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International Journal of Psychophysiology 59 (2006) 251 – 258
INTERNATIONAL JOURNAL OF PSYCHOPHYSIOLOGY
www.elsevier.com/locate/ijpsycho

Tobacco usage interacts with postdisaster psychopathology on circadian salivary cortisol

Miranda Olff [a,*], Marie-Louise Meewisse [a], Rolf J. Kleber [b,c], Peter G. van der Velden [b], Annelieke N. Drogendijk [b], Jan G.C. van Amsterdam [d], Antoon Opperhuizen [d], Berthold P.R. Gersons [a]

[a] *Center for Psychological Trauma, Department of Psychiatry, Academic Medical Center/De Meren, Amsterdam, The Netherlands*
[b] *Institute for Psychotrauma, Zaltbommel, The Netherlands*
[c] *Department of Clinical Psychology, Utrecht University, Utrecht, The Netherlands*
[d] *Laboratory of Toxicology, Pathology and Genetics, National Institute of Public Health and Environment, Bilthoven, The Netherlands*

Received 13 October 2005; received in revised form 15 October 2005; accepted 20 October 2005
Available online 4 January 2006

Abstract

Posttraumatic stress disorder (PTSD) and major depressive disorder (MDD) have been associated with increased rates of tobacco usage as well as with dysregulations of the hypothalamus–pituitary–adrenal (HPA) axis. At the same time tobacco also affects the HPA axis. This paper examines the relationships between PTSD, posttraumatic MDD, smoking and levels of circadian cortisol 2–3 years postdisaster. Subjects were survivors of the Enschede fireworks disaster. The sample consisted of 38 healthy survivors, 40 subjects with PTSD, and 17 subjects with posttraumatic MDD. The Composite International Diagnostic Interview was used to determine mental disorders in accordance with DSM-IV criteria. Salivary cortisol samples were collected at home immediately upon awakening, 30 min after awakening, at noon, and at 10 p.m. Quantity of smoking was measured through self-report. The results of the study show that salivary cortisol concentrations were higher in smoking subjects. Survivors with MDD following the disaster had a flatter diurnal cortisol curve than subjects with PTSD or healthy survivors. In survivors with PTSD and healthy individuals the usual dynamic pattern of increase in cortisol past awakening was present, while we did not observe this in posttraumatic MDD. These survivors with MDD tended to use more tobacco per day, and the cortisol group differences could only be revealed when we adjusted for quantity of smoking. Smoking, which may be an important palliative coping style in dealing with posttraumatic arousal symptoms, seems to mediate the relationship between traumatic stress and the HPA-axis.

Keywords: Smoking; Posttraumatic stress disorder; Major depression; Cortisol; Disaster

1. Introduction

The majority of people will be exposed to at least one traumatic event during their lifetime (Kessler et al., 1995). Of trauma exposed individuals, 20–30% of woman and 8–13% of men will develop posttraumatic stress disorder (PTSD) and a substantial proportion will develop major depressive disorder (MDD), substance disorder or a combination of those (Kessler et al., 1995; Olff and de Vries, 2004). The DSM-IV diagnosis of PTSD consists of symptoms in three clusters: "reexperiencing" (intrusive recollections of the trauma that are triggered by exposure to cues symbolizing the trauma, nightmares, flashbacks); "avoidance and numbing" (diminished participation in activities and avoidance of thoughts, people, places, and memories associated with the trauma); and "hyperarousal" (difficulty sleeping, irritability, difficulty concentrating, hypervigilance, and exaggerated startle response).

Substance use, including tobacco use, has been previously described as a significant problem after traumatic events (e.g. the 9-11 attacks: Vlahov et al., 2004; sexual and physical assault: Acierno et al., 1996; exposure to childhood trauma: Walker et al., 1999; Springs and Friedrich, 1992; Felitti et al., 1998; American male veterans: Schnurr and Spiro, 1999;

* Corresponding author. Department of Psychiatry, Academic Medical Center/De Meren, Tafelbergweg 25, 1105 BC Amsterdam, The Netherlands. Tel.: +31 20 5662356; fax: +31 20 6919019.
E-mail address: m.olff@amc.uva.nl (M. Olff).

