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Research Article

Should the Full Array of Steroid Hormones be Measured in Trauma Research? A Pilot Study

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Abstract

Objectives: This pilot study was designed to determine whether future trauma research should gather information on the full array of steroid hormones.

Methods: Blood levels of cortisol, DHEA, testosterone, pregnenolone, estradiol and sex hormone binding globulin were obtained in a sample of 67 hospital trauma program inpatients.

Results: High and low blood levels of all hormones except pregnenolone were observed, with the most frequent being cortisol: 13 participants had high resting morning cortisol, and 6 had low levels.

Conclusions: Although the uncontrolled and cross-sectional nature of the data do not allow conclusions about causality, it appears that, in future studies of trauma physiology, blood levels should be obtained for the full array of steroid hormones, rather than for just cortisol and DHEA; these two steroid have received the most attention in prior trauma research.

Keywords: Steroid hormones; Cortisol; Posttraumatic stress disorder; Dissociative disorders

Abbreviations

DES: Dissociative Experiences Scale; SDQ: Somatoform Dissociation Questionnaire; BDI: Beck Depression Inventory; BHS: Beck Hopelessness Scale; SCL-90-R: Symptom Checklist-90-Revised; BSS: Beck Suicide Scale; DDIS: Dissociative Disorders Interview Schedule; SCID: Structured Clinical Interview for DSM-IV

Introduction

It is well established that cortisol is a mammalian stress response hormone [1-8]. Cortisol is elevated following acute trauma but resting blood levels may become lower than normal in response to chronic trauma. Similarly, the Hypothalamic-Pituitary-Adrenal (HPA) axis can become blunted in response to chronic trauma, with reduced responsiveness to psychological and biochemical challenges [9,10].

Although most of the attention in studies of HPA-axis trauma physiology has been on cortisol, recent studies suggest that Dehydroepiandrosterone (DHEA) may also be involved in both the trauma response and psychopathology [1,6,11-22] DHEA may also play a role in resiliency [23].

In the context of this literature, we decided to obtain a full panel of steroid hormones in a sample of hospital trauma program inpatients. We hypothesized that if cortisol and DHEA are dysregulated in trauma survivors, perhaps abnormalities in other steroid hormones might occur in this population. Our uncontrolled, cross-sectional methodology does not allow us to reach any causal conclusions, or to attribute causality to the participants' psychological trauma, but we nevertheless thought it would be instructive to examine the steroid hormone system as a whole in a sample of trauma survivors.

This study is analogous to an open label pilot study in pharmacology. It represents a first look, not an effort to provide definitive data or establish causality. If no abnormalities in the other steroid hormones were observed in our traumatized sample, then there would be no need to proceed with controlled, randomized or prospective studies. To our knowledge, the full array of steroid hormones has never been measured in a trauma population previously.

Methods and Methods

Participants and procedure

The authors interviewed a sample of 67 inpatients in a hospital-based Trauma Program. Participants were consecutively admitted patients who consented to participate. The average length of stay in the inpatient program is 12 days. All 67 participants completed blood work as part of the study, including cortisol, Sex Hormone Binding Globulin (SHBG), testosterone (free and total), estradiol, pregnenolone, and Dehydroepiandrosterone (DHEA). All participants provided written informed consent. The study was approved by the Medical Staff Committee of the hospital.

Measures

The DES is a 28-item self-report measure that has good reliability and has been used in hundreds of published studies [24]. The BHS [25], BSS [26] and BDI [27] all are widely used and have good reliability and validity. The SDQ is a measure of somatoform dissociation that is less widely used than the Beck measures and the DES, but it also has established reliability [28]. The SCL-90-R [29] is a widely used measure of general psychopathology that has good reliability and validity.

The DDIS is a structured interview that makes DSM-IV diagnoses of major depressive episode and the five different dissociative disorders [30]. The DDIS has good concurrent validity when compared to the

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Table 1: Correlations between the different steroid hormones.

Hormone	Pregnenolone	Free T	Total T	DHEA	Estradiol	Cortisol	SHBG
Pregnenolone							
Free T	0.14						
Total T	0.22	0.94***					
DHEA	0.51***	0.29*	0.28*				
Estradiol	0.22	-0.15	-0.11	0.27*			
Cortisol	0.46***	0.06	0.13	0.26*	0.26*		
SHBG	0.39**	-0.19	-0.11	-0.11	-0.16	0.15	

* = $p<.05$; ** = $p<.01$; *** = $p<.0001$; T = Testosterone; SHBG = Sex Hormone Binding Globulin

Structured Clinical Interview for DSM-IV Dissociative Disorders [31] the DES-Tax on [32] and a clinical interview [30]. The SCID is a widely used structured interview with good reliability and validity [33].

Data analysis

The frequencies of abnormalities on screening blood work were tabulated. Average scores on the different measures, and the percentage of participants meeting criteria for PTSD on the SCID and a dissociative disorder on the DDIS was tabulated, as were their childhood trauma histories on the DDIS. A Pearson correlation matrix was constructed using the average values for the different steroid hormones, and the average values for the self-report symptom measures, with significance set at p = 0.05.

Results

The participants included 11 men and 56 women with an average age of 43.2 years (SD=9.9); 28 were married and 39 were not married. Of the 67 participants, 42 (62.7 %) met criteria for PTSD on the SCID, 30 (44.8 %) met criteria for major depressive disorder on the DDIS, and 22 (32.8 %) met criteria for a dissociative disorder on the DDIS. Average values on the self-report measures for the 84 participants were: DES (M = 46.6, SD = 21.3); BDI (M = 37.9, SD = 12.2); BHS (M = 12.5, SD = 5.9); BSS (M = 17.1, SD = 11.4), SCL-90 (M = 2.2, SD = 0.6) and SDQ (M = 39.0, SD = 15.4).

