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Different profiles of mental and physical health and stress hormone response in women victims of intimate partner violence

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ABSTRACT

Objectives: To analyse the individual differences in the impact that intimate male partner violence (IPV) has on a woman's depressive and posttraumatic stress disorder (PTSD) symptomatology, and to determine the association of the different profiles of mental dysfunction with cortisol and dehydroepiandrosterone (DHEA) basal saliva levels as well as physical health symptoms. **Methods:** A cross-sectional study was carried out in which IPV victims (n=73) and control non-abused (n=31) women participated. Information was obtained through structured interviews and saliva samples were collected for hormonal assays under baseline conditions. **Results:** There were three profiles of mental symptoms in IPV subjects: no symptoms (n=19); with depressive symptoms (n=36), and depressive/PTSD symptom (n=18). None of the non-abused women had depressive or PTSD symptoms. The stress hormone response differed between groups. Only the IPV-depressive group had higher evening cortisol, and both morning and evening DHEA, but lower morning cortisol/DHEA ratio than non-abused women. Furthermore, there were differences between the IPV groups. The IPV-depressive group had lower morning cortisol and morning cortisol/DHEA ratio than the IPV-no symptoms and lower morning cortisol/DHEA ratio than the IPV-depressive/PTSD group. With respect to the physical symptoms there was an association between the mean of symptoms and the profile of mental health, the incidence being higher in the depressive/PTSD group than in the other groups. **Conclusions:** This study demonstrates that there are individual differences in the impact that IPV has on the stress response and health status in women victims.

1. Introduction

Intimate male partner violence (IPV) refers to actual or threatened physically, psychologically or sexually abusive acts committed against women by their current or former male partners. IPV is considered a chronic social stressor for women as this kind of abusive relationships can last for decades[1-3]. Social stress, defined as the stress derived from a social interaction among members in same species, is considered the main source of stress in human beings and, consequently, increases the risk of developing health alterations[4-6].

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Cross-sectional, prospective and retrospective studies have consistently demonstrated that living with a violent intimate male partner is a significant contributor to women's adverse mental and physical health outcomes. Studies which compare women exposed to IPV with those who are not show that common mental sequelae include depression, post-traumatic stress disorder (PTSD), anxiety, suicidal behavior, sleep and eating disorders, low self-esteem, personality disorders, increased likelihood of substance abuse, and social dysfunction[1,7-18]. To our knowledge, there are few studies that have tried to assess mental health profiles on IPV women victims by examining patterns of distress and adjustment[19]. Thus, it is clearly important to assess individual differences to the deleterious effects of IPV on mental health following a person-oriented perspective[17,19-24]. Recent studies have found depressive symptomatology following IPV in 54% to 78%, and PTSD in 18% to 74% of

women victims. Furthermore, these women have often comorbid disorders such as mood, anxiety and/or substance abuse disorders[15,17,19,25,26]. IPV has also a great impact on women's physical health with short- and long-term consequences. First, in case of physical violence, the most common and immediate consequences are injuries, and neurological sequelae of violent acts. However, it is the fear and stress experienced through violence that results in long-term chronic stress-related physical problems. In general, abused women report a low self-perceived health[2,27-29], and higher incidence of different signs somatic symptoms, and illnesses related to the cardiovascular, gastrointestinal, muscular, urinary, and reproductive systems[2,30,31]. The most frequent health problems reported in IPV studies are headaches, nightmares, loss of appetite, back, pelvic, muscular and stomach pain, hypertension, asthma, diabetes, and gynecological symptoms[2,31-34]. Futhermore, other physical disturbances have been studied such as different markers of immune system functioning[35,36], with different results depending on the violence experienced and other mediating factors.

IPV is a chronic stressful experience with high impact on women's health, as it has been widely endorsed in the literature[2,27,37]. With this in mind, the hypothalamic-pituitary-adrenocortical (HPA) axis is the mechanism by which stress regulates its physiological response, and a large number of studies include its markers to measure its impact. This is the main reason why cortisol (and also, but not so far DHEA), the hormone released during the stress response, is one of the most studied biomarker and recognized to have an impact on the rest of body systems[38-40]. In this sense, studies have associated hormone levels with mental health status. It has been demonstrated the impact of IPV on women's HPA axis[1,25,26,41-45]. Studies that compared non-traumatized healthy women with female victims of IPV found different results. While Griffin *et al*.[25], reported lower early morning plasma cortisol levels in female victims, Basu *et al*.[1], found no differences between non-traumatized and female victims. On the other hand, the comparison between female victims of IPV found a variety of results depending on the incidence of PTSD and/or depression. While some studies found higher cortisol levels in women with current PTSD[26] or even remitted PTSD[43], another study reported no difference between female victims with PTSD and those without it[45], and Griffin *et al*.[25], found lower cortisol levels in female victims with PTSD. Furthermore, those studies that compared female victims with PTSD and those with a co-morbid PTSD/depression found no differences[1,25].

Most studies have assessed the impact on IPV on women victims considered as a homogeneous group in comparison with nonabused women. However, studies on stress impact have started to assess individual differences on this impact related to factors of resilience and vulnerability as well as the different strength of the stress variables. This consideration of women victims as an homogeneous group has produced misunderstanding in professionals that deal with the care of these women, the health intervention as well as the justice system. Thus, it is necessary to start research on individual differences in the impact that IPV has on women victims' health. This approach would allow a more effective intervention in several levels (health system, advocacy, social services).

The aim of this study was twofold to analyse the individual differences in the impact that IPV has on a woman's mental and physical health and to determine the association of the different profiles of health impact with cortisol and dehydroepiandrosterone (DHEA) basal saliva levels.

2. Material and methods

2.1. Subjects

The present study is part of a larger research project on the impact of IPV on women's health carried out in the Valencian Community of Spain[15,46,47]. All participants were of Spanish nationality. Female victims of IPV (n=73) were recruited from the 24 h centers for helping women (which offer information, and help from lawyers and social workers, and some psychological interventions for the women) in the three provinces of the Valencian Community of Spain (Alicante, Castellon and Valencia). A control group of women not exposed to IPV (n=31) was recruited through women's clubs (a civil organization located in each city and town that only women can join and in which they develop a wide arrange of activities such as receiving information, courses, trips, *etc*.).

2.2. Ethical considerations

The study was approved by the University of Valencia research ethics committee, and prior informed written consent was obtained from all participants. Subjects did not receive any money or other inducement for their participation.

2.3. Procedure

The study consisted of a structured interview in which trained female psychologists asked women questions about their lives and health. In general, each woman was interviewed four to six times, and the duration of each session was approximately 1.5 h. A comprehensive questionnaire was designed for use in a face-to-face

interview. The majority of questions were designed to obtain objective factual reports. Additionally, women were asked to provide saliva samples for hormonal assays (details below).