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doi:10.1016/j.ijpsycho.2005.10.014

Dutch resistance veterans: Falger et al., 1992; and Israeli veterans: Shalev et al., 1990). Studies have shown that the degree of event exposure is associated with a greater degree of substance use after disasters (Beckham et al., 1997; Green et al., 1985), and subsequently that the number of cigarettes is related to higher morbidity and mortality after trauma. For instance, early death has been reported among smoking US veterans with a relative risk of 2.4 in very heavy smokers (Rogot and Murray, 1980). Relationships between psychopathology and smoking may explain part of these high mortality rates. Associations have also been found between smoking and MDD (Upadhyaya et al., 2002), and suicidal behaviour in psychiatric patients (McGee et al., 2005) and U.S. army personnel (Miller et al., 2000).

Associations between PTSD and substance use disorders have been reported in several studies (Kandel et al., 1997; Breslau et al., 1994, 2003, 1991). US data show that 60% of help-seeking PTSD patients smoke cigarettes, compared to 23% of the general population, and also that patients with PTSD are more likely to be heavy smokers (Beckham, 1999). Recently, Vlahov et al. (2004) demonstrated an increased prevalence of substance use among residents of New York City shortly after the 9-11 attacks, which persisted six to nine months later. Those persons who increased use of cigarettes were more likely to report symptoms consistent with PTSD and depression. Persons who experience major trauma may increase use of substances – either by starting to use, or by increasing in comparison to prior levels – to deal with arousal symptoms and negative affect. Smoking may thus be a coping mechanism following trauma exposure to reduce distress (Carmody, 1992), and thereby also affecting the neuroendocrine stress response (Olff et al., 2005).

Disparate results on the association between PTSD, depression and cortisol may partly be explained by the effects of smoking on the central nervous system and neuroendocrine parameters. Nicotine facilitates release of crucial neurotransmitters (e.g. acetylcholine, noradrenaline, vasopressin, dopamine, serotonin and beta-endorphin). After smoking of one cigarette both the systolic and diastolic blood pressure increase with 10 mmHg, heart frequency with 20 beats per minute and plasma adrenaline and noradrenaline with 250% and 40% respectively (Cryer et al., 1976). With heavy smoking the sympathetic nervous system is almost permanently stimulated. Smoking also activates HPA-axis. For instance, in chronic smokers compared to non-smokers increased cortisol levels have been found (e.g. Field et al., 1994), not only over the day, but as well as in response to waking (Steptoe and Ussher, in this issue). The early morning rise (EMR) of cortisol, typically with a peak half an hour after awakening, has been found to be an indicator of the stress response system and has been shown to be attenuated in e.g. PTSD (Neylan et al. 2005). Also acute effects of smoking on the HPA-axis have been found (Wilkins et al., 1982; Kirschbaum et al., 1992). On the other hand, results have not always been consistent and attenuated adrenocortical responses to stress have also been reported (e.g., al'Absi et al., 2003; Handa et al., 1994). Since nicotine facilitates neurotransmitters that modulate mood, smoking may relieve symptoms of anxiety, irritability and depression following a traumatic event, thereby reinforcing smoking behavior. As such, apart from well-known physical health implications smoking may be an important problem in relation to mental health. One of the World Health Organization's (WHO) top priorities is the Tobacco Free Initiative (TFI), aiming at reducing tobacco use worldwide. 168 countries have signed the Framework Convention on Tobacco Control (FCTC) in April 2005. However, too little attention has been given to smoking related to psychiatric disorder.

