Depression, prolactin and dissociated mind

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Abstract

OBJECTIVES: Usual neuroendocrinological manifestation of traumatic stress and dissociation is dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis. The aim of the present study is to perform examination of HPA axis as indexed by basal serum prolactin and test its relationship to dissociative symptoms and symptoms of traumatic stress.

PATIENTS AND METHODS: 25 inpatients treated at the university hospital with diagnosis of unipolar depression mean age 41.23 (SD=11.53) were assessed using psychometric measures of dissociation (DES) and traumatic symptoms (TSC-40), and using standard biochemical analytical methods basal serum prolactin levels were investigated.

RESULTS: Data show that prolactin manifests significant relationship to dissociative symptoms (r=0.52, p=0.004). Significant correlation was not found between prolactin and traumatic symptoms measured by TSC-40 (r=0.31, p=0.07).

CONCLUSIONS: The present data suggest that serum prolactin levels in unipolar depressive patients are related to dissociative symptoms that is likely caused by passive coping mechanisms leading to dissociation.

ORIGINAL ARTICLE

INTRODUCTION

According to recent evidence child abuse and other traumatic stress experiences represent significant conditions in pathophysiology of depression and often cause to increase dissociative symptoms (Teicher *et al*., 2003; Bob *et al*., 2005; Duman and Monteggia, 2006; Dranovsky and Hen, 2006). Traumatic stress leading to dissociation typically affects memory systems that may lead to memory loss restricted to a circumscribed period of time or category of events within the individual's life that causes exclusion of the experience from consciousness and the inaccessibility of voluntary recall of mental events associated with the trauma (Nemiah, 1991; Bob *et al*., 2006; Bob, 2007). Typical physiological reactions to traumatic stress and dissociation are disturbances of self-regulatory

systems such as HPA axis resulting in hyperarousal, tachycardia or other symptoms of autonomic nervous system instability (Newport and Nemeroff, 2000; Teicher *et al*., 2003; Read *et al*., 2001). HPA axis is functionally closely related to neuroendocrinological balance, control hormonal levels, energetic metabolism, neuroimmunomodulation and disturbances of memory during stress reaction (Kellner and Yehuda, 1999; Newport and Nemeroff, 2000; Mason *et al*., 2001; Payne et al., 2006; Plotsky *et al*., 1998; Teicher *et al*., 2003; Gavrilovic and Dronjak, 2005; Nakayama *et al.* 2005; Takahashi *et al.* 2005; Umegaki et al., 2006). According to neurodevelopmental research are most serious disturbances of HPA axis caused by traumatic events such as childhood abuse or neglect in the first years of life and often have long-term impact on emotional, behavioral, cognitive, social and physiological functions and vice versa love and social care also may influence these functions and improve dissociative disturbances (Teicher *et al.* 2003; Read *et al.* 2001; Esch and Stefano, 2005a,b; Stefano and Esch, 2005).

With respect to findings that traumatic stress history typically is associated with dissociation, the relationship between dissociative symptoms and HPA axis dysregulation presents important problem of psychiatry and clinical neuroendocrinology. This link seems to be particularly relevant for therapy that would take into consideration both of these aspects of the disease. The purpose of the present study is to perform examination of HPA axis functioning indexed by basal prolactin and its relationship to dissociative symptoms and symptoms of traumatic stress.

PATIENTS AND METHODS

Patients

For empirical examination of suggested hypothesis assessment of basal serum prolactin during rest conditions was performed in 25 inpatients with unipolar depression treated at the Psychiatric Clinic of university hospital in Prague. The patients have diagnosis of unipolar depressive disorder (i.e. patients with recurrent depression or depressive period) in relapse, confirmed according to DSM-IV criteria by clinical interview (American Psychiatric Association, 1994). The patients were treated by SSRI antidepressants in usual recommended doses. Exclusion criteria were organic illnesses involving the central nervous system, psychotic disorders, bipolar disorder, alcohol and/or drug abuse, any form of epilepsy and mental retardation, neuroendocrine and metabolic disorders, any hormonal, antipsychotic or other medication affecting prolactin blood level, ECT or rTMS therapy, and pregnancy or lactation in women. The patients were 6 males and 19 females in average age 41.23±11.53 (age range 28–55) predominantly with high-school education. All the patients gave written informed consent and the clinical study was approved by university ethical committee.

Psychometric measures

Psychic dissociative symptoms were assessed by Dissociative Experiences Scale (DES) (Bernstein and Putnam, 1986). DES represents 28 items self-reported questionnaire examining main dissociative phenomena such as absorption, amnesia, depersonalization, derealization, reality distortion, and others. Subjects indicate a degree of their experience on the continuum from 0% to 100%.

For investigation of childhood traumas, TSC-40 (Trauma Symptom Checklist) (Briere, 1996) was used. TSC-40 is a self-reported 40-item questionnaire done on a 4-point likert scale. TSC-40 evaluates symptomatology in adults associated with childhood or adult traumatic experiences and measures aspects of posttraumatic stress and other symptom clusters found in some traumatized individuals.

