PHENOMENOLOGY AND PSYCHOBIOLOGY OF THE INTERGENERATIONAL RESPONSE TO TRAUMA

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INTRODUCTION

The literature describing the effects of the Holocaust on offspring of survivors has developed in a parallel fashion to the literature describing the effects of the Holocaust on its survivors. Early descriptions of the "survivor syndrome" arose as clinicians began to realize that classical psychoanalytic views of depression, mourning, and responses to trauma did not provide an adequate framework for understanding and treating Holocaust survivors. The classic observations describing severe symptomatology, maladjustment, and impairment of functioning were made on treatment-seeking individuals, many of whom were being evaluated for compensation or reparations, who did not benefit from psychoanalytic therapy (e.g., Chodoff, 1963; Eitinger, 1961; Krystal, 1968; Neiderland, 1969).

The literature on the effects of offspring also began with clinical anecdotal observations that children of Holocaust survivors appeared to display an increased incidence of psychological problems (Rakoff, 1966; Rakoff, Sigal, & Epstein, 1976; Trossman, 1968) that were also not resolved by classic psychoanalytic therapy (Daniel), 1981; Barocas & Barocas, 1983). These observations appeared soon after the descriptions of concentration camp syndrome. The early observations comparing children of survivors, then mostly children and adolescents, to those of non-survivor children and adolescents are noteworthy. Rackoff et al (1976) and Sigal & Weinfeld

(1985) indicated a greater incidence of depression, anxiety and maladaptive behavior such as conduct disorder, personality problems, inadequate maturity, excessive dependence, and poor coping problems in them (Sigal & Epstein, 1976).

Offspring of Holocaust survivors were also reported to have more physical ailments (Waldfogel, 1991), and were described as having a general vulnerability to stress (Danieli, 1981; Barocas & Barocas, 1983). In one of the more provocative findings, Solomon, Kotler, & Miulincer (1988) report that offspring of Holocaust survivors were more likely than other soldiers to develop PTSD following deployment in the Lebanon War.

This finding further served to underscore the idea of offspring of survivors as more fragile and vulnerable. Barocas & Barocas (1983) commented not only on the alarming number of children of survivors seeking and requiring help, but also of the nature of their symptoms. They stated that offspring of Holocaust survivors "present symptomatology and psychiatric features that bear a striking resemblance to the concentration camp survivor syndrome described in the international literature", and that these children "show symptoms that would be expected if they actually lived through the Holocaust."

The observation that children of trauma survivors display PTSD symptoms, but to a lesser extent, was also observed by Rosenheck & Nathan (1985) in their study of children of Vietnam combat veterans. Rosenheck and Nathan termed this phenomenon "secondary traumatization. "

Interestingly, there was an apparent backlash to observations of symptomatology in Holocaust survivors and observations of pathology in their offspring. In contrast to the findings of impairment in Holocaust survivors, for example, a literature arose describing exceptional coping skills among survivors, that focused on predictors of subsequent wellbeing, particularly in non-clinical populations (Dimsdale, 1974; Harel, Kahana, & Kahana, 1988; Kahana, Harel, & Kahana, 1988; Leon, Butcher, Kleinman, Goldberg, & Almagor, 1981).

These studies focused on the remarkable adaptive and reintegrative capacities of Holocaust survivors, who demonstrated good social and family functioning, high socioeconomic achievement, good coping skills, and other personal achievements. Interestingly, the describers of coping and resilience chose to call into question the earlier observations of impairment in Holocaust survivors (Harel et al., 1988) on methodological and other grounds, rather than resolve the diversity of opinions and data by acknowledging the broad spectrum of responsivity to trauma, as, for example, Danieli (1981, 1982) was astutely able to do.

There were similar negative responses in the literature on offspring of Holocaust survivors. Many investigators reported a failure to observe differences in psychopathological features characterizing children of survivors (Aleksandrowicz, 1973): Studies of coping and adjustment again found no significant differences between offspring of Holocaust survivors and matched controls on measures of well being (Zlotogorski, 1983), MMPI derived measures of global mental health (Last & Klein, 1981), or anxiety, depression or adjustment (Rose & Garske, 1987).

