Acute hypernatremia dampens stress-induced enhancement of long-term potentiation in the dentate gyrus of rat hippocampus

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Stress is a common experience in daily life. It initiates adaptive processes that allow the organism to physiologically cope with environmental perturbations in maintaining homeostasis and promoting survival. Stress often occurs within the context of homeostatic threat, requiring integration of physiological and psychological demands to trigger appropriate behavioral, autonomic and endocrine responses. However, the neural mechanism underlying stress integration remains elusive. Using an acute hypernatremic challenge (2.0 M NaCl subcutaneous), we assessed whether physical state may affect subsequent responsiveness to psychogenic stressors. We found that experienced forced swimming (FS, 15 min in 25°C), a model of psychogenic stress, enhanced long-term potentiation (LTP) induction in the dentate gyrus (DG) of the rat hippocampus ex vivo. The effect of FS on LTP was prevented when the animals were adrenalectomized or given mineralocorticoid receptor antagonist RU28318 before experiencing stress. Intriguingly, relative to normonatremic controls, hypernatremic challenge effectively elevated plasma sodium concentration and dampened FS-induced enhancement of LTP, which was prevented by adrenalectomy. In addition, acute hypernatremic challenge resulted in increased ERK1/2 phosphorylation in the DG and occluded the subsequent activation of ERK1/2 by FS. Moreover, stress response dampening effects by acute hypernatremic challenge remained intact in conditional oxytocin receptor knockout mice. These results suggest that acute hypernatremic challenge evokes a sustained increase in plasma corticosterone concentration, which in turn produces stress-like changes in the DG, thereby occluding subsequent responsiveness to psychogenic stress.

Figure 1. Acute hypernatremic challenge dampens forced swimming (15 min in 25°C)-induced enhancement of
LTP. (C) Slices from stressed rats displayed an enhancement in HFS-induced LTP at the LPP-DG synapses that was persisted for at least 1 h. Administration of 2.0 M NaCl inhibited FS-induced enhancement of LTP. (D) Bar graph showing the effects of 0.15 M and 2.0 M NaCl administration on FS-induced enhancement of LTP.

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