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## Diurnal cortisol patterns and stress reactivity in child Holocaust survivors reaching old age

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**Objectives:** Late-life implications of early traumatic stress for the adreno-cortical system were examined in a sample of 133 child survivors of the Holocaust, who were subjected to Nazi persecution during infancy.

**Method:** In a non-convenience sample of child survivors, born between 1935 and 1944, basal circadian cortisol release and cortisol reactivity to a stressor were assessed.

**Results:** Age, parental loss during the Holocaust, current depression, post-traumatic stress disorder (PTSD) and physical illness were not associated with differences in basal diurnal cortisol levels. Neuro-endocrine effects, however, were found in stress reactivity through elevated cortisol levels in male respondents in the youngest age group (born 1941–1945), and in male respondents suffering from PTSD-related functional impairment.

**Conclusion:** The youngest survivors of Nazi persecution show late-life effects of traumatic stress during early childhood, evidenced by the early onset of differential neuroendocrine pathways to stress-regulating strategies.

**Keywords:** early childhood traumatic stress; neuroendocrine pathways; late life stress regulation; cortisol; PTSD; Holocaust

### Introduction

Over the last 20 years, Jewish child survivors of the Nazi Holocaust have become identified as a subgroup of Holocaust survivors with specific needs, differing from those of survivors who were adults during the Holocaust (Keilson, 1992; Kestenberg & Brenner, 1996; Krell, 1985, Moskowitz, 1985; Moskowitz & Krell, 1990; Tauber, 1996). They have become the focus of an increasing number of studies on the effects of childhood deprivation on coping with later-life challenges (Dasberg, 2001).

Several studies have been carried out among various groups of child Holocaust survivors with matched controls who did not suffer Nazi persecution (Amir & Lev-Wiesel, 2003; Brom, Durst & Aghassy, 2002; Cohen, Brom & Dasberg, 2001; Cohen, Dekel, Salomon & Lavie, 2003; Sagi, Van IJzendoorn, Joels, & Scharf, 2002). The overall outcomes of these studies show significantly more traumatic stress with child Holocaust survivor samples compared with controls, whereas treatment-seeking Holocaust survivors show significantly more severe post-traumatic stress symptomatology.

As a rule, studies of child survivors of the Holocaust include persons born between 1927 and 1945. Interestingly, only Keilson (1992) designed an empirical study taking into account differences in developmental age at the time of persecution. To our knowledge, no systematic research exists focusing exclusively on effects of Holocaust persecution and its aftermath on the life cycle of the youngest children,

born between 1935 and 1944. Aged from several months to 10 years at the end of the Second World War in 1945, many had to cope with the stress of deprivation and violence during their very first years of life.

The oldest of this group of survivors were born during the first years of the Nazi regime, when, although not in direct life danger, their families endured progressively deteriorating physical, social and economic living circumstances. The younger of these child survivors were born during persecution, when their families had disintegrated under death threat. Some parents succeeded in keeping these children alive in concentration and work camps, or while fleeing into forest or mountain areas, or to the harsh living conditions in Siberia and Uzbekistan. Other parents separated from their children, intuiting that the chances for surviving were slimmer if they stayed together. They handed them to Christian families, monasteries and other institutional care. Infants were left on doorsteps, hurled out of trains or over ghetto walls, and ‘smuggled’ out of deportation centers in waste bins and laundry baskets. Care provided to them by Gentile strangers varied from excellent to abusive in physical, sexual or emotional ways. Some children stayed with one care provider during the persecution period, others had to cope with and to adapt to several, and sometimes many, caretakers. After liberation, many of the children suffered social and relational estrangement. When they survived separated from their families, they were now reunited with surviving parents they remembered

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only vaguely, if at all. Others had to cope with the loss of their murdered parents.

