ADOLESCENT EXPOSURE TO COCAINE IMPAIRS COGNITIVE ABILITIES AND EMOTIONAL RESPONSE IN THE DEVELOPING

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Adolescence is a developmental period characterized by impulsive choices that may lead to the beginning and escalation of illicit drug use. In this stage of life, the brain is in a unique state of transition as it undergoes profound structural and synaptic changes and, therefore, interfering with brain development during this delicate period may cause adverse consequences. Such effects may be the result of long-term neuroadaptations that involve, among the others, critical determinants of synaptic plasticity such as glutamate neurotransmission or other systems such as the neurotrophin BDNF. The major aim of our work was to investigate the cognitive abilities and emotional response following a history of cocaine exposure trying to dissect their underlying neuroplastic mechanisms.

To this end, rats were exposed to repeated cocaine injections [20mg/kg/day, from postnatal day (PND) 28 to PND 42]. The behavioral cognitive response was evaluated at PND 43 and PND 56 employing the novel object recognition test, which is relatively simple, non-rewarding and ethologically relevant test based on the innate tendency of a rodent to explore a novel object more than a familiar object. Notably, we found different behaviors that seem to depend on the latency from the last exposure to cocaine. In fact, on PND 43, cocaine-treated rats spent more time exploring the novel object than saline-treated counterparts, suggesting an increased response to novelty; however, on PND 56, cocaine-treated rats spent significantly less time on the novel object, suggesting an impairment of cognitive processes caused, at least in part, by the developmental exposure to the psychostimulant. Of note, such changes were accompanied by alterations of a critical glutamate determinant of the glutamate synapse, i.e. PSD-95, which is increased in the medial prefrontal cortex of PND 43 rats while reduced in the same brain region of PND 56 rats.

In addition, we have also performed a series of experiments involving a single injection of cocaine at PND 35 and measured the behavioral response, at PND 42, i.e. a week after the single exposure. We found that a single administration of the psychostimulant causes an anhedonic phenotype in the rats exposed to the sucrose consumption test, i.e a test used as an indicator of anhedonia (lack of interest in rewarding stimuli), which is present in some forms of affective disorder, including depression. Notably, anhedonia in cocaine-treated rats was associated with an overall decrease of BDNF and BDNF signalling pathways, an effect that could contribute to explain, at least in part, the pro-depressive phenotype in these rats.

In conclusion, our data show that different cocaine interventions (i.e. single or repeated) during different windows of the developmental stages may lead to different changes in the expression of critical determinants of neuroplasticity such as PSD-95 or BDNF.