

'Dimmer switch' drug idea could tackle schizophrenia

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(Medical Xpress)—Discovery of a new mechanism of drug action could lead to the next generation of drugs to treat schizophrenia.

Affecting one per cent of the world's population, [schizophrenia](#) is a major health condition. It affects a person's ability to think, feel and act and is associated with distressing symptoms including hallucinations and delusions.

New Monash University findings, published today in the journal, *Nature*

Chemical Biology, offer hope of a new class of drug that can act as a "[dimmer switch](#)" to control schizophrenia, without causing some of the common side effects associated with current anti-psychotic medicines.

One of the lead researchers of the study, Dr Rob Lane from the Monash Institute for Pharmaceutical Sciences (MIPS) said all current anti-psychotic medicines block the action of dopamine, a neurotransmitter, at a brain protein called the dopamine D2 receptor, resulting in serious side effects.

"These medications frequently result in serious side effects because this protein is also important for the control of movement. The side-effects can sometimes persist even after the patient has stopped taking the medication," Dr Lane said.

Co-lead researcher Professor Arthur Christopoulos, said gaining a better understanding of the biology of schizophrenia will lead to more effective drugs.

"The idea behind our research is to develop a drug that doesn't completely block dopamine. We found a molecule that, rather than blocking the effect of dopamine at the D2 receptor, acts to subtly dial down [dopamine](#)'s effect, a bit like a dimmer switch," Professor Christopoulos said.

"This means that if we can get just the right amount of dial-down, we could treat the symptoms of the disease and avoid some of these [side-effects](#).

"We're a long way yet from developing a drug, but our dimmer switch approach to controlling schizophrenia means it's conceivable we could have a whole new class of anti-psychotics in the future."

The research team also found a unique twist with the molecule, its mechanism of action changed depending on the arrangement of the D2 receptor in the brain.

Dr Lane said not only does this represent a new approach to develop anti-psychotics, it gives researchers more information about the protein involved in the disease.

"This extra information will help researchers develop new drugs that target the protein," Dr Lane said.

The next phase of the research will see Dr Lane and Professor Christopoulos collaborate with chemists at MIPS to try to develop a better version of the [drug](#) used in the study.

More information: A new mechanism of allostery in a G protein-coupled receptor dimer, *Nature Chemical Biology*, [DOI: 10.1038/nchembio.1593](#)

Provided by Monash University

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