The current study focused on assessing influences of early childhood exposure to the traumatic stress of these Holocaust survivors, now in their mid-sixties to mid-seventies. For the youngest survivors, in particular when born during persecution, the ability of their primary caregivers to stay fully attuned to their needs for proximity and safety could have been compromised (Bar-On et al., 1998; Siegel, 1999). We therefore examined the effects of their early childhood experiences on the level of psycho-physiological functioning, in particular the adreno-cortical system. At older age, more vulnerability to stress-related health impairments has been observed (Graham, Christian, & Kiecolt-Glaser, 2006).

Pre-clinical, animal and human studies showed that maternal separation and loss during infancy may have a long-term effect on social adjustment, cognitive functioning and behavioral responses to stress (Gunnar & Nelson, 1994; Lui et al., 1997; Sanchez, Ladd, & Plotsky, 2001; Sapolsky & Meaney, 1986; Weaver et al., 2004). Physiological responses to stress involve the sympathetic nervous system, the neurotransmitter system, the immune system and the hypothalamic-pituitary-adrenal (HPA) axis. During stress the hypothalamus signals the pituitary gland to stimulate the release of cortisol from the adrenal gland, which is regulated through an intricate neuroendocrinological feedback system. The production of cortisol follows a circadian rhythm with the highest level around 30 min after morning wake-up. During the day cortisol levels decrease first sharply, and more gradually into the evening, and can be observed in children as early as 3 months of age (Larson, Prudhomme White, Cochran, Donzella, & Gunnar 1998).

At the same time, cortisol levels are also sensitive to emotional and physical stressors (Kirschbaum & Hellhammer, 1989, 1994). Therefore, superimposed upon the diurnal patterns, cortisol secretion is activated by environmental cues related to threats, unfulfilled expectations, pain, infection or metabolic crises (Glaser, 2000).

Adverse experiences in childhood have been associated with altered stress reactivity and altered diurnal cortisol levels, but different studies vary in outcomes as higher as well as lower than normal levels of cortisol have been shown – hypo- or hyper-cortisolism (Heim et al., 2000). Yehuda and colleagues consistently found lower than normative diurnal cortisol levels in adult Holocaust survivors and their offspring, who also suffered from post-traumatic stress disorder (PTSD; Yehuda, 2002; Yehuda, Golier, & Kaufman, 2005).

Gender as well as age may influence cortisol reactivity to a stressor as reported in several studies. Elzinga et al. (2008) found blunted cortisol responses to the Trier Social Stress Test only in young adult males who had experienced maltreatment in their childhood, but not in females with similar experiences.

Their basal cortisol patterns did not differ from non-traumatized comparisons. Kudielka & Kirschbaum (2005) found that, in reaction to an acute psychological stressor, elderly men showed larger free cortisol responses than women. They hypothesized that stronger male stress reactivity could be causally related to higher risk for diseases associated with high cortisol levels, e.g. diabetes and cardiovascular diseases, which may explain a higher prevalence of these conditions in men. Lower cortisol responses to acute stressors in women may be related to a lower reactivity of the HPA-axis in general, which is associated with a greater risk for autoimmune diseases that are more prevalent in women.

We assessed the influences of early childhood exposure to the traumatic stress of the Holocaust on both diurnal cortisol patterns and cortisol reactivity to a stressor. We expected to find that the youngest child survivors, who experienced persecution at the most critical stage of their lives, would show a deviating diurnal cortisol pattern, related to suffering from PTSD, depression and physical illnesses. Second, we expected the youngest Holocaust child survivors, who lacked the prewar experience of a relatively protected family life, to show the most elevated cortisol responses to a stressful challenge, with men showing stronger responses than women.

## Method

### Participants

Participants were 203 child Holocaust survivors, who were born between 1935 and 1944 in countries occupied by the Nazi regime, and immigrated to Israel after 1945. A non-convenience sample was created by recruiting through demographic information provided by the Israel Ministry of Interior Affairs, including name, year and country of birth, and date of immigration into Israel. Invitations to participate in the study were sent by mail to 410 addresses. In a follow-up telephone call 293 survivors who met our criteria could be reached. Forty-nine survivors refused to participate, while 41 candidates were not available for participation during the time frame of the study. Non-participants explained their refusal by their need to let the past rest, or lacking strength to relate to their Holocaust experiences. All participants signed forms of informed consent after they had received an explanation of the purpose of the study.