Neuroendocrine measures

For biochemical assessment, the blood samples of 5 ml volumes were collected in rest conditions according to common procedures at the time from 7:30 to 8 a. m. in laboratory of Psychiatry department. The blood samples were carefully transferred (about 10 minutes) in icebox at the temperature of 4 °C to university biochemical department and immediately centrifuged at the temperature of 4 °C. After that prolactin serum levels have been assessed in biochemical laboratory according to common analytical procedures.

Prolactin serum levels were assessed by technique of chemiluminiscent immunoassay (CLIA) using analysator ADVIA (Centaur Bayer). The intra- and interassay coeficients of variance were 2.9 and 12.2%.

Statistical methods

Statistical evaluation for results of serum prolactin and psychometric measures included common methods of descriptive and inferential statistics i.e. mean and standard deviation, and Pearson product-moment correlation for independent samples were used for description of functional relationship. For the statistical evaluation the software package Statistica version 6 was used.

RESULTS

Results of the present study confirm dysregulation of the HPA-axis reactivity with respect to psychosocial stress and dissociative symptoms in the depressive patients. Data indicate that prolactin as a characteristic of HPA axis functioning displays significant relationship to dissociative symptoms measured by DES ($r=0.52$, $p=0.004$) (Figure 1). Significant correlation was not found between prolactin and traumatic symptoms measured by TSC-40 ($r=0.31$, $p=0.07$). Significant correlations was found between DES and TSC-40 ($r=0.58$, $p=0.001$). Hyperprolactinemia (higher than 30 microg/l) was found in 4 women.

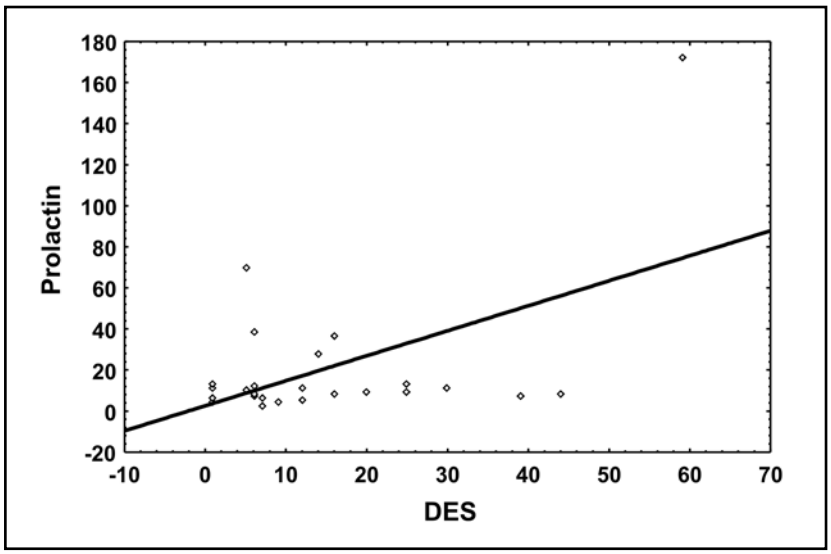

Figure 1. Dependency graph between DES and prolactin serum levels (microg/l) (r=0.52, p=0.004).

DISCUSSION

The result of this study indicate relationship between HPA-axis reactivity indexed by basal serum prolactin level and dissociative symptoms. This observed relationship between DES and serum prolactin (r=0.52, p=0.004) is in agreement with reported findings that increased or decreased prolactin level could be linked to psychological stressors (Sonino *et al*., 2004; Uhart *et al*., 2006; Theorell, 1992). This reason is consistent with reported data that patients with hyperprolactinemia often suffer from emotional difficulties that may persist even after successful treatment. It is mainly because prolactin influences CNS and variations in its concentrations are significantly related to mood, emotions and behavior (Sobrinho, 1998). In addition, there is evidence linking clinical onset of prolactinomas with stressful life-events, that more frequently occur in women. This suggests that psychological factors are especially important (Sobrinho, 1998). Specifically the present data suggest that not only traumatic stress symptoms leads to HPA disturbances but specific changes in the mental state linked to unresolved conflict and dissociation are needed for pathological neuroendocrine response. This is in agreement with findings that show relationship between passive coping response to stress and increased plasma prolactin levels; whereas stress situations associated with active coping are associated with unchanged or even lowered levels (Theorell, 1992). Passive coping mechanisms are typically associated with cognitive strategies such as withdrawal or disengagement, dissociation, and the immobility response (Schore, 1994, 2001). At this point dissociation presents typical form of human response to inescapable and threatening stress with the defensive tendency toward passive and avoidant coping that emerge as hopelessness, emotional withdrawal and disengagement (van der Kolk *et al*., 1985; Nijenhuis *et al*., 1998).

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