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Cortisol response to acute trauma and risk of posttraumatic stress disorder

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Summary This study sought to characterize the variability of the acute cortisol response following trauma and its relationship to posttraumatic stress disorder (PTSD). Forty eight participants were recruited within 24 h of a traumatic accident requiring hospital admission. A saliva sample was collected at 08.00 h and 16.00 h 2 days, 1 month and 6 months after hospital admission, together with 24-h urine collection. Participants completed a dexamethasone suppression test (0.5 mg DEX at 21.00 h) at each follow up, together with self-report questionnaires. The Clinician Administered PTSD Scale (CAPS) was administered at 1 and 6 months to identify PTSD. Prevalence of PTSD was 27% at 1 month and 21% at 6 months. PTSD symptoms at 6 months were negatively correlated with salivary cortisol at 08.00 h on day 2 ($r = -0.36$, $p = 0.04$), but positively correlated with 16.00 h cortisols ($r = 0.41$, $p = 0.03$). A lower rise in cortisol at 08.00 h on day 2 was associated with an increase in risk of PTSD at both 1 month (OR = 1.411 (1.017, 1.957)) and 6 months (OR = 1.411 (1.066, 1.866)). At 1 month, 70% of participants with PTSD suppressed cortisol to more than 90% of pre-dex levels compared with 25% without PTSD ($\chi^2 = 6.77$, $p = 0.034$). Urinary cortisol excretion was not different between groups at any time point. The findings support a hypothesis that sensitization of the HPA axis and enhanced suppression of cortisol following the dexamethasone suppression test are established early in the disease process.

1. Introduction

An increasing body of evidence suggests that mounting an adequate cortisol response at the time of exposure to a traumatic event has a protective effect against posttraumatic stress symptoms (Yehuda, 2002). Yet, practically

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speaking, there are several reasons why it is difficult to study this process in individuals who have been exposed to traumatic events. First, this is a time in which there is substantial disruption in people's lives and increased chaos as individuals deal with the many details involved in restoring their lives post-trauma. Second, the biological methodologies and instruments for tracking biological changes have not been well standardized for this purpose, and have, in fact, yielded conflicting results.

Despite the challenging nature of this work, the research in the aggregate supports the idea that there is an attenuated cortisol response during the peritraumatic and early post-traumatic period that contributes to longer-term disruption of the sympathetic nervous system in those that develop posttraumatic stress disorder (PTSD) (Yehuda, 2002; Ehring et al., 2008; Delahanty and Nugent, 2006). Most recently, Ehring et al. (2008) found that lower levels of salivary cortisol measured in the emergency room within 12 h of a motor vehicle accident predicted greater symptom levels of PTSD and depression 6 months later. Similarly, a study of rape victims that assessed plasma cortisol measured within 51 h of the rape found that those with a prior history of assault had lower cortisol levels and were more likely to develop post-traumatic stress disorder than those without a trauma history (Resnick et al., 1995). Further, another study of motor vehicle accident victims (McFarlane et al., 1997) demonstrated a trend toward lower cortisol levels in those who subsequently showed PTSD compared to those who did not develop the disorder, but cortisol levels were significantly lower than in individuals who developed depression.

Another study of 99 accident victims who gave urine samples in the first 15 h following admission showed significantly lower urinary cortisol levels in those diagnosed with acute stress disorder 5 weeks later, compared with those who did not have a disorder in this initial period after the accident (Delahanty et al., 2000). This study also found that the initial cortisol levels were negatively correlated with the subsequent symptoms of intrusion and avoidance.

In contrast, a large study of mixed civilian trauma, found no biological predictors of PTSD diagnosed 5 months later (Bonne et al., 2003). In this study, PTSD was diagnosed 5 months following the trauma and survivors with and without PTSD had similar levels of hormones 1 week after the trauma and again at 5 months. Similarly, Shalev et al. (2008) found no relationship between PTSD and plasma cortisol levels assessed at 10 am in the morning, 10 days, 1 month and 5 months after Emergency Department attendance amongst 155 civilians who had experienced mixed traumatic events.

The discrepancy in the literature may reflect differences in when cortisol levels are measured, and when PTSD is assessed during the post-trauma period. Although it has generally been assumed that cortisol levels remain stable, this may not be the case as illustrated in a study of 31 UN soldiers who had been exposed to a mine accident (Aardal-Eriksson et al., 2001). A negative correlation was found between morning saliva cortisols and concurrent PTSD at 5 days, but a positive correlation between cortisol level and PTSD symptoms 2 and 9 months later.

Indeed, although cortisol levels are easy to measure, they do not always produce stable results in either acute or chronic PTSD, owing to both the fact that cortisol levels might be responsive to environmental perturbations and may yield different estimates depending on whether integrated (e.g. 24-h urinary samples) or single time point estimates are obtained. A more reliable parameter in studies of hypothalamic–pituitary–adrenal (HPA) axis function in PTSD has been cortisol suppression in response to dexamethasone, which reflects the responsiveness of glucocorticoid receptors mediating negative feedback inhibition. To date, no study has examined the reactivity of the HPA axis to challenge in the immediate aftermath of a traumatic exposure.

The present study aimed to prospectively investigate the cortisol response to a traumatic accident in the 24–48 h period of the accident, and then 1 month and 6 months following the trauma to understand the relationship between cortisol production and posttraumatic stress symptoms in the 6 months period of follow up. The degree of HPA axis suppression to low dose dexamethasone 2 days, 1 month and 6 months after the accident was also investigated to study whether super-suppression of cortisol is a vulnerability factor for PTSD or an acquired abnormality.

Specifically, it was hypothesized that salivary cortisol level at 08.00 h and 16.00 h would be lower in individuals who developed PTSD 1 month and 6 months after the trauma. The PTSD group was hypothesized to suppress cortisol to a greater extent than those who did not develop PTSD in response to the low dose dexamethasone suppression test.

2. Methods

2.1. Study design

The study involved longitudinal follow-up of individuals who experienced acute trauma requiring admission to the Royal Adelaide Hospital, South Australia. Participants completed self-administered questionnaires, structured interviews, and provided saliva and urine samples 2 days, 1 month and 6 months after the trauma.

Ethical approval for this study was granted by the University of Adelaide Human Research Ethics Committee and the Royal Adelaide Hospital Ethics Committee.

2.2. Participants

Participants were recruited through the accident and trauma department of the Royal Adelaide Hospital by a research nurse between July 1998 and March 2001. All participants were involved in an acute traumatic accident (motor vehicle accident, industrial accident, assault, or domestic accident) and had been admitted.

The flow of participants through the study is presented in Fig. 1. All participants were between the ages of 18 and 65, and were required to understand written and spoken English and to have an adequate recall of significant events relating to the trauma. Any individual who was unconscious or amnesic for 15 min or longer immediately prior to or following the accident was excluded from the study. All participants lived within the Adelaide metropolitan area or nearby townships.

Patients who were heavily sedated, ventilated in intensive care or unconscious at the time of recruitment were excluded from the study as were patients who were pregnant or planning a pregnancy. Given the likelihood of amphetamines