Annotated Bibliography for Articles on HPA-axis & Cortisol Function in PTSD


*Biological Psychiatry, 48, 940-947.*

Delahanty et al. (2000) collected 15-hour urine samples from MVA victims upon admission to the trauma unit after their accidents. Urine samples were used to examine MVA victims’ peri- and acute-phase posttraumatic endocrine responses to their accident and to assess their efficacy in predicting PTSD symptomatology 1 month after the accident. Results revealed that victims who reported experiencing intrusive thoughts had significantly lower urinary cortisol and epinephrine levels than victims who did not report having intrusive thoughts. In addition, PTSD patients had significantly lower levels of urinary cortisol in the immediate aftermath of their accidents than did patients who did not meet diagnostic criteria. In comparison with control participants (from another study), the participants in this study excreted elevated levels of cortisol, with PTSD patients demonstrating lower elevations. Urinary cortisol also predicted a significant percentage of the variance on IES scores (which included measures of intrusive and avoidant thoughts and behaviour). The authors concluded that initial cortisol levels may contribute, in part, to subsequent acute PTSD.


*A pilot study of noradrenergic and HPA axis function in PTSD vs. panic disorder.*

*Psychiatry Research, 110, 219-230.*
This pilot study compares patients with post-traumatic stress disorder to a panic disorder group and healthy controls with regard to their baseline levels of cortisol and MHPG and their response to clonidine challenge. Clonidine is an alpha-2 agonist that leads to the reduction of blood cortisol levels. The main finding of the study was that baseline and functional HPA axis and noradrenergic profiles appear recognizably different in PTSD and panic disorder. PTSD patients had lower baseline cortisol, lower baseline MHPG, reduced MHPG volatility to clonidine challenge, and marginally reduced cortisol volatility compared to patients with panic disorder. The study found PTSD and panic disorder to be on opposite sides of the spectrum with respect to baseline cortisol and baseline MHPG. These findings are consistent with and HPA axis model in PTSD that suggests both reduced baseline activity and increased reactivity to challenge.


In this study Bonne at al. were specifically interested in testing the hypothesis that insufficient activation of the HPA-axis, shortly after traumatic events, is a risk factor for PTSD. No study prior to this one had observed a direct link between early cortisol levels and chronic PTSD. The study prospectively tested the hypothesis that PTSD is predicted by lower levels of cortisol in the early aftermath of traumatic events. Eight subjects developed PTSD at six months (PTSD group) and 13 did not (non-PTSD group). The groups had similar IES scores at 1 week. PTSD subjects, however, were significantly more symptomatic at 6 months. Cortisol levels at 1 week did not significantly predict PTSD symptoms at 6 months. The study's main hypothesis was not confirmed as chronic PTSD was neither predicted by nor associated with lower morning cortisol.

This article explores potential considerations in cancer research relating to conceptualizing the diagnosis of cancer as a traumatic event and the accompanying altered dynamic range of cortisol production. Yehuda discusses the divergent literature on HPA axis activation and proposes some hypotheses on why there is variability in the findings. One explanation is that there might be different biological variants of PTSD with relatively similar phenotypes as is the case with MDD. Several recommendations are made with regard to research examining the relationship between alterations in HPA axis in PTSD and cancer. These include cortisol collection procedures, examining shorter rhythm stress reactivity, prior risk factors, and the influence of co-occurring cancer treatments on stress hormones.


The main aim of this review is to explore the role of HPA axis dysregulation in the link between child maltreatment and MDD/PTSD among women. According to the authors PTSD studies have indicated a down regulation of pituitary CHR receptors, attributed to stress-related increases in CRH drive. Another major conclusion of this article is that exposure to child maltreatment has been found to have negative effects on the HPA axis, but not all individuals go on to develop these disorders. It is more likely that vulnerable individuals may have an increased risk for psychopathology. Lastly, it was concluded that the combined effects of both psychiatric illness
and a history of maltreatment appear to result in the largest degree of HPA axis dysregulation. Clinical recommendations include better screening by child welfare agencies that include tests of children’s mental health functioning and better access for these children to evidence based interventions such as CBT.