We decided to introduce saliva collection procedures for cortisol assessments halfway through our study, resulting in a sub-sample of 133 survivors for whom cortisol data were available. These survivors were on average 65 years old, and 61% were female. For the purpose of analysis, the sample was divided into three age groups: born between 1935 and 1937 ( $n=43$ ), between 1938 and 1940 ( $n=43$ ) and between 1941 and 1944 ( $n=47$ ) (see Table 1 for background information of the three age groups).

Table 1. Differences in main variables between age-cohorts of Holocaust survivors.

Year of birth	1935–1937			1938–1940			1941–1944			Total			F	p
	M	(SD)	N	M	(SD)	N	M	(SD)	N	M	(SD)	N		
Age	68.0	(0.79)	43	64.8	(0.88)	43	61.3	(1.10)	47	64.6	(2.94)	133	583.27	<0.01
Parents alive after war	1.37	(0.76)	43	1.60	(0.69)	43	1.74	(0.53)	47	1.58	(0.68)	133	3.59	0.03
Physical illness	2.72	(2.61)	43	1.95	(1.77)	43	1.96	(1.69)	47	2.20	(2.07)	133	2.01	0.14
Depression	2.40	(2.95)	43	2.42	(2.31)	43	2.32	(2.82)	47	2.38	(2.69)	133	0.02	0.98
<i>Cortisol</i>														
Morning	0.91	(0.37)	37	0.84	(0.28)	41	0.88	(0.29)	44	0.87	(0.31)	122	0.50	0.61
Noon	0.48	(0.25)	39	0.51	(0.28)	39	0.49	(0.21)	42	0.49	(0.24)	120	0.09	0.91
Afternoon	0.30	(0.28)	41	0.18	(0.29)	41	0.13	(0.26)	46	0.20	(0.28)	128	4.03	0.02
Reactivity 20 min	-0.74	(0.97)	34	-0.61	(0.99)	34	-0.42	(1.21)	36	-0.59	(1.06)	104	0.79	0.46
Reactivity 40 min	-0.53	(1.08)	36	-0.48	(0.97)	36	-0.77	(1.13)	36	-0.59	(1.06)	108	0.77	0.47
Reactivity 60 min	-0.74	(1.18)	33	-0.46	(1.06)	34	-0.64	(0.91)	33	-0.61	(1.05)	100	0.60	0.55
Gender (female)	22	(51%)		25	(58%)		34	(72%)		81	(61%)		$\chi^2 = 4.43$	0.11
Medication	35	(81%)		27	(64%)		32	(74%)		94	(73%)		$\chi^2 = 3.22$	0.20

### Procedures and measurements

#### Cortisol

Research assistants instructed participants in their home or at the Amcha Center for Holocaust Survivors, depending on the preference of the participants. They provided oral and written explanations for taking three saliva samples for basal cortisol measurements during a normal day: upon awakening, before lunch and before dinner. Respondents were asked to note the exact time when they collected saliva, and to report stressful activities, their state of health and medications taken during the sampling day. Saliva samples were frozen immediately after collection.

Several days to two weeks later, respondents participated in a stressful task which consisted of completing self-report questionnaires. A more detailed description of this stressor can be found below. Three saliva samples were collected at 20 min intervals during the procedure, with the first sample taken 20 min after the start. After a resting period of 40 min, a fourth sample was taken to assess the post-stress cortisol level. All samples were frozen until assayed for cortisol concentration. Research assistants were present during the whole procedure, and were available for emotional support at the time of the stressor, and by phone at any time afterwards.

The saliva samples were stored at  $-20^{\circ}\text{C}$  until analysis. The samples were analyzed in the laboratories of Trier University, Germany (Department of Clinical and Theoretical Psychobiology).

