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Cortisol Response Following Exposure Treatment for PTSD in Rape Victims

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Abstract

This study examined changes in salivary cortisol levels pre-to-post-treatment in adult female rape victims diagnosed with post traumatic stress disorder (PTSD) randomly assigned to be treated with either Prolonged Exposure Therapy or Eye Movement Desensitization and Reprocessing. Salivary cortisol was collected at baseline, session 3, and session 9. A significant decrease in salivary cortisol levels was observed in individuals classified as treatment responders in both treatment conditions. Findings suggest that successful exposure-based treatments for PTSD which result in trauma-related and depressive symptom reduction may impact the action of the hypothalamic-pituitary-adrenal axis as measured by changes in level of salivary cortisol from pre-to-post-treatment.

Keywords

salivary cortisol; PTSD; HPA axis; prolonged exposure; eye movement desensitization and reprocessing

Research on neuroendocrine correlates of post traumatic stress disorder (PTSD) has examined the hypothalamic-pituitary-adrenal (HPA) axis, the hormonal system involved in response to stress (Yehuda, 2002). Corticotrophin-releasing hormone (CRH) and adrenocorticotrophic hormone (ACTH) are activated in response to stress and ultimately result in the release of a glucocorticoid, cortisol, from the adrenal cortex into the bloodstream. The stress response is kept in check via a negative feedback loop, with the cortisol present in the bloodstream acting upon brain areas to shut down the release of CRH (Griffin, Nishith, Resick, & Yehuda, 1997). Cortisol alterations in PTSD appear to be different from those observed in acute and chronic stress, as well as those associated with major depressive disorder, although cortisol levels in persons with PTSD are within the normal endocrinologic range (Yehuda, 2002; Yehuda, 2006).

Early research in the area of urinary and plasma cortisol levels in PTSD yielded inconsistent results, with some studies indicating lower levels of cortisol in combat veterans with PTSD

(Kellner, Baker, & Yehuda; 1997; Mason, Giller, Kosten, Ostroff, & Harkness, 1986; Yehuda, Teicher, Trestman, Levengood, & Siever, 1996), while other studies indicated higher levels of cortisol in traumatized individuals. Elevated urinary cortisol levels were found in sexually abused women with PTSD (Lemieux & Coe, 1995), as well as in civilian disaster trauma survivors (Maes et al., 1998). Other recent studies have found no significant difference in urinary cortisol levels between groups of traumatized individuals with and without PTSD (Young & Breslau, 2004).

Levels of cortisol have also been measured via the dexamethasone suppression test. Depressed individuals show a lack of suppression in cortisol levels in response to dexamethasone administration, which interrupts the normal HPA negative feedback loop. Both male veteran and female civilian groups with PTSD exhibit enhanced suppression of the HPA cortisol response to the administration of dexamethasone (Stein, Yehuda, Koverola, & Hanna, 1997; Yehuda et al., 1993).

In one study, plasma cortisol reactivity was examined in individuals with PTSD, alcohol dependence and PTSD, and controls (Santa Ana et al., 2006). Results indicated that the childhood trauma group had significantly lower baseline and post-stressor cortisol levels than the adult trauma or no trauma history groups. This result is consistent with other studies which have indicated that low basal cortisol may be associated with early traumatization (Heim, Newport, Bonsall, Miller, & Nemeroff, 2001; Rasmusson et al., 2001).

In a recent study, Olf, Vries, Yener, Assies, and Gersons (2007) examined the association between psychological treatment for PTSD (brief eclectic psychotherapy) and HPA-axis-related stress hormones. Twenty-one patients with chronic PTSD due to a type I civilian trauma (e.g., assault, traffic accident, medical event, work accident) were treated in a manualized therapy over 16 weeks, which included psychoeducation, imaginary exposure, writing assignments, cognitive restructuring, giving meaning to the event, and a farewell ritual. The main result from the study indicated that effective psychotherapy may improve low cortisol and dehydroepiandrosterone (DHEA) levels. In this study, the effects of psychotherapy were found when taking depressive symptoms into account. In treatment responders, cortisol levels increased, while in non-responders, cortisol levels decreased post-treatment. Level of cortisol was also influenced by depressive symptoms at the beginning of treatment and the degree of change in depressive symptoms after treatment, and the authors postulate that depressive symptoms may obscure the effects of psychotherapy on cortisol, possibly because of opposite mechanisms of action. Heber, Kellner, and Yehuda (2002) also found an increase in cortisol following psychological treatment for PTSD. In this single case study of a 41-year-old female with chronic PTSD, treatment consisted of four weekly sessions of eye-movement desensitization and reprocessing (EMDR) and results indicated moderate symptom improvement and an increase in basal cortisol levels along with a more attenuated cortisol hypersuppression in response to the dexamethasone suppression test following treatment.

