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Salivary cortisol and dehydroepiandrosterone sulfate in adolescent rape victims with post traumatic stress disorder

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Dexamethasone suppression test (DST)

Summary
Background: In chronic sexual abuse victims with post traumatic stress disorder (PTSD), the hypothalamic pituitary adrenal (HPA) axis can be dysregulated. In single rape victims, PTSD symptoms are hypothesized to function as a chronic stressor leading to similar HPA-axis dysregulation. The objective of the current study was to assess HPA-axis functioning in female adolescents with rape-related PTSD, but no prior sexual trauma, in comparison to non-victimized controls.
Method: Salivary cortisol and dehydroepiandrosterone sulfate (DHEAS) were measured in 52 female adolescent rape victims with PTSD and 37 healthy adolescents at 0, 15, 30, 45 and 60 min after awakening, both under basal conditions and after 0.5 mg dexamethasone administration.
Results: Compared to age-matched controls, adolescent rape victims with PTSD showed significantly reduced cortisol and DHEAS levels. No group differences for the effect of dexamethasone suppression were found. Both the event of rape and PTSD diagnosis, and not factors such as sleep duration, smoking, education or oral contraceptives, accounted for the neuroendocrine differences between rape victims and controls.
Conclusions: The results show evidence for a dysregulated HPA-axis in female adolescent victims of single sexual trauma with PTSD. The finding of hypocortisolism is consistent with endocrine dysfunctioning in chronic sexual abuse victims and may have clinical implications with regard to treatment possibilities.

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The hypothalamic pituitary adrenal (HPA)-axis has been widely studied in traumatized individuals, either with or without post traumatic stress disorder (PTSD), reflecting the need to comprehend the pathophysiological changes that occur in the biological stress system after trauma and to find clues for possible treatment of PTSD. It is hypothesized by Hellhammer and Wade (1993) that after trauma, the HPA-axis is initially hyperactive corresponding with the acute stress response. As a consequence, pituitary corticotrophin releasing factor (CRF) receptors may down-regulate over the course of time. The authors assume that a normalization of hypothalamic CRF secretion at this point would result in a diminished adrenocorticotropin (ACTH) secretion, ultimately producing cortisol levels below the normal baseline. Analogue to this hypothesis, the more recent 'attenuation hypothesis' states that after trauma, initial pituitary—adrenal hyperactivity is followed by hypoactivity when stress persists over a long period of time (Fries et al., 2005; Trickett et al., 2010), as indicated by hypocortisolism. Hypocortisolism refers to a relative deficiency of cortisol, possibly due to reduced adrenocortical (re)activity or enhanced negative feedback inhibition of the HPA-axis (Yehuda et al., 1991).

In the context of trauma and stress, childhood sexual abuse emerges as a pronounced chronic stressor. HPA-axis dysregulation has been found in women with PTSD exposed to childhood sexual abuse, manifesting itself as hypocortisolism (Bremner et al., 2007; Meewisse et al., 2007) and cortisol hypersuppression in the dexamethasone suppression test (DST; Stein et al., 1997; Newport et al., 2004). Another hormone secreted by the adrenal cortex in response to ACTH stimulation, dehydroepiandosterone sulfate (DHEAS), has been shown to be increased in chronic sexual abuse victims with PTSD (Bremner et al., 2007; Kellner et al., 2010).

In sexually abused children and adolescents, increased cortisol levels (De Bellis et al., 1999), decreased cortisol levels (King et al., 2001), as well as similar levels (Kaufman et al., 1997; Duval et al., 2004) have been found, when compared to non-traumatized controls. These conflicting findings may be the result of methodological differences (Bicanic et al., 2008).

Both in adult and adolescent victims of single sexual trauma, such as rape, endocrine studies are lacking. An increase of our understanding of the functioning of the biological stress system following single sexual trauma, could help us to improve treatment of rape victims. We hypothesized that the HPA axis is dysregulated in adolescent victims of rape, because a single traumatic event may induce a prolonged stress experience, due to recurrent memories and continuous appraisals of situations as being threatening (Baum et al., 1993). The aim of this study was therefore to assess cortisol levels (in response to DST) and DHEAS levels in adolescent rape victims with PTSD in comparison to age-matched healthy controls. Based on findings in chronic sexual abuse victims, we hypothesized to find lower cortisol levels, higher DHEAS levels and an increased negative feedback inhibition (i.e. lower cortisol levels after DST) in the rape victims.

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The novelty of this study is that the HPA-axis is studied in a homogenous group with regard to age, sex and type of trauma, i.e. rape on *a single* occasion during adolescence with no history of sexual, physical or emotional abuse. Previous endocrine studies in sexual trauma victims have not differentiated between those victimized by single, multiple or chronic sexual trauma. Differentiation is important as prior sexual trauma has been shown to affect the HPA-axis response to rape (Resnick et al., 1995).

1. Methods

1.1. Subjects

Between April 2008 and November 2009, adolescent girls who experienced a single rape event were recruited into the study from consecutive referrals to the Psychotrauma Centre of the University Medical Centre in Utrecht and the Psychotrauma Centre for Children and Youth, GGZ Rivierduinen in Leiden. All rape victims presented themselves voluntarily at the participating centres for psychotherapeutic treatment of rape-related problems. Rape was defined as a single event that occurred without the victim's consent that involved the use or threat of force in vaginal, anal or oral intercourse. The definition includes both attempted and completed rape (Tjaden and Thoennes, 2006).

All rape victims were evaluated with a standardized psychological assessment procedure, consisting of (I) an assessment interview on trauma history, trauma characteristics, prior treatment, and lifetime number and types of trauma experienced (II), self-report questionnaires, and (III) the Dutch version of the Anxiety Disorders Interview Schedule — Children's version (ADIS-C; Silverman and Albano, 1996; Siebelink and Treffers, 2001), a DSM-IV based, semi-structured clinical interview to determine the presence of PTSD and potential other psychopathology.

Included were those who experienced a single rape event at minimum four weeks post-rape. Of the 82 rape victims admitted, 21 were excluded because of: a history of sexual trauma ($n = 11$); a history of physical or emotional abuse other than the single rape ($n = 8$); presence of a somatic illness known to cause endocrinological changes ($n = 2$). Eight eligible subjects refused to participate. This resulted in 53 participating rape victims.

Forty-two age-matched healthy controls, recruited from high schools and via personal contacts, were asked to fill out self-report questionnaires and a checklist to determine whether the subject experienced sexual trauma in the past. Three controls were excluded from participation, either because of corticosteroid medication ($n = 2$) or the experience of prior sexual abuse ($n = 1$). None of the remaining 39 controls reported a history of physical or emotional abuse.

Endocrine data were collected from 53 rape victims and 39 controls. One rape victim and two controls did not comply with the saliva sampling protocol, and were excluded from analysis. The final test population consisted of 52 rape victims and 37 controls.

The study was approved by the Medical Ethics Committee of the University Medical Centre Utrecht. All rape victims and controls, as well as their parents, provided written informed consent.