#### Stressor

Through the questionnaire participants were confronted with questions about their Holocaust survival experiences and exposure to other shocking life events, e.g. sexual, physical or emotional abuse, traumatic experiences during the wars and the terrorist attacks in Israel, combat trauma, death of close relatives after the Holocaust, life-threatening illnesses and traffic accidents. In addition, they completed several standard

psychological assessment questionnaires. The procedure took 90 min on average.

### Instruments

#### Physical health status

Physical health status was assessed by a self-report questionnaire developed by the Herczeg Institute on Aging (Tel-Aviv University), listing 18 chronic physical illnesses. Respondents were asked to indicate which illness(es) they had suffered during the last month. This questionnaire is widely used for socio-demographic research in Israel.

#### Beck depression inventory for primal care

This instrument (Beck, Guth, Steer, & Ball, 1997), is a seven-item self-report questionnaire. The items pertain to feelings of sadness, discouragement about the future, perceived decreases in self-confidence, a sense of being overly self-critical, the ability to derive pleasure from a suicidal ideation. Each question is answered on a scale of 0–3 (0, least; 3, most). Sensitivity and specificity rates are 82%, which is slightly lower than the longer version. The internal consistency of the short form showed adequate internal consistency ( $\alpha = 0.83$ ), and scores were not related to sex, age, ethnicity or type of medical diagnosis. Alpha reliability in the current sample was 0.75 ( $n = 133$ ).

#### Post-traumatic stress diagnostic scale

PTSD functional impairment was assessed by means of the Post-traumatic stress diagnostic scale (PDS) (Foa, Riggs, Dancu, & Rothbaum, 1993). The 49-item self-report scale assesses DMS-IV symptoms of PTSD. It provides a categorical diagnosis of PTSD, as well as an overall measurement of symptom severity. The instrument showed good internal consistency and test-retest reliability (0.91 and 0.74, respectively, Foa et al., 1993). The test items correspond to DSM-IV (American

Psychiatric Association, 1994) diagnostic criteria for PTSD, indicating satisfactory convergent validity and concurrent validity assessed by self-report measures of depression and anxiety (Foa, Cashman, Jaycox, & Perry, 1997). The PDS correctly classified PTSD positive patients with a sensitivity rate of 89%, a specificity rate of 65% and an overall correct classification rate of 74% (Foa et al., 1993). In the current study we used the PTSD F-criterion for functional impairment as a stringent index of PTSD with implications for daily functioning of the participant. It consists of nine questions on perceived disturbances in daily functioning during the last month as a result of a traumatic experience. The scale showed adequate internal consistency in our sample,  $\alpha = 0.82$  ( $n = 108$ ).

### Holocaust survival experience

In the current study, we interviewed the participants about their age and experiences during persecution, and parental loss as a result of the Holocaust.

## Results

### Preliminary analyses

Participants in the oldest age group more often lost one or both of their parents during the war,

$F(2, 131) = 3.59$ ,  $p = 0.03$ . No difference in physical illness among the groups was found (see Table 1). The three age groups did not differ on depression, gender or medication use.

Survivors with PTSD functional impairments suffered significantly more physical illnesses and they were significantly more depressed than the other survivors (Table 2). They did not, however, differ in the use of medication. Since the group of survivors who did not relate to any traumatic experience as disturbing them did not significantly differ from the group without PTSD functional impairments on any of the variables, they were collapsed in the analyses (see Table 3).

Survivors with more physical illnesses were more depressed,  $r(131) = 0.23$ ,  $p \leq 0.01$ . Depression scores were significantly higher in the group of survivors who lost both parents (mean,  $M = 4.29$ ,  $SD = 4.38$ ,  $n = 14$ ) compared with survivors who lost one parent ( $M = 1.82$ ,  $SD = 2.36$ ,  $n = 28$ ) or who lost no parents ( $M = 2.25$ ,  $SD = 2.35$ ,  $n = 91$ ) during the Holocaust ( $F[2, 130] = 4.44$ ,  $p = 0.01$ ). Physical health status did not differ for groups with varying parental losses.

