The Ottawa Hospital | L'Hôpital d'Ottawa

Research project summary

Role of Postsynaptic Density Proteins in Dopamine Receptor Function and Crosstalk

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- Co-Investigator: Diane Lagace
- Awarded $803,250 from the Canadian Institutes of Health Research (CIHR) in May 2017

Dopamine is an important chemical of the brain. Dopamine communicates with the exterior of nerve cells by attaching to specialized group of proteins called D1, D2, D3, D4 and D5 receptors to unlock signals inside the cells. A crosstalk exists between the dopamine D1 receptor and another type of receptor that attaches to glutamate, which also a key brain chemical. Abnormal dopamine and glutamate receptors have been implicated in mental illnesses. Our research has identified a novel partner of the dopamine D1 receptor called synaptic-associated protein 102 or SAP102. SAP102 attaches to a part of the D1 receptor located in the interior of cells. As SAP102 has been previously shown to also attach to glutamate receptors, we hypothesize that SAP102 is important in the cross-talk between dopamine and glutamate receptors. The present research project will test how SAP102 facilitates the crosstalk between dopamine D1 and glutamate receptors. We will also study the role of SAP102 is involved in the control of brain functions by the D1 receptor such as movement, learning and memory using mice. These functions are abnormal in human brain illnesses such as Parkinson's disease, schizophrenia, depression and obsessive-compulsive disorder. To do our research, we will use cultured cells, mouse brain slices, mouse behavior testing, electrophysiology, microscopy and biochemical assays to identify the SAP102 mechanisms controlling the crosstalk between D1 and glutamate receptors. It is hoped that our research will improve our knowledge of the crosstalk between the SAP102, the D1 receptor and the glutamate receptor in normal and diseased brains. We believe that our research will help developing novel drugs that target specifically the cross-talk between these three proteins to restore normal dopamine and glutamate function in individuals suffering from mental illnesses such as Parkinson's disease and schizophrenia.

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