Again, the best defense mounted against the studies depicting severe psychopathology was a methodological attack. Solkoff's critical review (1992) concluded that almost no study of children of Holocaust survivors fulfilled the necessary methodological criteria of subject selection and other experimental biases. This indictment attempted to render all conclusions in the literature about pathology in offspring practically useless. It is noteworthy that others also reacted quite sharply to methodological biases in studies of offspring that demonstrate weaknesses in these individuals as a group (e.g., Silverman, 1987).

Nonetheless, the clinical literature, seemingly oblivious to the implications of these studies, continued to provide case reports and other anecdotal observations of pathology in offspring (Danieli, 1981), and continued to explore treatment strategies for this group (e.g., Kestenberg, 1980; Kinsler, 1981). Thus, with few exceptions, the literature on offspring of Holocaust survivors is divided into two "camps": those who described the adverse effects of the Holocaust, and those failing to note these detrimental effects.

The polarized spectrum of opinions regarding the long-term effects of the Holocaust, and the failure to deal systematically or scientifically with this wide diversity is unusual, and also informative. Also interesting is the relative failure of the Holocaust literature to become integrated with the larger emerging literature focusing on the effects of other types of trauma exposure. Of particular note in this regard is the conspicuous absence of the concept of PTSD from the Holocaust literature, especially in articles that have been published after 1980, which marked the formal entrance of PTSD into the psychiatric nosology.

The heterogeneity reflected in the Holocaust literature is certainly compatible with (and may have contributed to the development of) the now well-established idea that the long-lasting effects of trauma, as reflected by the presence of PTSD, appear in some, but not all severely traumatized individuals. Yet only very few studies to date have applied the formal diagnostic criteria for PTSD to Holocaust survivors (Kaminer & Lavie, 1991; Kuch & Cox, 1992; Yehuda, Kahana, Binder-Brynes, Southwick, Zemelman, Mason, Giller, 1995b; Yehuda, Kahana, Schmeidler, Southwick, Wilson, Giller, l995c; Yehuda, Kahana, Southwick, Giller, 1994b), and even fewer have invoked this idea in considering intergenerational syndrome (see for exception Solomon et al., 1988).

It is clear that if Holocaust survivors and their children had been considered from the vantage point of either having or not having posttraumatic stress syndrome this might have helped clarify prior observations of other aspects of posttraumatic adaptation such as affect dysregulation, character changes, psychiatric comorbidity, and resilience, and might have provided a more cohesive literature. Similarly exploring the effects of the Holocaust on offspring based on whether they may have been raised by more or less symptomatic parents might yield similar clarity with regard to intergenerational syndromes.

The opposing views of survivors and offspring speaks to the ambivalence of mental health professionals who are searching for the most appropriate way to describe and view victims of trauma (Danieli, 1982; Yehuda & Giller, 1994a). To describe severe symptoms as a consequence of trauma exposure, on the one hand, serves to validate the experience of the victim by acknowledging that the traumatic events, rather than some personal flaw, was the cause of resulting symptoms. On the other hand, an acknowledgment of the profound effects of trauma may also serve to further victimize and stigmatize the survivor by implicitly suggesting a permanent damage, which may be quite contradictory to the survivors' perception that s/he has overcome adversity. Such a view may also promote hopelessness and pessimism in survivors, who may already be prone to these experiences. This issue is further compounded by the catastrophic magnitude of the Holocaust itself. Because the Holocaust was not only a personal trauma for the survivor, but also a conspiracy to eradicate the entire Jewish race, the Holocaust literature becomes much more than a vehicle for describing an individual's struggle with the effects of trauma, but also becomes a historical record of the persecution of the Jews and their ability to overcome this oppression.

Thus, the dilemma that is invariably created is how one goes about documenting the horrors and the permanent scars created by the racial prejudice as a result of the Holocaust while at the same time demonstrating the dignity of the Jewish people and their capacity to survive. To describe Holocaust survivors and their children as vulnerable, particularly if this has biological dimensions, is to document traits similar to the ones that were actually used to justify the extermination of the Jews. On the other hand, to mitigate the scars of the Holocaust is equally problematic, and serves as an obstacle to providing the needed resources to help survivors overcome their mental health symptoms. The scientist investigating the effects of the Holocaust must acknowledge the social, political and humanistic forces that may serve to shape mental health descriptions of the Holocaust in no less serious a manner than the clinician who must explore these very same issues in the context of their implications for counter transference.

