Molecular neuropsychopharmacology of stress-related diseases

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Pathophysiology and pharmacology of stress-induced inflammatory and disfunctional processes in the gut.

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Role of innate immune receptors on brain response to stress

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Neuroinflammation by cocaine. Effects of stress exposure.

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Hormonal regulation of stress inflammatory response. Role of nuclear receptors.
**Scientific aims**

All organisms are exposed to stressful stimuli. This is especially important in humans, since a correct stress response is essential for survival, even having beneficial consequences. Nevertheless, an inadequate response (when the stimulus is of high intensity or duration), can lead to diseases or even death. According to ample surveys, up to two thirds of the GP visits are related to stress exposure. Numerous cardiovascular or neuropsychiatric diseases, some cognitive alterations and some chronic metabolic diseases are consequence of stress.

We have been involved for years in the study of the pathophysiological basis of the stress response in the brain. The neuroinflammatory reactions induced by exposure to stressful stimuli appear in numerous neuropsychiatric pathologies. Our main objective is to contribute from the basic research to the development of strategies aiming to the reduction of the incidence of pathological reactions to stress and the search of markers of susceptibility to neuropsychiatric pathologies. Overall, to identify and develop pharmacological tools to improve the quality of treatments of stress induced pathologies, both in the brain as in other systems.

**Objectives:**

1. Study of protective mechanisms against oxidative and inflammatory cell damage alter stress exposure. Possible therapeutic targets and neuroprotective strategies.
2. Mechanisms of vulnerability to stress induced cell damage.
5. Mechanisms by which stress exposure increase susceptibility to cell damage in experimental models on Alzheimer and Parkinson diseases, hipoxic-ischaemic damage and demyelinating pathologies. Possible therapeutic targets and neuroprotective strategies.
6. Study of mechanisms by which stress increase susceptibility to gastrointestinal damage. Possible therapeutic targets and citoprotective strategies.
7. The neuropharmacological characterization and the study of the therapeutic potential of the endocannabinoid system in stress-related neuropsychiatric and gastrointestinal pathologies.

**Collaborative research with other scientific teams:**
- Dr. J Rodrigo (I. Cajal CSIC) NOX and COX neuroanatomy
- Dr. L Boscá (I. Bioquímica UCM/CSIC; CNIC) Regulation of NOS (NFkB)
- Dr. C Scavone (Univ. Sao Paulo, Brasil) Stress and NFkB, ATPase, TLRs
- Dr. J Manzanares (Inst. Neurociencias Alicante) Characterisation KO CB1/2
- Dr. JL Trejo (I. Cajal, CSIC) Stress and neurogenesis
- Dr. J Fernández-Ruiz (Dpto. Bioquímica, Medicina UCM). Neuroinflammation in Parkinson disease. Role of ECS.
- Dra. R F-Durango (Unid. Investigación HCUSC) Inflammatory damage in glaucoma
- Dr. M Heneka (Univ. Münster, Alemania) Stress and Alzheimer disease
- Dra. C Guaza (I. Cajal, CSIC, Madrid) Endocannabinoid regulation by chemokines
- Dra. C Guerri (I. Principe Felipe, Valencia) Neuroinflammatory damage by ethanol
**Selected grants** (see complete references in the spanish version)


Scientific networks in Biomedicine and Health. Coord (group): JC Leza


Stress exposure on Alzheimer disease, an experimental study. Coord. JC Leza

Study of brain PG-PPARγ antiinflammatory pathway and possible pharmacological modulation in an stress model in rat. Coord. JC Leza


Effects of psychosocial stress on the activity of several oxidative/nitrosative biomarkers in colonia mucosa in human ulcerative colitis and in an experimental model of IBD. Coord. L Menchén.

Nitric oxide and other oxidative stress markers in brain damage. Study of therapeutic strategies (part II). Coord. P.Lorenzo.


Stress induced brain damage. Study of mechanisms of oxidative cell damage. Coord. JC Leza.

**PhD Thesis:**

Our groups is specially devoted to the formation of scientists in Pharmacology. Apart from pregraduate (scientific formation of medical or pharmaceutical students, students with collaboration grants (national and regional agencies) as well as postgraduates, members of the group have completed several PhD Thesis on diverse aspects of neuropsychopharmacology of stress:


- Mecanismos de disfunción de la barrera mucosa e inflamación en el colon de ratas tras exposición a estrés. Angel Ponferrada, 2006.


Available in whole in Thesis Databases:
http://teseo.mec.es/teseo/jsp/teseo.jsp
http://cisne.sim.ucm.es/screens/opacmenu_spi_s2.html

Selected papers


**Reviews**


**Textbooks:**
