Dissociative symptoms and neuroendocrine dysregulation in depression

Petr Bob1,2, Peter Fedor-Freybergh1,2, Denisa Jasova1, Gustav Bizik1, Marek Susta1, Josef Pavlat1, Tomas Zima3, Hana Benakova3, Jiri Raboch1

1 Department of Psychiatry, 1st Faculty of Medicine, Charles University, Prague, Czech Republic
2 Department of Psychology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic
3 Department of Clinical Biochemistry and Laboratory Diagnostics, 1st Faculty of Medicine, Charles University, Prague, Czech Republic

Source of support: This work was supported by research grant by Ministry of Health IGA MZ NR 8824-4 and for support by research projects MSM0021620849, MSM0021622404 and Centre for Neuropsychiatric Research of Traumatic Stress 1M06039

Summary

Background: Dissociative symptoms are traditionally attributed to psychological stressors that produce dissociated memories related to stressful life events. Dissociative disorders and dissociative symptoms including psychogenic amnesia, fugue, dissociative identity-disorder, depersonalization, derealization and other symptoms or syndromes have been reported as an epidemic psychiatric condition that may be coexistent with various psychiatric diagnoses such as depression, schizophrenia, borderline personality disorder or anxiety disorders. According to recent findings also the somatic components of dissociation may occur and influence brain, autonomic and neuroendocrine functions. At this time there are only few studies examining neuroendocrine response related to dissociative symptoms that suggest significant dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis. The aim of the present study is to perform examination of HPA axis functioning indexed by basal cortisol and prolactin and test their relationship to psychic and somatoform dissociative symptoms.

Material/Methods: Basal cortisol and prolactin and psychic and somatoform dissociative symptoms were assessed in 40 consecutive inpatients with diagnosis of unipolar depression mean age 43.37 (SD=12.21).

Results: The results show that prolactin and cortisol as indices of HPA axis functioning manifest significant relationship to dissociative symptoms. Main results represent highly significant correlations obtained by simple regression between psychic dissociative symptoms (DES) and serum prolactin (R=0.55, p=0.00027), and between somatoform dissociation (SDQ-20) and serum cortisol (R=–0.38, p=0.015).

Conclusions: These results indicate relationship between HPA-axis reactivity and dissociative symptoms in unipolar depressive patients that could reflect passive coping behavior and disengagement.

key words: depression • traumatic stress • dissociation • prolactin • cortisol

Full-text PDF: http://www.medscimonit.com/fulltxt.php?ICID=869411

Word count: 2604
Tables: 1
Figures: 2
References: 64

Author’s address: Petr Bob, Department of Psychiatry, 1st Faculty of Medicine, Charles University, Ke Karlovu 11, 12800 Prague, Czech Republic, e-mail: petr.bob@f1.cuni.cz
**Background**

At the beginnings of the term dissociation is the French psychiatrist Pierre Janet [1,2] whose work is the source for most of the dissociation theory. Dissociation is traditionally attributed to trauma and other psychological stressors that are linked to dissociated traumatic memories [3–6]. According to existing evidence in most such cases, the loss of episodic and/or emotional memories is related to traumatic stress; nevertheless brain insult, injury or other organic brain disease may play a role in this process [5,6]. Dissociative disorders and dissociative symptoms including psychogenic amnesia, fugue, dissociative identity disorder, depersonalization, derealization and other symptoms or syndromes have been reported as an epidemic psychiatric condition that may be coexistent with various psychiatric diagnoses such as schizophrenia, depression, borderline personality disorder or anxiety disorders [7–11].

Etiology of these disorders is often related to a great occurrence of child abuse and experienced traumatic stress [9–11]. According to modern definition, dissociation could be defined as partial or total disconnection between memories of the past, awareness of identity and of immediate sensations, and control of bodily movements often resulting from traumatic experiences, intolerable problems, or distorted relationships [12]. DSM-IV defines dissociation as “a disturbance or alteration in the normally integrative functions of identity, memory or consciousness” [13]. Dissociation on the psychological level emerges as memory losses, fragmentation of knowledge of the self and experience, splitting of emotional and cognitive aspects of experiences, numbing of affect, psychological escape from unpleasant stimuli, trance-like states, increased suggestibility and greater hypnotizability [1,4,10,14,15]. According to historical and recent findings not only the psychological, but also the somatic components of dissociation have a profound role in the long-term adaptation to traumatic experience and lead to a lack of integration of somatoform components of experience, reactions, and functions [16,17]. Historically are these pathological manifestations associated with the term stress-related conversion at first systematically described in 1859 by Pierre Briquet and later comprehensively studied by Pierre Janet, Joseph Breuer and Sigmund Freud. In this concept mental and somatic factors are closely connected by Pierre Janet, Joseph Breuer and Sigmund Freud. In this context the aim of the present study is to perform examination of stress-related disturbances of HPA axis functioning indexed by basal cortisol and prolactin caused by chronic stress conditions, and test their relationship to psychiatric symptoms, somatoform dissociative symptoms, symptoms of depression and traumatic stress in depressive patients.

