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Variations in Psychometric Profiles and Awakening Cortisol Responses in Men with Chronic Prostatitis/Chronic Pelvic Pain Syndrome

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Introduction

The diurnal rhythm of the cortisol cycle is marked by two main characteristics • a peak in cortisol levels within 30 min. after awakening in the morning (awakening cortisol response) and a gradually decreasing slope throughout the day, reaching the lowest levels in the evening. These endocrine patterns are consistent, show high intra-individual stability across time and appear to be markers for subtle changes in hypothalamic-pituitary-adrenal (HPA) axis regulation.

Stress triggers a cascade of pathophysiological events that involve activation of two pathways, the HPA axis and the autonomic nervous system. Chronic activation of the physiologic stress response induces putative glucocorticoid resistance and altered immunity, release of proinflammatory cytokines and prostaglandins that may contribute to pelvic tension myalgia, and ultimately to cycling psychological distress. Clinicians have observed that stress exacerbates prostatitis, and chronic stress has been shown to specifically induce inflammatory histological changes in the prostate of a rat model. Abnormal regulation of the HPA axis and diurnal cortisol rhythms has been associated with several pain and chronic inflammatory conditions (e.g., fibromyalgia, back pain).

Personality traits may modulate reactivity and vulnerability to stress. We have strong preliminary evidence from studies of our patients with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) that manual physiotherapy with myofascial trigger point release and progressive relaxation therapy, proven methods to relieve stress, can provide pain relief in some CPPS sufferers. Once it is understood how stress-induced neuro-biochemical changes may relate to pelvic pain in men, it may be possible to modulate these effects and develop new and innovative approaches for the prevention and treatment of CPPS. Despite the likely relevance of stress-related neurohormones in the disease process of CPPS, these factors have not been systematically evaluated.

The primary aim of the study was to test the hypothesis that CP/CPPS is associated with psychological dysfunction as well as endocrine dysregulation of the HPA axis.

Methods

Patients

- Men (• 18 y. o.) with symptoms of CP/CPPS (NIH category III A&B) for at least 3 months within the last 6 months
- NIH-CPSI total score • 15 (scale 0-43); non-zero pain domain score
- No analgesics, psychotropic drugs, systemic corticosteroids allowed at least 2 weeks before study.
- Control subjects: healthy, age-matched men recruited from same socio-economic community; no history or evidence of GU disease or chronic pain conditions

Psychometric Evaluations

- **Brief Symptom Inventory (BSI)**: scores depression, anxiety, somatization, obsessive-compulsive behavior, interpersonal sensitivity, hostility, phobic activity, paranoid ideation (social alienation), and psychoticism.

  Global Severity Index (GSI) of the BSI provides an overall measure of distress
- **Beck Anxiety Inventory**
- **Perceived Stress Scale**: assesses unpredictability, lack of control, burden overload and inquiries about current levels of experienced stress
- **Bortner Type A Behavior Pattern**

Salivary Cortisol Collection and Assessment

- Saliva collected on two consecutive days at 9 specific time points with strict reference to each subject's time of awakening; awakening was either spontaneous or by alarm clock
- Saliva collected into sterile Salivette® tubes. To assure compliance, subjects used an electronic watch that beeps at designated time intervals and kept a collection time log
- Samples assayed in duplicate using luminescence immunoassay reagents (Immuno-Biological Labs, Hamburg, Germany)

Sampling times for salivary cortisol after awakening and throughout the day

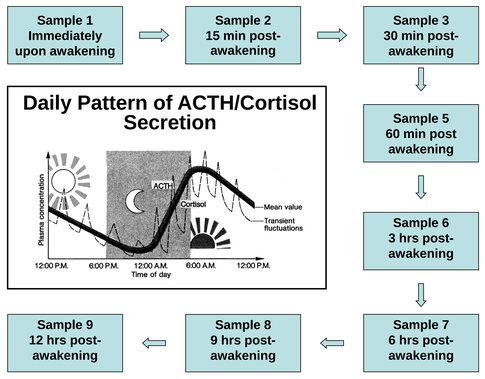


Table 1. Patient Characteristics

	CPPS (33)	Controls (18)
Mean age in years, (range)	43 (21-70)	46 (24-66)
Mean duration of CPPS, months (range)	81 (6-336)	0
NIH-CPSI total score, mean	24.5 (12-36)	0.7 (0-4)
Pain sub score, mean	12 (3-18)	0.1 (0-2)
Ethnicity/race, % of sample		
Caucasian	75	55
Asian	12	28
African American	6	6
Hispanic	6	11
Education, % of sample		
Less than college degree	24	28
College/Graduate school	76	72