The present study sought to examine changes in salivary cortisol levels related to treatment outcome in a sample of females with PTSD. The hypothesis was that cortisol levels would be impacted by a course of successful treatment, resulting in a decrease in salivary cortisol level, acutely, at the end of the treatment session. Cortisol levels were to be collected at the end of the first exposure treatment session and at the end of the last exposure treatment session. Subjects were adult female rape victim participants in a study which examined the relative efficacy of Eye Movement Desensitization and Reprocessing (EMDR) vs. Prolonged Exposure (PE) in the treatment of PTSD (Rothbaum, Astin, & Marsteller, 2005).

Method

Participants

Study subjects were female victims of a rape at least 3 months prior to study entry; no maximum time since the index rape was imposed. Inclusion criteria were that the index event must have been a rape in adulthood (i.e., age 12 or older) or a single incident of rape in childhood (ages 0–11). Participants were not excluded if they had other traumas in addition to a rape in adulthood, including childhood sexual abuse. Participants were required to be stabilized on any previously prescribed psychotropic medication for 30 days prior to study entry and to agree not to change medication or dosage for the duration of the study.

Seventy-four participants were randomly assigned to one of two active treatment groups (EMDR or PE) or a wait list control group (WAIT). WAIT participants were randomly assigned to either PE or EMDR after the post-treatment assessment. Sixty women completed the protocol. Mean participant age was 33.8 years ($SD = 11.0$). As assessed by the SCID, 35% ($n = 21$) of participants had only a PTSD diagnosis, 40% ($n = 24$) had one comorbid diagnosis, and 25% ($n = 15$) had two or more diagnoses in addition to PTSD.

Procedure

Both EMDR and PE were delivered by trained doctoral level psychologists in nine 90-minute, twice weekly sessions. Session tapes were independently rated by experts for treatment integrity. In both treatment conditions, the first two sessions consisted of information gathering, education about trauma effects, a rationale for treatment, and treatment preparation. During sessions 3 through 9, EMDR involved having the patient imagine a scene representing the worst part of the trauma, focusing on bodily sensations and rehearsing negative thoughts that match the picture, while simultaneously following the therapist's fingers moving back and forth, a minimum of 20 times per repetition. A subjective units of discomfort (SUDs) scale rating was used to monitor distress. When ratings decreased to 0 or 1, the patient was asked to track the therapist's fingers while rehearsing a new, preferred belief about the scene until this felt true to the patient. During sessions 3 through 9, the PE condition involved the patient reliving the rape scene in imagination as vividly as possible and describing it out loud. SUDs ratings were monitored while the patient recounted the traumatic event in its entirety several times during each session. Narratives were tape-recorded and patients were instructed to listen to the tapes at home at least once daily. The patient's reactions were discussed following exposure and a homework assignment relating to that day's exposure was assigned. Both techniques depended on imaginal exposure, were presumed to aid emotional processing of the trauma, and aimed to achieve cognitive modifications via treatment (Rothbaum et al., 2005). Assessments were conducted at pre-treatment, post-treatment, and follow-up of 6 and 12 months post-treatment.

Subjects were administered the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1990; Blake et al., 1995), the Assault Information Interview (AII; Rothbaum, Foa, Riggs, Murdock, & Walsh, 1992), and the SCID Non-Patient Version (First, Gibbon, Spitzer, & Williams, 1996). Self-report scales included the PTSD Symptom Scale Self-Report (PSS-SR; Foa, Riggs, Dancu, & Rothbaum, 1993), the Impact of Event Scale- Revised (IES-R; Weiss & Marmar, 1997), and the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961).

Salivary cortisol was collected at baseline, treatment session 3 (the first exposure session in both treatment conditions), and at treatment session 9 (the last exposure session in both treatment conditions). Saliva samples were collected immediately post-exposure. Participants were given privacy and asked to spit saliva into a test tube. Samples were frozen at -20 degrees

and were analyzed in batches. Cortisol was assayed in duplicate 0.2 ml-aliquots of centrifuged saliva using materials from Incstar Corp. (now DiaSorin, Stillwater, Minn.). The sensitivity was 0.1 ng/ml, and the intra-assay coefficient of variation was 3.7%.