Loss of parents, depression and physical health were not significantly correlated with any of the cortisol measures. Correlations ranged from  $r = -0.18$  ( $p = 0.06$ ,  $n = 109$ , for the relation between noon

Table 2. Presence of PTSD (absent, present, unreported) and background variables.

PTSD	No PTSD		PTSD, functional impairment		PTSD, not reported		Total		F	p
	M (SD)	N	M (SD)	N	M (SD)	N	M (SD)	N		
Age	65.0 (2.87)	32	65.0 (2.84)	38	64.2 (3.01)	63	64.6 (2.94)	133	1.46	0.24
Parents alive after war	1.63 (0.66)	32	1.37 (0.85)	38	1.68 (0.53)	63	1.58 (0.68)	133	2.72	0.07
Physical illness	2.00 (1.32)	32	3.08 (3.03)	38	1.78 (1.46)	63	2.20 (2.07)	133	5.18	0.007
Depression	1.84 (2.64)	32	3.53 (3.17)	38	1.95 (2.19)	63	2.38 (2.69)	133	5.19	0.007
Gender (female)	18 (56%)		25 (66%)		38 (61%)		81 (61%)		$\chi^2 = 0.68$	0.71
Medication	25 (86%)		28 (74%)		41 (67%)		94 (73%)		$\chi^2 = 3.64$	0.16

Table 3. Presence of PTSD (present or not), background and cortisol variables.

PTSD	PTSD not reported			PTSD, functional impairment			Total			F	p
	M	(SD)	N	M	(SD)	N	M	(SD)	N		
Age	64.5	(2.97)	95	65.0	(2.84)	38	64.6	(2.94)	133	1.04	0.31
Parents alive after war	1.66	(0.58)	95	1.37	(0.85)	38	1.58	(0.68)	133	5.32	0.02
Physical illness	1.85	(1.41)	95	3.08	(3.03)	38	2.20	(2.07)	133	10.15	<0.01
Depression	1.92	(2.34)	95	3.53	(3.17)	38	2.38	(2.69)	133	10.42	<0.01
Gender (female)	56	(59%)		25	(66%)		81	(61%)		0.53	0.47
Medication	66	(73%)		28	(74%)		94	(73%)		0.00	0.97
<i>Cortisol</i>											
Morning	0.87	(0.30)	86	0.89	(0.34)	36	0.87	(0.31)	122	0.21	0.65
Noon	0.47	(0.26)	84	0.53	(0.19)	36	0.49	(0.24)	120	1.59	0.21
Afternoon	0.18	(0.29)	92	0.25	(0.27)	36	0.20	(0.28)	128	1.78	0.18
Reactivity 20 min	-0.60	(1.06)	73	-0.56	(1.07)	31	-0.59	(1.06)	104	0.04	0.85
Reactivity 40 min	-0.57	(1.02)	74	-0.65	(1.16)	34	-0.59	(1.06)	108	0.13	0.72
Reactivity 60 min	-0.58	(1.00)	67	-0.69	(1.17)	33	-0.61	(1.05)	100	0.24	0.63

cortisol and health) to  $r=0.15$  ( $p=0.10$ ,  $n=120$ , for the relation between noon cortisol and loss of parents).

**Diurnal cortisol**

For the total group the basal cortisol curve showed a peak in the morning ( $M=9.49$ ,  $SD=7.05$ ,  $n=122$ ), with a decline to the noon ( $M=3.63$ ;  $SD=2.20$ ,  $n=120$ ) and afternoon levels ( $M=1.96$ ;  $SD=1.48$ ,  $n=128$ ). For the oldest age group, the cortisol curve was less steep (morning, 0.91; noon, 0.45; afternoon, 0.26) than those of the other two age groups (morning, 0.84 and 0.90; noon, 0.49 and 0.51; afternoon, 0.15 and 0.10, respectively), also when we controlled for loss of parents and health status (see Figure 1). In a repeated measure analysis of covariance with morning, noon and afternoon cortisol values as within-subject measures, loss of parents, depression and physical health as covariates and age cohort as between-subject factors, the multivariate interaction between diurnal cortisol and age cohort, however, was not significant,  $F(4, 204)=2.22$ ,  $p=0.07$ . The oldest age group tended to show a less steep decline from noon to afternoon cortisol level in comparison with the other two age groups [quadratic  $F(2, 102)=2.58$ ,  $p=0.08$ ]. There were no main or interaction effects for gender.