2.4. Questionnaires

The questionnaires from which information for the present study was obtained are described below, and more detailed information is given in our previous articles[44,46].

The sociodemographic profile included age, education-level and marital status items. The relationship with the aggressor/partner included data on the cohabitation with him at the time of the interviews and during the last year.

2.5. Characteristics of intimate male partner violence

A questionnaire was constructed to obtain detailed information about the different types of violence (physical, psychological and sexual) toward the women perpetrated by their partners (see 46 for more detailed information). Women gave answers of either "yes" or "no" regarding the experience of each act.

2.6. Mental health assessment

The Beck Depression Inventory (BDI) was used to assess depressive symptoms[48], and the total scores on the BDI ranged from 0 to 63. Women with BDI scores ranging from 0 to 8 were considered as having no symptoms of depression, from 9 to 18 as mild, from 9 to 29 as moderate, and from 30 to 63 to severe depressive symptoms. The Spanish version of the BDI that was used in our study has been validated by Conde and Useros[49], who obtained an internal consistency coefficient of 0.88. In our study, the cut-off score was set to 18. The incidence and severity of symptoms of current PTSD were assessed with Echeburúa's Severity of Symptom Scale of Posttraumatic Stress Disorder[50]. This is a structured interview based on DSM-IV criteria. The instrument has a high internal consistency with a Cronbach's α coefficient of 0.92 and a high test-retest reliability as well as a good discriminant, concurrent, and construct validity. A stressor was assessed by asking the woman if she had experienced an unusual, extremely distressful event (irrespective of whether or not it was IPV-related). Either type of event was considered a qualifying trauma when it met the DSM-IV criteria for PTSD and when distressing symptoms persisted for at least 4 weeks. Women were also asked about the lifetime incidence of thoughts and attempts of suicide. Detailed information about women's mental health assessment is given in Picó-Alfonso *et al*[15].

2.7. Physical health assessment

Self-report physical health status was assessed using a questionnaire designed by the research team. A symptom is defined as a subjective evidence of physical disturbance observed by the patient. The symptom inventory consisted of 35 symptoms and women were queried about their incidence in the year preceding the study. Furthermore, a total number of symptoms as well as a summatory of specific system symptoms was also calculated.

2.8. Saliva samples

Saliva samples for the analysis of the level of cortisol and DHEA were also collected. The participants provided a minimum of 0.5 mL of saliva in a plastic tube twice a day (between 08:00 and 09:00, and between 20:00 and 21:00) for four consecutive days at home, starting the fourth day after the beginning of menstruation. Saliva samples were frozen in women's freezer and brought to the freezer of the Department of Psychobiology in a mobile freezer, and then kept frozen at -21 ℃. Finally, all samples were sent to the Department of Clinical Neurosciences at University of Cambridge, UK, for analysis.

2.8.1. Hormone assays

Cortisol was measured by validated ELISA on 20 μL samples of saliva (antibody Cambio UK) without extraction (intra-assay variation: 4.1%; inter-assay: 7.6%). DHEA was measured by validated radioimmunoassay on 333 μL samples after extraction into hexane/ether (4:1) (antibody Bioclin; intra-assay variation: 5.1%; inter-assay: 11.2%). Details are given in Harris *et al*.[51]. Data from the four daily morning and evening collections were summed to give a mean value at each time point.

2.9. Statistical analyses

Women were classified into four groups depending on the incidence of IPV and their mental health status: non-abused women, and abused women with no depressive or PTSD symptoms (IPV-no symptoms), with depressive symptoms (IPV-depressive symptoms), and with both depressive and PTSD symptoms (IPV-depressive/PTSD symptoms). The four groups were compared with respect to age, and the profile of physical symptoms and mental health status using One-way analysis of variance (ANOVAs). Regarding the level of education, marital status, types of IPV, the incidence of clinical depression and PTSD the comparisons were assessed by using Pearson's *Chi*-square tests. Comparisons between groups with respect to endocrine measures (cortisol and DHEA analysis were carried out after logarithmic transformation of the data) were assessed by ANOVAs with

Bonferroni *post hoc* comparisons. When the criteria of ANOVA were not fulfilled, Welch's tests were calculated, and Games-Howell *post hoc* comparisons applied. A significance level of $P<0.05$ was established for all analyses. All statistical analyses were conducted using the SPSS for Windows statistical package Version 19.0.

3. Results

3.1. Participant's characteristics and health profiles

There were no differences between groups in either age ($V_w[3, 49.13]=1.25$) or education [χ^2 (18, $N=104$)=16.60] (Table 1). There was a significant association between the marital status and group [χ^2 (12, $N=104$)=33.40, $P<0.001$]. The percentage of "married" women was higher than expected by chance in the non-abused group, whereas the contrary pattern was observed in the category of "separated/divorced". There were no significant association between this variable and any of the three IPV-groups [χ^2 (8, $N=73$)=9.63]. On the other hand, there was a significant association between the cohabitation with the aggressor/partner at the time of the interviews and the group [χ^2(3, $N=104$)=19.95, $P<0.001$]. The proportion of women cohabiting with the aggressor/partner was significantly higher than expected in the nonabused group (96.8%) and lower in the IPV-no symptoms group (42.1%). However, this was not apparent during the year previous to the interviews [χ^2(3, $N=104$)=5.43]. In the IPV-groups, there was no significant association between the cohabitation and the group either during the previous year [χ^2(2, $N=73$)=3.06] or at the time of the interviews: [χ2 (2, $N=73$)=1.47].

All women (100%) in the IPV groups were exposed to psychological abuse by their partners. Furthermore, over a half of women on each IPV group were physically abused, and around one third of them were sexually abused by their partners. There was no association between the incidence of physical and sexual abuse and the mental health profile of women victims of IPV: physical [χ^2(2, $N=73$)=2.19, n.s.], and sexual [χ^2(2, $N=73$)=1.33].

3.2. Different profiles of depressive and PTSD symptomatology

One hundred and four women participated in this study. Seventy three were female victims of IPV and 31 were women no exposed to IPV (non-abused women). Depending on the incidence of symptoms of depression and PTSD female victims were distributed into three groups: (1) Female victims of IPV with no symptoms of depression or PTSD (IPV-no symptoms group; $n=19$); (2) Female victims of IPV

Table 1
Characteristics of nonabused women and women victims of intimate male partner violence with no symptoms, depressive symptoms, and depressive and posttraumatic stress disorder symptoms.

