The activation of the immune/inflammatory system is associated with the stress-induced anhedonia in rats: effect of pharmacological intervention.

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ABSTRACT

Major depression (MD) is a common psychiatric disorder that represents a leading cause of disability in the world. It is known that this complex disease originates from the interaction between many factors of different nature -a genetic background of susceptibility, biological, social and environmental stimuli- that act in concert leading to the development of the illness. Despite the increased knowledge of MD neurobiology, an effective improvement in the overall impact of pharmacotherapy is still lacking, possibly because a number of systems that are affected in mood disorders may not be adequately modulated by pharmacological treatments. Currently there is strong evidence that depression involves alterations of the immune/inflammatory system. In particular MD shows an elevated comorbidity with cancer, rheumatoid arthritis, cardiovascular and neurodegenerative diseases, all characterized by inflammatory alterations. Moreover, the treatment of Hepatitis C virus with IFNα predisposes to the development of clinically significant depression. On these bases, the purpose of our study was to analyze the cerebral expression of several mediators of the immune/inflammatory system in an animal model of depression based on the environmental component of the disease -the rat exposed to chronic mild stress (CMS)-, to elucidate the role of inflammation on the generation of the anhedonic phenotype and to evaluate the ability of pharmacological intervention in modulating the behavioral-associated inflammatory alterations. To this aim, rats exposed to CMS for two weeks were tested with the sucrose consumption test to assess the insurgence of an anhedonic phenotype, then molecular analyses were carried out on dorsal, ventral hippocampus and on prefrontal cortex, three brain regions mainly involved in the etiology of depression. Afterward a group of anhedonic animals underwent to five further weeks of CMS with a parallel treatment with the tricyclic antidepressant imipramine and the atipical antipsychotic lurasidone. At the end of the treatment, molecular analyses on inflammatory mediators were conducted. Our findings indicate that the stress-induced anhedonic phenotype is associated to an altered expression of specific mediators of immune/inflammatory system and that pharmacological treatment is not only able to normalize the anhedonic phenotype, but also inflammatory changes. These data suggest that the immune/inflammatory alterations are not a merely consequence of stress exposure, but they may contribute to the subject's vulnerability to depression and support the idea that this system may serve as a viable therapeutic target for more effective antidepressant drugs.