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Role of Wnt/β-catenin signaling pathway in cocaine induced sensitization

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Wnt signaling pathways are essential for development of many tissues and organs, including the mammalian brain. Wnt factors are cistein rich secreted proteins which interact with one of the 2 membrane receptors: Frizzled and Ryk. As a result of the interaction Dishevelled (DVL) is activated, and consequently, one of the three pathways: Wnt/β-catenin, Planar Cell Polarity, and Wnt/calcium pathways. These three pathways participate in different cell fate decisions like synaptogenesis, cell and tissue polarity and cell movement. In the case of the Wnt/β-catenin pathway, DVL activation inhibits GSK-3β which stabilizes β-catenin. Recently, it has been shown that Wnt signaling pathways are involved in neuropsychiatric diseases like Alzheimer and schizophrenia. Moreover chronic amphetamine decreased protein levels of GSK-3β and β-catenin while dopaminergic antagonists increased them in dopaminergic neurons and in their projections. Since schizophrenia and cocaine neuroadaptations targeted the mesolimbic system, and cocaine induces changes similar to those observed in mammalian development that could involve the Wnt signaling pathway; the main goal was to elucidate the role of the Wnt/β-catenin pathway in cocaine induced neuroadaptations underlying sensitization. Until now, the data shows that cocaine differentially changed this pathway depending on brain area, and whether animals show behavioral sensitization or not. Thus, after 7 days of cocaine injections Wnt/β-catenin pathway effectors are decreased in the PFC, Amyg and DS only in sensitized animals. More recently, it was found that a pretreatment with Wnt/β-catenin pathway activator (e.g. LiCl) block cocaine behavioral effects by restoring β-catenin levels. Furthermore, we reproduce the development of cocaine induced sensitization by repeatedly administering Sulindac (a DVL antagonist) into de PFC. Further studies are studying the relationship between these changes and spine morphology in the PFC. All these findings will be discussed considering that a possible protective role of Wnt pathways in cocaine addiction could lead to new treatment strategies.

Biography

Pacchioni A M completed her PhD at Universidad Nacional de Cordoba in Argentina (1999-2004) and her Postdoctoral studies at Medical University of South Carolina (2004-2009). She has received national and internationals awards. She is now an Assistant Professor at Universidad Nacional de Rosario and Associate Researcher at Argentina´s National Research Council (CONICET). She is a PI of a couple of grants and has published 17 papers in peer reviewed journals. She is interested in the search of new molecular pathways that underlies cocaine induced behavioral changes which could lead to new treatment strategies.

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