When our research group began investigating the phenomenology and neurobiology of posttraumatic adaptations in Holocaust survivors, our aim was to try to view the Holocaust survivor with a lens similar to that which we had been using to study combat veterans. For example, we attempted to utilize the diagnosis of PTSD to subgroup Holocaust survivors. Further, we were interested in examining Holocaust survivors on the same psychological and biological measures that had served to differentiate combat veterans from normal controls. Although we recognized that there were substantial differences between combat veterans (especially Vietnam veterans) and Holocaust survivors (e.g., in length of time since the focal trauma, nature and severity of the trauma, occupational functioning of survivors, incidence of substance abuse, etc.) we believed that it was essential to study Holocaust survivors with the same paradigm so that both similarities and differences between these groups could be explored.

We hypothesized that to the extent that there were commonalties in behavioral and neuroendocrine parameters between Holocaust survivors and other groups of trauma survivors, the variables being examined would explain core features of the response to trauma. To the extent that there would be differences between groups of trauma survivors based on the nature of the trauma, the findings would be less applicable to features of the general response to trauma. This approach allowed an operational scientific perspective with relatively unbiased observation, and was hypothesis driven. Indeed, to date we have been able to demonstrate both similarities (Yehuda et al., l995b; Yehuda et al., 1994b) and differences (Yehuda et al., in press a) between Holocaust survivors and other trauma survivors using this approach.

In our studies of adult offspring of Holocaust survivors, we attempted to utilize a similar approach to the one used in the study of Holocaust survivors. We believed that by using the same descriptive and biological measures that have been used to study Holocaust survivors, it would be possible to determine similarities and differences between these two groups in a more precise way, and to specifically test the hypothesis that adult children of Holocaust survivors are similar to Holocaust survivors. To the extent that there are commonalties in behavioral and neuroendocrine parameters between Holocaust survivors and other groups of trauma survivors, we hypothesized that these variables might explain core features of the intergenerational syndrome. However, since one of the main features of our work with Holocaust survivors has been the recognition of heterogeneity in this group (Danieli, 1984), a critical variable in our studies of offspring has been to try to determine the parameters which describe individual differences.

Indeed, the problem of how to select appropriate offspring for study and conceptualize their clinical or psychological status has been challenging. In this context, one of the major methodological criticisms that has arisen in studies of Holocaust survivors and offspring of survivors concerns potential biases in the selection of subjects. It is clearly recognized that individuals who agree to participate in this kind of research are a self-selected group and may be

quite different from individuals that choose not to participate. Although this kind of bias is inherent in all clinical research studies, it is important to keep this caveat in mind. Obviously, one can only speculate about what could be learned from individuals who decide not to participate in research.

This chapter will illustrate the approaches used by our group to arrive at different types of comparisons. Three such approaches and studies will be described:

- **The first** approach has been to try and examine the relationships between offspring and their own parents.
- **A second** approach has been to compare first and second generation Holocaust survivors without consideration of familial relationship (i.e., comparing a group of Holocaust survivors to a group of similarly selected, but not related offspring of Holocaust survivors) on variables of interest.
- **A third** approach is been to explore different subgroups of second generation offspring and compare these subgroups to demographically-matched controls (i.e., Jewish adults with non-European born parents).

The following represents preliminary findings from work-in-progress.

STUDY 1:

EXAMINING THE RELATIONSHIP BETWEEN PTSD SYMPTOMS IN PARENTS AND THEIR OFFSPRING

Rationale: Barocas & Barocas (1983) and Rosenheck & Nathan (1985) suggested that offspring of Holocaust survivors have similar symptoms to those of their parents. The implicit suggestion in these studies was that children "acquire" symptoms that they see their parents experience. Indeed, Solomon et al. (1988) suggested that the increased incidence of PTSD following the Lebanon War in the offspring of Holocaust survivors may have been a direct result of the PTSD in the parents: "The PTSD in the second generation may involve an unmasking of Holocaust-related disturbances or reflect responses that the children "learned" from their survivor parents. For example, the second generation PTSD casualty may have more war-related nightmares than his control group peers because he had seen and heard his parents venting their emotion."

