Psychoneuroendocrinology (2012) 37, 299—306

available at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/psyneuen

Comparison of the cortisol awakening response in women with shoulder and neck pain and women with fibromyalgia

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Received 28 February 2011; received in revised form 16 June 2011; accepted 20 June 2011

KEYWORDS
Salivary cortisol;
Hypothalamic—pituitary—adrenal axis;
Regional musculoskeletal pain;
Widespread musculoskeletal pain;
Stress;
Fibromyalgia syndrome;
Cortisol awakening response

Summary Shoulder and neck pain (SNP) and fibromyalgia syndrome (FMS), two musculoskeletal conditions of unknown pathogenesis, share some common features in terms of altered neuroendocrine responses, pain and stress perception. However, the pain distribution in SNP is localized, whereas in FMS is more widespread. Because regional musculoskeletal pain may represent an intermediate stage along a continuum towards widespread musculoskeletal pain we compared the cortisol awakening response (CAR) in women with SNP with the CAR in FMS patients and healthy controls (HC) in a controlled hospital—hotel setting. The aim of the study was to investigate whether SNP is related to a deviant regulation of the hypothalamic—pituitary—adrenal (HPA) axis. Eighteen women with SNP, 29 female FMS patients, and 27 female HC participated in the study. Cortisol samples were collected upon awakening, 30 and 60 min later. Questionnaires measuring pain levels, sleeping problems, perceived stress, and psychological characteristics were administered to the participants. Compared with HC, women with SNP had a tendency towards higher cortisol levels, whereas FMS had lower cortisol levels. Adjustment for potential confounders did not influence the results. Women with SNP and FMS patients reported more health complaints, pain, and perceived stress than the HC, but women with SNP were less affected than the FMS patients. Women with SNP showed a tendency towards an elevated HPA axis activity compared with HC. The current findings may indicate that the hypercortisolism in regional musculoskeletal pain represent an intermediate stage towards the development of a hypocortisolism in widespread musculoskeletal pain.

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doi:10.1016/j.psyneuen.2011.06.014

1 Introduction

The pathogenesis of widespread and regional chronic musculoskeletal pain conditions is still unknown. Psychosocial stress seems to play an important role in the onset and in the development of these disorders (Linton, 2000; van der Windt et al., 2000; McFarlane, 2007). Chronic shoulder and neck pain (SNP) is highly prevalent in the population of the Western countries (30—50% in the general population), particularly in women (Picavet and Schouten, 2003; Larsson et al., 2007; Côté et al., 2008). The pain distribution in women with SNP is localized in the shoulder and neck area, but the diagnostic criteria are relatively vague and several specific and partly overlapping diagnoses exist in clinical practice and epidemiological research (Larsson et al., 2007). Fibromyalgia syndrome (FMS) is a condition characterized by chronic widespread musculoskeletal pain and multiple tender points with reduced pressure pain threshold (Wolfe et al., 1990). Comorbid symptoms commonly associated with FMS include poor sleep quality, morning stiffness, fatigue, anxiety, depression, and psychosocial stress (Wolfe et al., 1990; Krag et al., 1994).

Whether widespread and regional musculoskeletal pain conditions represent a continuum with a common pathogenesis or are different entities has been debated in the scientific community (McCain and Scudds, 1988; Goldenberg, 1999; Buskila, 2001). To compare two pain-related conditions, such as SNP and FMS, may provide new insight into the pathogenesis and the development from regional to widespread pain conditions. Several authors have demonstrated that mental and psychosocial stress worsen pain in both conditions (Bansevicius et al., 2001; Van Houdenhove and Egle, 2004). Moreover, altered responses of the hypothalamic—pituitary—adrenal (HPA) axis have been observed in individuals with regional as well as widespread pain (McBeth et al., 2007; McFarlane, 2007; Turner-Cobb et al., 2010). Dysregulation of the HPA axis may lead to an inadequate adaptation to stress thereby representing a possible risk factor for the development of stress-related diseases (de Kloet et al., 2008). Moreover, some studies have found that individuals with a deviant regulation of the secretion of cortisol, the end-product of the HPA axis, have an increased risk for chronic pain development (Blackburn-Munro, 2004; McBeth et al., 2007). Both abnormal increase and decrease in cortisol secretion may lead to pathology (Miller et al., 2007). Hypocortisolism (i.e., low cortisol levels) has been associated with the pathogenesis of widespread and regional chronic musculoskeletal pain conditions, e.g., chronic pelvic pain (Heim et al., 1998) and FMS (Heim et al., 2000). However, findings for FMS are inconsistent also showing higher or normal cortisol levels compared with healthy controls (Tak et al., 2011). In contrast, several authors have found that women with SNP and healthy controls (HC) had comparable cortisol levels in saliva (Sjörs et al., 2010), in blood (Theorell et al., 2000; Nilsen et al., 2007), and in urine (Larsson et al., 2008). However, women with SNP showed a tendency towards higher serum cortisol levels than HC after a prolonged and stressful reaction-time test (Nilsen et al., 2007).