Summarizing, although there seem to be associations between traumatic stress and smoking, traumatic stress and cortisol, and between smoking and cortisol, the relationships between traumatic stress, smoking, and cortisol have not yet received much attention. This is the first study to explore the relationships between PTSD, posttraumatic depression, smoking and levels of cortisol in a sample of trauma survivors. The aim is to examine how smoking would interact with the effects of a large disaster in the Netherlands on salivary cortisol in subjects with PTSD, posttraumatic MDD or no disorder. The cortisol response to awakening is a discrete and distinctive part of the cortisol circadian cycle (Clow et al., 2004), therefore we address both the diurnal pattern, overall production, and early morning rise of cortisol. We hypothesized that smoking would be associated with increased cortisol levels and that smoking would be an important mediator in the relationship between traumatic stress disorders and salivary cortisol.

2. Methods

2.1. Subjects

Participants of the present study were 95 Dutch speaking adults aged 20–80 years (mean 48.12, S.D. 15.38), living in the affected area at the time of the fireworks disaster in the city of Enschede, the Netherlands, on May 13, 2000. That day, the surrounding residential district was completely destroyed by the explosion of a fireworks storage depot. Twenty-two people were killed and almost one thousand were injured. Over 10,000 local residents were evacuated for one or more days, while over 1200 people lost their homes completely (Roorda et al., 2004). The participants were recruited as part of a large prospective study monitoring health after the disaster (Kamp and van der Velden, 2001). Most subjects were invited by a letter of the Dutch Ministry of Health Welfare and Sports to participate. In addition, announcements for the study were made in the media.

Two to three years after the disaster a subsample of subjects were invited by telephone to participate in an additional study concerning prevalence and predictors of postdisaster psychopathology. Of them, 263 subjects were interviewed at their homes, face to face by research employees with the Dutch version of the Composite International Diagnostic Interview (CIDI; WHO, 1997) to determine mental disorders in accordance with DSM-IV criteria (APA, 1994) and demographic data. Research employees underwent 3 days of didactic and supervised practical training in CIDI administration. The following modules of the CIDI were administered to determine

the prevalence of axis I diagnoses that are common after traumatic events: mood, anxiety, substance-related disorder and somatoform disorder. The CIDI has shown to have excellent inter-rater reliability, good test–retest reliability and good validity (Andrews and Peters, 1998). Those subjects with PTSD, MDD and a comparison group of survivors without a lifetime history of any DSM-IV Axis I disorder were invited to participate in neuroendocrine assessment.

Subsequently, the 95 participants in the present study were those who completed neuroendocrine assessment and had a diagnosis of disaster-related PTSD ($N=40$), disaster-related MDD ($N=17$) – obtained by including only data from depressive participants with onset of the diagnosis in the year of the disaster – and 38 healthy survivors. In 25 of the 40 subjects with PTSD comorbid depression was found (post-disaster onset $N=18$). Since several studies found no differences in cortisol levels between subjects with PTSD with or without comorbid depression (Altemus et al., 2003; Bonne et al., 2003; Lindley et al., 2004) we regarded PTSD with or without depression as one single group. Four survivors with PTSD were excluded because their symptoms were due to a focal trauma other than the fireworks disaster. In the MDD group comorbid PTSD was not allowed. Three survivors with MDD were excluded because of onset of MDD prior to the disaster. Additional exclusion criteria for all groups were psychotic symptoms, bipolar disorder, and pregnancy.

The study was approved by the Institutional Review Board of the Academic Medical Center, and all subjects provided written informed consent.

2.2. Self-report instruments

2.2.1. Smoking

Current smoking status and number of cigarettes, cigars and pipe tobaccos a day were measured through self-report. The quantity of smoking reported by an individual was obtained by adding the number of cigarettes, cigars or pipe tobacco smoked a day.