No significant differences were found between the values of the diurnal cortisol curve of the survivors with PTSD functional impairment and survivors without PTSD,  $F(2, 103)=0.28$ ,  $p=0.76$ . Nor was there any interaction between PTSD and cortisol assessment, implying that there was no difference between the curves.

**Stress reactivity**

Reactivity at 20 min after onset of the test session was established by subtracting the standardized residual of the regression of the basal cortisol on the cortisol level after the stressor, from the time equivalent basal cortisol level after 20 min, thereby controlling for differences in baseline cortisol level. We tested for

difference in stress reactivity among the three age groups with gender as a second factor and loss of parents, depression and physical health as covariates. The interaction between age group and gender was significant,  $F(2, 95)=3.13$ ,  $p=0.048$ , see Figure 2. The males in the youngest age group showed the strongest reactivity. No significant main or interaction effects were found at 40 and 60 min after the test session began, although differences were in the same direction.

In an analysis of covariance between the two PTSD groups with gender as a second factor and loss of parents, depression and physical health as covariates, the interaction between PTSD functional impairment and gender was significant for reactivity at 20 min from the beginning of the session,  $F(1, 97)=3.97$ ,  $p=0.049$ , see Figure 3. Males with functional PTSD impairment showed the strongest reactivity. No significant main or interaction effects were found at 40 and 60 min after the test session began, although, again, differences were in the same direction.

**Discussion**

The current study provides evidence that the youngest survivors of the Nazi persecution bear late life effects of traumatic stress during early childhood. In our

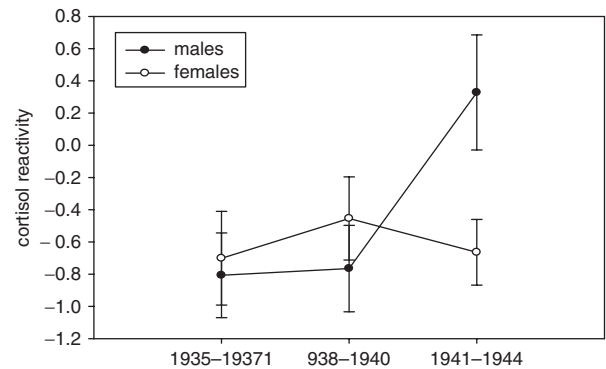


Figure 2. Cortisol reactivity to the test session for the various birth cohorts.

Note: Reactivity controlled for physical health, depression, and loss of parents during war.

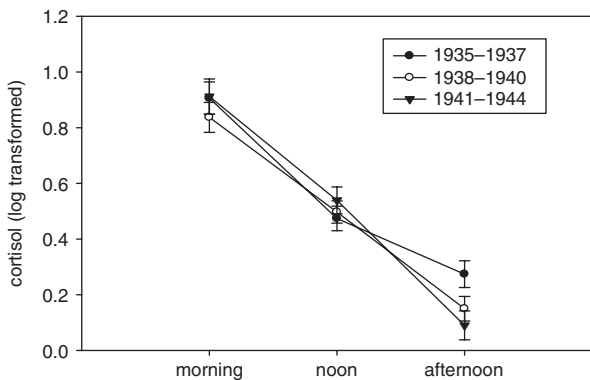


Figure 1. Diurnal cortisol for the three birth cohorts. Note: Diurnal cortisol controlled for physical health, depression, and loss of parents during war.