Variable	Nonabused $n=31$	IPV			P value
		No symptoms $n=19$	Depressive $n=36$	Depressive/PTSD $n=18$	
Age (mean±SD)	46.03±12.92	49.42±10.50	43.75±10.61	47.00±8.50	n.s.
Education level					
Illiterate	0	0	0	5.6	
Able to read and write	3.2	15.8	13.9	5.6	
Uncompleted primary school	12.9	26.3	19.4	33.3	
Primary school	35.5	36.8	38.9	33.3	
Secondary school	38.7	15.8	19.4	16.7	
University studies: 3-4 years	3.2	5.3	2.8	0	
University studies: 5-6 years	6.5	0	5.6	5.6	
Marital status					$P<0.001$
Widow	3.2	10.5	0	5.6	
Single not living with partner	0	15.8	8.3	11.1	
Separated/Divorced from husband	0	31.6	47.2	22.2	
Single living with partner	9.7	0	2.8	11.1	
Married	87.1	42.1	41.7	50	
Cohabitation with aggressor/partner					
At time of interviews	96.8	42.1	55.6	61.1	$P<0.001$
During the last year	96.8	78.9	94.4	88.9	n.s.
Intimate partner violence					
Physical	-	52.6	72.2	61.1	n.s.
Psychological	-	100	100	100	n.s.
Sexual	-	21.1	27.8	27.8	n.s.

IPV: Intimate male partner violence; PTSD: Posttraumatic stress disorder; n.s.: Not significant.

with symptoms of depression (IPV-depressive group; n=36), and (3) Female victims of IPV with symptoms of depression and PTSD (IPV-depressive/PTSD group; n=18). None of the non-abused women had either symptoms of depression or PTSD (non-abused group; n=31).

The scores for depression were significantly higher in both the IPV-depressive and the IPV-depressive/PTSD groups than in the IPV-no symptoms and non-abused groups (P<0.001). Moreover, the IPV-depressive/PTSD group had higher scores than the IPV-depressive group (P<0.05). In the IPV-depressive group women were distributed mainly among "mild" (72.2%) symptoms, while the highest level of severity was found in IPV-depressive/PTSD group: 38.9% of women suffered "severe" symptoms, these percentages being higher than expected by chance in both groups. On the other hand, PTSD scores were significantly higher, not only in those with clinical PTSD, but also in the IPV-depressive group than in the IPV-no symptoms and non-abused groups (P<0.001). Furthermore, the IPV-depressive/PTSD group had higher scores than all the other groups (P<0.001). Regarding suicide, the incidence of both suicidal thoughts and attempts was associated with the group: thoughts [χ^2 (3, N=104)=28.67, P<0.001] and attempts [χ^2(3, N=104)=12.21, P<0.01]. In the case of thoughts, the incidence was higher than expected in both IPV-depressive and IPV-depressive/PTSD groups, and only in the latter group regarding suicidal attempts. On the contrary, the incidence of both thoughts and attempts of suicide were lower than expected in the nonabused group (Table 2).

3.3. Association of the different profiles of mental health dysfunction with physical health

The four groups of women were compared with regards to the incidence of perceived physical symptoms during the year prior to the interviews. Detailed information of total amount of physical symptoms as well as the incidence of each specific symptom is given in Table 3.

There were differences between groups in the total amount of physical symptoms (V_w [3, 44.14]=52.71; P<0.001). *Post hoc* comparisons indicated that the IPV-depressive/PTSD group had higher incidence of symptoms than the other three groups (P<0.001), and the IPV-depressive group showed a higher mean than non-abused (P<0.001) and IPV-no symptoms group (P<0.05).

There were differences between groups in the total amount of symptoms of specific systems: nervous (V_w [3, 45.28]= 38.02; P<0.001), muscular (V_w [3, 48.13]=26.39; P<0.001), reproductive (F [3, 103]=4.04; P<0.01), digestive (V_w [3, 44.92] =14.25; P<0.001), circulatory (V_w [3, 44.30]=22.38; P<0.001) and the endocrine system (V_w [3, 41.83]=60.92; P<0.001) with the only exception of urinary system and skin (F [3, 103] =0.60). *Post hoc* comparisons showed a higher amount of symptoms in both IPV-depressive/PTSD and IPV-depressive groups than in the non-abused group (P<0.001, reproductive system: P<0.05). The IPV-depressive/PTSD group showed a higher amount of symptoms in nervous, muscular and endocrine systems (P<0.001), as well as in digestive and circulatory systems (P<0.05) than the IPV-no symptom group, and a higher number of symptoms in nervous and

Table 2
Characteristics of depressive and PTSD symptoms in nonabused women and in women victims of intimate male partner violence.

Variable	Nonabused n=31	IPV			P value
		No symptoms n=19	Depressive n=36	Depressive/PTSD n=18	
BDI	3.26±3.16	4.11±3.00	16.25±5.21$^{***/aaa}$	27.06±12.96$^{***/aaa/b}$	P<0.001
Clinical cut-off	–	–	27.8	66.7	P<0.01
Severity of depressive symptoms					P<0.001
No depression	–	–	0	0	
Mild	–	–	72.2	33.3	
Moderate	–	–	25.0	27.8	
Severe	–	–	2.8	38.9	
PTSD	–	–	–	100	
Total score	1.77±2.91	3.26±3.46	11.44±5.25$^{***/aaa}$	29.11±8.15$^{***/aaa/bbb}$	P<0.001
Subscales PTSD score					
Re-experiencing	0.94±1.46	1.26±1.48	3.75±2.92$^{***/aaa}$	9.00±2.74$^{***/aaa/bbb}$	P<0.001
Avoidance	0.61±1.89	1.05±1.31	4.14±3.01$^{***/aaa}$	10.89±4.17$^{***/aaa/bbb}$	P<0.001
Arousal	0.23±0.56	0.95±1.39	3.56±2.25$^{***/aaa}$	9.22±2.65$^{***/aaa/bbb}$	P<0.001
Suicidal thoughts	3.2	31.6	52.8	72.2	P<0.001
Suicidal attempts	3.2	10.5	27.8	38.9	P<0.01

IPV: Intimate male partner violence; PTSD: Posttraumatic stress disorder; BDI: Beck depression inventory.
***: Differs from nonabused group, P<0.001; ^{aaa}: Differs from IPV-No symptoms group, P<0.001; ^{b}: Differs from IPV-Depressive group, P<0.05; ^{bbb}: P<0.001.

Table 3

Physical symptoms suffered by nonabused women and women victims of violence with no symptoms, depressive symptoms, and depressive and PTSD symptoms during the last year.

