## Relevance of allostasis and allostatic load in bipolar disorder

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Introduction: Bipolar disorder (BD) is a disabling illness associated with high rates of medical comorbidities, including obesity, diabetes, hypertension and metabolic syndrome, poor functioning and cognitive decline. The mechanisms underlying these processes are under debate and investigation. Despite research concerning new paradigms other than neurotransmitter systems, such as second messengers, oxidative stress and neuroplasticity, the mechanisms underlying these processes are not well elucidated. New concepts in the study of stress have been introduced during the last two decades and we intend to review their relevance for BD.

Method: Review of the current literature.

Results and Discussion: There have been an increasing number of studies about allostasis and its relationship to animal and human biology. Allostasis is the capacity to achieve stability through the change of internal parameters in order to maintain normal function in face with perceived or anticipated demands. Although the adaptive mechanisms of allostasis can be protective for the individual, there is a price to pay for this forced re-setting. The cost related to adaptation is called allostatic load. It is the wear and tear on the body and brain resulting from chronic overactivity or inactivity of physiological systems that are involved in adaptation to environmental challenge. In recent years the concepts of allostasis and allostatic load have been integrated in neuroscience research. The mediators of allostasis include various systems of the body, such as the cardiovascular, autonomous and immune systems and hypothalamic-pituitary-adrenal axis. The brain is a primary target and some structures are particularly sensitive. Effects of chronic stress have been described in important brain structures such as the hippocampus, the amygdala and the prefrontal cortex. Dysfunction in these structures is also associated with mood disorders, including BD. Furthermore, evidence of severe alterations in the mediators of allostasis described above is found in depressive and manic episodes but also in euthymic phases. We intend to present at the Conference evidence that support the hypothesis that bipolar patients experience a chronic allostatic state even when in remission, what may explain the cognitive and functional impairment associated with the disease.

Keywords: bipolar disorder, allostasis, allostatic load