2.2.2. Symptom severity measures

To determine the severity of PTSD and MDD symptoms, participants completed three self-report measures. The Dutch version of the Impact of Event Scale (IES; Brom and Kleber, 1985) was administered to obtain sumscores on a 4-point Likert scale for intrusion and avoidance in the past week. The Self-Rating Scale for PTSD (SRS-PTSD; Carlier et al., 1998) was administered to obtain the number of PTSD symptoms based on DSM-IV criteria. For both the IES and the SRS-PTSD, participants were asked specifically to consider the fireworks disaster when completing these measures. The internal consistency and interjudge reliability of these self-reports were found to be satisfactory (Carlier et al., 1998; van der Ploeg et al., 2004). The Dutch version of the Symptom Check List-90 (SCL-90; Arrindell and Ettema, 1986, 2003) was administered to measure the severity of depressive symptoms (16 items). These items are scored on a 5-point Likert scale. The internal consistency of the test is good, and both the construct and the predictive validity are adequate.

2.2.3. Salivary cortisol

Samples were collected at home over a 1-day period using plain cotton rolls Salivettes (Sarstedt): immediately upon awakening, 30 min after awakening, at noon, and at 10 p.m. Subjects sampled saliva on week-days with a similar schedule as they normally have, within 4 days from their appointment. They were instructed to avoid eating, drinking, brushing their teeth, or smoking for at least one hour before sampling. Samples were stored in domestic freezers until their appointment. At the laboratory, saliva samples were centrifuged 3000 U/min for 5 min and stored at −20 °C until analysis.

Cortisol was measured in duplicate by enzyme immunoassay kit (Salimetrics, State College, Pennsylvania). According to the manufacturer the mean intra- and inter-assay coefficients of variation were $\leq 7.12\%$ and $\leq 6.88\%$, respectively. The lower limit of sensitivity is ≤ 0.19 nmol/L.

2.3. Statistical analysis

Chi-square tests were used to examine whether survivor groups differed in terms of socio-demographic features and symptom severity. The general linear models (GLM) procedure for univariate and repeated measures analysis of variance (ANOVA) were used to examine if the diagnostic groups differed in salivary cortisol measures. We included diagnostic group, gender, age, smoking (number of cigarettes, cigars and/or pipe tobacco), and group by smoking interactions in the model.

The cortisol response to awakening (early morning rise; EMR) was calculated by subtracting the awakening sample from the awakening+30 min sample. Overall cortisol production through the day was calculated as the area under the curve (AUC) with reference to zero. Data sets with one or two missing samples were not excluded for calculating AUC. In order to benefit from the incomplete data sets median values for that specific time sample were imputed. Imputed missing values in this way represented 3.7% of the samples (a total of 14 of the 376 samples were missing).

Correlation analyses were calculated using Pearson Product–Moment correlation coefficients. All statistical tests were two-tailed, and p values of less than .05 were considered statistically significant.

3. Results

3.1. Subjects characteristics

Subjects with PTSD with or without coexisting MDD did not differ on demographic data, PTSD symptom severity, smoking habit and cortisol profile, therefore these subjects were taken together in the analyses. Moreover, in favour of this strategy was the fact that MDD-only subjects had significantly

Table 1
Demographic characteristics for disaster-related PTSD and MDD diagnosed survivors and healthy survivors

	PTSD (N=40)	MDD (N=17)	Healthy survivors (N=38)	F or χ^2	df	p
Gender (N, %)						
Male	16 (16.8)	5 (5.3)	17 (17.9)	1.15	2	.58
female	24 (25.3)	12 (12.6)	21 (22.1)			
Age (years)	45.11 (12.61)	49.94 (15.86)	53.58 (16.91)	3.11	2,92	.049
Education (years)	13.85 (4.39)	12.41 (3.97)	11.95 (3.53)	2.33	2,92	.103
Smoking (N, %)	13 (32.5)	4 (23.5)	8 (21.1)	1.23[a]		.56
Cigarettes, cigars, pipe tobacco per day	12.67 (7.11)	25.50 (13.20)	13.63 (8.77)	3.07	2,18	.071
Coexisting disorders within the past year (N, %)						
Depression	25 (62.5)	–	–			
Dysthymic disorder	2 (5)	0	–			
Alcohol dependence	2 (5)	1 (5.9)	–			
Specific phobia	14 (35)	7 (41.2)	–			
Obsessive compulsive disorder	1 (2.5)	0	–			
Conversion disorder	4 (10)	2 (11.8)	–			
Symptom ratings						
IES	38.44 (18.33)	28.00 (22.30)	17.40 (14.93)	11.91	2,83	.000
SRS-PTSD	9.00 (3.84)	5.94 (4.07)	3.39 (3.50)	14.18	2,85	.000
SCL-90 depression	34.06 (13.81)	26.47 (9.79)	20.16 (5.25)	16.59	2,86	.000

