Neuroplastic alterations in rats exposed to prenatal stress: preventive effect of lurasidone treatment during adolescence.

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Environmental factors, which might occur as early as during in utero life, exert profound influences on the structural and functional development of individuals, giving rise to changes that can persist throughout life. The perinatal modifications on the phenotypic plasticity of the progeny may result in the development of long-term diseases, from metabolic syndrome to psychiatric disorders.
With this respect, animal models are very useful to characterize the molecular and functional mechanisms that may be persistently affected after exposure to early-life stressors (ELS). In the present study we used a model of prenatal stress in rats consisting in repetitive immobilization stress three times a day for 45 minutes from E14 until delivery. Considering that neuronal plasticity has emerged as a major vulnerability element in psychiatric disorders, we investigated the postnatal developmental profile of brain derived neurotrophic factor (BDNF) in male and female rats following exposure to prenatal stress (ELS). We found that exposure to ELS results in adult impairment of neuroplasticity and reduced expression of BDNF that develops post-puberty, with major changes occurring on long 3'-UTR BDNF mRNA levels, the pool of neurotrophin transcripts that undergoes dendritic targeting. Moreover, ELS rats displayed an altered responsiveness of BDNF when exposed to an acute challenge during adulthood, which is suggestive of an impairment in coping mechanisms.
We also tested the ability of a chronic treatment with the novel antipsychotic drug lurasidone administered during adolescence in preventing the changes produced by ELS exposure. We found that lurasidone administration increased total BDNF expression in the prefrontal cortex of prenatally stressed rats, as measured 24 hours or two weeks post treatment. Furthermore, we found that chronic drug treatment also increased the expression of the long 3'-UTR BDNF at 24 h and, more importantly, it was able to prevent the reduction of long 3'-UTR BDNF mRNA levels occurring at PND 60 in rats that were exposed to ELS.
Collectively, our results provide further support to the notion that exposure to early life stress has a negative impact on neuronal plasticity and that preventive pharmacological intervention during critical time windows may prove effective in preventing neuroplastic dysfunctions. The ability of lurasidone to normalize defects associated with environmental animal models of stress-related disorders may ameliorate functional capacities closely associated with alteration in neuronal plasticity, a core feature common to several psychiatric conditions.