Dysregulation of the HPA axis can be investigated with the assessment of the cortisol awakening response (CAR). The peak level of cortisol in healthy individuals generally occurs about 30 min after awakening and deviating responses from this pattern may indicate altered HPA axis regulation (Wüst et al., 2000; Clow et al., 2004; Federenko et al., 2004).

There are still few studies in the literature that have systematically investigated salivary CAR under controlled conditions in groups with such pain conditions. The aim of this study was therefore to compare women with SNP with FMS patients and HC in terms of free salivary cortisol levels during the morning, self-reported pain, sleep disturbances, and psychological features. In a previous study, the comparison between FMS patients and HC of the same study sample showed that FMS patients presented an attenuated HPA axis activity with low CAR (Riva et al., 2010). However, in the current study we added new data on women with SNP because SNP might represent a preliminary stage towards the development of FMS, as it has been already hypothesized for chronic local and widespread musculoskeletal pain conditions (McEwen, 1998; Rosmond and Björntorp, 2000; Van Houdenhove and Egle, 2004; Miller et al., 2007). We therefore hypothesize that the HPA axis in women with SNP is dysregulated and characterized by elevated cortisol secretion. Moreover, we hypothesize that women with SNP show more self-reported pain, sleep disturbances, perceived stress, and health complaints than HC, but less than FMS patients.

2 Methods

2.1 Participants

Eighteen women with SNP, 29 female FMS patients and 27 female HC participated in the study (Table 1). Women with SNP were recruited among staff at the University and at a secondary school, FMS patients were mainly recruited through the local fibromyalgia association in Trondheim (Norway), and the HC were recruited among donors to the hospital blood bank. Eligible women with SNP were included if they scored 3 or more on a scale from 0 to 6 representing frequency and intensity of shoulder and neck pain during the last 6 months. HC included in the study scored below 3 on the same scale. The cut-off score of 3 was in a previous study associated with a 45% chance of seeking medical consultation due to shoulder and neck symptoms (Westgaard and Jansen, 1992; Jensen et al., 1993; Mork and Westgaard, 2006). Inclusion criteria for eligible FMS patients were a verified diagnosis of FMS as defined by the American College of Rheumatology (Wolfe et al., 1990). Number of tender points (M = 15.7; SD = 5.9; range 11—18), number of years since first symptoms (M = 13.1; SD = 8.6; range 3—36), and number of years with confirmed diagnosis (M = 5.5; SD = 6.0; range 0—26) was retrieved from each FMS patient's medical record. Participants were excluded if they had: (a) cardiorespiratory, cerebrovascular, neurologic, neuromuscular, endocrine, infectious, metabolic, lung, or cancer disease, (b) injury that affected function, (c) connective tissue disorder, (d) tendinitis or capsular affection of the shoulder joint, (e), high blood-pressure (i.e., systolic pressure $>$ 140 mmHg or diastolic pressure $>$ 90 mmHg) or were taking anti-hypertensive medication. Participants were also excluded if they were taking medication that may interact with neural, vascular, or muscular function or the physiological measurements to be performed (e.g. antidepressants, antiepileptics, β-blockers). Participants that used analgesics and/or sleep medicine