This study examined the relationship between urinary hormone levels in children immediately following exposure to a traumatic event and the later development of acute PTSD symptoms six weeks post-trauma. The study focused on children exposed to a first-time, acute-duration, trauma. Acute PTSD symptoms were significantly correlated with initial cortisol levels. Within-gender analysis suggested that, in boys, urinary epinephrine, norepinephrine and cortisol levels were significantly correlated with acute PTSD symptoms. However, urinary hormones were not related to acute PTSD symptoms in girls. Initial urinary cortisol levels significantly predicted acute PTSD symptoms. The present findings suggest the observed alterations may be present soon after the trauma, and that initial levels of stress hormones may help to distinguish child trauma patients at risk for PTSD. Results of this study suggest that elevated levels of urinary cortisol and epinephrine shortly following exposure are positively related to levels of PTSD symptoms in children measured six weeks post-trauma. These findings contradict Delahanty et al.’s (2000) prior findings in adult trauma victims.

This study examined whether cumulative critical incident exposure, independent from PTSD symptoms, would predict lower cortisol levels. Active duty to the saucers were used as they are an ideal study population to test these questions as they express a broad range of PTSD symptomatology, have higher rates of both critical incident and routine work environment stressors, are ambulatory, and are physically active. No relationship was found between cumulative critical incident exposure or routine work environment stressors and either pre- or post-dexamethasone cortisol levels. As predicted, higher peritraumatic distress, peritraumatic dissociation and PTSD symptoms were associated with lower pre-dexamethasone cortisol levels, the counter to be author’s predictions were not associated with post-dexamethasone cortisol levels or with amount of post-dexamethasone cortisol suppression. The results indicate a relationship between greater PTSD symptoms and lower levels of basal cortisol on awakening.


This paper provides an overview of the finding of 34 articles examining non-pharmacological challenges and different pharmacological challenges, including the dexamethasone suppression test (DST), ACTH-, CRH-, and naloxone challenges, dexamethasone CRH test and metyrapone challenge designs. Leukocyte glucocorticoid receptor studies are also briefly discussed because
in vitro leukocyte GR studies have been used as a surrogate measure for central HPA axis feedback regulation. A discussion is provided linking findings of reported alterations to clinical and preclinical findings. Some key findings reported were an enhanced salivary cortisol levels in response to cognitive challenge, as well as enhanced plasma cortisol suppression after administration of 0.5 mg of dexamethasone. An enhanced GR sensitivity in PTSD patients was reported in leukocyte GR function studies.


This study's primary aim was to determine whether patients with chronic PTSD due to mixed civilian trauma and healthy volunteers differed in basal cortisol levels. The study also evaluated other hormones, including DHEA(S), prolactin, TSH, and fT4 levels, because they are all components of or related to HPA axis functioning. This study clearly demonstrated lower plasma cortisol levels in patients with chronic PTSD compared to the comparison group. These findings were robust, whether or not controlling for sex, age, BMI, or smoking. The authors hypothesize that the discrepancies in the literature on the relationship between PTSD and cortisol might be due to the severity of symptoms in the PTSD samples. In concordance with earlier studies, the study found a linear negative relationship between cortisol levels and the severity of PTSD symptoms.

This article briefly reviews the multiple moderating factors that help account for the divergent patterns in HPA function as well as methodological advances that will continue to improve the assessment of HPA function in youth exposed to violence and trauma. Both the locus coeruleus-norepinephrine (LC/NE) system and the hypothalamic pituitary adrenal axis are briefly discussed. The dissimilar patterns of neurobiological response to violence and trauma are discussed, such as hyper- and hypocortisolism as well as the normal expected diurnal pattern of cortisol secretion. Several theories are advanced to account for the variability in response patterns. HPA-priming may be influenced by early traumatic experiences and may be more likely to occur among adults and adolescents than in children because adaptation of the HPA-axis may take years to occur. Promising assessment techniques considered include salivary cortisol assays and neuroimaging.


The aim of this article was to conduct a meta-analysis in order to compare basal cortisol levels in adults with current PTSD and in people without psychiatric disorder. A total of 1628 people were included from 37 studies, with 828 with PTSD and 800 controls with no current Axis 1 disorder or history of PTSD. Results indicated that across the 37 studies, people with PTSD did not differ in cortisol levels. Meewisse et al. conducted subgroup analyses and found that studies assessing plasma or serum showed significantly lower levels in people with PTSD than in controls. The same result was found in studies including females only, in studies on physical and sexual abuse.
and in afternoon samples. The authors concluded that low cortisol levels do not relate to PTSD in general, but rather seem to mirror trauma exposure and PTSD subgroups.


