

New dopamine brain target discovered

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A team of Canadian researchers, lead by Dr. Susan George and Dr. Brian O'Dowd at the Centre for Addiction and Mental health (CAMH), discovered a distinct dopamine signalling complex in the brain. Composed of two different types of dopamine receptors, this novel target may have a significant role in understanding and treating schizophrenia.

Published in the *Proceedings of the National Academy of Sciences USA* (Rashid et al., 2007), this important discovery demonstrates the existence of a Gq/11-coupled signalling unit that triggers a calcium signal, which is turned on by stimulating D1 and D2 dopamine receptors. Unlike other dopamine receptors, this novel unit will only create brain signals when both receptors are stimulated at the same time.

Using animal models. Drs. George and O'Dowd and their team identified this complex by its unique reaction to dopamine or specific drug triggers. Strikingly, stimulating this target with dopamine or specific drugs triggered a rise in calcium in the brain. As calcium has a profound effect on almost all brain function, this rise in calcium causes a cascade of events in the brain. This is the first time that a direct connection between dopamine and calcium signals has been reported.

"This distinct unit provides a novel signalling pathway through which dopamine can impact the function of brain cells", said Dr. George. "This is significant because signalling through calcium release is a major mechanism regulating many important functions in the brain and we have provided the first direct mechanism by which dopamine can

activate a calcium signal."

This data has significant implications for schizophrenia. Research tells us that people with schizophrenia may have disordered calcium signals, and the major treatments for this disease target the dopamine system. Drs. George and O'Dowd state, "our data links these two pieces of evidence, creating better understanding of the disease and opening the door for a new generation of highly specific drugs that may help alleviate the devastating symptoms of schizophrenia."

Source: Centre for Addiction and Mental Health

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