Variable	Nonabused *n*=31	IPV			*P* value
		No symptoms *n*=19	Depressive *n*=36	Depressive/PTSD *n*=18	
Total physical symptoms	4.16±3.43	8.16±6.61	13.50±5.30$^{***/a}$	19.17±4.97$^{***/aaa/bbb}$	*P*<0.001
Nervous system	0.97±1.30	2.26±2.13	3.64±2.27***	5.89±1.78$^{***/aaa/bbb}$	*P*<0.001
Headache	32.3	42.1	72.2	77.8	*P*<0.001
Faintness	19.4	36.8	47.2	94.4	*P*<0.001
Numbness	3.2	26.3	47.2	72.2	*P*<0.001
Trembling hand	6.5	26.3	41.7	77.8	*P*<0.001
Ringing ears	9.7	31.6	27.8	72.2	*P*<0.001
Dizziness	16.1	21.1	41.7	77.8	*P*<0.001
Blurred vision	6.5	26.3	47.2	44.4	*P*<0.01
Nightmares	3.2	15.8	38.9	72.2	*P*<0.001
Muscular system	1.19±1.25	1.89±1.59	3.14±1.44$^{***/a}$	4.00±1.03$^{***/aaa}$	*P*<0.001
Low energy	12.9	42.1	75.0	83.3	*P*<0.001
Fatigue	12.9	31.6	47.2	83.3	*P*<0.001
Cramp	16.1	21.1	41.7	50.0	*P*<0.05
Muscular pain	29.0	36.8	69.4	88.9	*P*<0.001
Back pain	48.4	57.9	80.6	94.4	*P*<0.01
Reproductive system	0.39±0.72	0.68±1.16	1.03±0.91*	1.22±1.06*	*P*<0.01
Amenorrhoea	3.2	10.5	8.3	5.6	n.s.
Menstrual pain	19.4	21.1	22.2	27.8	n.s.
Vaginal bleeding	6.5	5.3	16.7	11.1	n.s.
Vaginal pain	3.2	15.8	19.4	27.8	n.s.
Painful intercourse	6.5	10.5	22.2	27.8	n.s.
Pelvic pain	0.0	5.3	14.3	23.5	*P*<0.05
Digestive system	1.00±1.06	1.53±1.65	2.69±1.82***	3.39±1.61$^{***/aa}$	*P*<0.001
Nausea	19.9	21.1	30.6	55.6	*P*<0.05
Vomiting	9.7	0.0	25.0	44.4	*P*<0.01
Heartburn	16.1	15.8	41.7	61.1	*P*<0.01
Stomach pain	12.9	21.1	41.7	72.2	*P*<0.001
Diarrhea	6.5	10.5	11.1	38.9	*P*<0.05
Constipation	16.1	47.4	38.9	22.2	n.s.
Bloating	25.8	21.1	55.6	38.9	*P*<0.05
Anal bleeding	0.0	15.8	25.0	5.6	*P*<0.05
Urinary system					
Leakage of urine	0.0	10.5	22.2	33.3	n.s.
Circulatory system	0.16±0.45	0.58±0.69	1.11±0.75***	1.50±0.79$^{***/aa}$	*P*<0.001
Chest pain	6.5	42.1	61.1	72.2	*P*<0.001
Palpitations	9.7	15.8	50.0	77.8	*P*<0.001
Respiratory system					
Shortness of breath	9.7	21.1	47.2	66.7	*P*<0.001
Skin	0.16±0.45	0.16±0.37	0.19±0.47	0.33±0.59	n.s.
Pruritus	6.5	5.3	11.1	16.7	n.s.
Eruptions	9.7	10.5	8.3	16.7	n.s.
Endocrine system	0.10±0.30	0.74±0.87*	1.00±0.89***	1.83±0.51$^{***/aaa/bbb}$	*P*<0.001
Weight change	6.5	36.8	52.8	88.9	*P*<0.001
Appetite lost	3.2	36.8	47.8	94.4	*P*<0.001

*: Differs from nonabused group, *P*<0.05; ***: *P*<0.001. ^{a}: Differs from no symptoms group, *P*<0.05; ^{aa}: *P*<0.01; ^{aaa}: *P*<0.001. ^{bbb}: Differs from depressive group, *P*<0.001.

endocrine systems than the IPV-depressive group (*P*<0.001). Furthermore, IPV-depressive group showed a higher amount of muscular symptoms than the IPV-no symptom group (*P*<0.05). The only difference between IPV-no symptoms and the non-abused group was a higher amount of symptoms in the endocrine system in the former group (*P*<0.05).

Twenty-six specific symptoms out of 35 were significantly associated with the group: headache [χ^2 (3, *N*=104)=15.87, *P*<0.001], faintness [χ^2 (3, *N*=104)=26.58, *P*<0.001], numbness [χ^2 (3, *N*=104)=27.85, *P*<0.001], trembling hands [χ^2 (3, *N*=104)=27.05, *P*<0.001], ringing ears [χ^2(3, *N*=104)=21.51, *P*<0.001], dizziness [χ^2 (3, *N*=104)=21.14,

Table 4

Basal saliva levels of cortisol, DHEA (ng/ml, and ratio C/DHEA (nMol/L in the morning and evening in Nonabused women and women victims of Intimate male partner violence with no symptoms, depressive symptoms, and depressive/posttraumatic stress disorder symptoms. (Mean and standard deviation, SD.

Variable	Nonabused n=31	IPV			P value
		No symptoms n=19	Depressive n=36	Depressive/PTSD n=18	
Cortisol (ng/mL)					
AM	2.93±1.11	3.38±1.14	2.34±1.02[a]	3.31±1.62	P<0.01
PM	0.37±0.14	0.58±0.58	0.83±0.67[**]	0.67±.53	P<0.01
DHEA(ng/mL)					
AM	0.34±0.22	0.48±0.31	0.63±0.43[**]	0.43±.29	P<0.01
PM	0.20±0.09	0.34±0.35	0.44±0.38[**]	0.28±0.25	P<0.01
RATIO C/DHEA (nMol/L)					
AM	7.87±4.20	7.31±5.64	4.09±3.34[***/a/bb]	8.72±6.41	P<0.001
PM	1.59±0.72	1.42±0.76	1.99±2.14	2.42±2.23	n.s.

IPV: Intimate male partner violence; PTSD: Posttraumatic stress disorder; n.s.: Not significant.

[**]: Differs from nonabused group, P<0.01; [***]: P<0.001. [a]: Differs from IPV-No symptoms group, P<0.05. [bb]: Differs from IPV-Depressive/PTSD group, P<0.01.