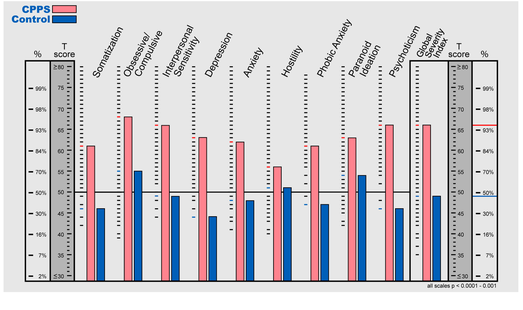
Results

Table 2. Psychometric Profiles: median scores (Q1/Q2)

Evaluation	CPPS (n=33)	Controls (n= 18)	p Value*
Type A Behavior	101 (80/113)	98 (90/110)	0.82
Perceived Stress Scale	19 (14/22)	12 (11/15)	<0.002
Beck Anxiety Inventory	9 (6/16)	1 (.25/4.75)	<0.001
Global Severity Indexof BSI			
T score	66 (55/73)	49 (44/58)	<0.0001
Centile rank	94%	47%	

*Mann-Whitney U test

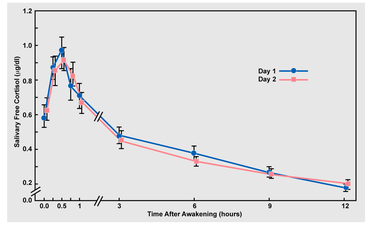
Fig. 1 Brief Symptom Inventory Median T Scores and Centile Ranks



- CPPS patients had significantly more perceived stress and anxiety than controls (p<0.002, both PSS and BAI); but similar Type A behavior patterns (Table 2)
- BSI scores were significantly elevated in CPPS for all nine scales (p< 0.0001-0.006) (Fig.1)
  CPPS: median range 70th to 96th centile
  Controls: median range 27th to 54th centile
- The Global Severity Index (GSI) of BSI • summary score indicative of current degree of each subject's distress, median scores •

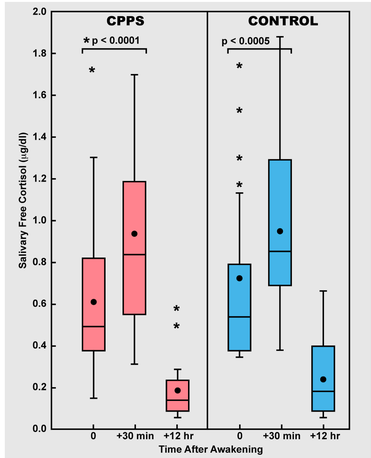
  CPPS at 94th centile vs. 47th centile for controls (p<0.0001)
- No significant correlation was found between psychometric scores and duration of CPPS or NIH-CPSI total scores

Fig. 2 Salivary Free Cortisol (Mean ± SE) on Two Days After Awakening in CPPS Men



- Diurnal cortisol profiles showed good intra-individual stability, and stability within the CPPS and control cohorts, for 2 days of saliva sampling (Fig. 2, shown for CPPS men only, similar stability for controls)
- Awakening cortisol response (wake +30 min) • cortisol increased significantly (p < 0.0001) and peaked 30 min after awakening in both groups (Fig. 3)
  54% (0.61 - 0.93 µg/dl) increase for CPPS men
  32% (0.72 - 0.95 µg/dl) increase for controls

Fig. 3 Changes in Salivary Free Cortisol With Awakening Rise (Wake + 30 min) and to Nadir (Wake + 12 hr)



Box plot of salivary cortisol sampled on two consecutive days. Mean (dot in box); median (line in box). Box boundary closest to zero is 25th percentile; farthest is 75th percentile; whiskers are 90th and 10th percentiles.

- The mean slope of the natural log-cortisol levels (awakening cortisol response) showed hyperactive responses for the CPPS men
  CPPS slope 0.90
  Control slope 0.59 p = 0.05
- Both groups showed a decline (wake +12 hr) with similar mean daytime log-cortisol slopes (p >0.05)
  CPPS slope -0.106
  Control slope -0.116

Summary

- Psychometric profiles of the CPPS men showed significantly higher levels of self-reported perceived stress, feelings of depression and anxiety, somatization, obsessive-compulsive behavior and other psychological symptoms than the age-matched controls.
- The Global Severity Index (of BSI), a single composite score indicating respondent's quantity and intensity of symptoms, affirmed high levels of psychosocial distress (median 94th centile) in the CPPS cohort.
- Men with CPPS show evidence HPA dysregulation indicated by the significantly greater slope of the awakening cortisol response compared to healthy, pain-free controls.

Conclusions

CPPS men scored exceedingly high on all psychosocial variables and showed evidence of dysfunctional HPA axis function reflected in augmented awakening cortisol responses compared with healthy, age-matched controls.

Whether these observations represent preexisting characteristics of individuals before the onset of CPPS which are activated by chronic pain, or as a consequence of stress associated with this condition, remain in question.

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