

Neuroendocrine perturbations in fibromyalgia and chronic fatigue syndrome

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A large body of data from a number of different laboratories worldwide has demonstrated a general tendency for reduced adrenocortical responsiveness in CFS. It is still not clear if this is secondary to CNS abnormalities leading to decreased activity of CRH- or AVP-producing hypothalamic neurons. Primary hypofunction of the CRH neurons has been described on the basis of genetic and environmental influences. Other pathways could secondarily influence HPAaxis activity, however. For example, serotonergic and noradrenergic input acts to stimulate HPAaxis activity. Deficient serotonergic activity in CFS has been suggested by some of the studies as reviewed here.

In addition, hypofunction of sympathetic nervous system function has been described and could contribute to abnormalities of central components of the HPAaxis. One could interpret the clinical trial of glucocorticoid replacement in patients with CFS as confirmation of adrenal insufficiency if one were convinced of a positive therapeutic effect. If patient symptoms were related to impaired activation of central components of the axis, replacing glucocorticoids would merely exacerbate symptoms caused by enhanced negative feedback. Further study of specific components of the HPAaxis should ultimately clarify the reproducible abnormalities associated with a clinical picture of CFS.

In contrast to CFS, the results of the different hormonal axes in FMS support the assumption that the distortion of the hormonal pattern observed can be attributed to hyperactivity of CRH neurons. This hyperactivity may be driven and sustained by stress exerted by chronic pain originating in the musculoskeletal system or by an alteration of the CNS mechanism of nociception. The elevated activity of CRH neurons also seems to cause alteration of the set point of other hormonal axes. In addition to its control of the adrenal hormones, CRH stimulates somatostatin secretion at the hypothalamic level, which, in turn, causes inhibition of growth hormone and thyroid-stimulating hormone at the pituitary level. The suppression of gonadal function may also be attributed to elevated CRH because of its ability to inhibit hypothalamic luteinizing hormone-releasing hormone release; however, a remote effect on the ovary by the inhibition of follicle-stimulating hormone-stimulated estrogen production must also be considered. Serotonin (5-HT) precursors such as tryptophan (5-HTP), drugs that release 5-HT, or drugs that act directly on 5-HT receptors stimulate the HPAaxis, indicating a stimulatory effect of serotonergic input on HPAaxis function. Hyperfunction of the HPAaxis could also reflect an elevated serotonergic tone in the CNS of FMS patients.

The authors conclude that the observed pattern of hormonal deviations in patients with FMS is a CNS adjustment to chronic pain and stress, constitutes a specific entity of FMS, and is primarily evoked by activated CRH neurons.