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Role of the Dorsomedial Hypothalamus in Responses Evoked from the Preoptic Area and by Systemic Administration of Interleukin-1β

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Abstract:

Recent studies in anesthetized rats suggest that autonomic effects relating to thermoregulation that are evoked from the preoptic area (POA) may be mediated through activation of neurons in the dorsomedial hypothalamus (DMH). Disinhibition of neurons in the DMH produces not only cardiovascular changes but also increases in plasma adrenocorticotropic hormone (ACTH) and locomotor activity mimicking those evoked by microinjection of muscimol, a GABAA receptor agonist and neuronal inhibitor, into the POA. Therefore, I tested the hypothesis that all of these effects evoked from the POA are

mediated through neurons in the DMH by assessing the effect of bilateral microinjection of muscimol into the DMH on the changes evoked by microinjection of muscimol into the POA in conscious rats. In addition, I tested the hypothesis that neurons in the DMH mediate a specific response that is thought to signal through the POA, the activation of the HPA axis evoked by systemic administration of the inflammatory cytokine IL-1β. After injection of vehicle into the DMH, injection of muscimol into the POA elicited marked increases in heart rate, arterial pressure, body temperature, plasma ACTH and locomotor activity and also increased Fos expression in the hypothalamic paraventricular nucleus (PVN), a region known to control the release of ACTH from the adenohypophysis, and the raphe pallidus, a medullary region known to mediate POA-evoked sympathetic responses. Prior microinjection of muscimol into the DMH produced a modest depression of baseline heart rate, arterial pressure, and body temperature but completely abolished all changes evoked from the POA. Microinjection of muscimol just anterior to the DMH had no effect on POA-evoked autonomic and neuroendocrine changes. Inhibition of neuronal activity in the DMH only partially attenuated the increased activity of the HPA axis following systemic injections of IL-1β. Thus, neurons in the DMH mediate a diverse array of physiological and behavioral responses elicited from the POA, suggesting that the POA represents an important source of inhibitory tone to key neurons in the DMH. However, it is clear that the inflammatory cytokine IL-1β must employ other pathways that are DMH-, and possibly POA-, independent to activate the HPA axis.

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