Values are expressed as mean (S.D.) unless otherwise indicated.
Abbreviations: PTSD, posttraumatic stress disorder; MDD, major depressive disorder; SRS-PTSD, Self-Rating Scale for PTSD; IES, Impact of Event Scale; SCL-90, Symptom Checklist.
[a] Fisher's exact test.

fewer PTSD symptoms [SRS-PTSD: $t(41)=-2,03$; $p=.049$] than the PTSD–MDD subjects.

Table 1 summarizes the demographic characteristics of subjects assigned to each group. The PTSD group turned out to be slightly younger than healthy survivors [$t(68.35)=-2,50$; $p=.015$]. Symptom severity of PTSD and depression were significantly higher in the PTSD subjects than in MDD or healthy survivors. The number of persons smoking (i.e. smoking status yes/no) did not differ significantly per diagnostic group. However, there was a trend for subjects with MDD to use more tobacco per day than subjects with PTSD or healthy survivors.

Among those subjects smoking a significant correlation was found between depressive symptoms and the quantity of tobacco use [$r=.45$, $N=25$, $p=.025$].

3.2. Diurnal pattern of salivary cortisol

The GLM repeated measures ANOVA of the diurnal salivary cortisol concentrations, corrected for age and gender, revealed no main effects for diagnostic groups when samples were not adjusted for smoking [$F(2,78)=.43$, $p=.65$]. However, when adjusted for smoking, we found significant main effects of smoking [$F(1,73)=7.24$, $p=.009$], group by

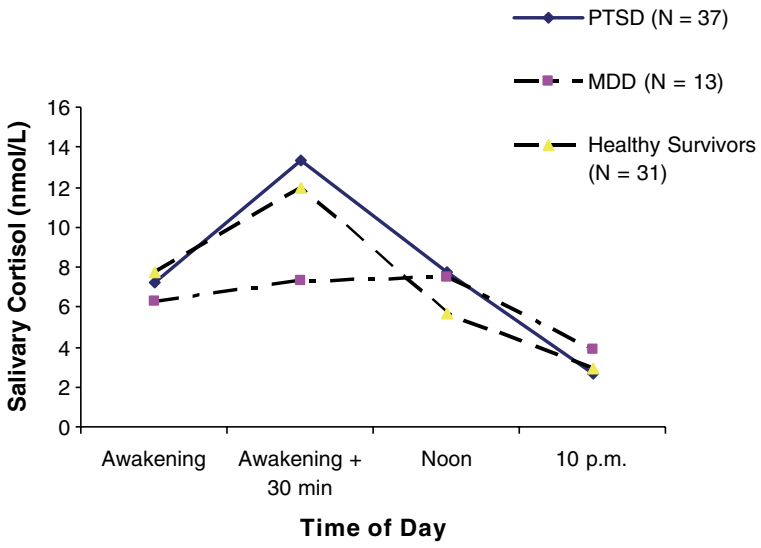

Fig. 1. Diurnal salivary cortisol levels in survivors with PTSD, posttraumatic MDD, and in healthy survivors. Data represent estimated marginal means of cortisol adjusted for quantity of smoking, age and gender. For the four time points the estimated marginal means in nmol/L±SE per group from awakening to 10 p.m. were as follows: PTSD 7.19±1.20, 13. 36±1.07, 7.74±.90, and 2.68±.52; posttraumatic MDD 6.28±2.00, 7.28±1.78, 7.46±1.50, and 3.90±.87; healthy survivors 7.70±1.29, 11.92±1.15, 5.67±.96, 2.94±.56.

