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Analysis of the transcriptome in an animal model of alcohol addiction - Evidence for a new pathway for the control and maintenance of the phenotype

Ana Lucia Brunialti Godard
Federal University of Minas Gerais, Brazil

The recreational and controlled use of alcohol is distinct from its scaled and uncontrolled use. The progression of controlled use for addition is influenced by many factors, including the drug itself, user behavior (psychological factors), environmental influences and genetic and epigenetic factors. In order to try to elucidate the genetic factors predisposing to addictive behavior to alcohol, we have studied the transcriptome of an animal model that has free choice for ethanol consumption. We used non-inbred, Swiss mice exposed to a three-bottle free-choice model (water, 5% v/v ethanol, and 10% v/v ethanol) that consisted of four phases: Acquisition (AC), withdrawal (W), re-exposure (RE), and quinine-adulteration (AD). Based on individual ethanol intake, the mice were classified into three groups: "addict" (A group; preference for ethanol and high levels of consumption during all phases), "heavy" (H group; preference for ethanol and high levels of consumption during the AC phase and a reduction in intake in the AD phase), and "light" (L group; preference for water during all phases). In order to highlight new avenues of gene regulation that may be involved with the addict phenotype, we evaluated the transcriptome of three brain areas (hippocampus, striatum and prefrontal cortex) of animals of all developed experimental groups. Through this analysis, we demonstrated that the striatum of these animals has transcriptional differences in several genes that constitute a pathway related to the flow and recycling of synaptic vesicles, called LRRK2. This pathway contributes to the maintenance of the dopaminergic tone in striatal neurons and possibly their dysfunction works for characteristic dopaminergic deficit of additions. Our hypothesis is that the change in gene regulation of this pathway is involved in the establishment and maintenance of the addict phenotype, providing evidences of potential new targets for prevention and treatment of the addiction.

Biography

Ana Lucia Brunialti Godard graduated in Biological Sciences from the Catholic University of Campinas (1988), Master in Human Genetics, Université Pierre et Marie Curie (1993) and PhD in Human Genetics, Universite Pierre et Marie Curie (1997). She is an Associate Professor of the Federal University of Minas Gerais. She is currently a Doc consultant to various funding agencies and the National Council for Animal Experiments Control CONCEA, MCT, Coordinator of the Program of MBA in Genetics, Federal University of Minas Gerais. She has experience in human genetics, with emphasis in animal models of human disease, acting on the following topics: Functional genomics, genetic of the alcoholism, molecular mechanisms of addiction and compulsion.

brunialt@ufmg.br

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