Results

Change from Pre-Treatment to Post-Treatment

Overall results of the study indicated that improvement in PTSD symptoms was significantly greater in both the PE and EMDR groups as compared with the WAIT group, and that PE and EMDR groups did not differ significantly from each other on measures of outcome at post-treatment and at 6 month follow-up. Baseline resting cortisol levels measured prior to initiation of treatment indicated no group differences. This sample was obtained at home at approximately the same time of day as study appointment times: PE condition, $M = 2.97$ ng/ml ($SD = 1.97$) vs. EMDR condition, $M = 3.25$ ng/ml ($SD = 2.41$), $t(56) = -0.476$, $p = 0.64$. Table 1 presents the results of the analysis of the change in cortisol over time across groups (PE and EMDR). The available case means and repeated measures analysis of variance are presented. Results indicate that the difference between active treatments (PE vs. EMDR) was not significant, $F(1, 57) = 0.23$, $p = .635$. There was also no significant decrease in cortisol levels over time in the total group, $F(1, 47) = 0.13$, $p = .724$. However, given that not all patients responded to treatment, it was tested whether there might be a response-specific decrease in cortisol level which was unrelated to treatment condition. Post-treatment response was defined in two domains of symptoms: PTSD-related symptoms (50% reduction in CAPS) and depression-related symptoms (50% reduction in BDI scores).

Table 2 presents the cortisol levels classified by PTSD-related symptom response ($n = 50$). Results indicate a larger change in cortisol level in those who responded to either treatment as measured by a greater than 50% reduction in symptoms on the CAPS, with a significant interaction effect on cortisol levels indicating a significant decrease in responders but not in nonresponders, $F(1, 47) = 4.86$, $p = .03$.

This response-specific decrease in symptoms over time was also apparent in the analysis of depression symptom response (response group $\times$ time interaction, $F(1, 47) = 6.34$, $p = .02$; see Table 3). The data also indicate a possible increase in cortisol levels in BDI nonresponders, $F(1, 47) = 3.09$, $p = 0.08$. BDI responders evidenced higher cortisol levels when compared to nonresponders at either time point, total, $F(1, 49) = 8.37$, $p = .006$. In summary, results of the present study indicated a significant decrease in salivary cortisol levels from pre- to post-treatment in this sample of female rape victims who responded to either PE or EMDR.

Discussion

Past research has not yielded an established range of cortisol for individuals with PTSD, nor have group differences in cortisol levels been demonstrated on the basis of diagnosis (Yehuda, 2006). Rather than looking at basal cortisol differences, the present study examined response-to-treatment associated changes in the salivary cortisol levels of individuals diagnosed with PTSD. Observed changes in cortisol levels over time of treatment were not associated with a lifetime or current diagnosis of depression, nor were the differences significantly correlated with time since assault or number of past traumas. While cortisol values were within the normal endocrinologic range, these values significantly decreased pre- to post-treatment in individuals who evidenced a response to treatment characterized by a greater than 50% reduction in PTSD and depressive symptomology.

These preliminary results suggest that exposure-based treatment (either PE or EMDR) that results in trauma-related and depressive symptom reduction may influence the dynamic action

of the HPA axis as measured by level of salivary cortisol. This difference might be conceptualized as decreased reactivity to the stressor or as an underlying change in the system. If subjects are no longer avoiding the traumatic event due to successful emotional processing and/or cognitive modifications based on a model of exposure-based treatment, it may be possible that trauma-related autonomic distress is impacted, and this may be reflected by changes in levels of salivary cortisol pre-to-post treatment. It is also interesting to note the trend toward significance for increased cortisol levels over time in those individuals who did not respond to treatment. Limitations of the present study include changes in salivary cortisol levels which may be related to diurnal variation or other extraneous factors such as pattern of sleep. It is hoped that the preliminary results from this study will encourage further exploration of the cortisol response in female rape victims with PTSD in order to clarify a possible pattern of change in cortisol level which may be a neurochemical indicator related to treatment outcome.

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Table 1 Mean Cortisol Levels ng/ml, Treatment Condition $\times$ Time

Treatment Condition	Pre- treatment	Post- treatment	Total
	M (SD)	M (SD)	M (SD)
PE	3.09 (2.53) n=30	2.22 (0.74) n=25	2.70 (1.97)
EMDR	2.74 (1.48) n=28	2.67 (0.93) n=25	2.71 (1.24)
Total	2.93 (2.08)	2.45 (0.87)	

Table 2

Mean Cortisol Levels ng/ml (CAPS)

	Pre- treatment	Post- treatment	Total
	M (SD)	M (SD)	M (SD)
CAPS Nonresponders (<50% sx reduction) n = 14	2.40 (0.94)	2.55 (1.18) n = 14	2.47 (1.05)
CAPS Responders (>50% sx reduction) n = 36	3.23 (2.51) n = 36	2.41 (0.73) n = 36	2.82 (1.88)
Total	3.00 (2.21)	2.45 (0.87)	

Table 3

Mean Cortisol Levels ng/ml (BDI)

	Pre- treatment	Post- treatment	Total
	M (SD)	M (SD)	M (SD)
BDI Nonresponders (<50% sx reduction) n = 13	2.27 (0.96)	2.56 (1.19) n = 14	2.42 (1.07)
BDI Responders (>50% sx reduction) n = 37	3.25 (2.47)	2.41 (0.72) n = 36	2.84 (1.86)
Total	3.00 (2.21)	2.45 (0.87)	