbreaking study, published today in *Molecular Psychiatry*, crucially identifies a peptide that stabilises DISC1 levels, paving the way for a possible treatment for schizophrenia and related conditions.

For the first time, scientists identified the protein, FBXW7, which tags the DISC1 protein for destruction. They discovered that by disrupting the interaction between these two proteins with and inhibitory peptide, DISC1 deficiencies could be counteracted.

Lead author George Baillie, Professor of Molecular Pharmacology at the Institute of Cardiovascular and Medical Sciences, said: "My colleagues and I decided to look specifically at the DISC1 protein. Our idea was simple: what would happen if we could simply raise the concentration of DISC1 in patients' brains?

"We looked at the turnover of DISC1 in the brain and found it was rapidly made and then degraded by brain cells. We thought, if we can stop the natural destruction of DISC1, people with low levels would see it naturally increase. Using our peptide, we can now restore DISC1 concentrations in psychiatric patient derived brain cells back to the levels of control subjects."

Schizophrenia affects around 1 in 100 people over the course of their life. It is present in twice as many people as Alzheimer's Disease and five times as many people as Multiple Sclerosis, with an estimated cost to the economy of £6.7 billion each year.

Professor Baillie added: "Many patients respond inadequately or adversely to current psychiatric medications, so the development of new drugs to treat mental illness is needed, but unfortunately no substantial innovations in drug treatments for these debilitating disorders have emerged in the last 60 years. We are hopeful that our peptide can be a stepping stone toward a novel therapeutic in the future to counteract this unmet need"

"As positive as our discovery is, we have some way to go between laboratory findings and the clinical application, but we are hopeful that our research is the first step on a journey towards a potential new drug treatment option for a range of psychiatric illnesses."

The paper, 'FBXW7 regulates DISC1 stability via the ubiquitin-proteosome system' is published in Molecular Psychiatry. The research was funded by Pfizer. The paper was funded by an award from the Translational Medicine Research Collaboration – a consortium made up of the Universities of Aberdeen, Dundee, Edinburgh and Glasgow; the four associated NHS Health Boards (Grampian, Tayside, Lothian and Greater Glasgow & Clyde), Scottish Enterprise and Pfizer. Part funding also came from grants from the MRC, National Institutes of Health and the Connecticut Regenerative Medicine Research Fund.

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