Brain Dysfunction Precedes the Development of Fibromyalgia

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by Janis Kelly
MANCHESTER, UK—Subjects with abnormal function of the hypothalamic-pituitary-adrenal (HPA) axis have a reduced ability to cope with psychosocial stress and are at increased risk for the onset of chronic widespread musculoskeletal pain in the wake of stressful events, according to research reported in *Arthritis & Rheumatism*.[1]

"HPA dysfunction precedes the onset of symptoms." —John McBeth, PhD.

Lead author John McBeth, PhD, writes, "We would argue that the current data support our hypothesis that psychosocial factors are moderated through the presence of HPA axis dysfunction, leading to the onset of chronic widespread pain." Dr. McBeth is a member of the Arthritis Research Campaign Epidemiology Unit, at the University of Manchester, in the UK.

Somatization, health-seeking behavior identify "at risk" subjects

The population-based, prospective cohort study included 463 patients who were free of chronic widespread pain at baseline but "at future risk based on their psychosocial profile." These subjects had high scores on measures of somatization and health-seeking behavior (as measured by the Somatic Symptom Checklist and by the Illness Behavior subscale of the Illness Attitude Scales questionnaire). The researchers had previously shown that these two scales predicted the onset of new chronic widespread pain (fibromyalgia, as defined by the American College of Rheumatology criteria) in a population-based prospective study.[2]

In the prospective study of HPA function in 463 randomly selected "high risk" subjects, 267 (57.7%) agreed to participate; of these, 241 subjects completed the 15-month follow-up study, and among them, 28 (11.6%) reported new-onset fibromyalgia during the follow-up.

HPA axis function was measured at baseline. As explained by the investigators, "Four measures of HPA axis function were selected as being appropriate for use in large samples of community-dwelling subjects: serum cortisol levels in response to an acute stressor (a pain-threshold examination), serum cortisol levels in response to a low-dose dexamethasone suppression test, and salivary cortisol levels obtained in the morning and in the evening to assess diurnal HPA tone. All tests were performed and all samples were collected in the subjects' homes or at the offices of their local general practitioners." Female subjects were studied during the early follicular phase of the menstrual cycle to control for variations in HPA function during the cycle.

Disturbed HPA axis function precedes chronic pain symptoms

Fifteen months later the subjects were mailed a second set of questionnaires including a manikin line illustration on which to indicate sites of pain lasting at least 24 hours during the previous month. The follow-up questionnaires also included the List of Threatening Life Experiences, which includes questions about adverse experiences in the subject's personal relationships, employment, illness, and financial and legal situation during the previous 6 months.

Baseline cortisol levels were not significantly different in the patients who developed fibromyalgia. Age-adjusted post-dexamethasone cortisol levels were strong predictors of subsequent pain problems. Subjects whose post-dexamethasone cortisol readings were in the middle third (183-324 nmoles/L) were three times as likely to have developed chronic widespread pain as those in the lowest third (30-179 nmoles/L), and subjects with cortisol levels above 324 nmoles/L were at even higher risk (OR 3.53, 95% CI 1.17-10.65).

The patients who developed fibromyalgia also had lower median morning salivary cortisol levels and higher median evening cortisol levels at baseline. "[S]ubjects whose morning saliva values were in the lowest third [<1-3 nmoles/L] were nearly 1.5 times more likely to report symptoms, while those whose evening saliva values were in the middle and highest thirds were more than twice as likely to report symptoms," the authors write. They note that higher post-dexamethasone serum levels indicate a failure to suppress the HPA axis, and lower morning and higher evening salivary cortisol levels indicate a blunting of the diurnal rhythm.

"Conclusions from these studies support the concept of disturbed HPA axis function in subjects with chronic pain, and specifically, with fibromyalgia. The focus would appear to be functional deficits in CRH [corticotropin-releasing hormone] release from the hypothalamus," Dr. McBeth says. " ... Central CRH tone itself therefore appears to lie at the heart of the interrelationships between stress stimuli and response

adaptation. The current results further elucidate their temporal relationships, having determined that HPA dysfunction precedes the onset of symptoms."
E-mail any comments to **info@ciaomed.org**.

Reference

1. McBeth J, Silman AJ, Gupta A, et al. Moderation of psychosocial risk factors through dysfunction of the hypothalamic-pituitary-adrenal stress axis in the onset of chronic widespread musculoskeletal pain. Findings of a population-based prospective cohort study. *Arthritis Rheum*. 2007;56:360-371.
2. McBeth J, Macfarlane GJ, Benjamin S, et al. Features of somatization predict the onset of chronic widespread pain: results of a large population-based study. *Arthritis Rheum*. 2001;44:940-946.

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