No study that we knew of systematically assessed psychiatric diagnoses in parents and their offspring. We were specifically interested in determining whether there would be significant correlations between the PTSD symptoms of the parents and the offspring.

Subject recruitment: Our initial recruitment began by asking the Holocaust survivors we had studied whether they would be interested in telling their children about the research project. The Holocaust survivors in these studies had all been interned in Nazi concentration camps. They were randomly selected from publicly available lists of Holocaust survivors provided by the local historical society and local synagogue membership rosters. They were invited through a mailing to participate in studies exploring the biological basis of survival and adaptation. Subjects who agreed to participate provided written informed consent and received medical clearance by one of the study physicians. None of the subjects were treatment seekers. Almost all of the Holocaust

survivors with children that we studied were amenable to telling their children about the study. Parents were told that children interested in participating in the project contact the local study coordinator for further information. From this effort, 19 children called us and agreed to participate in the research. Note that although the sample size is relatively small, the subjects were recruited through a relatively non biased procedure.

Methods: The 19 second generation offspring were interviewed using the same structured instruments and ratings as their parents. They were asked whether they felt the Holocaust had been a traumatic they were further queried about PTSD symptoms. The Clinician Administered PTSD Scale (CAPS (Blake, Weathers, Nagy, Kaloupek, Klauminzer, Charney, & Keane, 1990)) was used to quantify the frequency and intensity of current and lifetime PTSD in response to the trauma of the Holocaust in these offspring. Subjects also filled out the Dissociative Experiences Scale (DES) (Bernstein & Putnam, 1986). Additional information included presence of current and lifetime psychiatric diagnoses, as determined by the Structured Clinical Interview for the DSM-III (Spitzer, Williams, Gibbon, 1987). A comprehensive trauma history was obtained using the Antonovsky Scale (Antonovsky, 1979), and the Recent Life Events Scale (Kahana & Kahana, 1982).

The responses of the 19 parents and offspring on each individual item of the CAPS and the DES were correlated. Nine of the parents were men and 10 were women. Eleven of the 19 pairs were of the same sex. Given the small number of subjects and the large number of correlations, the results should not be considered definitive. These are pilot data that are being presented to illustrate the approach we have been trying to develop in our studies

Results and Conclusions: Nine of the 19 parents met diagnostic criteria for current PTSD according to the CAPS, and 11 of the 19 met diagnostic criteria for past PTSD. Table 1 shows the correlations between the individual PTSD symptoms in the parents and children. Most of the symptoms were not correlated, however, positive correlations were present for flashbacks, avoidance of situations that are reminders of the Holocaust, emotional detachment, and physiological reactivity. Additionally, there was a significant association between dissociative experiences as reflected by DES scores in parents and children.

There are several reasons to be cautious in interpreting these findings. Primarily, the number of subjects is small and the number of correlations relatively large. Secondly, it is unclear from this study whether these current symptoms in either the parent of the children reflected long term symptoms. However, according to the diagnostic interview, all but two of the parents that did not meet current criteria for PTSD also did not meet past criteria for PTSD. Similarly, the parents who did meet criteria for PTSD reported suffering from PTSD symptoms on a chronic basis, but generally tended to indicate that symptoms currently were less severe than they had been in the past.

Table 1: Correlations Between PTSD Symptom Severity in Holocaust Survivors and their Biological Offspring (n=38).

Symptom	r	p*
B1 -- intrusive thoughts	.06	
B2 -- distress at reminders	.00	
B3 -- flashbacks	.46	.025
B4 -- nightmares	.33	.085
C1 -- avoidance of thoughts	.09	
C2 -- avoidance of situations	.43	.03
C3 -- psychogenic amnesia	.24	

C4 -- diminished interest	**	
C5 -- emotional detachment	.52	.01
C6 -- restricted range of affect	.26	
C7 -- sense of foreshortened future	.28	
D1 -- difficulties with sleep	.10	
D2 -- irritability	.08	
D3 -- impaired concentration	.12	
D4 -- hypervigilence	.09	
D5 -- increased startle	.10	
D6 -- physiological reactivity	.63	.002
DES scores	.55	.01