**Material and Methods**

**Participants**

For empirical examination of suggested hypothesis assessment of basal serum prolactin and cortisol levels during rest conditions were performed in 40 consecutive inpatients with unipolar depression. The patients were at the time of recruitment treated at the university hospital, Psychiatry department and the clinical assessments were performed during two weeks from the beginning of hospitalization. The patients have diagnosis of unipolar depressive disorder (i.e. patients with recurrent depression or depressive period) in relapse without posttraumatic stress disorder (PTSD) and other comorbid diagnoses confirmed according to DSM IV criteria by clinical interview [13]. With the purpose to re-examine diagnosis and exclude PTSD or other comorbidities all the patients were also screened using structured psychiatric interview M.I.N.I. version 5.0.0. [45]. The patients were treated only by SSRI antidepressants in usual recommended doses according psychiatric guidelines. Exclusion criteria were organic illnesses involving the central nervous system, psychotic disorders, PTSD, bipolar disorder, alcohol and/or drug abuse, any form of epilepsy and mental retardation (IQ Raven higher than 90), neuroendocrine and metabolic disorders, any hormonal or antipsychotic medication, tricyclic antidepressant, methyldopa, prednisolone and cimetidine medication, ECT or rTMS therapy and pregnancy or lactation in women. The patients were 10 males and 30 females in average age 43.47±12.21 (age range 30–60) predominantly with high-school education, non-smokers with adequate nutritional status and body mass index (17–29). 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) [46] DES represents 28 items self-reported questionnaire examining main dissociative phe-
nomena such as absorption, amnesia, depersonalization, de-realization, reality distortion, and others. Subjects indicate a degree of their experience on the continuum from 0% to 100%. In the present study we have used the Czech version of the DES that similarly as original English version displays high reliability and internal consistency (Cronbach’s alpha 0.92, test-retest reliability after week 0.91).

Somatoform dissociative symptoms were assessed using the 20-item self-reported somatoform dissociation questionnaire SDQ-20 [17]. Somatoform dissociative symptoms represent alterations in sensations of pain (analgiesia, kinesthetic anesthesia), alterations of perception, loss of motor control, gastrointestinal symptoms, etc. Subjects indicate the degree of their experience on 5-point Likert scale. We have used the Czech version of the SDQ-20 that displays high reliability and internal consistency (Cronbach’s alpha 0.91, test-retest reliability after week 0.90).

For investigation of childhood traumas, TSC-40 (Trauma Symptom Checklist) [47] 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 post-traumatic stress and other symptom clusters found in some traumatized individuals. The Czech version of the TSC-40 has high reliability and internal consistency (Cronbach’s alpha 0.91, test-retest reliability after week 0.88).

For the assessment of depressive symptoms was used Beck depression inventory BDI-II [48] that represents 21-items questionnaire for assessing depression (Cronbach’s alpha 0.89, test-retest reliability after week 0.85). Subjects indicate degree of their experience on 4-point Likert scale.

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 and cortisol serum levels have been assessed in biochemical laboratory according to common analytical procedures.

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

Statistical methods

Statistical evaluation for results of serum prolactin, cortisol and psychometric measures included common methods of descriptive and inferential statistics. For quantitative description means, standard deviations and measures aspects of post-traumatic stress and other symptom clusters found in some traumatized individuals. The Czech version of the TSC-40 has high reliability and internal consistency (Cronbach’s alpha 0.91, test-retest reliability after week 0.90).

For investigation of childhood traumas, TSC-40 (Trauma Symptom Checklist) [47] 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 post-traumatic stress and other symptom clusters found in some traumatized individuals. The Czech version of the TSC-40 has high reliability and internal consistency (Cronbach’s alpha 0.91, test-retest reliability after week 0.88).