For the blood work that did not differ by gender, the values were: pregnenolone (M = 20.52, SD = 22.4), and cortisol (M = 13.26, SD = 7.6). For blood work that did differ by gender, the values were: sex hormone binding globulin (SHBG), men (M = 34.5, SD = 18.3), women (M = 51.2, SD = 33.7); DHEA, men (M = 164.4, SD = 133.7), women (M = 117.0, SD = 109.8); estradiol, men (M = 34.9, SD = 11.9), women (M = 72.4, SD = 88.7); total testosterone, men (M = 400.2, SD = 155.9), women (M = 23.6, SD = 16.3); and free testosterone, men (M =9.2, SD = 3.3), women (M = 0.5, SD = 0.4).

For men, the normal range for sex hormone binding globulin is 14.5-48.4 nmol/l; the normal range for total testosterone is 193-740 ng/dl, and for free testosterone it is 6.6-18.1 pg/ml; for estradiol it is 7.6-42.6 pg/ml; and for DHEA it is 51.7—295 ug/dl. For women, the normal range for sex hormone binding globulin is 17.3-125.0 nmol/l; the normal range for total testosterone is 3-41 ng/dl, and for free testosterone it is0-2.2 pg/ml; for estradiol it is <498 pg/ml during ovulation; and for DHEA it is 35.4-256 ug/dl. For both genders, for pregenolone, the normal range is <151 ng/dl, and for A.M. cortisol, the normal range is 6.2-19.4 mcg/dl.

No participants had elevated pregnenolone. For unknown reasons, not all the steroid hormone results on the 12 male participants were reported by the laboratory. Of11 men, two had low cortisol; of 56 women, 11 had low cortisol and 6 had high cortisol. Of 10 men: two had high sex hormone binding globulin and one had a low value; of 10 men, two had low DHEA; of 11 men, three had high estradiol; of 11 men, one had low total testosterone and two had low free testosterone. Of 56 women, seven had low DHEA and one had high DHEA; four had low total testosterone, seven had high total testosterone and none had abnormal free testosterone. Estradiol levels could not be interpreted for the women because we did not gather information about their menstrual cycles, however none had values above 498 pg/ml. Overall, the most frequently abnormal cholesterol-derived hormone was cortisol, with 19 of 67 participants (28.4%) having an abnormal value, of which 13 were high and 6 low.

The correlation matrix is shown in (Table 1). There were no significant correlations between any of the blood values and any of the clinical symptom measures.

Discussion

Our results indicate that abnormal levels of cortisol, DHEA, testosterone, estradiol and sex hormone binding globulin occur in our population. There is no consistent pattern and blood levels can be either high or low. The most frequent abnormality was in cortisol, with 6 participants out of 67 having low levels and 13 having high levels. This variability is consistent with the literature on trauma and cortisol, in that some trauma survivors exhibit more of an acute trauma response with elevated cortisol, while others have a more exhausted, depleted or blunted HPA-axis. We think that the same logic may apply to the rest of the steroid system.

In terms of correlations, it makes sense that, in general, there is an inverse correlation between levels of SHBG and the steroid hormone blood levels, since higher levels of binding globulin should result in lower levels of free hormone. Also, the high correlation between free and total testosterone is not surprising. The most interesting significant correlations are with pregnenolone, which supports our conclusion that future research should examine the whole steroid system not just cortisol and DHEA. Overall, there were no significant correlations between any of the clinical symptom measures and any of the blood values. This is not surprising, given the large standard deviations in the steroid hormone values, including patients being both above and below the normal reference range. Future research involving larger samples should attempt to identify subgroups with

either high or low hormone levels, or any possible correlations between hormone levels and symptoms in those subgroups.

Because of the cross-sectional nature of the sample, and the absence of any experimental challenges, our findings are preliminary, and they cannot be attributed to the participants' reported trauma in any causal fashion. Our purpose was simply to determine whether abnormal levels of an array of steroid hormones occur in the population; since they do, further study is warranted. Psychological trauma could increase the demand for production of some steroid hormones, and thereby shunt synthesis away from others; it could deplete precursors if the trauma is chronic; or it could cause other dysregulations of the system as a whole. Alternatively, the abnormalities found in our sample may be entirely unrelated to their trauma histories; although this is logically possible, it is also plausible that trauma could cause dysregulation in the steroid system as a whole.

We suggest that, in future research on trauma and the HPA axis, attention should be paid to the system as a whole, rather than to one or two steroid hormones at a time. Our study has several limitations: the sample size is relatively small; the results may not be generalizable to other populations; there was no randomization, and no comparison group; and we did not include children or adolescents. Even if some or all of the steroid abnormalities we observed are unrelated to the participants' trauma, from a public health perspective it is clear that further study of steroid physiology in the population is required, at both clinical and research levels.

This study is the conceptual equivalent of an open label pilot study in pharmacology or a twin concordance study in psychopathology: a high twin concordance for psychopathology does not prove genetic causation, but it means that further investigation is warranted. Inversely, a low concordance means that further genetic research is unlikely to yield significant findings. Our conclusion is that further study is warranted based on our preliminary data. To our knowledge, no such data have been presented previously in the literature.

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