New insights on the lateral habenula: its contribution to the emotional hyperthermia

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The lateral habenula (LHb) has an important role in behavioural response to aversive situations. The corrective behavioral response to aversive stimuli is mediated via a powerful inhibitory influence of LHb on dopamine neurons in the ventral tegmental area (VTA) [1]. Physiological responses to the same situations include emotional hyperthermia, which is mediated by thermogenesis in brown adipose tissue (BAT) and vasoconstriction in cutaneous vascular bed. We recently showed that activation of neurons in the LHb elicits BAT thermogenesis and cutaneous vasoconstriction [2]. The neural circuits underlying the habenula-elicited autonomic physiological response are unknown. The LHb, via the the VTA dopamine system, may be also involved in the emotional hyperthermia. We test this possibility in the present study. We measured BAT and body temperature with pre-implanted thermistors in conscious freely-moving Sprague-Dawley. Psychological stress was performed by sudden introduction of an intruder rat confined to a small cage into the resident rat cage. Chronic electrical lesions of the LHb attenuated BAT thermogenesis and emotional hyperthermia of the resident rat elicited by the intruder stimulus. The stress-induced BAT thermogenesis was also attenuated by quinpirole (0.25mg/kg i.p.), a selective D2 receptor agonist. In anesthetized rats, inhibition of neurons in the VTA with muscimol (1nmol in 100nl) increased BAT sympathetic nerve discharges and BAT temperature. These results suggest that the LHb, via the VTA-dopamine system, may contribute to the emotional hyperthermia. 1. Hikosaka, Nat Rev Neurosci (2010, 11, 503), 2. Ootsuka and Mohammed, Physiol Rep (2015, 3 e12297).

New insights on Amygdala: The role of Basomedial Amygdala on the regulation of the autonomic and behavioral response to social stress.

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The amygdala has been associated with a variety of functions linked to physiological, behavioural and endocrine responses during emotional situations. This brain region is comprised of multiple sub-nuclei. These sub-nuclei belong to the same structure, but may be involved in different functions. The involvement of a particular sub-nucleus, the basomedial amygdala (BMA) in the regulation of emotional states has been neglected. We have investigated the regulatory role of the BMA on the responses evoked during a social novelty model and whether the regulatory role depended on an interaction with the dorsomedial hypothalamus (DMH). Our results showed that the chemical inhibition of the BMA promotes increases in mean arterial pressure (MAP) and heart rate (HR). In contrast, the BMA chemical activation by the bilateral microinjection of *bicuculline methiodide* ($GABA_A$ antagonist), blocked the increases in MAP and HR observed when an intruder rat was suddenly introduced into the cage of a resident rat, and confined to the small cage for 15 minutes. Additionally, the increase in HR and MAP induced by BMA inhibition were eliminated by DMH chemical inhibition. The BMA gabaergic chemical inhibition decreased and gabarergic disinibition increased the duration of social interaction. Our data suggest that BMA has an essential regulatory role in social anxiety, in which its inhibition has an anxiogenic effects and its activation has anxiolytic effects. Thus, our data reveals that the BMA is under continuous GABAergic influence, and that its hyperactivation can reduce the autonomic and behavioral response induced by a social novelty condition.

Contribution of serotonergic neurons in the defense response

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Stress causes several physiological responses including tachycardia, hyperthermia and hyperactivity. Activation of neurons in the medullary raphe (MR) causes an increase in heart rate and body temperature. The MR region contains the serotonin synthesizing B1-B3 bulbospinal neurons, suggesting contribution of these serotonergic neurons to the stress-induced defense responses. In the present study, we tested this possibility by taking an optogenetic approach. We used transgenic mice in which archaerhodopsin-T, a green light-driven neuronal silencer, was expressed selectively in serotonergic neurons in the central nervous system. An optic fiber and telemetry device were surgically implanted and, after recovery, the mice were subjected to a series of stress-inducing tests. Social stress (intruder) and physical stress (drop cage; may be relevant to an earthquake) were applied. Optical inhibition of serotonergic neurons in the MR significantly attenuated the stress-induced tachycardia ($P<0.05$), but did not attenuate hyperthermia or hyperactivity in both types of the stress tests. These results suggest that the MR serotonergic neurons selectively mediate tachycardia in the stressful conditions so far tested.