smoking interaction [$F(2,73)=5.31$, $p=.007$], and a trend for the diagnostic group [$F(2,73)=3.04$, $p=.054$]. No main effects were found for gender [$F(1,73)=.14$, $p=.71$], or age [$F(1,73)=.073$, $p=.78$]. Fig. 1 shows the estimated marginal means of the diurnal pattern of salivary cortisol levels in the diagnostic groups (means and SE are presented in the legend of Fig. 1). Post hoc pairwise comparisons showed that subjects with posttraumatic MDD had significantly different diurnal cortisol patterns than subjects with PTSD and healthy survivors. There were no significant differences between subjects with PTSD and healthy survivors.

Depressive symptoms correlated negatively with cortisol at awakening ($r=-.24$, $p=.025$, $N=86$). None of the other symptom severity measures correlated with any of the single cortisol sampling times.

3.3. Early morning rise (EMR) of salivary cortisol

The GLM univariate ANOVA procedure adjusted for age, gender, and smoking, again showed main effects for smoking in cortisol EMR [$F(1,79)=6.14$, $p=.015$], with higher levels of cortisol for smoking subjects. No effects of diagnosis [$F(2,79)=1.82$, $p=.17$], or interaction between smoking and diagnosis [$F(2,79)=1.15$, $p=.32$] were found for cortisol EMR (see Fig. 2). No main effects for age or gender were found either.

Depressive symptoms correlated positively with EMR [$r=.22$, $p=.047$, $N=83$], but none of the other symptom severity measures did.

3.4. Area under the curve (AUC) of salivary cortisol

For the cortisol AUC (adjusted for age, gender, and smoking), there was a trend for a main effect of smoking [$F(1,85)=3.84$, $p=.053$]. No main effects of diagnosis [$F(2,85)=2.75$, $p=.07$], or interaction [$F(2,85)=.87$, $p=.43$] between smoking and diagnosis were found for cortisol AUC.

Smoking significantly correlated with cortisol AUC ($r=.26$, $p=.012$, $N=93$). When we examined this correlation within each diagnostic group separately, this relation turned out to be only significant within the MDD group ($r=.57$, $p=.017$, $N=17$). Men and women did not differ in AUC cortisol [$F(1,85)=.03$, $p=.86$]. Age was not significantly correlated with cortisol AUC, nor were any of the symptom severity measures. When we divided each diagnostic groups in *smokers versus non-smokers*, we found significant differences between the groups in AUC [$F(5,88)=2,36$, $p=.047$]. Post hoc analyses revealed that non-smoking depressive survivors had significant lower cortisol AUC, than non-smoking PTSD survivors [non-smoking PTSD: mean=25.97 nmol/L, S.D.=11.79, $N=27$; non-smoking MDD: mean=16.81 nmol/L, S.D.=9.38, $N=13$; $t(37.89)=3.40$, $p=.002$].

4. Discussion

This is the first study to investigate smoking related to salivary circadian cortisol in disaster-related psychopathology. In a sample of people victimized by a large disaster we found that smoking was associated with an increase in cortisol levels during the day in all groups. There was also a linear positive relationship between the number of cigarettes smoked and cortisol levels, particularly in the MDD group. The finding of increased cortisol levels in smoking subjects is in accordance with other studies (e.g. Wilkins et al., 1982; Steptoe and Ussher, in this issue).

Examining how smoking would interact with posttraumatic disorders on salivary cortisol we found that survivors with MDD since the disaster had a flatter diurnal cortisol curve than subjects with PTSD and healthy survivors. In survivors with PTSD and healthy individuals the usual dynamic pattern of increase in cortisol past awakening was present, while we did not observe this in posttraumatic MDD. Although we could only reveal these group differences when we controlled for quantity of smoking, this correction was essential because smoking was associated with substantially elevated salivary cortisol levels. Since survivors with MDD tended to use more tobacco per day, smoking may have concealed this effect. Thus, smoking seems to mediate HPA-axis differences in disaster-related psychopathology.