*** one-tailed**

The results indicate that the level of severity of some PTSD symptoms in parents and their own children are correlated, which supports the suggestions of Barocas & Barocas (1983), Rosenheck & Nathan (1985) and Solomon et al. (1988). There appears to be no specific pattern regarding which of the 17 core symptoms of PTSD are more likely to be correlated between parent and child. In fact, at least one symptom from each of the three symptoms clusters were correlated. Thus, to the extent that the symptoms of PTSD are correlated between parent and child, there does not appear to be a systematic preference for a particular symptom cluster. These results provide at least preliminary support that offspring may be influenced by the symptoms of their parents.

STUDY 2:

COMPARING FIRST AND SECOND GENERATION SURVIVORS ON BIOLOGICAL VARIABLES: A PILOT STUDY

Rationale: Given that parents and offspring may share symptoms in common, it was reasonable to explore the extent to which first and second generation survivors are similar in regard to a biological alteration. Our objective was to compare the urinary cortisol excretion of Holocaust survivors with and without PTSD to those of offspring.

We chose to measure cortisol because levels of this hormone have been found to be altered in individuals with PTSD. Cortisol is a hormone that is released by the adrenal gland. In response to stress, several biological systems are activated in order to allow the body to become mobilized for the "fight-or-flight" reaction (Munck et al., 1984). During stress the brain also signals the pituitary gland to stimulate the release of cortisol from the adrenal gland. The function of cortisol in response to stress is to shut down the other biological reactions that have been turned on in order to cope with the short term demands of a stressor (Munck et al., 1984). If cortisol did not shut off these other reactions, they would do long-term damage to the body. Therefore, it is possible to conceptualize cortisol as an "anti-stress" hormone, because if an organism was unable to produce cortisol in sufficient amounts in response to stress, this would have deleterious consequences.

In conditions of acute and chronic stress, and in certain types of psychiatric disorders that are associated with stress, such as major depression, cortisol levels are high (Mason, 1986; Sachar, Hellman, & Roffwarg, 1973), but this sometimes reflects the fact that the HPA axis has grown

resistant to the effects of cortisol (Yehuda, Southwick, Krystal, Charney, Mason, 1993b). The dexamethasone suppression test (DST) has been used as a probe of the HPA axis (Carroll, 1982). Dexamethasone is a synthetic glucocorticoid that mimics the effects of cortisol and allows testing of the effectiveness of the HPA axis in shutting off a stress response. Under normal conditions, the administration of dexamethasone results in a suppression of the body's own cortisol. This indicates that the negative feedback of cortisol is intact and the body is capable of responding to stress or glucocorticoids. However, under conditions of hypercortisolism, such as is observed in major depression, dexamethasone often fails to shut down cortisol levels, resulting in a response called a "nonsuppression." Such a response suggests a defect in the sensitivity of cortisol receptors.

Studies in combat veterans PTSD have shown that cortisol levels are lower in trauma survivors with PTSD compared to normals and other psychiatric groups (Yehuda, Southwick, Nussbaum, Wahby, Giller, & Mason, 1990; Yehuda et al., 1993b). Further, individuals with PTSD respond to the administration of dexamethasone by suppressing their own cortisol levels to a greater extent than normals do (Yehuda et al., 1993b, Yehuda, Boisoneau, Lowy, & Giller, 1995a). The hypersuppression of cortisol in response to dexamethasone suggests that the cortisol (or glucocorticoid) receptors in PTSD are very sensitive (Yehuda, Giller, Southwick, Lowy, & Mason, 1991; Yehuda et al., 1995a). Importantly, the hypersuppression is the opposite of the nonsuppression response to dexamethasone observed in depression (Yehuda et al., 1991; Yehuda et al., in press b). These and other (Yehuda et al., in press b) results suggest that unlike depressed patients who seem relatively unresponsive to the environment, trauma survivors with PTSD may be exquisitely sensitive to external events. The more sensitive cortisol system may account for why trauma survivors show exaggerated responses even to non dangerous environmental stimuli (Yehuda et al., in press b).

