Role of CRF system in a model of binge eating in female rats

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The present study evaluated the role of the corticotrophin releasing factor 1 receptor (CRF-1R) system in female rats, in which Binge Eating (BE) forhighly palatable food(HPF) was evoked by stress and repeated food restrictions [1]. Episodes of BE in humans are characterized by compulsive, non-homeostatic consumption of an unusually large quantity of HPF in a short period of time. Considerable evidence suggests that BE may be caused by a unique interaction between dieting and stress.In consideration of the high prevalenceof BE disorders in adolescent and young adult women, young female rats were used.

Four groups of rats were used: NR+NS was normally fed and not stressed on the test day (d25); NR+S was fed as NR+NS and stressed on d25; R+NS was exposed to 3 cycles of yo-yo dieting (8-day cycles of food restriction/refeeding (4d 66% of the standard chow food intake, 4d food *ad libitum*) but not stressed; R+S was fed as R+NS and stressed on d25. All groups were fed HPF for 2 h on day 5-6 and 13-14. Stress was induced by preventing access to HPF for 15 min, while rats were able to see and smell it. After the stressful procedure the rats had free access to HPF and standard chow.

Results revealed that BE was selectively elicited in R+S, that showed a marked increase in HPF intake in comparison to NR+NS. Intake of standard chow pellets was not significantly modified. HPF intake in R+NS and NR+S was not significantly different from that of NR+NS. Systemic injections of the selective CRF-1R antagonist R121919 (10-20 mg/kg) significantly reduced HPF intake in the R+S, but had no effect in the other 3 groups.

To explore the significance of hypothalamic CRF related mechanisms in BE, HPA axis activity in the R+S and NR+NS groups was monitored by measuring serum corticosterone (CORT) levels. Data showed a marked increase of CORT levels in the R+S group that lasted for about 30 min. On the other hand, treatment with metyrapone (50 and 100 mg/kg), a CORT synthesis inhibitor, failed to prevent BE. Consistent with this finding, CORT injection (2.5 and 10 mg/kg) did not induce BE.

In a subsequent in situ hybridization experiment the expression of CRHR1 transcript in the R+S and NR+NS groups was monitored. Results revealed an up regulation of CRHR1 mRNA signal in the BNST, central (CeA) and basolateral amygdala (BLA) of R+S rats. Of note, when the non selective CRF receptor antagonist D-Phe-CRF(12-41) (50 ng/rat) was bilaterally injected into the BNST it significantly and selectively reduced BE in the R+S group thus replicating the results obtained following systemic administration of R121919. On the other hand, the same dose of D-Phe-CRF(12-41), injected in lateral ventricle, was ineffective.

Altogether these findings demonstrated that extra-hypothalamic CRF-1R mechanisms rather than the endocrine function of these receptors are involved in BE. Selective antagonism at CRF1 receptor could represent a novel pharmacological treatment for binge eating and other eating disorders with a compulsive component.

[1] Cifani et al. (2009) Psychopharmacology 204:113-25