For the assessment of depressive symptoms was used Beck depression inventory BDI-II [48] that represents 21-items questionnaire for assessing depression (Cronbach’s alpha 0.89, test-retest reliability after week 0.85). Subjects indicate degree of their experience on 4-point Likert scale.

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 and cortisol serum levels have been assessed in biochemical laboratory according to common analytical procedures.

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

Statistical methods

Statistical evaluation for results of serum prolactin, cortisol and psychometric measures included common methods of descriptive and inferential statistics. For quantitative description means, standard deviations and multiple and simple regression for the study of the relationship between several independent or predictor variables and a dependent or criterion variable the methods of simple or multiple regression were used. For description of functional relationship between psychometric measures Pearson product-moment correlation for independent samples was used. All the methods of statistical evaluation were performed using the software package Statistica version 6.

RESULTS

Results of the present study confirm relationship between HPA-axis reactivity and psychosocial stressors leading to dissociative symptoms in the depressive patients. Data show that prolactin and cortisol as indices of HPA axis functioning manifest significant relationship to dissociative symptoms. Main result represents highly significant correlation obtained by simple regression between psychic dissociative symptoms measured by Dissociative Experiences Scale and serum prolactin (R=0.55, p=0.00027, F=16.11) (Figure 1). Significant correlation was also found between somatoform dissociative symptoms measured by SDQ-20 and serum cortisol (R=0.38, p=0.015, F=6.39) (Figure 2). Other correlations assessed by simple regression among prolactin, cortisol and psychometric measures were not statistically significant (Table 1). Significant relationships indicate also Pearson product-moment correlations for psychometric measures
Coefﬁcient of multiple determination R=0.62 obtained by multiple regression is highly statistically signiﬁcant for prolactin as linear function of independent variables DES and SDQ-20, i.e. prolactin=f (DES,SDQ-20); F=11.34, p=0.00014, df=2.37, R-square=0.38, standard error of estimate is 25.62.

Coefficient of multiple determination R=0.45 obtained by multiple regression is statistically signiﬁcant also for cortisol as linear function of independent variables DES and SDQ-20, i.e. cortisol=f (DES,SDQ-20); F=4.67, p=0.015, df=2.37, R-square=0.201, standard error of estimate is 172.46.

Hypoprolactinemia or hypocortisolemia was not present in any of the patients. On the other hand hyperprolactinemia (higher than 30 microg/l) was found in 9 patients (1 man) and hypercortisolemia (higher than 620 nmol/l) in 15 patients (1 man). Simultaneous occurrence of hyperprolactinemia and hypercortisolemia was found in 5 women.

### DISCUSSION

The results of this study similarly as previous studies [40–44] indicate relationship between HPA axis reactivity and dissociative symptoms. The present study in depressive patients shows close relationship among HPA axis functioning indexed by cortisol and prolactin, and psychic and somatoform dissociative symptoms. This observed relationship between DES and serum prolactin (R=0.55, p=0.00027) is in agreement with ﬁndings that increased or decreased level of prolactin could be linked to psychological stressors [31,59]. Recent ﬁndings including also longitudinal studies indicate that stressful experiences associated with passive coping behavior are associated with increased plasma prolactin levels whereas stress situations associated with active coping are associated with unchanged or even lowered levels [51,52]. Theorell [51] found that serum prolactin reacts in a bimodal fashion in conjunction with stress, i.e. it increases in subjects that experience passive helplessness, whereas it decreases in conjunction with increased anxiety and active coping. In comparison to the results obtained during acute (phasic) emotional states that report decreased prolactin [52,53], Theorell focused his research on chronic (tonic) stress condition [51,52]. Because the regulation of plasma prolactin is part of a dopaminergic system it is possible that increased prolactin levels might be needed for preservation of vital functions during withdrawal [51].

In this context also animal studies have found increased prolactin levels in submissive subjects but decreased levels in dominant subjects [54].

At this point there are clinical experiences that dissociation could be a parallel process to animal defensive and recuperative states that are evoked in the face of severe threat. Empirical data and clinical observations seem to be supportive of the idea that there are similarities between freezing, concomitant development of analgesia and anesthesia, and acute pain in threatened animals [55,56]. These primary defense strategies supported by the parasympathetic nervous system involve energy conservation that cause passive coping strategies such as withdrawal or disengagement, dissociation, and the immobility response [56,57]. Typical emotions associated with parasympathetic functions have a negative valence, such as shame, disgust, hopelessness, and despair [56,57]. Dissociation is an analogical form of human response to inescapable and threatening stress with the same defensive tendency toward passive and avoidant coping that emerge as hopelessness, learned helplessness, social and emotional withdrawal and disengagement [55,58]. With respect to these ﬁndings the present study presents supporting material that documents close relationship between prolactin and dissociation as a typical form of passive coping behavior related to withdrawal and disengagement related to chronic stress conditions.