P<0.001], blurred vision [χ^2 (3, N=104)=14.94, P<0.01], nightmares [χ^2 (3, N=104)=27.95, P<0.001], low energy [χ^2 (3, N=104)=34.44, P<0.001], fatigue [χ^2 (3, N=104)=24.83, P<0.001], muscular pain [χ^2 (3, N=104)=22.35, P<0.001], back pain [χ^2 (3, N=104)=15.01, P<0.01], pelvic pain [χ^2 (3, N=104)=8.05, P<0.05], nausea [χ^2 (3, N=104)=10.88, P<0.05], vomiting [χ^2 (3, N=104)=14.48, P<0.01], heartburn [χ^2 (3, N=104)=14.26, P<0.01], stomach pain [χ^2 (3, N=104)=20.04, P<0.001], diarrhea [χ^2 (3, N=104)=10.88, P<0.05], bloating [χ^2 (3, N=104)=9.02, P<0.05], anal bleeding [χ^2 (3, N=104)=10.55, P<0.05], chest pain [χ^2 (3, N=104)=27.95, P<0.001], palpitations [χ^2 (3, N=104)=29.19, P<0.001], shortness of breath [χ^2 (3, N=104)=20.76, P<0.001], weight change [χ^2 (3, N=104)=34.18, P<0.001], and appetite lost [χ^2 (3, N=104)=40.43, P<0.001], with the exception of most symptoms of the reproductive system: amenorrhoea [χ^2 (3, N=104)=1.23], menstrual pain [χ^2 (3, N=104)=0.48], vaginal bleeding [χ^2 (3, N=104)=2.54], vaginal pain [χ^2 (3, N=104)=6.10], painful intercourse [χ^2 (3, N=104)=5.32], constipation [χ^2 (3, N=104)=7.31], leakage of urine [χ^2 (3, N=104)=5.41], pruritus [χ^2 (3, N=104)=1.89] and eruptions [χ^2 (3, N=104)=0.92] (Table 3).

The incidence of the following symptoms was higher than expected by chance in the IPV-depressive/PTSD group: headache, faintness, numbness, trembling hands, ringing ears, dizziness, nightmares, low energy, fatigue, muscular pain, back pain, pelvic pain, nausea, vomiting, heartburn, stomach pain, diarrhea, chest pain, palpitations, shortness of breath, weight change, and loose of appetite. Also in the IPV-depressive group eight symptoms had a higher incidence than expected: headache, blurred vision, low energy, muscular pain, bloating, anal bleeding, chest pain, palpitations, and shortness of breath. On the contrary, just two symptoms, vomiting and palpitations, had a lower incidence than expected in IPV-no symptoms group. Regarding non-abused group, almost all symptoms showed a lower incidence than expected, with the exception of vomiting, diarrhea, and bloating.

3.4. Association of the different profiles of mental health dysfunction with cortisol and DHEA basal saliva levels

The four groups of women were compared with regards to the basal level of cortisol and DHEA as well as the ratio cortisol/DHEA (C/DHEA). Mean basal levels and comparisons between groups are given in Table 4. There were significant differences in mean morning and evening cortisol levels between the groups [ANOVA: morning: F [3, 103]=4.14; P=.008; evening: V_w [3, 42.89]=5.34; P=.003 F (1, 115)]. *Post hoc* comparisons revealed that morning levels were lower in the IPV-depressive group than in the IPV-no symptoms group (P<0.05), while evening cortisol levels were significantly higher in IPV-depressive group than in the non-abused group (P<0.01). Both morning and evening DHEA were significantly different between groups (morning: F [3, 103]=4.51; P=0.005); evening: V_w [3, 45.19]=4.45; P=0.008). *Post hoc* comparisons showed that both morning and evening DHEA levels were higher in the IPV-depressive group than in the non-abused group (P<0.01).

As it is shown in Figure 1, morning C/DHEA ratio was significantly different between the groups (V_w [3,48.86]=7.51; P<0.001). *Post hoc* comparisons indicated that the ratio was lower in the IPV-depressive group than in all the other groups (non-abused: P<0.001; IPV-no symptoms: P<0.05; and IPV-depressive/PTSD: P<0.01).

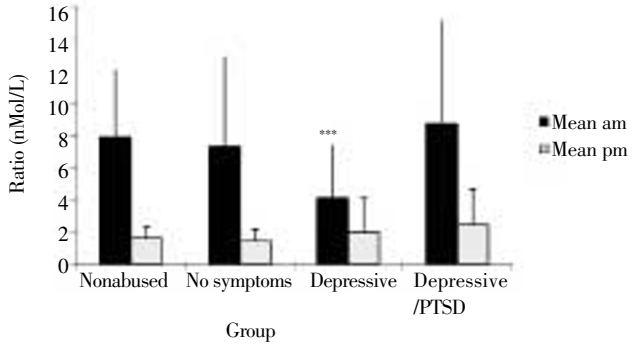

Figure 1. Mean±SD of morning C/DHEA ratio (nMol/L) in evening in nonabused women and women victims of intimate male partner violence with no symptoms, depressive symptoms, and depressive/posttraumatic stress disorder symptoms.

***: Differs from nonabused group; $P<0.001$, IPV-No symptoms; $P<0.05$, and IPV-depressive/PTSD; $P<0.01$.

4. Discussion

Our results show that there are individual differences in the impact that the exposure to IPV has on women's health. Thus, while some women show no symptoms of either depression or PTSD (the IPV-no symptoms group), others develop mostly mild depression (IPV-depressive group), and the rest women a comorbid more severe depression and PTSD (IPV-depressive/PTSD group). Thus, exposure to IPV does not necessarily lead to the development of psychopathology in all women or to a unique pattern of mental ill-health. A more detailed assessment of mental health in female victims may aid the design of appropriate intervention policies[15,19,20,23,24].

With respect to physical health there is an association between the amount of somatic symptoms and mental health deterioration profile. The main results shown that the IPV-depressive/PTSD group had the highest incidence in the total amount of symptoms followed by the IPV-depressive group in comparison with the IPV-no symptoms group and the non-abused group. Furthermore, the incidence of the specific symptoms headache, faintness, numbness, trembling hands, ringing ears, dizziness, nightmares, low energy, fatigue, muscular pain, back pain, pelvic pain, nausea, vomiting, heartburn, stomach pain, diarrhea, chest pain, palpitations, shortness of breath, weight change, and loose of appetite was higher than expected by chance in the IPV-depressive/PTSD group, while headache, blurred vision, low energy, muscular pain, bloating, anal bleeding, chest pain, palpitations, and shortness of breath was higher than expected by chance in the IPV-depressive group. These results are consistent with other studies that analyzed physical symptomatology in women victims[32,34].

