Psychoneuroendocrinology (2014) 45, 179—186

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

The role of acute cortisol and DHEAS in predicting acute and chronic PTSD symptoms

Joanne Mouthaan [a,*], Marit Sijbrandij [b,c], Jan S.K. Luitse [d], J. Carel Goslings [d], Berthold P.R. Gersons [a,e], Miranda Olff [a,e]

[a] Department of Psychiatry, Center for Anxiety Disorders, Research Group Psychotrauma, Academic Medical Center, Amsterdam, The Netherlands
[b] Department of Clinical Psychology, VU University, Amsterdam, The Netherlands
[c] EMGO Institute for Health and Care Research, The Netherlands
[d] Trauma Unit, Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands
[e] Arq Psychotrauma Expert Group, Diemen, The Netherlands

Received 11 July 2013; received in revised form 1 April 2014; accepted 1 April 2014

KEYWORDS
Posttraumatic stress disorder;
Cortisol;
DHEAS;
Traumatic injury;
Predictors;
Prospective study

Summary
Background: Decreased activation of the hypothalamus—pituitary—adrenal (HPA) axis in response to stress is suspected to be a vulnerability factor for posttraumatic stress disorder (PTSD). Previous studies showed inconsistent findings regarding the role of cortisol in predicting PTSD. In addition, no prospective studies have examined the role of dehydroepiandrosterone (DHEA), or its sulfate form DHEAS, and the cortisol-to-DHEA(S) ratio in predicting PTSD. In this study, we tested whether acute plasma cortisol, DHEAS and the cortisol-to-DHEAS ratio predicted PTSD symptoms at 6 weeks and 6 months post-trauma.
Methods: Blood samples of 397 adult level-1 trauma center patients, taken at the trauma resuscitation room within hours after the injury, were analyzed for cortisol and DHEAS levels. PTSD symptoms were assessed at 6 weeks and 6 months post-trauma with the Clinician Administered PTSD Scale.
Results: Multivariate linear regression analyses showed that lower cortisol predicted PTSD symptoms at both 6 weeks and 6 months, controlling for age, gender, time of blood sampling, injury, trauma history, and admission to intensive care. Higher DHEAS and a smaller cortisol-to-DHEAS ratio predicted PTSD symptoms at 6 weeks, but not after controlling for the same variables, and not at 6 months.
Conclusions: Our study provides important new evidence on the crucial role of the HPA-axis in response to trauma by showing that acute cortisol and DHEAS levels predict PTSD symptoms in survivors of recent trauma.

* Corresponding author at: Academic Medical Center, Department of Psychiatry, Meibergdreef 5 (PA.3-127), 1105 AZ Amsterdam, The Netherlands. Tel.: +31 20 891 3552; fax: +31 20 891 3664.
E-mail address: j.mouthaan@amc.uva.nl (J. Mouthaan).

http://dx.doi.org/10.1016/j.psyneuen.2014.04.001
0306-4530/

1. Introduction

Injury victims presenting to an emergency room have an increased risk of developing trauma-related psychopathology, such as posttraumatic stress disorder (PTSD). Prevalence rates of PTSD following a traffic accident, one of the most common injury causing traumatic events (de Vries and Olff, 2009), vary greatly, from 8–45% at 1 month to 7–26% at 12 months (for a review, see Heron-Delaney et al., 2013). To explain why some develop PTSD and others do not, studies have examined the role of the hypothalamus–pituitary–adrenal (HPA) axis (Delahanty et al., 2000, 2003, 2005; McFarlane et al., 1997, 2011; Resnick et al., 1995, 1997; Shalev et al., 2008; Yehuda et al., 1998b). It has been hypothesized that an insufficient activation of the HPA-axis in response to stress serves as vulnerability for PTSD (Yehuda et al., 1998a; Yehuda, 2002). During acute stress, the hypothalamus secretes corticotrophin-releasing hormone. This in turn stimulates the pituitary gland to release adrenocorticotropic hormone, which leads to the production of glucocorticoids (cortisol) and dehydroepiandrosterone (DHEA) by the adrenal cortex (Vinson et al., 2007). Cortisol suppresses metabolic, immuno- and neurodefensive processes to adequately cope with the stressor, and triggers a negative feedback loop when sufficient circulating levels are reached. Low levels of circulating cortisol have been found to be a vulnerability factor for developing PTSD symptoms, either directly (Delahanty et al., 2003) or indirectly through prior trauma exposure (Resnick et al., 1995; Yehuda et al., 1998b). They fail to trigger the negative feedback loop, thus prolonging the adrenergic response, which may exacerbate consolidation of the traumatic memory. This may lead to intrusive symptoms, which may increase the risk for PTSD (Yehuda, 2002).