Analogical but reciprocal meaning has the observed relationship between SDQ-20 and serum cortisol (R=–0.38, p=0.015). The relationship between SDQ-20 and serum cortisol reﬂects a tendency that psychological stressors could be linked to decreased level of cortisol. The result is in agreement with ﬁndings that one of the neuroendocrine changes related to chronic mental stress exposure is decreased cortisol level related to defense mechanisms [31,59]. Similarly as in prolactin recent ﬁndings in both animals and humans indicate, that cortisol levels reﬂect not only emotional arousal but also active defensive or antiarousal intrapsychic mechanisms that should be conceptualized in psychological perspective as a balance between opposing intrapsychic forces. These intrapsychic forces relate to excitatory and inhibitory inﬂuences and are experienced as engagement that represents active emotional response with high cortisol levels, and disengagement (e.g. avoidance, withdrawal or denial) related to passive defense with low cortisol levels [31]. These ﬁndings suggest that the cortisol decrease related to somatoform dissociation reﬂects typical vulnerability to mental stress exposure that emerges as disengagement.
The relationship between SDQ-20 and basal serum cortisol (R=−0.58, p=0.015) related to chronic stress conditions found in the present study could be in principle in agreement with similar result by Simeon et al. [41] r=−0.32, p=0.03 between DES and plasma cortisol level during stress stimulation in 43 patients with dissociative disorders because of high correlation between DES and SDQ-20 (r=0.65, p=0.000005) that was reported also in other studies [16]. In the study by Simeon et al. [41] basal level of cortisol did not display significant relationship which suggests that the construct of somatoform dissociation used in the present study could be more sensitive to measurable physiological changes related to chronic stress exposure and associated defense mechanisms.

Recent studies indicate that there is a significant relationship between traumatic stress symptoms, dissociation and depression [29,60–62]. These data suggest that the patients assessed in this study presented typical sample of depressive patients that were not highly traumatized in comparison to other depressive inpatients. This presents important point because in many cases depression is related to elevated cortisol levels [53] while in the patients with PTSD who were excluded in this study the level of cortisol is decreased [25]. Recently unclear neuroendocrinology of dissociation may explain a certain decrease in cortisol in depression, because dissociation may be present without PTSD, although PTSD patients have significantly higher occurrence of dissociative symptoms in comparison with other patient groups including schizophrenia [46,63]. This suggests the hypothesis that several neuroendocrine abnormalities in PTSD could be explained by factors related to dissociation and that depressive patients with high dissociation could have neuroendocrine dysregulation similar to PTSD. This problem presents important topic for further research that could better explain neuroendocrinology of dissociation and its clinical and diagnostic consequences in various psychiatric diagnoses and diagnostic definitions [64].

**Conclusions**

In summary, results of the present study together with recent findings indicate that HPA axis plays a central role in neuroendocrinological consequences of traumatic stress in association with dissociation. Partial limitation of these results may present antidepressant medications that act against the symptoms, influence mental state and likely also the neuroendocrine activity. Although it is not too probable that the results are produced by medication, antidepressant treatment may influence the relationships between symptoms of dissociation and neuroendocrine changes. These preliminary results in depressive patients suggest significant occasion for future research in larger samples of patients that could help to find more specific criteria for dissociation related neuroendocrine disturbances in various psychiatric disorders.

**References:**

www.IndexCopernicus.com

One Stop Shop in Science

- Scientists networking & collaboration
- Online Research Team
- Scientists profiles
- Individual career monitor
- Personalized information delivery
- Information integration: literature/grants/patents/jobs

Index Copernicus International Plc.

International Office: 415 Madison Ave., 14th Floor, New York, NY 10017, U.S.A.
phone +1 (646) 673-8415, fax +1 (646) 673-8414
European Office: Ustrzycka 11, 01-141 Warsaw, Poland
phone +48 (0)22 868 1265, fax +48 (0)22 868 1273
e-mail: office@IndexCopernicus.com