Finally, there is also an association between levels of stress hormones and mental health deterioration. A disturbed HPA axis could either reflect or contribute to the array of mental stress-related disorders[40,52-54]. Our results clearly demonstrate that dysregulation of the HPA axis and basal levels of DHEA are particularly associated with depressive symptoms in women exposed to IPV. The IPV-depressive group had lower morning cortisol levels than the IPV-no symptoms group but higher evening cortisol levels and both higher morning and evening DHEA levels in comparison to the nonabused group. More significantly, they had a lower morning cortisol/DHEA ratio than all the other groups. However, no significant alterations compared to non-abused controls were found in those women with neither depressive nor PTSD symptoms (IPV-no symptoms) or those with comorbidity of these two disorders (IPV-depressive/PTSD group). Previous studies reported that female victims of IPV who developed PTSD had higher morning levels of cortisol than those that did not[25,26,43]. However, in general, studies on cortisol in patients with PTSD have revealed inconsistent results, while some studies reported no differences in cortisol levels between individuals with PTSD and controls or between trauma-exposed subjects with and without PTSD, and even others found higher levels[55-58]. On the other hand, the comorbidity of major depressive disorder and PTSD has received scant attention[59], studies reporting a variety of results[60-62]. The meta-analysis conducted by Morris *et al.*[63], on 47 studies revealed that daily cortisol output was lower in trauma-exposed individuals with comorbid major depressive disorder/PTSD in comparison to controls. Our results suggest that cortisol is altered specifically in those with depressive symptoms alone following IPV. It is not clear whether this indicates a distinct psychopathological state, or whether altered cortisol in some way influences the psychological response to IPV. It is possible that the presence of the two sets of symptoms in our subjects have opposite actions on cortisol, though we had no women with PTSD alone. This cannot be verified from our data. Since the risk for depression as well as depression itself, is associated with higher morning cortisol, it is unclear whether our results reflect an epiphenomenon of depressed state, or an antecedent risk for it.

Both lower and higher levels of DHEA have been reported in depressed subjects in comparison to controls[64-68]. It is interesting, in view of the finding that altered cortisol was restricted to the IPV-depressive group, that this was also the group in which DHEA was altered in comparison to controls. The high levels found in women of the IPV-depressive group in our study may have some protective effects against putative deleterious actions of cortisol[69]. However, as this is a cross-sectional study, it was not possible to assess whether

high levels of DHEA predicted a reduced incidence of depressive symptoms. Since altered cortisol and DHEA was limited to the IPV-depressive group, their C/DHEA ratio was also altered, as would be expected. Elevated C/DHEA ratios have reported as a state marker of depressive illness[64,70,71].

The present results indicate that women exposed to IPV show differences in the vulnerability and resilience to the development of psychopathology, somatic symptoms as well to the alterations in the endocrine system[71], and the two may be related. What makes some women more vulnerable to develop specific IPV-related health deterioration and others resilient is not well understood. Thus, discovering those variables that may contribute to the different vulnerability and resilience to develop health deterioration is important for advancing diagnostic screening, prevention and treatment[21,24,72,73].

A limitation of this study consists on the method used for the recruitment of the sample. Women victims of IPV were recruited from the Centers for Helping Women, while the recruitment from other settings such as Primary health care could gather a wider sample of victims.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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References

[1] Basu A, Levendosky AA, Lonstein JS. Trauma sequelae and cortisol levels in women exposed to intimate partner violence. *Psychodyn Psychiatry* 2013; **41**(2): 247-275.

[2] Campbell JC. Health consequences of intimate partner violence. *Lancet* 2002; **359**(9314): 1331-1336.

[3] Martínez M, García-Linares MI, Picó-Alfonso MA. Women victims of domestic violence: consequences for their health and the role of the health system. In: Klein R, Bernard W, editors. *Conflict, gender, and violence*. Vienna: Studien-Verlag; 2004. p. 127-155.

[4] Chuang CH, Cattoi AL, McCall-Hosenfeld JS, Camacho F, Dyer AM, Weisman CS. Longitudinal association of intimate partner violence and depressive symptoms. *Ment Health Fam Med* 2012; **9**(2): 107-114.

[5] Martinez M, Calvo-Torrent A, Pico-Alfonso MA. Social defeat and subordination as models of social stress in laboratory rodents: a review. *Aggress Behav* 1998; **24**(4): 241-256.

[6] Poirier GL, Cordero MI, Sandi C. Female vulnerability to the development of depression-like behavior in a rat model of intimate partner violence is related to anxious temperament, coping responses and amygdala vasopressin receptor 1a expression. *Front Behav Neurosci* 2013; **7**: 35.

[7] Aguilar RJ, Nightingale NN. The impact of specific battering experiences on the self-esteem of abused women. *J Fam Violence* 1994; **9**(1): 35-45.

[8] Bergman B, Brismar B. A 5-year follow-up study of 117 battered women. *Am J Public Health* 1991; **81**(11): 1486-1489.

[9] Coker AL, Davis KE, Arias I, Desai S, Sanderson M, Brandt HM, et al. Physical and mental health effects of intimate partner violence for men and women. *Am J Prev Med* 2002; **23**(4): 260-268.

[10] Ehrensaft MK, Moffitt TE, Caspi A. Is domestic violence followed by an increased risk of psychiatric disorders among women but not among men? A longitudinal cohort study. *Am J Psychiatry* 2006; **163**(5): 885-892.

[11] Houry D, Kemball R, Rhodes KV, Kaslow NJ. Intimate partner violence and mental health symptoms in African American female ED patients. *Am J Emerg Med* 2006; **24**(4): 444-450.

[12] Humphreys JC, Lee KA, Neylan TC, Marmar CR. Sleep patterns of sheltered battered women. *Image J Nurs Sch* 1999; **31**(2): 139-143.

[13] McCaw B, Golding JM, Farley M, Minkoff JR. Domestic violence and abuse, health status, and social functioning. *Women Health* 2007; **45**(2): 1-23.

[14] Pico-Alfonso MA, Echeburúa E, Martinez M. Personality disorder symptoms in women as a result of chronic intimate male partner violence. *J Fam Viol* 2008; **23**(7): 577-588.

[15] Pico-Alfonso MA, Garcia-Linares MI, Celda-Navarro N, Blasco-Ros C, Echeburúa E, Martinez M. The impact of physical, psychological, and sexual intimate male partner violence on women's mental health: depressive symptoms, posttraumatic stress disorder, state anxiety, and suicide. *J Womens Health* (Larchmt) 2006; **15**(5): 599-611.

