EMOTIONAL BEHAVIOR IS MODULATED BY LIRAGUTIDE IN AN AGE AND GENDER MANNER IN RATS FROM FOOD RESTRICTION MOTHERS

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INTRODUCTION

Food restriction (FR) of mothers during the perinatal period, can generate disorders such as anxiety an hypersensitivity to stress in offspring and predisposes to the development of disturbances in emotional behaviour and psychological disorders in adulthood. In rodents, these alterations include changes in exploratory behaviour and increased behaviour associated to anxiety. Liraglutide, a GLP-1 receptor agonist, used as a treatment for Type 2 Diabetes Mellitus, is known to have several effects in the central nervous system, regulating the hypothalamic-pituitary-adrenal function, food intake and stress response, but also having important neuroprotective activities.

The aim of this study was to assess liraglutide given to pregnant rats may prevent the deleterious effects of FR in the anxiety-like behaviour in pups at 21 days and two months of age males.

MATERIAL AND METHODS

Separation of rats in individual cages and randomly determining groups (CT/VEH, CT/LIRA, 50FR/VEH, 50FR/LIRA).

Start of treatment with liraglutide (100μg/kg, s.c/12h) or vehicle (acetic acid (0.4%)+NaCl; s.c/12h).

DAY 6

DAY 14

DAY 21 before weaning

Open field test to determine anxiety-like behavior in 40° and 30°.

DAY 23

FR 30% ad libitum for 21 days

Open field test to determine anxiety-like behavior in 40°.

VAGINAL SMEAR

Control of the estrous cycle and mating (25±2) and 10 Sprague-Dawley rats (12 weeks old) were used.

DAY 1 Vaginal plug

DAY 12 Food restriction 50% in 50FR rats; ad libitum feeding in CT rats.

DAY 21 Birth

Statistical analysis was performed using the statistical program GraphPad Prism, test two-way ANOVA was used, considering as variables sex and treatment. The test of multiple comparisons was used to compare sex was the Sidak, and for comparing treatment was Tukey. Differences were considered significant when p<0.05.

*** Statistically different between CT / VEH and 50FR / LIRA; ** Statistically different between CT / LIRA and 50FR / VEH; * Statistically different between 50FR / 50FR VEH; *a* statistically different between males and females 50FR / LIRA.

RESULTS

Study of the anxiety-like behavior in males and females in the corner, 10, 20, 30cm and in the center, at day 21.

There were no differences in the time spent in 10 (A), 20 (B), 30 (C) cm or corner (D), nor in anxiety-like behavior between vehicle treated males or females (50FR or CT). However treatment with liraglutide decreased significantly the time spent in 10 cm and corner, and increased the time spent in 20 or 30 cm only in 50FR males but not in females. Liraglutide has anxiolytic effects, increasing the percentage of time that 50FR-animals spent in the center (E), and the number of crossings they made (F). In females no significant differences were observed.

When compared results obtained in males and females no significant differences were observed in the number of crossings or the percentage of time that the offspring spent in the center in the control groups, but there were differences among the male and the female of FR group treated with liraglutide, since males spent more time in the center, and the number of crossings was higher.

CONCLUSIONS

In conclusion besides FR did not induce behavioral alterations at 21 days or two months of age, liraglutide reduced the % of time in the center only in 50FR male pups, indicating an age-dependent effect of liraglutide under non-stressed conditions.