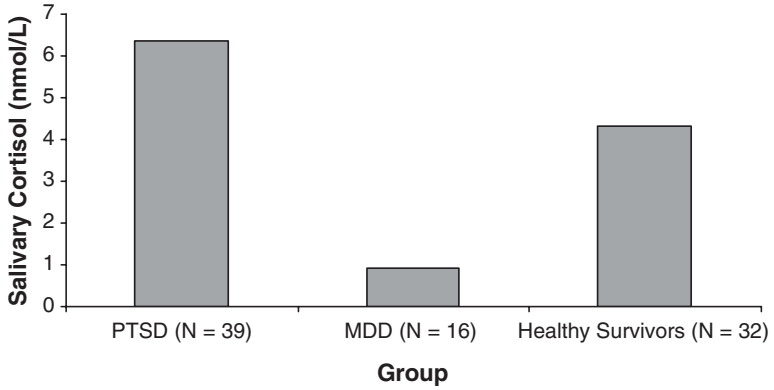

Fig. 2. Early morning rise of salivary cortisol levels in survivors with PTSD, posttraumatic MDD, and in healthy survivors. Data represent estimated marginal means of early morning rise in cortisol adjusted for quantity of smoking, age and gender. The estimated marginal means in nmol/L±SE per group were: PTSD 6.38±1.19; posttraumatic MDD .93±1.85; healthy survivors 4.31±1.30.

Little is known about cortisol in posttraumatic depression. Major depressive disorder has been associated with high cortisol levels, but this was usually the case in hospitalized severely depressed patients with for instance psychotic depression (i.e. biologically induced) (Nelson and Davis, 1997). Our sample was a community sample with moderate depression, which was induced by a traumatic experience (specifically selected by posttraumatic onset). Peeters and colleagues (2004), who studied salivary cortisol in a community population, suggested that erratic cortisol secretion might be a more characteristic feature of HPA axis dysregulation in MDD than hypercortisolism. The few studies that have been examining the relationship between posttraumatic depression and cortisol levels have shown disparate results. Both higher levels of plasma (Halbreich et al., 1989; Oquendo et al., 2003) and normal levels of 24 h urinary cortisol (Young and Breslau, 2004) have been found in posttraumatic depression. Our findings indicated no differences in total cortisol production over the day (cortisol AUC) between survivors with MDD and healthy subjects also. However, total cortisol production – whether assessed in saliva or urine, or cortisol assessed in plasma at one single fixed clock time point – cannot reveal deviations in *patterns* of cortisol excretion as we found.

Similarly to studies in depression, there is lack of consistent data on cortisol levels in PTSD. Our study could not confirm the lower levels of basal cortisol in PTSD found in some studies with or without comorbid depression (Yehuda et al., 1990, 1995a,b,c, 2004; Thaller et al., 1999). However, these low levels were found in subjects with war-related trauma and again cortisol was measured in plasma at fixed time points or in 24 h urine. Halbreich et al. (1989) also studied veterans and found normal plasma cortisol levels in PTSD with comorbid depression. In civilian samples with PTSD no differences in plasma cortisol were found either (e.g. Bonne et al., 2003; Stein et al., 1997). Circadian salivary levels of basal cortisol have only been rarely investigated and those studies demonstrated contradictory results also. Lindley and colleagues (2004) found higher concentrations of cortisol in PTSD. In contrast, Rohleder and colleagues (2004) found lower levels of salivary cortisol throughout the day and lower early morning rise in their PTSD group compared to a combined group of exposed and non-exposed healthy controls. Yehuda and colleagues (2005) also found lower morning levels in holocaust survivors with PTSD, but only in comparing them to non-exposed healthy individuals. In accordance with our results, no differences were found when survivors with PTSD were compared to healthy exposed subjects, and no differences were found between these groups in total production of cortisol throughout the day. Unfortunately, none of these studies controlled for quantity of tobacco use in their study groups. Consistent with our results is the study on women with PTSD related to childhood abuse (Altemus et al., 2003). In this study smoking was controlled for by excluding subjects who regularly used tobacco, resulting in no differences in circadian salivary cortisol between PTSD and healthy comparisons. When smoking subjects are included, quantity of smoking seems to be an important mediator of the relationship between posttraumatic psychopathology and hormone levels and if not taken into account it may help explain the divergent results in the relationship between stress-related disorders and cortisol.