[16] Ruiz-Pérez I1, Plazaola-Castaño J. Intimate partner violence

and mental health consequences in women attending family practice in Spain. *Psychosom Med* 2005; **67**(5): 791-797.

[17] Young-Wolff KC, Hellmuth J, Jaquier V, Swan SC, Connell C, Sullivan TP. Patterns of resource utilization and mental health symptoms among women exposed to multiple types of victimization: a latent class analysis. *J Interpers Violence* 2013; **28**(15): 3059-3083.

[18] Zlotnick C, Johnson DM, Kohn R. Intimate partner violence and long-term psychosocial functioning in a national sample of American Women. *J Interpers Violence* 2006; **21**(2): 262-275.

[19] Hughes HM, Cangiano C, Hopper EK. Profiles of distress in sheltered battered women: implications for intervention. *Violence Vict* 2011; **26**(4): 445-460.

[20] Anderson KM, Renner LM, Danis FS. Recovery: resilience and growth in the aftermath of domestic violence. *Violence Against Wom* 2012; **18**(11): 1279-1299.

[21] Bogat GA, Levendosky AA, von Eye A. The future of research on intimate partner violence: person-oriented and variable-oriented perspectives. *Am J Community Psychol* 2005; **36**(1-2): 49-70.

[22] Karatsoreos IN, McEwen BS. Psychobiological allostasis: resistance, resilience and vulnerability. *Trends Cogn Sci* 2011; **15**(12): 576-584.

[23] Nurius PS, MacY RJ. Heterogeneity among violence-exposed women: applying person-oriented research methods. *J Interpers Violence* 2008; **23**(3): 389-415.

[24] Nurius PS, Macy RJ. Person-oriented methods in partner violence research: distinct biopsychosocial profiles among battered women. *J Interpers Violence* 2010; **25**(6): 1064-1093.

[25] Griffin MG, Resick PA, Yehuda R. Enhanced cortisol suppression following dexamethasone administration in domestic violence survivors. *Am J Psychiatry* 2005; **162**(6): 1192-1199.

[26] Johnson DM, Delahanty DL, Pinna K. The cortisol awakening response as a function of PTSD severity and abuse chronicity in sheltered battered women. *J Anxiety Disord* 2008; **22**(5): 793-800.

[27] Ellsberg M, Jansen HAFM, Heise L, Watts CH, Garcia-Moreno C, WHO Multi-country Study on Women's Health and Domestic Violence against Women Study Team. Intimate partner violence and women's physical and mental health in the WHO multi-country study on women's health and domestic violence: an observational study. *Lancet* 2008; **371**(9619): 1165-1172.

[28] Hellemans S, Buysse A, De Smet O, Wietzker A. Intimate partner violence in Belgium: prevalence, individual health outcomes, and relational correlates. *Psychol Belg* 2014; **54**(1): 79-96.

[29] Vives-Cases C, Torrubiano-Domínguez J, Escribà-Agüir V, Ruiz-Pérez I, Montero-Piñar MI, Gil-González D. Social determinants and health effects of low and high severity intimate partner violence. *Ann Epidemiol* 2011; **21**(12): 907-913.

[30] Campbell JC, Lewandowski LA. Mental and physical health effects of intimate partner violence on women and children. *Psychiatr Clin North Am* 1997; **20**(2): 353-374.

[31] de Sousa J, Burgess W, Fanslow J. Intimate partner violence and women's reproductive health. *Obstet, Gynaecol Reprod Med* 2014; **24**(7): 195-203.

[32] Ruiz-Pérez I, Plazaola-Castaño J, Del Río-Lozano M. Physical health consequences of intimate partner violence in Spanish women. *Eur J Public Health* 2007; **17**(5): 437-443.

[33] Sanchez-Lorente S, Blasco-Ros C, Martínez M. Factors that contribute or impede the physical health recovery of women exposed to intimate partner violence: a longitudinal study. *Womens Health Issues* 2012; **22**(5): e491-e500.

[34] Watkins LE, Jaffe AE, Hoffman L, Gratz KL, Messman-Moore TL, DiLillo D. The longitudinal impact of intimate partner aggression and relationship status on women's physical health and depression symptoms. *J Fam Psychol* 2014; **28**(5): 655-665.

[35] Garcia-Linares MI, Sanchez-Lorente S, Coe CL, Martinez M. Intimate male partner violence impairs immune control over herpes simplex virus type 1 in physically and psychologically abused women. *Psychosom Med* 2004; **66**(6): 965-972.

[36] Newton TL, Fernandez-Botran R, Miller JJ, Lorenz DJ, Burns VE, Fleming KN. Markers of inflammation in midlife women with intimate partner violence histories. *J Womens Health (Larchmnt)* 2011; **20**(12): 1871-1880.

[37] Krug EG, Mercy JA, Dahlberg LL, Zwi AB. The world report on violence and health. *Lancet* 2002; **360**(9339): 1083-1088.

[38] Bowes L, Jaffee SR. Biology, genes, and resilience: toward a multidisciplinary approach. *Trauma Violence Abuse* 2013; **14**(3): 195-208.

[39] Chrousos GP. Stress and disorders of the stress system. *Nat Rev Endocrinol* 2009; **5**(7): 374-381.

[40] Koolhaas JM, Bartolomucci A, Buwalda B, de Boer SF, Flügge G, Korte SM, et al. Stress revisited: a critical evaluation of the stress concept. *Neurosci Biobehav Rev* 2011; **35**(5): 1291-1301.

[41] Constantino RE, Sekula LK, Rabin B, Stone C. Negative life experiences, depression, and immune function in abused and nonabused women. *Biol Res Nurs* 2000; **1**(3): 190-198.

[42] Feinberg ME, Jones DE, Granger DA, Bontempo D. Relation of intimate partner violence to salivary cortisol among couples expecting a first child. *Aggress Behav* 2011; **37**(6): 492-502.

[43] Inslicht SS, Marmar CR, Neylan TC, Metzler TJ, Hart SL, Otte C, et al. Increased cortisol in women with intimate partner violence-related posttraumatic stress disorder. *Psychoneuroendocrinology* 2006; **31**(10): 825-838.

[44] Pico-Alfonso MA, Garcia-Linares MI, Celda-Navarro N, Herbert J, Martinez M. Changes in cortisol and dehydroepiandrosterone in women victims of physical and psychological intimate partner violence. *Biol Psychiatry* 2004; **56**(4): 233-240.

[45] Seedat S, Stein MB, Kennedy CM, Hauger RL. Plasma cortisol and neuropeptide Y in female victims of intimate partner violence. *Psychoneuroendocrinology* 2003; **28**(6): 796-808.