Whereas high cortisol has catabolic properties, DHEA and its sulfate form DHEAS have been found to possess anabolic, neuroprotective and antiglucocorticoid effects, showing neurogenerative effects in the hippocampus (Karishma and Herbert, 2002) and protection against the neurotoxic effects of cortisol in studies in rodents (Kaminska et al., 2000; Kimonides et al., 1998, 1999). This may contribute to an upregulation of HPA-axis responses as well as mitigate possible deleterious effects of high cortisol levels on the brain in PTSD (Rasmusson et al., 2003). As such, it may be hypothesized that dysregulations in the HPA-axis function associated with PTSD may also be evident in an abnormal DHEA-response. DHEAS is much more abundant than DHEA, because DHEAS has longer half-life and lower clearance (Lennartsson et al., 2012). Because DHEAS levels are also more stable and show no diurnal variation (Kroboth et al., 1999), they are often preferred in studies on long term effects of stress. Studies on acute stress, on the other hand, often assess DHEA, since DHEAS serves as a reservoir for DHEA biosynthesis and DHEA rather than DHEAS is expected to respond to acute psychosocial stress (Izawa et al., 2008; Morgan et al., 2004; Oberbeck et al., 1998; Pico-Alfonso et al., 2004; Shirotsuki et al., 2009). However, in a recent study, although the response of DHEA was more pronounced, both DHEA and DHEAS were found to increase in response to acute psychosocial stress (Lennartsson et al., 2012). In addition, DHEAS was found to increase in response to low, but not high, intensity military stress exposure (Morgan et al., 2004; Taylor et al., 2007). Cortisol and DHEA(S) are often addressed as a ratio, representing the balance between anabolic and catabolic hormones (Maninger et al., 2009). A high ratio of cortisol-to-DHEA(S), or conversely a low DHEA(S)-to-cortisol ratio, represents a catabolic balance. A low cortisol-to-DHEA(S) ratio, or a high DHEA(S)-to-cortisol ratio, reflects an anabolic balance. A higher cortisol-to-DHEA ratio has been linked to a chronic stress response in depressed adolescents and adults (Goodyer et al., 1998; Young et al., 2002), as well as more resilient functioning in both maltreated and non-maltreated children (Cicchetti and Rogosch, 2007), whereas a higher DHEAS-to-cortisol ratio was positively correlated with fewer dissociative symptoms after prolonged and extreme training stress (Morgan et al., 2004; Taylor et al., 2007). Thus, previous findings are inconclusive with respect to the role of the cortisol-to-DHEA(S) ratio in the onset of psychiatric disorders such as PTSD.

Findings from prospective studies on acute cortisol levels as a predictor for PTSD so far are inconsistent. Some studies have found that low cortisol levels immediately or in the first days following trauma predict PTSD diagnosis (Delahanty et al., 2000; McFarlane et al., 1997) or symptoms (Aardal-Eriksson et al., 2001; Ehring et al., 2008; McFarlane et al., 2011). In some of these studies, however, the association disappeared when controlling for possible confounding variables, such as injury severity and history of PTSD (Delahanty et al., 2000), and time of the accident or blood sampling (McFarlane et al., 1997). Other studies found no direct relationship between initial cortisol and subsequent PTSD (Bonne et al., 2003; McFarlane et al., 1997; Resnick et al., 1995; Shalev et al., 2008). Variations in methodology, for example, when (i.e., immediately post-trauma up to several days after the event) or how (i.e., saliva, urine or plasma) cortisol was measured, might explain these differences. Lack of power due to a small sample size has been referred to by some studies as a possibility for not finding a significant association (Delahanty et al., 2000; Ehring et al., 2008). Therefore, it has been argued that the predictive effect of cortisol should be replicated in large, consecutively recruited samples, taking into account the important confounders. Until now, no prospective studies examining whether the DHEA or DHEAS response is implicated in the development of PTSD have been carried out yet.

In this study, we investigated whether plasma cortisol, DHEAS and cortisol-to-DHEAS ratio, collected immediately following traumatic injury, predicted PTSD symptoms at 6 weeks and 6 months post-trauma in a sample of 397 acutely injured trauma victims. We hypothesized that lower levels of cortisol predict greater PTSD symptoms at 6 weeks and 6 months. Although the role of DHEAS in the development of PTSD is yet unclear, we also expected that lower levels of DHEAS and a smaller cortisol-to-DHEAS ratio predict PTSD symptoms at 6 weeks and 6 months.

2. Methods and materials

2.1. Subjects and procedure

Patients were recruited between 2005 and 2009 as part of a large ongoing prospective study of psychopathology following