Recently, we observed that Holocaust survivors with PTSD also showed significantly lower mean 24-hr cortisol excretion compared to both Holocaust survivors without PTSD and comparison subjects not exposed to the Holocaust (Yehuda et al., l995b). In this study, 24-hr urine samples were collected, and the following day, subjects were evaluated for the presence and severity of past and current PTSD and other psychiatric conditions. The results demonstrated a significant relationship between cortisol levels and avoidance symptoms. We concluded from these findings that low cortisol levels are associated with PTSD symptoms of a clinically significant nature, rather than occurring as a results of exposure to trauma per se.

Recruitment: For the present study, rather than asking the children of survivors of parents we had already identified to participate as we had done in Study One, we placed ads in local newspapers around the New York Metropolitan area. Many offspring also called us in response to hearing about our research through local T.V. and newspaper articles, and seeing advertisements for our group therapy program.

Methods: Twenty-four offspring participated in the study. For this first preliminary study, the only inclusion criteria was that the subjects have at least one parent who was a Holocaust survivor. Typically, however, most were the offspring of two Holocaust survivors, and almost all had at least one parent who survived concentration camps. None of the offspring were taking any psychotropic medications or drugs that could interfere with cortisol levels. This group was compared to a sample of Holocaust survivors who were further subgrouped according to the presence (n=31) or absence (n=34) of a PTSD diagnoses (as determined using the CAPS). Data from 46/65 of these patients have recently been reported in Yehuda et al., l995b. However, for that study, subjects with comorbid Axis I diagnoses, and those taking psychotropic medications were excluded from the analysis. Since the completion of the study the sample of survivors has been expanded. Furthermore, because presence of Axis I disorder was not an exclusion criterion in the offspring, we included Holocaust survivors who also had Axis I conditions (n=10): Of the

24 offspring studied, 4 were men and 20 were women. Of the Holocaust survivors studied, 23 were men and 42 were women.

Urine was collected beginning at 9:00 a.m. in exact 24-hr portions in 2-liter polyethylene bottles kept in freezers in the subjects residences in order to ensure stability of cortisol. Collections were scheduled to occur on days when subjects planned to be home for the 24-hr period. Clinical assessments took place following the completion of the 24-hr collection, usually within the same week. Urinary-free cortisol levels were determined by using an extraction procedure and radio immunoassay kit from Clinical Assays, Inc.

Results and Conclusions: Overall Anova demonstrated a main effect of group ($F=4.04$; $df=2,86$; $p=.02$). The mean urinary cortisol excretion of Holocaust survivors with and without PTSD was significantly different. The mean cortisol levels were comparable to what we reported previously, however, the PTSD group contains a larger range of values due to the inclusion of some subjects with comorbid major depressive disorder. Post hoc testing using the Scheffe test showed that the offspring group was not significantly different from the either survivor group. The results are graphically portrayed in Figure 1. As can be seen by examining the individual scatter points, many of the offspring had cortisol levels that could be considered extremely low (i.e., under 25 ug/day).

STUDY 3:

EXPLORING SUBGROUPS OF OFFSPRING AND COMPARING URINARY CORTISOL EXCRETION IN OFFSPRING TO THAT OF DEMOGRAPHICALLY-MATCHED NORMALS

Rationale: As more offspring began calling in response to advertisements to participate in the research, we searched for ways to subgroup these individuals based on traumatic experiences or clinical symptomatology. Just as considering Holocaust survivors as a group without consideration of PTSD diagnoses would have obscured important findings, we felt that equally, the offspring of Holocaust survivors should be subgrouped according to similar parameters.

Method: We considered two possible ways to subgroup the offspring of Holocaust survivors. The first was on the basis of whether or not these individuals met or not meet the diagnostic criteria for an Axis I psychiatric disorder, as assessed by the SCID. In reviewing the diagnostic history of the 23 offspring described in Figure 1 (one SCID could not be completed), we learned that only 10 of these subjects had no current or past psychiatric disorder. Seven of the 23 met criteria for past major depression and three met diagnostic criteria for anxiety disorder (i.e., two with past panic disorder and one with past generalized anxiety disorder). Five had current psychiatric disorder (one met criteria for major depression; one for generalized anxiety disorder; one for both major depression and generalized anxiety disorder; one for attention deficit disorder with depression, and one for bulimia with dysthymia and secondary depression).