Laboratory studies have shown a stress reducing effect of smoking (Gilbert et al., 1989). In victims of traumatic experiences smoking may even have a larger impact. The physiological arousal symptoms of PTSD may be characterized as panic reactions that were experienced during initial exposure to a traumatic event, and such reactions are reexperienced in response to reminders of the traumatic event (e.g. Resnick et al., 1992). Tobacco use is then theorized to be an attempt to decrease this arousal, as well as to decrease sleep disturbances and nightmares. In a traumatic stress coping model as described by Olff et al. (2005) smoking serves as a palliative coping style reducing physiological arousal. In learning theoretical terms smoking is negatively reinforced, because it reduces posttraumatic distress. It may also be more difficult to quit smoking for persons with PTSD or other anxiety disorders, because they seem to suffer from exacerbated withdrawal symptoms, particularly irritability or nervousness (Beckham et al., 1996). In neurobiological terms the facilitation of dopamine neurotransmission in the mesocorticolimbic dopamine system seems to be critical for the acute reinforcing actions of smoking, and cortisol interacts with neurotransmitters that are involved in nicotine's reinforcing properties (Koob and Le Moal, 1997).

This study has some limitations. We had relatively low sample sizes, making within group comparisons difficult. It should also be noted that we only used a comparison group of healthy survivors who did experience the traumatic event. Stronger effects may be found using a non-traumatized healthy control group as well, although in that case it is unclear whether differences are due to experiencing trauma or to the development of posttraumatic disorder. Another limitation is the cross-sectional design, which does not allow any conclusions about causality or mechanisms. Although the negative reinforcement theory sounds plausible, little is actually known about the causal pathways that might explain the associations between posttraumatic psychopathology and smoking. For instance, it is possible smoking subjects are more susceptible to develop a posttraumatic disorder following trauma. Previously, tobacco smoking in adolescence or early adulthood has been found to predict major depression (Upadhyaya et al., 2002). Another possibility is that both smoking and posttraumatic psychopathology share genetic factors, as has been reported for alcohol (McLeod et al., 2001; Xian et al., 2000). It is also possible that shared environmental factors (i.e. exposure to trauma) induce both smoking and posttraumatic psychopathology. In those persons where trauma induces PTSD, depression or other disorders (depending on the persons' vulnerabilities) negative reinforcement of smoking may be even stronger. Interestingly, early studies of the acute psychological effects after the September 11 attacks suggested high prevalences of stress, PTSD, and depression, whereas follow-up studies (Galea et al., 2002) showed substantial resolution of PTSD and depression among New York City residents six months after September 11. However, the resolution of PTSD and depression was not followed by a resolution of smoking behavior. Thus, even if

there is a causal pathway for increased smoking after trauma and posttraumatic disorders, the resolution of trauma and subsequent disorders does not automatically reduce smoking behavior. Longitudinal studies on trauma disaster survivors will give more insight in the causal relations and the mechanism of smoking while in distress. Clearly, more research is needed examining the relationships between posttraumatic stress, substance use and psychobiological mechanisms.

In summary, in this study we found that smoking subjects who have experienced a major disaster have higher cortisol levels during the day — regardless of whether they developed PTSD, depression or no disorder. Comparing diagnostic groups revealed differences in diurnal cortisol only when controlling for smoking, particularly for subjects with posttraumatic depression. Smoking, which may be an important palliative coping style in dealing with posttraumatic arousal symptoms, seems to be a significant mediator in the relationship between traumatic stress and the HPA-axis.

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