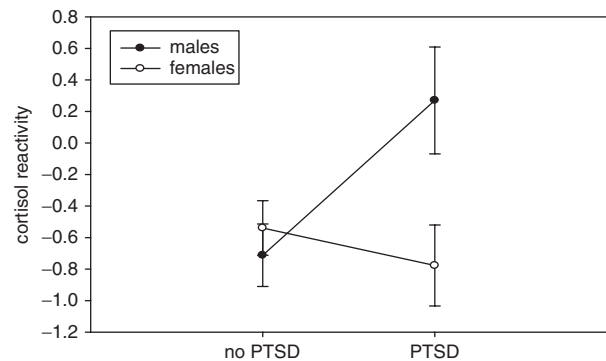


Figure 3. Cortisol reactivity for respondents with and without functional PTSD impairment.

Note: Reactivity controlled for physical health, depression, and loss of parents during war.

study age, parental loss during the Holocaust, current depression and physical illness were not associated with differences in basal diurnal cortisol levels. However, we noticed neuroendocrine effects in stress reactivity through elevated cortisol levels in the youngest male age group, and in male respondents suffering from PTSD-related functional impairment even when controlling for differences in loss of parents, depression and physical health. We found a prominent association of depression with parental loss during the war. Child survivors who had lost both parents during the Holocaust were significantly more depressed than survivors who lost one parent, or did not suffer parental loss. Finally, survivors affected by PTSD-functional impairment also suffered significantly more often from physical illnesses and depression.

### *Limitations*

One important limitation of our study concerns the absence of a control group of the same age cohort, not persecuted by the Nazis or in other ways affected by the consequences of the Second World War. Selecting a matched comparison group was not possible within the time frame available for the current study. We therefore focused on individual differences among child Holocaust survivors, with special emphasis on birth cohort. Another limitation may be non-response to our call for participation in a study stirring memories and emotions around the Holocaust. Non-responders may constitute a biased (more severely affected) selection but in the current study it was impossible to quantify this bias. The incomplete data on cortisol due to the start of data collection halfway through our study did not lead to additional selection bias as the cortisol group was not different from the total sample in any relevant respect. A further limitation concerns the lack of homogeneity in survival circumstances, complicated by the absence of reliable data on emotional and physical deprivations, or on peri-trauma physical health status of these young survivors (see also Keilson, 1992). As a proxy for these variations in Holocaust experiences we controlled for three important factors, namely loss of parents during the Holocaust, and current depression and physical health. Future studies might try and collect more detailed reports of what exactly did happen during the Holocaust, maybe even from camp records or case records from social services or medical reports just after the war. It should be doubted, however, whether this approach would yield more valid information, as even Keilson (1992), analyzing peritraumatic data collected immediately after the Holocaust, was unable to derive solid conclusions from these reports.

### *Loss and depression*

One explanation why the oldest group of survivors in our sample more often suffered the loss of both parents

than the two younger groups could be that the older children were more often handed over to the care of strangers to keep them hidden from persecution. Parents probably more often intuitively kept their babies in their own charge, and survived or perished together.

The association between the adversity of early parental loss and depression in later life that we found was also observed by Keilson (1992) in his longitudinal study on Dutch-born orphaned child survivors. On the other hand, Robinson, Rapaport-Bar-Sever, and Rapaport (1997) found no differences in depressive complaints between survivors who lost both parents and those who lost none or one parent. In non-Holocaust-related studies, Agid et al. (1999) found that parental loss during childhood, especially before the age of 9, contributed significantly to developing major depression in adult life, with loss due to permanent separation being even more devastating than loss due to death.

### *Diurnal cortisol*

Our data show little evidence for associations between diurnal cortisol and coping with the hardships of traumatic early life experiences, such as parental loss as a result of the war. To our knowledge no other studies of these measures involving child Holocaust survivors have been published. Nicolson (2004) found higher basal cortisol levels in healthy adult men who had lost a parent during childhood compared with controls who did not suffer parental loss. Luecken (2000) noted that subsequent quality of care after the loss of a parent, or other adversities during childhood, contribute as additional risk factors for neuro-endocrine effects related to parental loss. From these findings we infer that appropriate care after parental loss may be a reason for the absence of deviating diurnal cortisol patterns in our sample (Van der Hal-Van Raalte, Van IJzendoorn, & Bakermans-Kranenburg, 2007).