A major focus of the assessment of offspring was their own history of traumatic events. We were interested in determining whether offspring of Holocaust survivors would be more vulnerable to developing PTSD in response to stressful events. We used several scales to help offspring identify their traumatic events including the Traumatic History Questionnaire (Green et al., unpublished) and the Antonovsky Scale (Antonovsky, 1979). We then queried subjects about PTSD using the Clinician Administered PTSD Scale (Blake et al., 1990).

This interview was done by asking the subject which traumatic event or events they experienced as the the worst, and perhaps might be the focus of PTSD symptomatology. In response to this question, 12/23 of the offspring spontaneously indicated that hearing about their parents' experiences in the Holocaust constituted their trauma (even though almost all of them had undergone extremely stressful events such as being mugged or assaulted, being in motor vehicle accidents, etc.). As being "confronted" with information about trauma exposure in others qualifies in the DSM-IV conception of Criterion A, we felt that we could consider the possibility that offspring may indeed develop PTSD symptoms in response to hearing about their parents' experiences during the Holocaust, particularly if they subjectively stated that such information elicited fear, helplessness or horror. The other 11 either indicated no traumatic event or stressful events that would not meet the criteria for PTSD under the current DSM-IV stressor criterion (such as losing a sibling or father, having an illness, etc.).

The subgroups were similar to each other in total scores on the Traumatic History Questionnaire (i.e., the groups were comparable in the extent of "trauma" exposure exclusive of the Holocaust trauma). Subjects also filled out the Civilian Mississippi PTSD Scale (Keane, Caddell, Taylor, 1991), and the Impact of Events Scale (Horowitz, Wilner, Alvarez, 1979). In filling out the latter scale, subjects were instructed to use the "Holocaust" as the "event".

Using both these methods to subgroup patients, cortisol levels and PTSD symptoms were assessed and compared with a non-offspring comparison group.

Results and Conclusions: Figure 2 shows the scatterplot of 24-hr urinary cortisol excretion in the offspring group when they are divided based on meeting and not-meeting criteria for other Axis I disorders. As can be clearly seen when the offspring group was subdivided in this manner, significantly lower cortisol values were observed in the group without Axis I disorder. An overall ANOVA demonstrated a significant main effect of group F=4.98; df=2.30; p=.01. Post hoc testing revealed that the offspring group without Axis I disorder had significantly lower cortisol levels compared to the other two groups. The mean +/- S.D. urinary cortisol excretion for the offspring group without Axis I disorder was 37.9 +/- 20.8. In contrast the mean cortisol level in the offspring group with Axis I disorder was 60.0 +/- 24.0. The mean for comparison subjects was 66.5 +/- 30.

Table 2: Mean + S.D. for Mississippi and Impact of Event Scores in Offspring subgrouped on the basis of meeting or not meeting diagnostic criteria for an Axis I disorder and comparison subjects:

Scale	Offspring: Axis I	Offspring: No Axis I	Comparison Group
Mississippi PTSD Scale	75.0 + 20.8*	77.65 + 20.4*	59.9 + 7.0
IES Total	10.6 + 8.4*	13.9 + 9.3*	1.1 + 2.6
IES Intrusive	6.6 + 5.3*	7.1 + 5.4*	0.9 + 2.5
IES Avoidance	4.0 + 4.0*	0.2 + 0.6*	0.2 + 0.6

*** Significantly different than comparison group.**

When scores on the Civilian Mississippi PTSD Scale and the Impact of Events Scale were tabulated, overall ANOVA revealed significant group differences on the Mississippi Scale (F=3.36; df=2.29; p=.05), the Impact of Event Total Score (F=8.65; df=2.27; p=.001), and Intrusive (F=5.76; df=2.27; p=.008)) and Avoidance (F=8.99; df=2.27; p=.001) subscale scores. In all cases, however, the F tests reflected the fact that both offspring groups were significantly higher on these measures than the comparison group. Post hoc testing showed that the two offspring groups were comparable on these self-reports as indicated in Table 2.

