

Female rats are resistant to the long-lasting neurobehavioral changes induced by adolescent stress exposure

Katharina Klinger^{1,#}, Felipe V. Gomes^{1,*}, Millie Rincón-Cortés¹, Anthony A. Grace¹

Departments of Neuroscience, Psychiatry and Psychology, University of Pittsburgh

[#]Current affiliation: University of Magdeburg; Institute of Genetic and molecular Neurobiology Otto-von-Guericke University, Universitätsplatz 2, 39106 Magdeburg Germany

^{*}Current affiliation: Department of Pharmacology, Ribeirao Preto Medical School, University of Sao Paulo, 3900 Bandeirantes Ave, Ribeirao Preto, SP, 14049-900, Brazil

Stress during adolescence is a risk factor for neuropsychiatric diseases, including schizophrenia. We recently observed that peripubertal male rats exposed to a combination of daily footshock plus restraint stress exhibited schizophrenia-like changes including cognitive impairment, anxiety, and dysregulation of the dopaminergic (DA) system. However, sex differences are present in nearly all aspects of psychiatric disorders, such as prevalence, symptom expression and severity. Furthermore, these sex differences may involve the hypothalamic-pituitary-adrenal axis response to stress and a possible interaction with the DA system. Although females are more susceptible to affective dysfunction and exhibit greater sensitivity to stress than males, as suggested by the higher incidence of depression and anxiety disorders, the preclinical research is dominated by results obtained in male animals and the effects of adolescent stress on ventral tegmental area (VTA) DA neuron activity in females have not been examined. To get a more complete picture of the role of stress in developing neuropsychiatric diseases, this study evaluated the impact of stress exposure in females during adolescence or early adulthood on social interaction, anxiety, cognitive function, as well as the activity of the DA system. Stress during adolescence has short-term effects on the firing rate of VTA DA neurons. Furthermore, stress during adulthood improved cognitive performance but decreased the VTA DA neuron population activity in a short-term manner. Our results show that female rodents appear to be more resilient to developmental stress-induced persistent changes than males. This may contribute to the delayed onset and lesser severity of schizophrenia in females.