[46] Garcia-Linares MI, Pico-Alfonso MA, Sanchez-Lorente S, Savall-Rodriguez F, Celda-Navarro N, Blasco-Ros C, et al. Assessing physical, sexual, and psychological violence perpetrated by intimate male partners toward women: a Spanish cross-sectional study. *Violence Vict* 2005; **20**(1): 99-123.

[47] Blasco-Ros C, Sánchez-Lorente S, Martinez M. Recovery from depressive symptoms, state anxiety and post-traumatic stress disorder in women exposed to physical and psychological, but not to psychological intimate partner violence alone: a longitudinal study. *BMC Psychiatry* 2010; **10**: 98.

[48] Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961; **4**: 561-571.

[49] Conde V, Useros E. Adaptación castellana de la escala de evaluación conductual para la depresión de Beck. *Rev Psiquiatr Psicol Med Eur Am* 1975; **12**: 217-236.

[50] Echeburúa E, Corral P, Amor PJ, Zubizarreta L, Sarasúa B. Escala de gravedad de síntomas de trastorno de estrés postraumático: propiedades psicométricas. *Anal Modificación Conducta* 1997; **23**: 503-526.

[51] Harris TO, Borsanyi S, Messari S, Stanford K, Cleary SE, Shiers HM, et al. Morning cortisol as a risk factor for subsequent major depressive disorder in adult women. *Br J Psychiatry* 2000; **177**: 505-510.

[52] Herbert J. Neurosteroids, brain damage, and mental illness. *Exp Gerontol* 1998; **33**(7-8): 713-727.

[53] Dettenborn L, Muhtz C, Skoluda N, Stalder T, Steudte S, Hinkelmann K, et al. Introducing a novel method to assess cumulative steroid concentrations: increased hair cortisol concentrations over 6 months in medicated patients with depression. *Stress* 2012; **15**(3): 348-353.

[54] Herbert J. Cortisol and depression: three questions for psychiatry. *Psychol Med* 2013; **43**(3): 449-469.

[55] Klaassens ER, Giltay EJ, Cuijpers P, van Veen T, Zitman FG. Adulthood trauma and HPA-axis functioning in healthy subjects and PTSD patients: a meta-analysis. *Psychoneuroendocrinology* 2012; **37**(3): 317-331.

[56] Lemieux AM, Coe CL. Abuse-related posttraumatic stress disorder: evidence for chronic neuroendocrine activation in women. *Psychosom Med* 1995; **57**(2): 105-115.

[57] Meewisse ML, Reitsma JB, de Vries GJ, Gersons BP, Olff M. Cortisol and post-traumatic stress disorder in adults: systematic review and meta-analysis. *Br J Psychiatry* 2007; **191**: 387-392.

[58] Pervanidou P, Chrousos GP. Neuroendocrinology of post-traumatic stress disorder. *Prog Brain Res* 2010; **182**: 149-160.

[59] Vythilingam M, Gill JM, Luckenbaugh DA, Gold PW, Collin C, Bonne O, et al. Low early morning plasma cortisol in posttraumatic stress disorder is associated with co-morbid depression but not with enhanced glucocorticoid feedback inhibition. *Psychoneuroendocrinology* 2010; **35**(3): 442-450.

[60] Gill J, Vythilingam M, Page GG. Low cortisol, high DHEA, and high levels of stimulated TNF-alpha, and IL-6 in women with PTSD. *J Trauma Stress* 2008; **21**(6): 530-539.

[61] Oquendo MA, Friend JM, Halberstam B, Brodsky BS, Burke AK, Grunebaum MF, et al. Association of comorbid posttraumatic stress disorder and major depression with greater risk for suicidal behavior. *Am J Psychiatry* 2003; **160**(3): 580-582.

[62] Young EA, Breslau N. Saliva cortisol in posttraumatic stress disorder: a community epidemiologic study. *Biol Psychiatry* 2004; **2**(3): 205-209.

[63] Morris MC, Compas BE, Garber J. Relations among posttraumatic stress disorder, comorbid major depression, and HPA function: a systematic review and meta-analysis. *Clin Psychol Rev* 2012; **32**(4): 301-315.

[64] Goodyer IM, Herbert J, Altham PM, Pearson J, Secher SM, Shiers HM. Adrenal secretion during major depression in 8- to 16-year-olds, I. Altered diurnal rhythms in salivary cortisol and dehydroepiandrosterone (DHEA) at presentation. *Psychol Med* 1996; **26**(2): 245-256.

[65] Heuser I, Deuschle M, Luppa P, Schweiger U, Standhardt H, Weber B. Increased diurnal plasma concentrations of dehydroepiandrosterone in depressed patients. *J Clin Endocrinol Metab* 1998; **83**(9): 3130-3133.

[66] Michael A, Jenaway A, Paykel ES, Herbert J. Altered salivary dehydroepiandrosterone levels in major depression in adults. *Biol Psychiatry* 2000; **48**(10): 989-995.

[67] Lopes RP, Grassi-Oliveira R, de Almeida LR, Stein LM, Luz C, Teixeira AL, et al. Neuroimmunoendocrine interactions in patients with recurrent major depression, increased early life stress and long-standing posttraumatic stress sisorder symptoms. *Neuroimmunomodulation* 2012; **19**(1): 33-42.

[68] Phillips AC, Batty GD, Gale CR, Lord JM, Arlt W, Carroll D. Major depressive disorder, generalised anxiety disorder, and their comorbidity: associations with cortisol in the Vietnam experience study. *Psychoneuroendocrinology* 2011; **36**(5): 682-690.

[69] Yehuda R, Brand SR, Golier JA, Yang RK. Clinical correlates of DHEA associated with post-traumatic stress disorder. *Acta Psychiatr Scand* 2006; **114**(3): 187-193.

[70] Markopoulou K, Papadopoulos A, Juruena MF, Poon L, Pariante CM, Cleare AJ. The ratio of cortisol/DHEA in treatment resistant depression. *Psychoneuroendocrinology* 2009; **34**(1): 19-26.

[71] Young AH, Gallagher P, Porter RJ. Elevation of the cortisol-dehydroepiandrosterone ratio in drug-free depressed patients. *Am J Psychiatry* 2002; **159**(7): 1237-1239.

[72] Adams TB, Wharton CM, Quilter L, Hirsch T. The association between mental health and acute infectious illness among a national sample of 18- to 24-year-old college students. *J Am Coll Health* 2008; **56**(6): 657-663.

[73] Olff M, de Vries GJ, Güzelcan Y, Assies J, Gersons BP. Changes in cortisol and DHEA plasma levels after psychotherapy for PTSD. *Psychoneuroendocrinology* 2007; **32**(6): 619-626.