BLUNTED HPA AXIS ACTIVITY DURING ISCHEMIA PROTECTS ADULT RATS NEONATALLY EXPOSED TO GLUCOCORTICOIDS AGAINST BRAIN DAMAGE

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Early-life environmental factors may cause structural and functional changes in the CNS, which persist for the life span. A slight increase of corticosterone, through mother's milk, during lactation, induces enhanced learning, a blunted Hypothalamus-Pituitary-Adrenal (HPA) axis response to restraint stress and an increase of mineralcorticoid (MR) receptors in the hippocampus of adult rats.
Glucocorticoids play an important role in many physiologic functions and pathologic conditions. It is established that high levels of glucocorticoids increase neuronal vulnerability versus many insults, such as ischemia. Hence, we hypothesised that animals lactated by mothers supplemented with corticosterone in the drinking water (CORT-nursed) could be neuroprotected against an ischemic insult. We induced a transient (10 min) global brain ischemia by clamping both carotid arteries and by reducing the systolic blood pressure to 50±5 mmHg with a subcutaneous injection of sodium nitroprusside (2,5mg/kg). We collected blood samples to assess plasma corticosterone concentrations in both control and CORT-nursed animals in basal condition, 15 minutes and 24 hours after the end of the ischemia; seven days after the insult, brains were collected for histological assessment of neural damage. Interestingly, 15 min after reperfusion we found that CORT-nursed animals had significantly lower plasma level of corticosterone compared to controls, while they did not differ in the basal and 24 h levels of the hormone. The assessment of viable hippocampal neurons of the CA1 subfield, the most vulnerable brain area, revealed that CORT-nursed animals were partially neuroprotected respect to control animals. These results, together with previous data demonstrating a better learning ability of ischemic CORT-nursed animals compared to ischemic controls, suggest that the lower incretion of corticosterone induced by ischemia in CORT-nursed rats play a major role in the protection against neuronal damage and consequent learning deficit. This animal model may be useful to study several neuroadaptive changes which follow an early perturbation of plasma corticosterone levels.