Effect of maternal exposure to low levels of corticosterone during lactation on the susceptibility to the TNBS-induced colitis in rat adult male and female offspring

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It is well known that important events occurring in early infancy induce long-lasting changes that result to be key pathogenic factors in the development of some intestinal diseases, in which inflammatory and stress stimuli play a primary role.

A non invasive postnatal rat model, the 'CORT-nursed', in which the drinking water of mother during lactation is supplemented with corticosterone, at the moderate dose of 0.2 mg/ml, comparable to that increased by mild stressful environmental events, has been shown to improve the ability of adult progeny to meet the demands of the environment (improved cognitive capabilities, reduced fearfulness in anxiogenic situations, reduced stress response, etc).

Aim of this work was to study the susceptibility to TNBS-induced colitis in CORT-nursed (CR) adult males and females in comparison with their controls i.e., H_2O-nursed (HR) rats.

In order to do this, overnight fasted HR and CR rats, under anaesthesia, were intra-colonically infused with saline or TNBS (30 mg/kg in 0.3 mL of 50% ethanol) into the distal colon. In female rats, TNBS was infused in the luteal phase of the cycle. Four days after TNBS instillation, animals were sacrificed and, in each experimental group, were evaluated: 1) intestinal length, 2) body weight and food intake variation, 3) colonic histological damage, 4) colonic myeloperoxidase (MPO) activity, 5) plasma level of corticosterone.

HR and CR healthy males showed similar values of intestinal length (22.50 ± 0.33vs 22.05 ± 0.29 cm), body weight increase (10%vs 11% of initial weight), food intake increase (10%vs 11% of initial food), histological damage (score = 0), colonic MPO activity (145.46 ± 23.16 vs 196.33 ± 28.92 U/g protein), and plasma corticosterone (1.54 ± 0.12 vs 1.23 ± 0.21 μg/100ml). In both HR and CR male rats, in comparison with healthy animals, the induction of colitis caused a significant decrease of the intestinal length (18.38 ± 0.34vs 18.25 ± 0.31 cm), body weight (4%vs 0.1% weight lost) and food intake (11% vs 17% of consumed food), and a significant increase of histological damage (6.66 ± 0.38 vs 6.14 ± 0.52), colonic MPO activity (969.13 ± 172.41vs 592.08 ± 69.32 U/g protein) and corticosterone levels (4.47 ± 1.21vs 3.15 ± 1.14 μg/100ml). Interestingly, in CR colitic rats the reduction in body weight and food intake together with the increase in MPO activity were significantly lower than those observed in colitic HR rats. No differences in intestinal length, macroscopic score and plasmatic corticosterone levels in HR and CR colitic rats, were found.

In HR and CR healthy females, all parameters studied did not result to be different. However, their colonic MPO activity (266.56 ± 47.21 in HR and 271.29 ± 43.9 U/g protein in CR) and plasmatic corticosterone levels (7.77 ± 1.96 in HR and 8.97 ± 1.98 μg/100ml in CR) were significantly higher than those observed in healthy male rats. In both HR and CR female rats, in comparison with healthy animals, the induction of colitis caused a significant decrease of the intestinal length (9.8%vs 9.6%), body weight (1%vs 3% weight lost) and food intake (7%vs 10% of consumed food), but a significant increase of histological damage (5.6 times higher both in HR and CR) and colonic MPO activity (3.9 times higher both in HR and CR). No difference in corticosterone levels was seen. Differentially from what found in male, in CR females all parameters analyzed after colitis induction did not differ from those observed in HR female rats.

The data presented in this study highlight how a moderate corticosterone increase in lactating mothers, by changing some events occurring early in life, can exert a permanent programmed gender-specific susceptibility to TNBS colitis in adult progeny. In particular, male rats result to be more resistant to the TNBS-induced colonic damages in comparison with female rats.