Figure 3 shows the scatterplot of 24-hr urinary cortisol excretion in the offspring group when they are divided on the bases of reporting the Holocaust as their major traumatic event during the clinician-rated PTSD interview. As can be clearly seen, when the offspring group was subdivided in this manner, significantly lower cortisol values were observed in the group reporting distress in response to Holocaust-related material. An overall ANOVA demonstrated a significant main effect of group $F=5.93$; $df=2.30$; $p=.007$. The mean +/- S.D. urinary cortisol excretion for the offspring group without Holocaust trauma was 54.1 +/- 25.7. In contrast the mean cortisol level in the offspring group with Holocaust trauma was 32.4 +/- 14.2. The mean for comparison subjects was 66.53 +/- 30. These distinctions do not consider current diagnostic status of the subjects.

When scores on the Civilian Mississippi PTSD Scale and the Impact of Events Scale were tabulated, overall ANOVA revealed significant group differences on the Mississippi Scale ($F=6.66$; $df=2.29$; $p=.004$). However in this case, the offspring groups with and without Holocaust trauma were significantly different. The mean Mississippi PTSD Scale score for offspring without Holocaust trauma was 68.3 +/- 14.5, and the mean score for offspring with Holocaust trauma was 84.3 +/- 21.6. Note that the mean Mississippi PTSD Scales score for offspring without Holocaust trauma did not differ from the mean Mississippi PTSD Scale score for the comparison subjects (i.e., 59.9 +/- 7.0).

Figure 4 graphs the mean Impact of Events Scores in the three groups. ANOVA showed a significant main effect for total IES scores ($F=10.9$; $df=2.27$; $p=.009$), Intrusive subscale scores ($F=8.46$; $df= 2,27$; $p=.001$), and Avoidance subscale scores ($F=8.90$; $df=2.27$; $p=.001$). Figure 5 shows that offspring with Holocaust trauma were significantly more symptomatic on almost each symptoms as assessed by the CAPS. Thus, offspring who report that the Holocaust was the significant traumatic event in their lives also appear to suffer from PTSD symptoms in response to the Holocaust. As Figure 5 indicates, the most common symptoms endorsed were: distress at reminders of the Holocaust, emotional detachment, intrusive and distressing thoughts about the Holocaust, sense of foreshortened future, restricted affect, and sleep difficulties. By comparison, offspring without Holocaust trauma reported negligible levels of these symptoms.

In sum, the results indicate that low cortisol levels in offspring of Holocaust survivors was associated with the tendency of these individuals to indicate distress about the trauma of the Holocaust, and to have PTSD symptoms in response to Holocaust-related events that they heard about.

The etiology of the PTSD symptoms and low cortisol levels in the offspring studied is currently unknown. There are many potential models that could explain these findings, but more information must be acquired before any of these models can be confidently applied to these observations. The absence of objective and definitive knowledge about the diagnostic status or severity of the trauma of the parent(s)) is a critical omission to the biological data obtained in this study. However, such knowledge is not typically available in studies of offspring of trauma survivors. In fact, except for the preliminary observations in Study one, no investigation of which we are aware has actually compared the level of PTSD or other psychiatric symptoms in parents and offspring.

By omitting these data, studies of offspring assume a homogenous syndrome in the parents. However, our studies of Holocaust survivors have clearly indicated that not all survivors have suffered chronic PTSD symptoms, regardless of the magnitude in all survivors. Therefore, information about parental symptoms and trauma exposure must be considered in formulating a hypothesis of the etiology of PTSD symptoms and biological alterations in offspring. To the extent that such knowledge could be obtained, then it might be possible to determine whether the same biological or psychological risk factors that contribute to the chronic nature of symptoms in the Holocaust survivor parent are relevant to the biological and clinical picture of offspring, or

whether symptoms in offspring are due to the impact of psychological or biological impairments in their parents.

Although the present studies have not addressed the larger question of the etiology of the intergenerational syndrome, they do provide the first biological validation that the symptoms described by offspring as being related to the Holocaust appear, indeed, to reflect a type of post-traumatic response. The best conclusion from these studies to date is that the offspring of Holocaust survivors may be more psychologically and "biologically" vulnerable to stress and trauma for a host of reasons yet to be elucidated.

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