Elevated levels of basal cortisol have rather consistently been associated with mood disorders (Heim, Plotsky, & Nemeroff, 2004; Plotsky, Owens, & Nemeroff, 1998). We did not find such a connection, nor were there any associations between decreased levels of diurnal cortisol and physical impairment or PTSD. The associations we found between PTSD functional impairment, physical illness and depression are consistent with findings in non-Holocaust-related studies of military veterans and civilian populations (Deykin et al., 2001; Dobie et al., 2004; Ford et al., 2001; Zatzick et al., 1997). Our findings are also consistent with other studies reflecting on clinical observations of heightened psycho-social vulnerability of child survivors, even when they seem outwardly well-adapted (Cohen et al., 2001; Dasberg, Bartura, & Amit, 2001).

The tendency in the oldest age group to show a less steep decline of cortisol level over the day converges

with findings of Ferrari et al. (2001). They noticed that, with physiological and in particular pathological aging (e.g. dementia and Alzheimer's disease), a relative increase of cortisol serum levels in the evening and at night-time is responsible for a flattened cortisol circadian profile. Yehuda et al. (1995) found lower mean 24 h urinary cortisol excretion in Holocaust survivors with PTSD than in Holocaust survivors without PTSD. In that study, cortisol levels were significantly related to the severity of PTSD, due to a substantial association between cortisol levels and scores on the PTSD avoidance subscale. In the current study, we did not find similar associations with the PTSD functional impairment.

### Cortisol reactivity

Although the literature concerning cortisol reactivity to a stressor is not entirely consistent, many studies report stronger cortisol reactivity with aged male participants (Kudielka, Buske-Kirschbaum, Hellhammer, & Kirschbaum, 2004, 1998; Traustadottir, Bosch, & Matt, 2003; Wang et al., 2007; Wolf, Schommer, Hellhammer, McEwen, & Kirschbaum, 2001). The finding of higher cortisol reactivity of the males in our sample was thus not unexpected. An interaction effect for cortisol reactivity between gender and PTSD was also found in Hawk, Dougall, Ursano, and Baum (2000). They reported elevated urinary cortisol levels among men with post-traumatic symptoms, but not among women, one month after a motor vehicle accident.

A most interesting outcome concerns the significant interaction between age group and gender, with males in the youngest age group showing more reactivity. Although the age differences between the groups are not large, they bear historical significance: the survivors in the youngest group were all born after the outbreak of the war and after the Nazi persecution had started. We infer from our results that the youngest survivors in our study show neuroendocrine reactions while under stress that are significantly different from the reactions of survivors born before the onset of persecution.

In view of the important role of sensitive and responsive parenting in buffering reactivity of the HPA system to potentially stressful events (Gunnar, 1998; Gunnar, Brodersen, & Kreuger, 1996; Gunnar & Quevedo, 2007; Larson et al., 1998; Leckman et al., 2005), it stands to reason that the older child survivors in our sample, born before the onset of the persecution, could more often rely on early parental care not yet compromised by the stresses of coping with moment-to-moment survival. They experienced their parents' 'good enough' support for regulating and buffering normal infantile internal and environmental stresses and anxieties, at least in the first years of their lives (Siegel, 1999; Stern, 1985). Born after the onset of Nazi persecution, the youngest participants in our study were, due to the circumstances, more often deprived

of unconditional care and attention by their parents or substitute parents. Furthermore, the youngest survivors may also have suffered more from pre- and perinatal stresses affecting HPA-axis functioning already before birth (De Weerth, Van Hees, & Buitelaar, 2003). Our findings leave room for prenatal programming of the neuroendocrine system (Bertram & Hanson, 2002) in infants of mothers who were stressed by the extreme circumstances of the Holocaust. Thus, our findings support the concept of an early onset of differential neuroendocrine pathways to stress-regulating strategies of aging male survivors, who were born in the midst of war and genocide.

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