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## ACCEPTED MANUSCRIPT

Defeat stress in rodents: from behavior to molecules

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- Social defeat produces behaviors resembling those observed in humans with depression
- Developed as a model for MD, social defeat reflects other psychiatric disorders too
- Social defeat is a model for stress-induced psychopathologies

#### Abstract

Mood and anxiety disorders are prevalent conditions affecting one out of four people during lifetime. The development of high validity animal models to study these disorders has been a major challenge in the past. When considering experimental approaches for studying affective disorders, the social defeat paradigm has been shown to have etiological, predictive and face validity. Here, we explain the general principle of social defeat stress paradigms, with a strong focus on the resident-intruder model and compare different experimental settings as published to date. We discuss behavioral changes described in defeated animals as well as changes in the animal's physiological parameters. In addition, we provide an overview of the molecular adaptations that are found in animals subjected to defeat stress, with special attention to neural circuits and neuroendocrine signaling. Defeat produces specific behaviors resembling the signs and symptoms of humans with affective disorders, such as anhedonia, social avoidance, despair and anxiety. These can be linked to a wide range of physiological changes -ranging from cardiovascular changes to alterations in the immune system- or by disturbances in specific neurotransmitter systems, in particular serotonin and dopamine. The defeat stress model thus impacts on several functional domains of behavior and may mimic cardinal features of a multitude of psychiatric disorders including depression, post-traumatic stress disorder and schizophrenia. This manuscript critically reviews the core findings, strengths and limitation of the range of animal studies in this field and provides future perspectives. Keywords

Social defeat, Resident - intruder, Stress, Animal model, Psychiatric disorders

#### 1. Introduction

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