Exposure to childhood maltreatment and cocaine-abuse: from the preclinical model to clinical research

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Childhood maltreatment frequently confers risk for multiple psychiatric diagnoses. The molecular and neurobiological substrates engaged during early traumatic events and mediating the risk for psychiatric diseases are poorly understood. In our laboratory, we have developed a preclinical model of “physical maltreatment” that has allowed us to study and identify several biological changes induced by this traumatic experience and associated with an increased tendency to cocaine-seeking behavior in adulthood.

In order to be able to translate our preclinical finding to the clinical research, we studied such changes not only in the brain but also in the blood. In this study, molecules altered in the blood of mice susceptible to cocaine seeking behavior because of their early life stress experience, were studied in the blood of cocaine abstinent individuals in treatment for the substance use disorder with or without exposure to childhood maltreatment. In these subjects we investigated the expression levels of molecules involved in several biological pathways such as: 1. Integrin signaling;2. Agiogenesis;3. Platelet growth signaling; and 4. Innate immune response mediated by Toll-like receptor 4 (TLR4). Our results showed that the cocaine was able to induce a strong inflammatory response mediated by the TLR4 receptors in both mice and humans. Interestingly such inflammatory response was significantly higher in cocaine abstinent individuals with a history of childhood abuse compared with abstinent individuals with no experience of maltreatment. Finally we observed a positive correlation between the expression levels of TLR4 receptors and levels of craving for the substance.