Neuroscience 2001 Abstract

Presentation Number:	665.5
Abstract Title:	Effects of chronic treatment with the small molecule CRF_1 antagonist R121919 in rats.
Authors:	**Gutman, D. A.***[1,2] ; Skelton, K. S.[1,2] ; Knight, D. L.[1,2] ; Owens, M. J.[1,2] ; Nemeroff, C. B.[1,2] [1]Laboratory of Neuropsychopharmacology, Emory University School of Medicine, Atlanta, GA [2]Department of Psychiatry & Behavioral Sciences, Emory University School of Medicine, Atlanta, GA
Primary Theme and Topics	Neurological and Psychiatric Conditions - Psychiatric Disorders -- Affective Disorders
Secondary Theme and Topics	Neurological and Psychiatric Conditions - Psychiatric Disorders -- Anxiety disorders
Session:	665. Psychiatric disorders: mood disorders--behavioral and biochemical drug effects Poster
Presentation Time:	Tuesday, November 13, 2001 1:00 PM-2:00 PM
Location:	Convention Center Exhibit Hall, Poster Board ZZ-48
Keywords:	depression, anxiety, crh

We have previously demonstrated that acute administration of R121919 can blunt the behavioral and endocrine responses to acute stressors. In this study, we examined the effects of long term treatment with the selective small molecule CRF_1 receptor antagonist, R121919, in rats. R121919 (0.0,1.0,3.16, or 10 mg/kg/day based on final body weight, n=10-12 per group) was administered via osmotic minipump for 27 days. R121919 had no effect on weight gain during the period investigated. Basal ACTH and corticosterone values obtained in the morning following 27 days of R121919 administration showed no group differences. There was no change in adrenal gland weight following R121919 treatment for 27 days. After 25 days of R121919 treatment, the animals were tested in a defensive withdrawal paradigm to assess anxiety. Previously, we have demonstrated that acute administration of R121919 reduces measures of anxiety as assessed in this paradigm. Following 25 days of R121919 administration, the total amount of time spent outside of the tube was not significantly different between vehicle treated animals and those receiving R121919. ACTH and corticosterone values obtained following defensive withdrawal via tail-nick also showed no significant differences. These results may suggest that tolerance to the behavioral and endocrine effects of R121919 may develop during chronic administration. These results will be correlated with in situ hybridization and receptor autoradiographic analysis to determine if changes in CRF_1 receptor mRNA and CRF peptide mRNA expression may explain these effects.

Supported by MH-42088