Miller et al. (2007) discuss the contradictory findings of both the increase and decrease of cortisol production in response to stress and the subsequent pathogenic conditions related to these deviations. The goal of this review is to synthesize the findings over the past 50 years of research and generate answers to how activity of the HPA axis is modified by exposure to chronic stress. A second objective of this review is to outline and evaluate five hypotheses that may help to sort out some of the confusion in the literature. Meta-analysis findings indicate that variability in HPA response is attributable to stressor and person features. Timing is a critical element as hormonal activity is elevated at stress onset but reduced as time passes. Stress that threatens physical integrity, is traumatic in nature, and is largely uncontrolled elicits a high, flat diurnal profile of cortisol secretion. Finally, APA activity is shaped by the person’s response to stress; cortisol output increases with the extent of subjective distress and is generally reduced in those with PTSD.

The authors of this article point out that previous studies examining HPA axis function in response to stress have typically evaluated small samples, male subjects, and have used a single peripheral measure of the HPA axis activity. None of these studies measured hormone levels immediately after exposure. This study evaluated both male and female survivors and biological measures were obtained within hours of traumatic events. Furthermore, several corroborating measures of HPA axis activity were obtained. The authors hypothesized that PTSD is associated with lower initial levels of plasma cortisol and that PTSD is associated with the time-dependent decrease in plasma cortisol levels. The studies hypothesis of an association between ER cortisol levels and PTSD was not confirmed. Likewise, the hypothesized time-dependent differential change in HPA axis measures was also not confirmed. The authors explain that these findings should prompt researchers to reconsider the role of the immediate response in the aetiology of PTSD.


The aim of this study was to investigate the longitudinal course of mean 24 hour urinary cortisol excretion in posttraumatic stress disorder (PTSD). The authors evaluated 24-hour cortisol excretion in 20 Holocaust survivors 10 years after obtaining an initial estimate. Cortisol levels increased in participants whose PTSD had remitted but declined in participants who developed PTSD or whose PTSD status did not change over time. Cortisol levels at time 1 predicted diagnostic status change better than psychological variables, including exposure to traumatic
events between assessments. The authors conclude that cortisol levels are affected by change in PTSD status and age.


This review examines the pattern of HPA-axis activity and reactivity in healthy individuals compared to individuals with PTSD and MDD using a number of measures including cortisol levels at rest, in response to the dexamethasone suppression test (DST), and in response to psychological stress. While PTSD and MDD share numerous overlapping symptoms, their HPA profiles are often strikingly different. Individuals with PTSD often display lower basal cortisol, hypersuppression in response to low-dose DST, and higher cortisol in response to stress. Individuals with MDD often display heightened basal cortisol, DST nonsuppression, and either normal or slightly blunted cortisol increases in response to stress. The authors conclude that despite the variability in the literature, the DST has produced the most consistent findings; though not sufficient to establish a formal diagnosis, it is likely to provide useful diagnostic information.


This study explored whether HPA axis dysregulation is associated with concurrent PTSD and MDD diagnoses. Participants were bereaved and non-bereaved spouses from September 11,
2001 terror attacks. The authors hypothesised that after terror-related spouse death, bereaved compared to non-bereaved spouses would have greater HPA axis activation, evidenced by higher basal salivary cortisol levels and less dexamethasone suppression of salivary cortisol; and persistent PTSD and MDD. Study results indicated that bereaved compared to non-bereaved had significantly higher rates of post-traumatic stress disorder (PTSD) and major depressive disorder (MDD) and had significantly higher morning basal cortisol and less afternoon postdexamethasone cortisol suppression than non-bereaved. An important finding was that among the bereaved, those with PTSD and without comorbid MDD had significantly greater afternoon postdexamethasone cortisol suppression compared to those without psychiatric disorders. The authors concluded that heightened glucocorticoid receptor sensitivity may explain why bereaved spouses who develop PTSD without depression had enhanced postdexamethasone cortisol suppression.


This study used an epidemiological sample of 1880 police officers and firefighters to examine associations of salivary cortisol with PTSD, negative life events (NLE) and exposure to a major air disaster more than 8 years earlier. Probable PTSD was not associated with basal salivary cortisol. However cortisol was associated with negative life events. Subjects who generally experienced more negative life events and specifically events in the past that threaten the subjects own life and social or occupational functioning or that of close relatives, have somewhat
lower basal cortisol levels. The authors conclude that this confirms previous suggestions that basal hypocorticolism is not a correlate of PTSD specifically, but that it is a widespread phenomenon even present in healthy individuals with a past or current condition of ongoing stress. Professional exposure to the air disaster in 1992 was not associated with abnormal cortisol levels. However, disaster exposed subjects reporting more intrusion symptoms had relatively lower cortisol levels. Results should be interpreted with caution as the data are cross-sectional and contain several methodological limitations such as assessment of basal functioning of the HPA axis with a single saliva sample.