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Title

The lateral habenula interacts with the hypothalamo-pituitary adrenal axis response upon stressful cognitive demand in rats

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Research highlights

- LHB inhibition induces spatial memory deficits in the Morris water maze
- Memory deficits are accompanied by an exacerbated release of corticosterone
- Memory deficits in the water maze could partly be due to a defective stress response
- The LHB is likely to be considered as an interface between emotion and cognition

ABSTRACT

The lateral habenula (LHb) is involved in emotional and cognitive behaviors. Recently, we have shown in rats that blockade of excitatory inputs to the LHb not only induced deficits of memory retrieval in the water maze, but also altered swim strategies (i.e., induced excessive thigmotaxis). The latter observation, although consistent with the occurrence of memory deficits, could also possibly be the consequence of an excessive level of stress, further suggesting a role for the LHb in the stress response in our behavioral paradigm. To test this hypothesis we performed in rats intra-LHb infusion of 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX, 267 ng/side in 0.3 μ L), or vehicle, and assessed the responsiveness of the hypothalamo-pituitary adrenal (HPA) axis to environmental stressful or non-stressful situations. We have measured plasma corticosterone (CORT) concentrations at different time points before and following intra-LHb infusion of CNQX - or of the same volume of vehicle - in three conditions: during the probe test of a water maze experiment; in an anxiety test, the elevated plus maze; and in a home cage condition. Whereas there were no differences in the home cage condition and in the elevated plus maze, in the water maze experiment we observed that CNQX-treated rats presented, along with memory deficits, a higher level of blood CORT than vehicle-treated rats. These results suggest that perturbations of the modulation of the HPA axis are consecutive to the alteration of LHb function, whether it is

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